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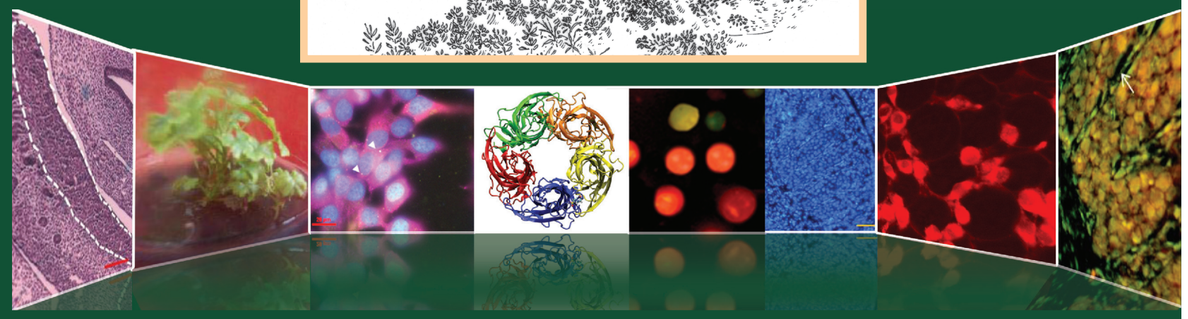

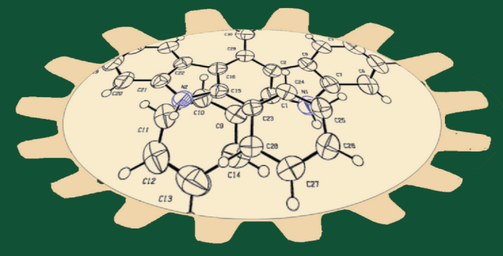

भारतीय रासायनिक जीवविज्ञान संस्थान
INDIAN INSTITUTE OF CHEMICAL BIOLOGY
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Annual Report
2009-2010

भारतीय रासायनिक जीवविज्ञान संस्थान
Indian Institute of Chemical Biology

(सी. एस. आई. आर. का एक प्रतिष्ठान)
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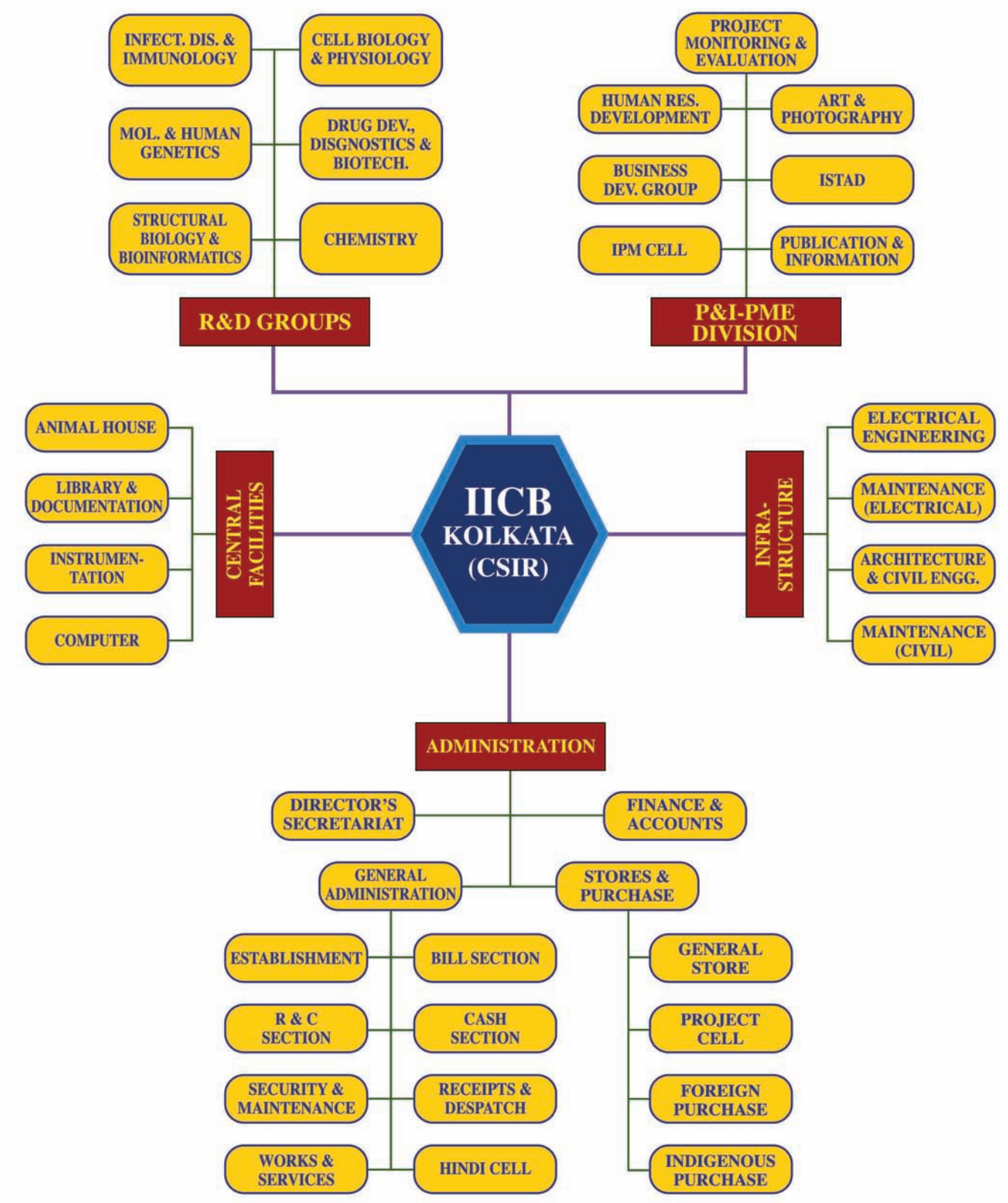
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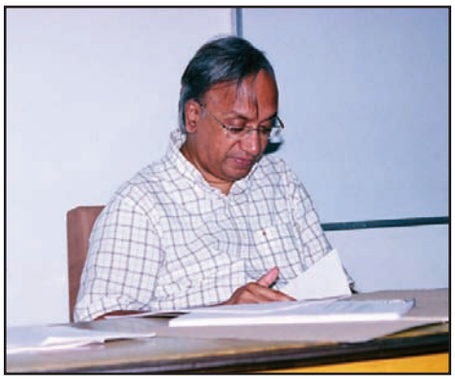


निदेशक की कलम से

निदेशक की कलम से

भारतीय रासायनिक जीवविज्ञान संस्थान का अप्रैल 2009 से मार्च 2010 तक की अवधि के लिए वार्षिक प्रतिवेदन प्रस्तुत करते हुए मुझे हार्दिक प्रसन्नता हो रही है। संस्थान प्रति वर्ष अपने वार्षिक प्रतिवेदन का प्रकाशन इसलिए करता है कि वह अपने वर्ष-व्यापी अनुसंधान क्रियाकलापों का संक्षिप्त विवरण सहकर्मियों एवं पूरे विश्व के वैज्ञानिक समुदाय को प्रदान कर सके। इस प्रतिवेदन में वैज्ञानिक क्षेत्र में किए गए योगदान के अतिरिक्त हमारी बुनियादी सुविधाओं, बाह्य निधियों की प्राप्ति, बौद्धिक संपदा तथा वैज्ञानिक प्रबंधन एवं प्रशासन के अन्य विभिन्न पहलुओं के बारे में गंभीर सूचनाएँ भी शामिल होती हैं।

भारतीय रासायनिक जीवविज्ञान संस्थान राष्ट्रीय महत्व के रोगों और वैश्विक हित की जैविक समस्याओं पर विशिष्ट अनुसंधान करने में संलग्न है, जिसके लिए वह तीव्र और अभूतपूर्व गतिशीलता बनाए रखकर स्टेट-ऑफ-द-आर्ट प्रौद्योगिकी का प्रयोग करता है जो पिछले 50 वर्षों से जीव विज्ञान के क्षेत्र में विश्व में छाया हुआ है। इस संस्थान का अनुसंधान एवं विकास के क्रियाकलापों में लगातार वृद्धि बनी हुई है और पिछले वर्षों की तरह भारतीय रासायनिक जीवविज्ञान संस्थान ने अपनी प्रगति जारी रखी और समीक्षाधीन अवधि में विज्ञान की गुणवत्ता को विकसित तथा परिवर्धित किया। अनेक नई परियोजनाओं की स्वीकृति दी गई है। सिंथेटिक बायोलोजी परियोजना का अनुमोदन किया गया है तथा वह बड़ा पोतवाहिनी कार्यक्रम बनने जा रहा है। भारतीय रासायनिक जीवविज्ञान संस्थान की बुनियादी सुविधाएँ क्रमशः उन्नत हो रही हैं। साल्ट लेक के कैंपस का निर्माण कार्य शुरू हो चुका है। भारतीय रासायनिक जीवविज्ञान संस्थान के कैंपस में जगह के विस्तार तथा एक आधुनिक पशु गृह और दस तल्ले के भवन के निर्माण हेतु अनुमोदन प्राप्त हो चुका है। संस्थान ने कोलकाता के निकट बरुईपुर में प्रस्तावित ज्ञान भंडार के अंग के रूप में ट्रांसलेशनल रिसर्च सेंटर बनाने की योजना बनाई है। भारतीय रासायनिक जीवविज्ञान संस्थान, नेशनल इंस्टिट्यूट ऑफ फार्मास्यूटिकल एडुकेशन एंड रिसर्च (एनआईपीइआर), कोलकाता के लिए परामर्शदाता संस्थान के रूप में कार्य कर रहा है और इस वर्ष उनतीस विद्यार्थियों के प्रथम बैच ने सफलतापूर्वक एमएस (फार्मा) के पाठ्यक्रम को पूरा किया है। इस संस्थान ने एनआईपीइआर-कोलकाता को राष्ट्रीय महत्ता प्राप्त करने के प्रयासों में मदद की है। हमारे संस्थान में छह बड़े अनुसंधान एवं विकास प्रभाग आपसी सहयोगात्मक कार्यों के साथ विभिन्न जीववैज्ञानिक एवं रासायनिक क्षेत्रों में कार्य कर रहे हैं ताकि कुछ बड़े रोगों के बारे में अध्ययन किया जा सके तथा स्वास्थ्य देखभाल विज्ञान में सुधार हो सके। हमने घरेलू एवं प्राकृतिक स्रोतों जैसे भारतीय पौधों से दवा का विकास करने पर काफी ध्यान दिया है।

रसायन विभाग के क्रियाकलापों में औषधीय पौधों से जैवसक्रिय प्राकृतिक उत्पादों के वियोजन पर विशेष ध्यान

दिया गया है ताकि कुछ बड़े रोगों के लिए भेषज औषधि निर्माण एवं उनकी प्रभावकता का निर्धारण किया जा सके। इस प्रभाग में जैवसक्रिय प्राकृति उत्पादों या बड़ी मात्रा में अणु जैसे प्राकृतिक उत्पादों का संश्लेषण बड़ा अनुसंधान कार्य रहा है जिनमें नए न्यूक्लियोसाइड/न्यूक्लियोटाइड, चाइरल/एर्चाइरल हिटेरोसाइकल, एंटी-लिशमानियल यौगिक आदि शामिल हैं। इनके अतिरिक्त यह प्रभाग बैक्टिरियल कोशिका सतह एंटीजेनों, पौधा पोलिसैकेराइडों तथा न्यूग्लाइकोप्रोटीनों और प्राकृतिक उत्पादों के नाभिकीय अम्ल बाइंडिंग गुणों का अध्ययन भी कर रहा है। इस प्रभाग के वैज्ञानिकों ने हरे रसायन पर भी कार्यक्रम प्रारंभ किए हैं जो पर्यावरण की दृष्टि से अधिक लाभकारी उत्पाद एवं प्रक्रियाओं को जन्म देंगे।

आणविक एवं मानव आनुवंशिकी प्रभाग भारतीय लोगों में आम तौर पर पाए जाने वाले रोगों के आणविक एवं आनुवंशिक आधारों को समझने के लिए कार्य कर रहा है। इस प्रभाग का विशेष उद्देश्यों में शामिल है -- सिर एवं गर्दन के कैंसर पैदा करने में शामिल पुटेटिव ट्यूमर सप्रेशर जीनों (एचएनएससीसी) की पहचान, *हेलिकोबैक्टर पाइरोली* से जुड़े गैस्ट्रोड्योडोनल रोगों में प्रवणता एलेल की पहचान, मौखिक सबम्युकस फाइब्रोसिस के आणविक पैथोजेनेसिस का अध्ययन, कीटों से स्व-रक्षा की क्रियाविधि में शामिल नन-होस्ट पौधों से जीन की पहचान, वियोजन एवं आशोधन तथा होस्ट पौधों में बायोपेस्टिसाइड के रूप में उन्हें अंतरित करना, हैमोफिलिया ग्लोकोमा, विलसन रोग तथा ओकुलो-क्युटेनियस अल्बिनिज्म जैसे मानव रोगों पर आणविक आनुवंशिकी का अध्ययन, ल्यूकोप्लाकिया एवं मौखिक कैंसर के लिए प्रवणशील जीनों की पहचान, आनुवंशिक टॉक्सीकोलॉजी का अध्ययन, जैवरासायनिक एवं प्रतिवर्त्य आनुवंशिक दृष्टिकोण के समन्वित रूप का प्रयोग करते हुए काइनेटोप्लास्टिड प्रोटोजून लिशमानिया के मिटोकोंड्रिया में नाभिकीय-एनकोडे टीआरएनए के आयात के आणविक आधार का अध्ययन।

संक्रामक रोग एवं प्रतिरक्षा विज्ञान प्रभाग लिशमानिया, कॉलेरा एवं मलेरिया पर विशेष रुचि दिखाते हुए जैविक विज्ञान के विभिन्न क्षेत्रों में कार्यरत है। इस प्रभाग के वैज्ञानिक आणविक आर्किटेक्चर एवं चिकित्सीय विकास, डीएनए मरम्मत एंजाइम की पहचान, टाइरोसिल डीएनए फॉस्फोडिस्टेरेज 1 (टीडीपी 1), संशोधित सियालिलेटेड संरचना की पहचान, सियालिलेशन के मोडुलेशन की महत्ता की समझ, उसकी जैविक भूमिका तथा ल्यूकेमिया एवं आंत्रिक लिशमानिया (वीएल) में संभावनायुक्त रोग-संबद्ध बायोमार्करों के रूप में उनकी उपयोगिता की समक्ष, *प्लाज्मोडियम* फैल्सिपेरम मैक्रोफेज प्रवर्जन निषेधक कारक की ऑक्सीडोरेडक्टेस क्रिया तथा ईएल टोर बायोटाइप द्वारा *वी. कॉलरे* के क्लासिकल बायोटाइप के प्रतिस्पर्धात्मक अपवर्जन के अध्ययन के संदर्भ में टाइप 1ए, 1बी तथा 1ए, 1बी तथा III डीएनए टोपोआइसोमेरेज के अध्ययन में शामिल हैं। इस प्रभाग के वैज्ञानिकों ने पहले यह दर्शाया कि मैक्रोफेज ऑक्सीडेटिव क्षति में लिशमानिया पारासाइट के प्रतिरोध के भिन्नात्मक-युग्मित प्रवेश का संबंध वर्धित इंट्रासेलुलर सीएएमपी और सीएएमपी-मध्यस्थ प्रतिक्रिया से जुड़ा हुआ है। उन्होंने लिशमानिया डोनोवनी प्रोमेस्टिगोट मेम्ब्रेन एंटीजेन (एलएजी) के साथ तीन केटआयोनिक निर्माणों की टीका सक्षमता की तुलना की और प्रयोगात्मक आंत्रिक लिशमानिया के विरुद्ध दीर्घावधि बचाव के लिए श्रेष्ठ वेसिकल के रूप में मूल्यांकन किय । इस प्रभाग के वैज्ञानिकों ने यह पाया कि फेनोलिक ग्लाइकोलिपिड--1 (पीजीएल-I)*एम. लेपरे* के लिए विशेष एंटीजेन नहीं है, क्योंकि वह लिशमानिया एंटीजेन के साथ क्रॉस-प्रतिक्रिया करता है। उन्होंने स्पॉट जीन कार्य के जेनेटिक विश्लेषण के द्वारा पोषकता दबाव के अधीन *वी. कोलरा* के जीवन्ता के आणविक आधार का भी अध्ययन किया है और एक नया (पी)पीपीजीपीपी सिंथेटेस जीन की पहचान की है।

कोशिका जीवविज्ञान एवं दैहिकी प्रभाग के कोशिका जीवविज्ञानियों, देहविज्ञानियों एवं आणविक जीवविज्ञानियों के एक दल ने कुछ खास मेटाबोलिक एवं डिजेनेरेटिव रोगों के पैथोफिजियोलोजी को समझने का सामान्य लक्ष्य प्राप्त किया। इस समूह द्वारा कैंसर, स्टेम सेल जीवविज्ञान, हृदीय हाइपरट्रोफी, मधुमेह, नशे की लत, न्यूरोडिजेनेरेटिव रोग, यूटेरो-ओवेरियन डिस्फंक्शन तथा हेमाटोपोएटिक पद्धति में पैथोजिन की प्रतिक्रिया पर कार्य किया गया। इस प्रभाग ने विभिन्न मानव रोगों के लिए अनेक मोडलों का विकास और उनकी जाँच का कार्य भी किया। इस प्रभाग के अनुसंधान के प्रमुख बिंदु हैं : पेरोक्सीरेडॉक्सिन II तथा मेलेटोनिन मध्यस्थ के द्वारा कार्डियोमाइकोसाइट मृत्यु का बचाव, एक्रोजम प्रतिक्रिया के दौरान मेम्ब्रेन फुशन के नए नियामकों के रूप में स्पर्म एक्टो-प्रोटीन किनेस तथा एंडोजेनस न्यूरोटॉक्सिन की खोज, 6-हाइड्रोक्सीडोपामाइन जो लंबे समय तक एल-डोपा देने के कारण मस्तिष्क में डोपामिनर्जिक कोशिका की मृत्यु का कारण बनता है। इस प्रभाग के वैज्ञानिकों ने नेत्र सतह की खराबी से ग्रस्त रोगियों में ट्रांसप्लांटेड कल्चर्ड लिंबल कोशिका को डालने में सफलता प्राप्त की है जिससे आँख की रोशनी वापस आ सकती है।

औषधि विकास, परीक्षण एवं जैवप्रौद्योगिकी प्रभाग जैवसक्रिय यौगिकों के अध्ययन में शामिल है ताकि स्वास्थ्य एवं जीवन की गुणवत्ता में सुधार हो सके और साथ ही जैवप्रौद्योगिकी में नवोत्थान के माध्यम से भावी आर्थिक विकास को बढ़ावा मिल सके। इनके क्रियाकलापों के बड़े क्षेत्र हैं -- उपयोगी चिकित्सीय क्रियाओं के लिए पौधों, माइक्रोब या विष से मुख्य जैवसक्रिय यौगिकों के वियोजन; गैस्ट्रिक घाव की क्रियाविधि; फार्मास्यूटिकल्स /न्यूट्रास्यूटिकल्स के बेहतर उत्पादन के लिए पौधा जीनों की आभियांत्रिकी; इम्युनोकंजुगेट निर्माण की कार्यनीति; प्रमस्तिष्कीय ऑक्सीडेटिव क्षति को रोकने के लिए नैनोकैप्सुलेटेड औषधि का प्रयोग; ट्रेहालूज मेटाबोलिज्म एवं माइक्रोबियल ग्लाइकोसिडेज एंजाइमों की आणविक क्रियाविधि।

संरचनागत जीवविज्ञान एवं जैव-सूचनाविज्ञान प्रभाग उन क्षेत्रों में अनुसंधान कार्य कर रहा है जिनका मुख्य विषय यक्ष्मा, लिशमानियसिस, कलरा, कैंसर, मधुमेह जैसे विभिन्न रोगों के लिए तथा अन्य एंटी-इनफ्लेमेटरी, एंटीकनवल्सेंट तथा इम्युन्मेमॉड्यूलेटरी क्रियाकलापों के लिए चिकित्सीय दृष्टि से संभावनायुक्त जैविक मैक्रोमोलेक्यूल एवं अन्य छोटे अणुओं का संरचनागत लक्षणनिर्धारण करना है। प्रोटीन कार्यों, प्रोटीन-प्रोटीन तथा प्रोटीन-न्यूक्लिक अम्ल अंतर्क्रियाओं का मौलिक अध्ययन किया जा रहा है जो नाभिकीय चुंबकीय निनाद (एनएमआर), एक्स-रे क्रिस्टेलोग्राफी, विश्लेषणात्मक अल्ट्रासेंट्रीफ्युज, फ्लुरोसेंस सहसंबंध स्पेक्ट्रोस्कोपी, डायोड ऐरे अवरुद्ध-प्रवाह स्पेक्ट्रोफोटोमेट्री, मास-स्पेक्ट्रोमेट्री, प्रमात्रात्मक संरचना कार्य संबंध (क्यूएसएआर) तथा 3डी-क्यूएसएआर जैसे आधुनिक परिष्कृत प्रौद्योगिकीयों के क्षेत्र में व्यवहार्य है। जेनोम/प्रोटियोम विश्लेषण, मैक्रोमोलेक्यूलर संरचनाओं की संभावना, आशोधन तथा विश्लेषण और जैव-सक्रिय अणुओं के साथ उनकी अंतर्क्रिया की व्याख्या हेतु सॉफ्टवेयर का विकास किया जा रहा है।

11वें पंचवर्षीय योजना में आईआईसीबी 18 परियोजनाओं में शामिल है, जिसमें 4 नोडल नेटवर्क परियोजना और 14 पार्टनर नेटवर्क परियोजनाएँ हैं। पार्टनर नेटवर्क परियोजनाओं में से दो, दसवीं योजना की विस्तार परियोजनाएँ हैं। सभी परियोजनाएँ अधिकांशतः जीवविज्ञान एवं जैवप्रौद्योगिकी क्षेत्र की हैं, सिवाय एक नोडल नेटवर्क परियोजना के जो फार्मास्यूटिकल्स, स्वास्थ्य देखभाल एवं औषधि क्षेत्र की है। इस वर्ष के दौरान दो नई परियोजनाओं के अनुसंधान एवं विकास कार्य प्रारंभ हुए हैं, जिनमें एक "सिंथेटिक बायोलोजी एंड मेटाबोलिक इंजीनियरिंग ऑफ एजाडिरैक्टिन बायोसिंथेसिस पाथवे" नामक इंटरएजेंसी परियोजना है और दूसरी "डिजाइनिंग पोटेंसियल लिड मोलेक्यूल्स फॉर इनहिबसन ऑफ साइड्रोफोर बायोसिंथेसिस इन *एम. ट्यूबरक्लूसिस*" नामक ओएसडीडी परियोजना है।

आईआईसीबी ने यादवपुर के अपने मूल कैंपस से लगभग पंद्रह किलोमीटर दूर साल्ट लेक, कोलकाता में अपने द्वितीय कैंपस के लिए **बुनियाद स्थापना समारोह** का आयोजन किया। इस मांगलिक समारोह में आईआईसीबी के सभी स्टाफ सदस्य एवं विद्यार्थियों और बड़ी संख्या प्रतिष्ठित अतिथियों ने भाग लिया। प्रो. समीर के ब्रह्मचारी, महानिदेशक, सीएसआईआर ने बुनियाद रखी। कलकत्ता विश्वविद्यालय के उप कुलपति प्रो. सुरंजन दास मुख्य अतिथि थे।

आईआईसीबी द्वारा "**जैवचिकित्सीय विज्ञान में पद्धति जीवविज्ञान तथा प्रोटियोमिक्स**" पर दो-दिवसीय लघु-संगोष्ठी आयोजित की गई। प्रो. समीर कुमार ब्रह्मचारी, महानिदेशक, सीएसआईआर उस कार्यक्रम में उपस्थित थे। इस संगोष्ठी की एक बड़ी उपलब्धि यह थी कि सीएसआईआर और सिस्टम बायोलोजी इंस्टिट्यूट (एसबीआई, टोक्यो जापान) ने भारत एवं जापान में अपने चिकित्सीय एवं पर्यावरण संबंधित व्यवहार हेतु पद्धति जीवविज्ञान को बढ़ावा देने के उद्देश्य से सहयोगात्मक क्रियाकलापों के लिए एक समझौते के ज्ञापन पर हस्ताक्षर किए। हमारा संस्थान सहयोगात्मक कार्यक्रम का समन्वय करेगा। संयुक्त अनुसंधान का प्रारंभिक स्वरूप पद्धति जीवविज्ञान दृष्टिकोण का उपयोग करके एक नया मल्टी-एजेंट कैंसररोधी दवा का निर्माण करने पर जोर देना है। भविष्य के अनुसंधान के विषय अन्य क्षेत्रों में भी विस्तृत किए जाएंगे जो भारत को पद्धति जीवविज्ञान की अगली पंक्ति में खड़ा करने के उद्देश्य से होगा। आईआईसीबी की पूरे कार्यक्रम में बड़ी भूमिका होगी।

भारत के युवा वैज्ञानिकों के लिए कैरियर विकास कार्यशाला का आयोजन आईआईसीबी द्वारा किया गया ताकि कोलकाता और उसके आसपास के विभिन्न अनुसंधान संस्थानों से युवा वैज्ञानिकों को सहयोगात्मक अनुसंधान करने के लिए भावी अवसरों तथा विदेशी अनुसंधान सहयोगात्मक कार्यों तथा समर्थन के लिए उपलब्ध योजनाओं के बारे में अद्यतन जानकारी दी जा सके, खासकर जैवचिकित्सीय अनुसंधान के क्षेत्र में।

संस्थान ने 10-14 सितंबर तक **हिंदी सप्ताह** का आयोजन किया और उस अवसर पर हिंदी टिप्पण एवं आलेखन, निबंध प्रतियोगिता एवं 'तकनीकी शब्दावली के प्रयोग में आनेवाली कठिनाईयों' पर एक कार्यशाला का आयोजन किया गया। संस्थान ने 14 सितंबर को राष्ट्रीय हिंदी दिवस का भी आयोजन किया। इस साल संस्थान में हिन्दी वेबसाइट का प्रारंभ किया गया।

मानव संसाधन समूह ने "**आईआईसीबी के गैर-तकनीकी ग्रेड डी स्टाफ सदस्यों के लिए बहु-कौशल प्रशिक्षण कार्यक्रम**" पर दो-दिवसीय कार्यक्रम का आयोजन किया। हमारे संस्थान के ग्रेड डी (गैर-तकनीकी) के कुल सोलह कर्मचारियों ने उस कार्यक्रम में भाग लिया। अन्य प्रयासों में तकनीकी समूह 2 के कर्मचारियों को तनाव से मुक्ति के लिए प्रेरणात्मक प्रशिक्षण कार्यक्रम में प्रशिक्षित किया गया, जिसका विषय था 'श्रेष्ठ तरीके से जीना'।

आईआईसीबी में **संमिश्र नेटवर्क : गतिकी एवं समक्रमण** पर **भारत-रूस कार्यशाला** का आयोजन किया गया। नौ रूसी प्रतिनिधियों ने उसमें भाग लिया और अपने कार्यों को प्रस्तुत किया। जर्मनी के दो वैज्ञानिक, एक स्पेन के तथा एक अमेरिका के वैज्ञानिक ने भी कार्यशाला में भाग लिया। उसमें कुल 55 (पचपन) प्रतिभागी थे, जिनमें हमारे देश के विभिन्न भागों के युवा अनुसंधानकर्ता भी शामिल थे। उसमें जिन विषयों को शामिल किया गया था उनमें भौतिक पद्धतियाँ तथा हृदयी-आंत्रिक पद्धति में न्यूरोन मोडल प्रमुख थे। व्याख्यानों के मुख्य बिंदु उन पद्धतियों में छोटी इकाइयों (यूनिट सेल या उत्तोलक) के सामूहिक व्यवहार थे। चिकित्साविज्ञानियों ने सैद्धांतिक मोडलों उल्लेख

किया और कुछ सीमित मामलों में कुछ छोटे प्रयोगों के बारे में चर्चा की, किंतु उन्होंने महसूस किया कि चिकित्सा के क्षेत्र से संकायों एवं जीवविज्ञानियों के साथ गहन विचार-विमर्श से वास्तविक जीववैज्ञानिक पद्धतियों में उनके अनुभव कारगर सिद्ध हो सकेंगे, जिससे ज्ञान का आदान-प्रदान होगा।

आईआईसीबी द्वारा 14**वां अखिल भारतीय साइटोलोजी एवं आनुवंशिकी कांग्रेस (एआईसीसीजी)** की मेजबानी की गई। संस्थान में यूनिवर्सिटी ऑफ कैलिफोर्निया, बर्कले, अमेरिका के साथ मिलकर फोगार्टी प्रशिक्षण कार्यक्रम आयोजित किया, जिसके लिए एनआईएच, अमेरिका से निधि प्राप्त हुई। इस वर्ष यह प्रशिक्षण कार्यशाला 14वें एआईसीसीजी के साथ ही आयोजित की गई। कार्यशाला का मुख्य विषय था "मोलेक्यूलर एपिडिमियोलोजी, इनवायरमेंटल हेल्थ एंड आर्सेनिक एक्सपोजर एसेसमेंट"। एआईसीसीजी बैठक और कार्यशाला का लक्ष्य साइटोलोजी, जेनेटिक्स के क्षेत्र में प्रगति तथा आर्सेनिक की संभावना के मूल्यांकन के संदर्भ में पर्यावरण स्वास्थ्य के क्षेत्र में अनुसंधान में प्रगति की समीक्षा करना था।

संक्रामक रोग-2009 पर **भारत-ब्राजिल संगोष्ठी** आईआईसीबी तथा जवाहरलाल नेहरू सेंटर फॉर एडवांस्ड साइंटिफिक रिसर्च (जेएनसीएएसआर), बेंगलूरु के तत्वावधान में कोलकाता में संपन्न हुई। ब्राजिल के छह प्रतिनिधियों ने इसमें भाग लिया और अपने कार्यों को प्रस्तुत किया। कुल मिलाकर 85 प्रतिभागी थे, जिसमें भारत के विभिन्न भागों के युवा वैज्ञानिक भी शामिल थे। संगोष्ठी के दौरान बत्तीस व्याख्यान दिए गए। संगोष्ठी ने आगामी वर्षों में संक्रामक रोगों पर भारत-ब्राजिल सहयोगात्मक कार्यों के बारे में और अधिक पथ खोले। इस संगोष्ठी के लिए भारत सरकार के विज्ञान और प्रौद्योगिकी विभाग द्वारा वित्तीय सहयोग प्रदान किया गया।

डॉ. के कस्तूरीरंगम, सदस्य, योजना आयोग, डॉ. ए के वर्मा, सलाहकार (एस एंड टी), योजना आयोग तथा डॉ. इंद्राणी चंद्रशेखरन, सलाहकार (इ एंड एफ), योजना आयोग इस अवधि के दौरान हमारे संस्थान में पधारे। डॉ. कस्तूरीरंगन ने अपनी लिखित टिप्पणी के द्वारा आईआईसीबी के बारे में अपने विचार प्रकट किए -- *"अणुओं, प्रोटीनों और इसी प्रकार की चीजों और प्रकृति की एक आश्चर्यजनक रचना मानव शरीर के स्वाभाविक संसार में एक अत्यंत आह्लादकारी यात्रा। आईआईसीबी में किया जाने वाला कार्य अग्रणी एवं नवोन्मेषकारी है तथा उनके प्रति प्रतिज्ञाबद्ध है जिन्हें इसकी अत्यंत आवश्यकता है और उनके लिए उसे सुलभ बनाता है।"* बड़ी संख्या में राष्ट्रीय एवं अंतरराष्ट्रीय स्तर के ख्यातनाम वैज्ञानिक इस वर्ष हमारे संस्थान में पधारे। इनमें डॉ. मैक्स गोट्समैन, कोलंबिया यूनिवर्सिटी, अमेरिका का "सेल साइकल रेगुलेशन ऑफ सीएएमपी लेवल" पर व्याख्यान देने हेतु आगमन, प्रो. रुइज आई अल्टाबा, यूनिवर्सिटी ऑफ जेनेवा, स्विटजरलैंड का "रोल ऑफ हेजहॉग -- जीएलआई सिग्नेलिंग इन स्टेम सेल्स, कैंसर एंड कैंसर स्टेम सेल्स" पर वैज्ञानिक व्याख्यान के लिए आगमन, प्रो. एस इ हसनैन, उप कुलपति, हैदराबाद यूनिवर्सिटी (आंध्र प्रदेश) का "मोलेक्यूलर मिमिक्री एंड हाइजैक ऑफ होस्ट मशीनरी बाई माइकोबैक्टिरियम ट्यूबरक्लोसिस फॉर इट्स ओन सरवाइवल एंड डिसेमिनेशन" पर वैज्ञानिक व्याख्यान देने हेतु आगमन, डॉ. श्रीनिवास वी. कावेरी, अनुसंधान निदेशक, आईएनएसइआरएम, पेरिस का "फंक्शन एंड डिस्फंक्शन ऑफ ऑवर इम्युन सिस्टम : नोवल कंसेप्ट चैलेंजेज एंड होप्स फॉर टुमॉरो" पर व्याख्यान देने हेतु आगमन तथा प्रो. हारुकी नाकामुरा, ओसाका यूनिवर्सटी का "न्यू एंड पावरफुल मेथड फॉर इनसिलिको ड्रग स्क्रीनिंग एंड इट्स एप्लिकेशन्स" पर वैज्ञानिक विचार-विमर्श तथा तकनीकी व्याख्यान हेतु आगमन अत्यंत उल्लेखनीय है।

इस अवधि के दौरान हमारे संस्थान ने अपने परिसर में एक प्रदर्शनी का आयोजन किया और कोलकाता एवं आसपास के जिलों में आठ प्रदर्शनियों में भाग लिया। इन सभी प्रदर्शनियों में आईआईसीबी की उपलब्धियों और चल रहे अनुसंधान एवं विकास कार्यक्रमों को आकर्षक ढंग से चित्रों एवं पोस्टरों के माध्यम से प्रदर्शित किया गया।

पश्चिम बंगाल में वर्ष 2009 में विज्ञान में नेतृत्व के लिए युवा पर सीएसआईआर कार्यक्रम (सीपीवाईएलएस 2009) का आयोजन आईआईसीबी द्वारा किया गया। इस कार्यक्रम में पश्चिम बंगाल के विभिन्न भागों से 110 विद्यार्थियों ने भाग लिया।

संस्था द्वारा अनुसंधान में की गई प्रगति के प्रमाणस्वरूप उच्च प्रभाव वाले गुणवत्तापूर्ण प्रकाशनों एवं पत्रिकाओं में बड़ी संख्या में आलेखों का प्रकाशन तथा औसत प्रभावशाली प्रकाशन लगातार बढ़ रहा है। मुझे यह जानकर गर्व होता है कि आईआईसीबी के प्रकाशनों का औसत प्रभाव कारक इस वर्ष लगभग 3 रहा है।

इस समीक्षाधीन अवधि में आईआईसीबी ने संश्लेषण, परीक्षण, टीकाकरण, मिटोकोंड्रियल डिस्फंक्शन के सुधार, कालज्वर, अंडकोष कैंसर, रक्त कैंसर, और अन्य सामान्य मानव रोगों को रोकने हेतु भेषज स्रोतों से जैवसक्रिय यौगिकों के निष्कर्षण से संबंधित ग्यारह राष्ट्रीय एवं अंतरराष्ट्रीय पेटेंट दर्ज किए हैं। इस अवधि में कुल दस पेटेंट विदेशों में स्वीकृत किए गए हैं।

निदेशक की कलम से

आईआईसीबी हमेशा संभावनायुक्त अनुसंधानकर्ताओं के लिए पसंदीदा केंद्र रहा है जिनकी महत्वाकांक्षा जीवविज्ञान एवं रसायन के क्षेत्रों में कार्य करने की रही है। इस वर्ष इस संस्थान ने पूरे देश से बड़ी संख्या में मेधावान, युवा अनुसंधान फेलो एवं अनुसंधान एसोसिएटों को आकर्षित किया है ताकि वह जीवविज्ञान एवं रसायन तथा संबंधित क्षेत्रों में पर्याप्त एवं प्रशिक्षित मानव संसाधन पैदा कर सके, जिससे बेहतर अनुसंधान की आवश्यकताओं की पूर्ति हो सके। वर्ष 2009-10 के दौरान लगभग 225 फेलो एवं अनुसंधान एसोसिएटों ने इस संस्था में कार्य किया। भारत एवं विदेशों से एक बड़ी संख्या में प्रख्यात वैज्ञानिकों ने हमारे संस्थान का दौरा किया और व्याख्यान दिए तथा आईआईसीबी के विभिन्न अनुसंधान समूहों से विचार-विमर्श किया। भारत के विभिन्न विश्वविद्यालयों एवं संस्थानों के लगभग 107 विद्यार्थियों ने ग्रीष्म प्रशिक्षण तथा अन्य प्रशिक्षण कार्यक्रमों में भाग लिया। बड़ी संख्या में वैज्ञानिक पड़ोसी विश्वविद्यालयों एवं संस्थानों में शिक्षण एवं प्रशिक्षण कार्यक्रमों में शामिल थे। संस्थान ने बेहतर तरीके से संस्थान के स्थापना दिवस और सीएसआईआर स्थापना दिवस का आयोजन किया।

मैं अपने संस्थान के सभी वैज्ञानिकों, तकनीकी एवं प्रशासनिक स्टाफ सदस्यों के प्रति हार्दिक कृतज्ञता ज्ञापित करता हूँ, जिन्होंने आईआईसीबी के विकास को बनाए रखने तथा प्रतिष्ठा को कायम रखने हेतु वर्ष भर गहन भाव से क्रियाकलापों को अंजाम दिया है तथा सहयोग किया है। मेरा यह भी विश्वास है कि मेरे सहकर्मियों द्वारा जो समर्पण और निष्ठा प्रदर्शित की जा रही है उससे यह संस्थान आगामी दिनों में नई ऊँचाइयाँ प्राप्त करेगा।

प्रो. सिद्धार्थ राय
आईआईसीबी, कोलकाता

उपलब्धियों की एक झलक

सम्मान

- प्रो. सिद्धार्थ राय को वर्ष 2009-10 के लिये भारतीय विज्ञान काँग्रेस एसोशियन (आई.एस.सी.ए) द्वारा प्रो. जी.पी. चटर्जी मेमोरियल पुरस्कार से पुरस्कृत किया गया।
- डॉ. चित्रा मंडल को वर्ष 2010 में भारतीय राष्ट्रीय विज्ञान अकादमी (एफ.एन.ए.) भारत के अध्येता (फेलो) के लिए मनोनीत किया गया।
- डॉ. चित्रा मंडल को वर्ष 2010 में पश्चिम बंगाल अकादमी विज्ञान और प्रौद्योगिकी (डब्लू.ए.एस.टी) के सदस्य के रूप में मनोनीत किया गया।
- डॉ. सुशान्त राय चौधुरी को राष्ट्रीय अकादमी तथा भारत विज्ञान (एफ.एन.ए.एस.सी) के अध्येता (फेलो) के लिए मनोनीत किया गया।
- डॉ. हेमंत के. मजुमदार का डी.एस.टी. भारत सरकार के द्वारा सर जे.सी. बोस राष्ट्रीय पुरस्कार से पुरस्कृत किया गया।
- डॉ. के.पी. मोहनाकुमार को अन्तरराष्ट्रीय सोसाइटी के तंत्रिका रसायन के लिए तंत्रिका रसायन (सी.ए.ई.एन) में एड्स और शिक्षा के लिए समिति के सदस्य के रूप में मनोनीत किया गया।
- डॉ. के.पी. मोहनाकुमार को एस.एन.सी.भारत का अध्यक्ष के लिए मनोनीत किया गया।
- डॉ. स्नेहसिक्ता स्वर्णकार को वर्ष 2009 में एस.बी.सी भारत के द्वारा प्रो. ए.एन. भादुरी मेमोरियल लेकचर पुरस्कार से पुरस्कृत किया गया।
- डॉ. सुभेन्द्रा भट्टाचार्य को लेडी टाटा मेमोरियल ट्रस्ट द्वारा यंग अनुसंधानकर्ता पुरस्कार से पुरस्कृत किया गया।
- डॉ. सुभेन्द्रा भट्टाचार्य को वेलकम ट्रस्ट, लंदन यू. के में अन्तरराष्ट्रीय वरिष्ठ अनुसंधान अध्येता के लिए चुना गया।
- डॉ. परशुरामन जयशंकर वर्ष 2010-2011 के लिए रमन अनुसंधान अध्येता (फेलो) के लिए मनोनीत किया गया।
- वर्ष 2009 के लिए डॉ. कृष्णानन्द चट्टोपाध्याय को इन्डो-यूएस अनुसंधान अध्येता के लिए मनोनीत किया गया।

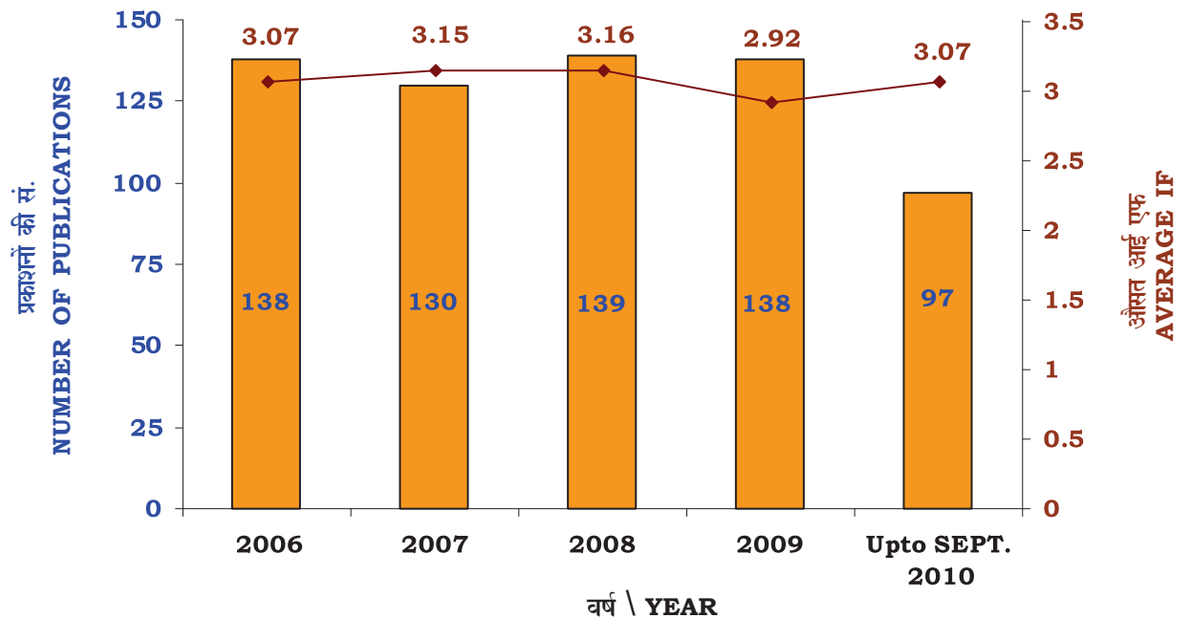
उपलब्धियों की एक झलक

प्रकाशन

संस्थान के अनुसंधान की प्रगति के लिए उच्चकोटि का प्रकाशन एक श्रेष्ठसूचक चिह्न आरएंडडी है। वार्षिक प्रकाशन तथा पिछले पांच वर्ष का औसत प्रभावी कारक (आईएफ) निम्नलिखित है :-

अनुसंधान प्रकाशन -- 2009

कुल प्रकाशित कागजात	--	--	138
कुल इम्पैक्ट फैक्टर	--	--	405.432
आई.एफ प्रति कागजात	--	--	2.92
आई.एफ. प्रति वैज्ञानिक	--	--	5.63
कागजातो की संख्या आई.एफ के संग ≥ 6 < 15	--	--	2
कागजातो की संख्या आई.एफ के संग ≥ 5 < 6	--	--	10
कागजातो की संख्या आई.एफ के संग ≥ 4 < 5	--	--	23
कागजातो की संख्या आई.एफ. के संग ≥ 3 < 4	--	--	27
कागजातो की संख्या आई.एफ. के संग ≥ 2 < 3	--	--	31
कागजातो की संख्या आई.एफ. के संग ≥ 1 < 2	--	--	29
कागजातो की संख्या आई.एफ. के संग ≥ 1	--	--	18

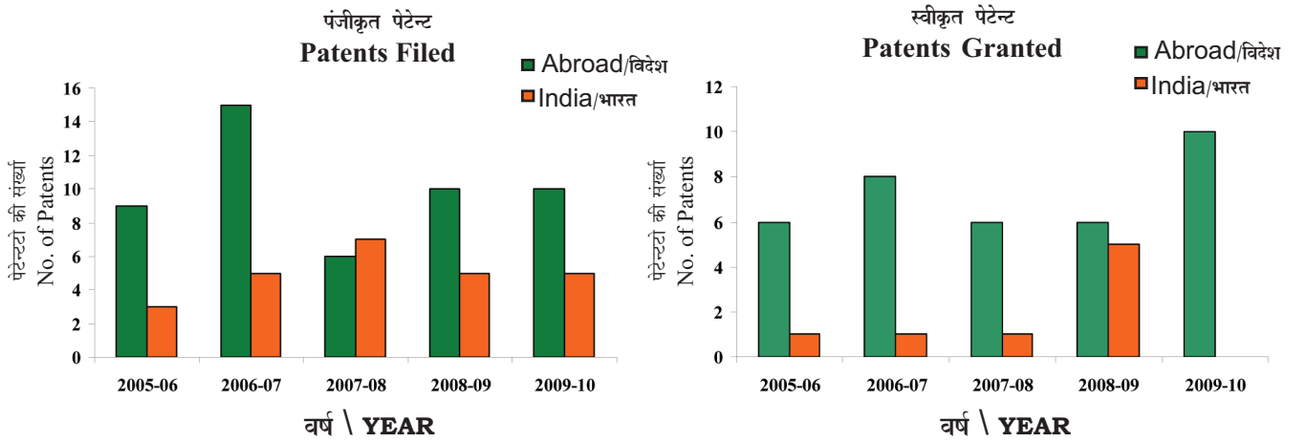


2009-10 के लिए प्रकाशनों की विस्तृत सूची अन्दर अलग दिया गया है।

उपलब्धियों की एक झलक

पेटेन्ट

संस्थान में प्रत्येक वर्ष स्थायी रूप से कई पेटेन्ट का पंजीकरण एवं स्वीकृति।



वर्ष 2009-10 में पंजीकृत एवं स्वीकृत पेटेन्ट की सूची संस्थान के प्रकाशन एवं सूचना विभाग के रिपोर्ट में दर्ज है।

उपलब्धियों की एक झलक

उद्योग - संस्थान का गठजोड़

संस्थान, उद्योग के साथ निरंतर एकीकरण बनाए रखा है एवं सफलतापूर्वक ज्ञान को धन में परिवर्तित कर रहा है। इस वर्ष आई.आई.सी.बी के वैज्ञानिको ने उद्योग के साथ पारस्परिक संबंध को बनाए रखने में एवं पर्याप्त मानवीय एवं वित्तीय संसाधन जुटाने में अपने को सक्षम बनाए रखा।

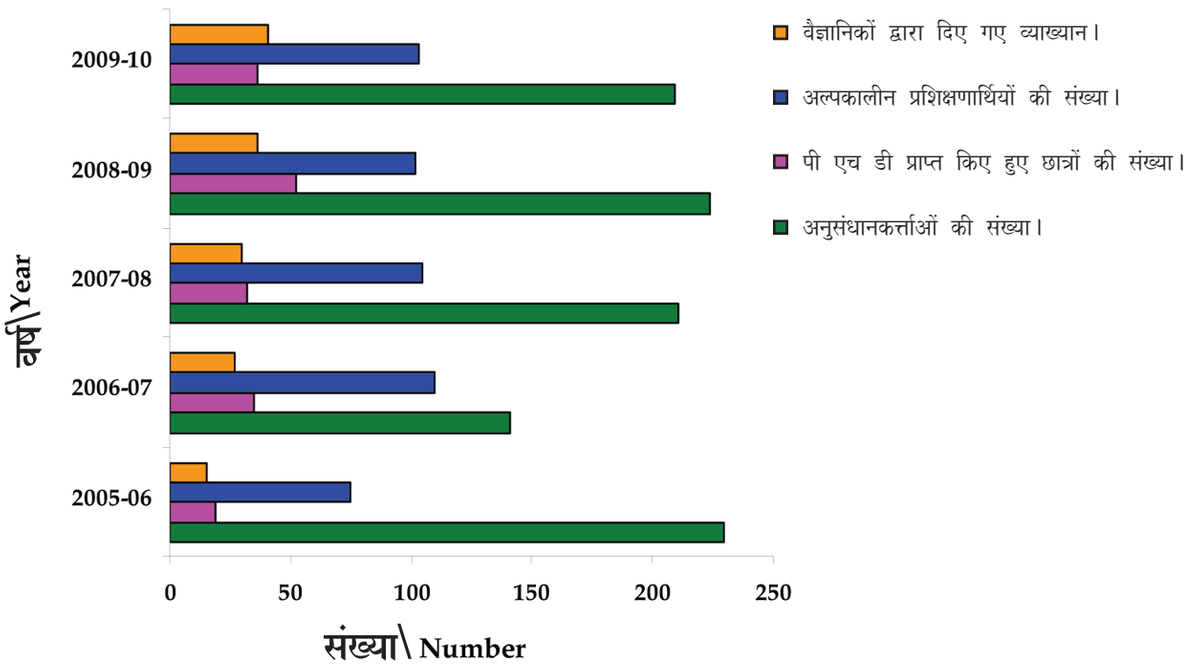
गेट (GATT)-भारत व्यवस्था के साथ सम्पूर्ण विकास के लिए हमारे सहायोगी इस प्रकार है:-

* चटर्जी मनेजमेन्ट सर्वीसेस प्राइवेट लिमिटेड, कोलकाता।
* ईस्ट इंडिया फार्मास्यूटिकल्स वर्क्स लिमिटेड, कोलकाता।
* एनर्जीओजेन फार्मास्यूटिकलस, आस्ट्रेलिया
* केमबायोटेक रिसर्च इन्टरनेशनल प्राइवेट लिमिटेड, कोलकाता।
* दे मेडिकल स्टोर्स (मैनुफैक्चरिंग) लिमिटेड, कोलकाता।
* बायोटेक कानसोरटीयम (आई) लिमिटेड, नई दिल्ली।
* शान्ता वायोटेकनिक्स लिमिटेड, हैदराबाद।
* पीरामल लाइफ सर्वीसेस लिमिटेड, मुंबई।
* क्वालप्रो डायग्नोस्टिक, गोवा।
* एलबर्ट डेविड लिमिटेड, कोलकाता
* जेफर बायोमेडिकल्स, गोवा।
* मेरियल एस ए एस लिन, फ्रांस।
* क्वायर बोर्ड, कोची।
* डी एन डी आई, फ्रांस।

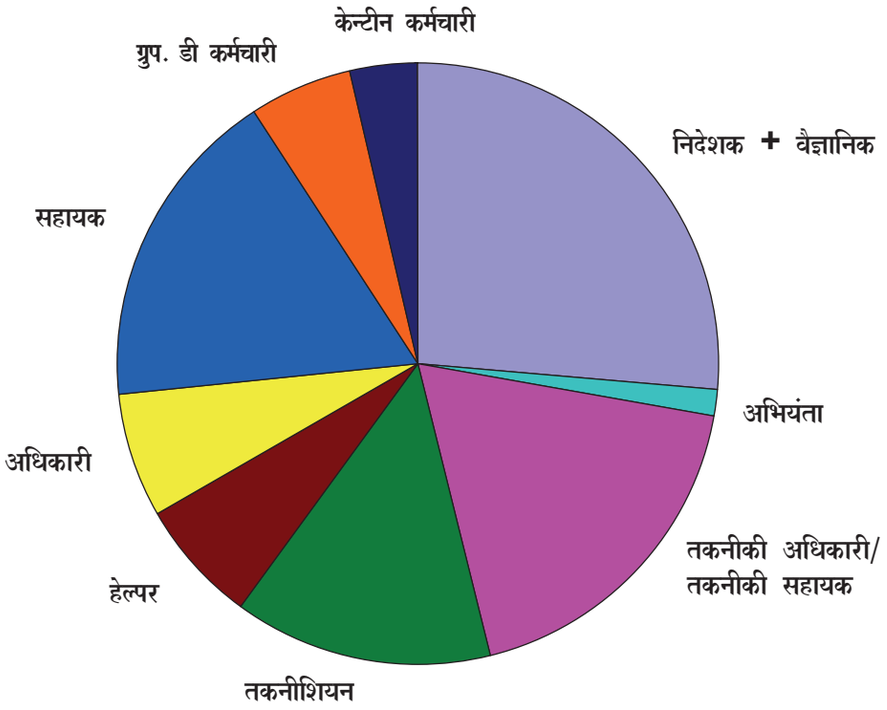
उपलब्धियों की एक झलक

मानव संसाधन विकास

हर वर्ष कई अनुसंधानकर्ता डॉक्टरेट एवं पोस्टडॉक्टेरेट स्तर पर अपना अनुसंधान जारी रखते हैं देश के विभिन्न विश्वविद्यालयों से अनेक विद्यार्थी यहाँ हर वर्ष अल्पकालीन प्रशिक्षण प्राप्त करते हैं। गत पाँच वर्षों का आँकड़ा ग्राफ के माध्यम से प्रस्तुत है:-



31 मार्च, 2010 तक कर्मचारी की संख्या



भारतीय रासायनिक जीवविज्ञान संस्थान

कुल कर्मचारी -- 273

वैज्ञानिक एवं तकनीकी कर्मचारी -- 182

निदेशक -- 1, वैज्ञानिक -- 71, अभिभन्ता -- 4, तकनीकी अधिकारी एवं सहायक -- 50, तकनीशियन -- 38, हेल्पर -- 18

प्रशासनिक कर्मचारी -- 91

अधिकारी -- 18, सहायक -- 48, ग्रुप डी -- 15, कैन्टीन -- 10

कर्मचारी अनुपात :

वैज्ञानिक : तकनीकी कर्मचारी : सहायक कर्मचारी -- 1:1.5:1.3

संस्थान में राजभाषा कार्यान्वयन

भारत रासायनिक जीवविज्ञान संस्थान कोलकाता में राजभाषा अधिनियम के तहत राजभाषा की आवश्यकताओं का सफलतापूर्वक कार्यान्वित किया गया। द्विभाषी पत्राचार किया गया एवं विभिन्न क्षेत्रो में नियम अनुसार भेजा गया। राजभाषा अधिनियम के नियम 3 (3) के संस्थान में अनुपालन किया गया जैसे ज्ञापन, निविदा, सूचना सामान्य आदेश इत्यादि को द्विभाषी रूप में जारी किया जाता है।

संस्थान में 10-14 सितम्बर, 2009 तक हिन्दी सप्ताह मनाया गया है। इस समारोह के अंतर्गत 10 सितंबर, 2009 को हिन्दी टिप्पण, आलेखन तथा निबंध लेखन आदि प्रतियोगिताओं का आयोजन किया गया।

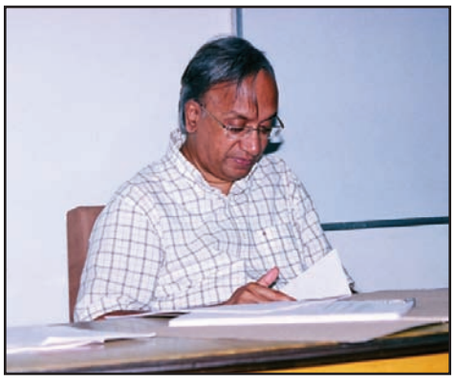
11 सितम्बर, 2009 को आयोजित हिन्दी कार्यशाला में तकनीकी शब्दावली के प्रयोग में आने वाली कठिनाईयों पर श्री सतीष पाण्डेय, केन्द्रीय अनुवाद प्रशिक्षण ब्यूरो, कोलकाता के प्रशिक्षण अधिकारी अपना वक्तव रखा एवं कार्यशाला का सुचारू रूप से संचालन किया। उन्होंने तकनीकी शब्दावली के प्रयोग करते हुए कई शब्दों का सटीक प्रयोग बताया एवं शब्दों के विभिन्न उपयोग तथा उनके विभिन्न व्यावहारिक प्रयोगों का उदाहरण देते हुए सभी को नए-नए तकनीकी शब्दों से अवगत कराया एवं तकनीकी शब्दों के प्रयोग में आने वाली कठिनाईयों का हल बताया।

14 सितंबर, 2009 हिन्दी दिवस पर प्रो. रत्ना मुखर्जी, हिन्दी के पूर्व प्राध्यापिका, सेंट जेवियर्स कॉलेज, कोलकाता, मुख्य अतिथि के रूप में तथा श्रीमती मंजू शीरीन, सहायक निदेशक, हिन्दी शिक्षण योजना, कोलकाता, विभिन्न प्रतियोगिताओं के निर्णायक के रूप में विराजमान थी। संस्थान के निदेशक प्रो. सिद्धार्थ राय, प्रतियोगिता में भाग लेनेवाले कर्मचारियो/अधिकारियों को पुरस्कार से प्रोत्साहित किए। हिन्दी दिवस पर आमंत्रित मुख्य अतिथि श्रीमती रत्ना मुखर्जी ने हिन्दी के विकास तथा राजभाषा हिन्दी के प्रगामी प्रयोग को कार्यान्वित करने पर प्रोत्साहित किया। संस्थान राजभाषा कार्यान्वयन में अभिरूची रखते हुए प्रतियोगिताएँ आयोजित करता है -- जिसकी सराहना करते हुए उन्होंने संस्थान में हिन्दी में काम करने की कार्य संस्कृति की प्रशंसा की। उन्होंने कहा कि हिन्दी एक ऐसी भाषा है जिसे देश के सभी लोग आसानी से समझ लेते हैं।

श्रीमती मंजू शीरीन ने भी संस्थान के हिन्दी कार्यकलापों पर अपनी खुशी व्यक्त की एवं इसे बनाए रखने के लिए सभी से आग्रह किया। सभा में दिए गए 50 सटीक हिन्दी शब्द को पुरस्कृत किया गया। इस दिन कई और प्रतियोगिताओं का आयोजन किया गया। जिसमें कई अधिकारी/कर्मचारी भाग लिए और पुरस्कार ग्रहण किए।

अन्त में संस्थान के प्रशासन नियंत्रक द्वारा धन्यवाद प्रस्तुत किया गया।

CONTENTS



From Director's Desk

From Director's Desk

It is my privilege to present the Annual Report of this Institute for the period from April 2009 to March 2010. The Institute publishes its Annual Report to provide a brief description of our year-long research activities to colleagues and scientific communities across the globe every year. Apart from the scientific contributions, this report also includes some critical information about our infrastructure, extramural funding, intellectual property and other various aspects of scientific management and administration.

IICB is engaged in quality research on diseases of national importance and biological problems of global interest, employing sophisticated state-of-the-art technology in keeping with the rapid and unprecedented momentum that life science research has gained globally over the last 50 years. This institute has a steady record of growth in its R&D activities and like preceding years IICB continued its progress in the reporting period through developing and enhancing quality of science. Several new projects have been sanctioned. The Synthetic Biology project has been approved and is going to be a major Flagship programme. IICB Infrastructure continues to be upgraded. The construction of Salt Lake campus has been started. Expansion of space in IICB campus including a modern animal house and the construction of a ten storied modern building has been approved. The institute is planning to have a Translational Research Centre as a part of the proposed Knowledge Hub at Baruipur, near Kolkata. IICB is functioning as the mentor institute for National Institute of Pharmaceutical Education and Research (NIPER), Kolkata and this year first batch of twenty nine students completed their MS (Pharm) course successfully. This institute has helped NIPER-Kolkata's effort to gain national prominence. The six major R&D divisions in our institute are working in different biological and chemical fields with active collaboration among them to study some major diseases and improve healthcare sciences. We have paid substantial attention in developing drug from our indigenous and natural resources like native Indian plants.

The activities of **Chemistry Division** are focused on isolation of bioactive natural products from medicinal plants for determining their efficacies as well as in formulating herbal preparations for treatment of some major ailments. Synthesis of bioactive natural products or natural product like molecules in large amount, which include synthesis of novel nucleosides/nucleotides, chiral/achiral heterocycles, anti-leishmanial compounds etc are the major areas of research in this division. Besides, the division is also conducting studies on bacterial cell surface antigens, plant polysaccharides and neoglycoproteins, and on nucleic acid binding properties of natural products. The scientists of this division also initiated programme on Green Chemistry that will deliver more environmentally benevolent products and processes.

The **Molecular and Human Genetics Division** is working to understand the molecular genetic basis of diseases common in Indian populations. The specific objectives of this division include identification of the putative tumor suppressor genes involved in the development of head and neck cancer (HNSCC), identification of susceptibility alleles in *Helicobacter pylori* associated gastroduodenal diseases, study of molecular pathogenesis of oral submucous fibrosis, identification, isolation and modification of genes from non-host plants involved in self-defence mechanisms against pests, and transferring them as bio-pesticides to host plants, study of molecular genetics on human diseases like haemophilia, glaucoma, Wilson disease, and oculo-cutaneous albinism, identification of susceptible genes for leukoplakia and oral cancer, study of genetic toxicology, study of the molecular basis of the import of nuclear-encoded tRNAs into the mitochondria of the kinetoplastid protozoon Leishmania using a combination of biochemical and reverse genetic approaches.

The **Infectious Disease and Immunology Division** is involved in various fields of biological sciences with special interest to Leishmania, Cholera and Malaria. Scientists of this division are involved in the studies of type IA, IB and III DNA topoisomerase with reference to molecular architecture and therapeutic development, identification of a DNA repair enzyme, tyrosyl DNA phosphodiesterase 1 (Tdp 1), identification of modified sialylated structures, understanding the importance of modulation of sialylation, its biological role and their utility as potential disease-associated biomarkers in leukemia and visceral leishmaniasis (VL), study of oxidoreductase activity of *Plasmodium falciparum* macrophage migration inhibitory factor and competitive exclusion of classical biotype of *V. cholerae* by El Tor biotype. The scientists in this division first showed that differentiation-coupled induction of resistance of Leishmania parasites to macrophage oxidative damage is associated with increased intracellular cAMP and cAMP-mediated response. They compared the vaccine potentiality of three cationic formulations with Leishmania donovani promastigote membrane antigens (LAg) and the best vesicle was evaluated for long-term protection against experimental visceral leishmaniasis. The scientists of this division found that Phenolic Glycolipid–I (PGL-I) is not a specific antigen for *M. leprae*, because it cross-reacts with leishmanial antigens. They have also studied Molecular basis of survival of *V. cholerae* under nutritional stress by genetic analysis of spot gene function and identified a novel (p)ppGpp synthetase gene.

A team of cell biologists, physiologists and molecular biologists of the **Cell Biology and Physiology Division**, share a common goal of understanding the pathophysiology of certain metabolic and degenerative diseases. Cancer, stem cell biology, cardiac hypertrophy, diabetes, drug addiction, neurodegenerative diseases, utero-ovarian dysfunction and responses to pathogens in hematopoietic system are dealt with by the group. This division has developed and tested a number of models for various human diseases. The research highlights from the Division are: protection of cardiomyocyte death via peroxiredoxin II and melatonin mediation, sperm ecto-protein kinase as novel regulators of membrane fusion during acrosome reaction and detection of an endogenous neurotoxin, 6-hydroxydopamine that causes dopaminergic cell death in the brain due to long-term L-DOPA administration. The scientists of this division have successfully transplanted cultured limbal cells in patients suffering from ocular surface disorder resulting in recovery of eyesight.

The **Drug Development, Diagnostics & Biotechnology Division** is involved in studies on bioactive compounds for improving health and quality of life, as also for promoting future

economic growth through innovation in biotechnology. The major field of activity includes – isolation of lead bioactive compounds from plants, microbe or venom for useful pharmacological activity; mechanism of gastric ulceration; engineering plant genes for improved production of pharmaceuticals / nutraceuticales; immunoconjugate preparation strategies; nanocapsulated drug delivery in combating cerebral oxidative damage; molecular mechanisms of trehalose metabolism and microbial glycosidase enzymes.

The **Structural Biology & Bio-informatics Division** is carrying out research in areas that focus on structural characterization of potentially prospective biological macromolecules and other small molecules of therapeutic interest against various diseases, e.g. tuberculosis, leishmaniasis, cholera, cancer, diabetes and for other anti-inflamatory, anticonvulsant and immunomodulatory activities. Fundamental studies on protein functions, protein-protein and protein-nucleic acid interactions applying modern sophisticated technologies like nuclear magnetic resonance (NMR), X-ray crystallography, analytical ultracentrifuge, fluorescence correlation spectroscopy, diode array stopped-flow spectrophotometry, mass-spectrometry, quantitative structure activity relationship (QSAR) and 3D-QSAR are also being pursued. Softwares are being developed for genome / proteome analysis, prediction, modification and analysis of macromolecular structures and for elucidating their interactions with bio-active molecules.

In **11th Five Year Plan**, IICB is involved in 18 projects consisting of 4 Nodal Network Projects and 14 Partner Network Projects. In Partner Network Projects there are two extension Projects of Tenth Plan. All the projects are mainly from Biology & Biotechnology sector except one nodal network project which is from Pharmaceuticals, Healthcare & Drugs sector. During this year R&D works of two new projects have been started, one is an Interagency Project entitled, "Synthetic Biology and metabolic engineering of Azadirachtin biosynthesis pathway" and the other is an OSDD Project entitled, "Designing potential lead molecules for inhibition of siderophore biosynthesis in *M. tuberculosis*".

IICB has organized the **Foundation Stone Laying Ceremony** for its second campus at Salt Lake, Kolkata, about fifteen kilometers from its original campus at Jadavpur. The auspicious ceremony was attended by all the Staff members and students of IICB alongwith a large number of distinguished guests. Prof. Samir K. Brahmachari, DG, CSIR laid the foundation stone. Prof. Suranjan Das, Vice Chancellor, Calcutta University was the Chief Guest

A two day mini-symposium on **"Systems Biology and Proteomics in Biomedical Sciences"** was organized by IICB. Prof. Samir Kumar Brahmachari, DG, CSIR was also present in the programme. As a major achievement of this symposium, CSIR and the Systems Biology Institute (SBI, Tokyo Japan) have signed a Memorandum of Understanding (MoU) to look for collaborative initiatives with a view to promote systems biology and its medical and environmental applications in India and Japan. Our institute will co-ordinate the collaborative programme. The initial scope of the joint research is focused on developing new multi-agent anti-cancer formulations using systems biology approach. Future research topics would be extended to other areas with the goal of bringing India to the forefront of systems biology. IICB will have a major role in the entire programme.

A **Career Development Workshop for Young Scientists of India** was organized by IICB with a view to update young scientists from different research institutes in and around Kolkata about the present and upcoming opportunities for doing collaborative research and available schemes for

foreign research collaborations and support, particularly in the field of biomedical research.

The Institute observed **Hindi Week** from 10-14 September by organizing different competitions like Hindi noting & drafting, essay competitions and a workshop was conducted on "Problems coming on the way of use of technical vocabulary". The Institute also celebrated National Hindi Day on 14th September. This year Hindi web-site was launched in the Institute

The Human Resource Group organized a two-day programme on **"Multi-Skill Training Programme for Non-Tech Gr. D Staff-Members of IICB"**. A total of sixteen numbers of Gr. D (Non Tech) employees of our institute participated in this programme. In another effort the Technical Group II employees were also provided with a motivational training programme entitled, "Living in excellence" to overcome stress.

The **Indo-Russian Workshop** on **Complex Networks: Dynamics and Synchronization** was held at the IICB. Nine Russian delegates attended and presented their works. Two scientists from Germany, one from Spain and one from United States also joined the workshop. There were 55 (fifty five) participants altogether including young researchers from different parts of our country. The topics covered ranged from physical systems, neuron models to cardio-vascular system. The talks focused on collective behaviors of small units (unit cells or oscillators) in such systems. The physicists discussed about theoretical models and in limited cases about some small experiments, but they felt that close interaction with biologists and faculties from medicine can translate their experience into real biological systems leading to exchange of knowledge.

The **14th All India Congress of Cytology and Genetics (AICCG)** was hosted by IICB. The institute has a Fogarty Training Program in collaboration with the University of California, Berkeley, USA funded by the NIH, USA. This year, this training workshop was organized along with the 14th AICCG meeting. The main topic of the workshop was "Molecular Epidemiology, Environmental Health and Arsenic Exposure Assessment". The AICCG meeting and workshop were intended to review the advances in the field of cytology, genetics and the advancement of research in the field of environmental health with special reference to arsenic exposure assessment.

The **Indo-Brazil Symposium** on **Infectious Diseases-2009** was held at Kolkata under the auspices of IICB and Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), Bangalore. Six Brazilian delegates attended and presented their works. There were 85 participants altogether including young researchers from different parts of India. Thirty two talks were presented during the symposium. The Symposium has opened more avenues regarding Indo-Brazil collaborative works on infectious diseases in coming years. The symposium was financially supported by DST, Govt. of India.

Dr. K Kasturirangan, Member, Planning Commission, Dr. A.K.Verma, Adviser (S&T), Planning Commission and Dr. Indrani Chandrasekharan, Adviser (E&F), Planning Commission visited our institute during this period. Dr. Kasturirangan has expressed his views about IICB through his written comments, *"A most fascinating journey into the world of molecules, proteins and so on in their natural habitat, the most amazing creation of nature, the human body. The work here at IICB is pioneering and pathbreaking and promises to bring success to those who need it urgently and can make it affordable"*. A large number of scientists of national and international repute visited our institute during this year. Among which a lecture on "Cell Cycle regulation of cAMP levels" by Dr. Max Gottesman, Columbia University, USA, visit of Prof. Ruiz I Altaba, University of

Geneva, Switzerland for Scientific Lecture on "Role of Hedgehog – GLI signaling in stem cells, cancer and cancer stem cells", visit of Prof. S. E. Hasnain, Vice-Chancellor, University of Hyderabad (A. P.) for Scientific Lecture on "Molecular mimicry and hijack of host machinery by Mycobacterium tuberculosis for its own survival and dissemination", visit of Dr. Srinivas V. Kaveri, Director of Research, INSERM, Paris with a Lecture on "Function and dysfunction of our Immune system: Novel concepts Challenges and hopes for tomorrow" and visit of Prof. Haruki Nakamura, Osaka University for scientific discussion and a technical lecture on "New and powerful method for insilico drug screening and its applications" are most significant.

During the period our institute arranged an exhibition in its premises and participated in eight exhibitions in Kolkata and adjacent districts. In all of these exhibitions the achievements and on going R&D works of IICB were presented in popular ways with posters and photographs.

The CSIR Programme on Youth for the Leadership in Science for the year 2009 (CPYLS-2009) in West Bengal was coordinated by IICB. The programme was attended by 110 students from various parts of West Bengal.

A steady number of quality publications in journals of high impact factors are the hallmark of the Institute's progress in research and the average impact factor of publications is increasing continuously. I am proud in finding that the average impact factor of publications of IICB is approximately 3 this year.

During the reporting period IICB has filed eleven national and international patents related to synthesis, diagnosis, vaccination, correction of mitochondrial dysfunction, extraction of bioactive compounds from herbal resources to combat kala azar, prostate cancer, blood cancer, and other common human diseases. Total ten patents have been granted abroad in this period.

IICB has always remained as a centre of choice for promising researchers with ambition to work in biological and chemical fields. This year the institute has attracted a large number of bright, young research fellows and research associates from all over the country to generate adequate and trained human resource in the different fields of Biology and Chemistry and related areas for meeting the requirement of cutting edge research. During 2009-10 around 225 fellows and research associates worked in this Institute. A large number of distinguished scientists both from India and abroad visited our institute, delivered lectures and held discussions with different research groups in IICB. About 107 students from different Universities and Institutes of India participated in summer training and other training programmes. A large number of Scientists were involved in teaching and training programmes of neighbouring universities and institutes. The institute also fittingly observed Institute Foundation day and CSIR Foundation day.

I extend my cordial gratitude to all the scientific, technical and administrative staff members of our Institute for their year long sincere activity and cooperation in sustaining the growth and maintaining the reputation of IICB. I also believe that the dedication offered by my colleagues will move up the Institute to a new height in coming days.

Prof. Siddhartha Roy
IICB, Kolkata

Performance at a Glance

The Laurels

- Prof. Siddhartha Roy received Prof. GP Chatterjee Memorial Award from Indian Science Congress Association (ISCA), for the year 2009 – 2010.
- Dr. Chitra Mandal was elected Fellow of The Indian National Science Academy (FNA), India in 2010.
- Dr. Chitra Mandal was elected as a Member of West Bengal Academy of Science and Technology (WAST), in 2010 .
- Dr. Susanta Roychoudhury was elected Fellow of National Academy of Sciences India (FNASc).
- Dr. Hemanta K. Majumder received Sir J.C. Bose National Award by DST, Govt. of India.
- Dr. K.P. Mohanakumar was elected Member of the "Committee for Aid & Education in Neurochemistry (CAEN)" of International Society for Neurochemistry.
- Dr. K.P. Mohanakumar was elected President of SNC, India.
- Dr. Snehasikta Swarnakar received Prof. AN Bhaduri Memorial Lecture Award by SBC India 2009.
- Dr. Suvendra Bhattacharyya received Young Researcher Award of the Lady Tata Memorial Trust.
- Dr. Suvendra Bhattacharyya was selected International Senior Research Fellow of the Wellcome Trust, London, UK.
- Dr. Parasuraman Jaisankar received Raman Research Fellowship 2010 – 2011.
- Dr. Krishnananda Chattopadhyay received Indo-US Research Fellowship Award for the Year 2009.

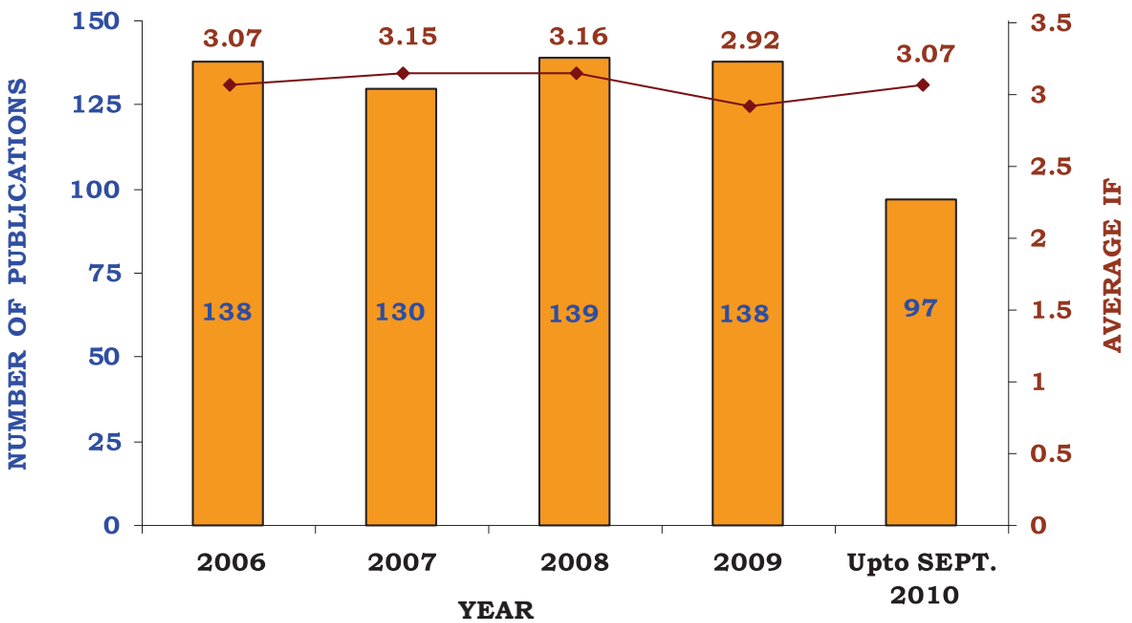
Performance at a Glance

PUBLICATIONS

A steady number of quality publications are the hallmark of the progress of our Institute in R&D. A schematic representation of year-wise publications* and average impact factor (IF) for the last five years is presented below:

Research Publication – 2009

Total Papers Published	...	...	138
Total Impact Factor	...	...	405.432
IF per Paper	...	...	2.92
IF per Scientist	...	...	5.63
No. of Papers with IF = 6 < 15	...	...	2
No. of Papers with IF = 5 < 6	...	...	10
No. of Papers with IF = 4 < 5	...	...	23
No. of Papers with IF = 3 < 4	...	...	27
No. of Papers with IF = 2 < 3	...	...	31
No. of Papers with IF = 1 < 2	...	...	29
No. of Papers with IF < 1	...	...	18

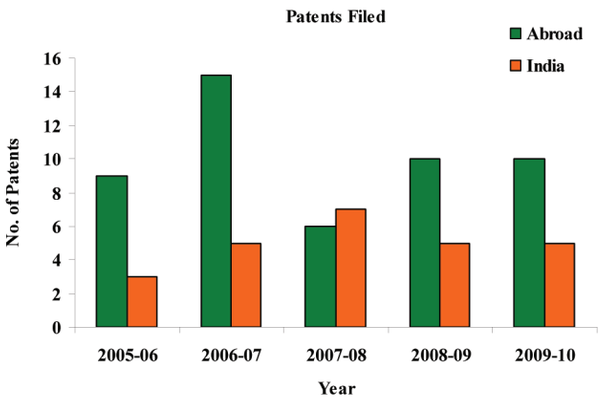


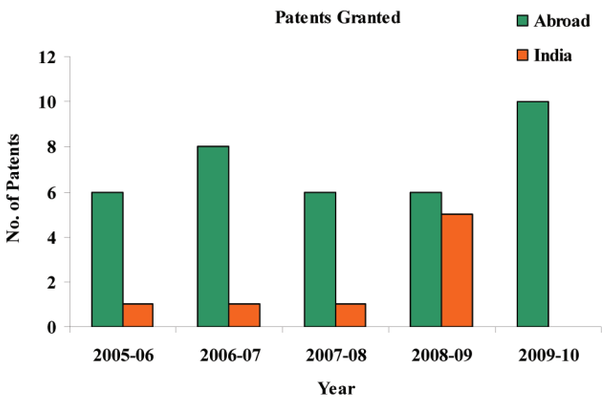
* Detailed list of publications for 2009-10 is given inside separately.

Performance at a Glance

PATENTS

A steady number of patents* are filed every year from the Institute and are granted.





* Lists of patents filed and granted in 2009-10 are given inside in the reports of P&I-PME Division.

Performance at a Glance

IICB-INDUSTRY PARTNERSHIP TIE-UPS

The Institute is continuously building synergy with the industries and successfully converting knowledge into wealth. This year, IICB scientists have managed to sustain the same level of interaction with the industry and earn a considerable amount of resources both human and financial.

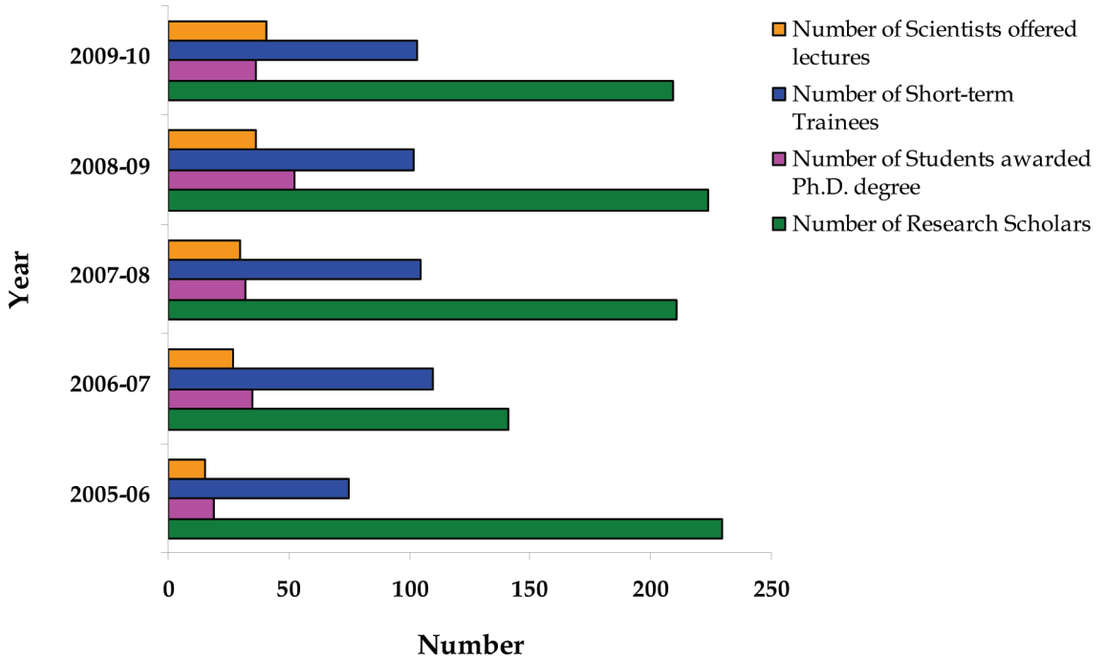
Our partners for the overall growth towards a GATI-India regime are as follows:

- Chatterjee Management Services Pvt. Ltd., Kolkata
- East India Pharmaceutical Works Ltd., Kolkata
- Angiogen Pharmaceuticals Pte. Ltd., Australia
- Chembiotech Research Int. Pvt. Ltd., Kolkata
- Dey's Medical Stores (Mfg.) Ltd., Kolkata
- Biotech Consortium (I) Ltd., New Delhi
- Santha Biotechnics Ltd., Hyderabad
- Piramal Life Sciences Ltd., Mumbai
- Qualpro Diagnostics, Goa
- Albert David Ltd., Kolkata
- Zephyr Biomedical, Goa
- Merial SAS Lyn, France
- Coir Board, Kochi
- DNDi, France

Performance at a Glance

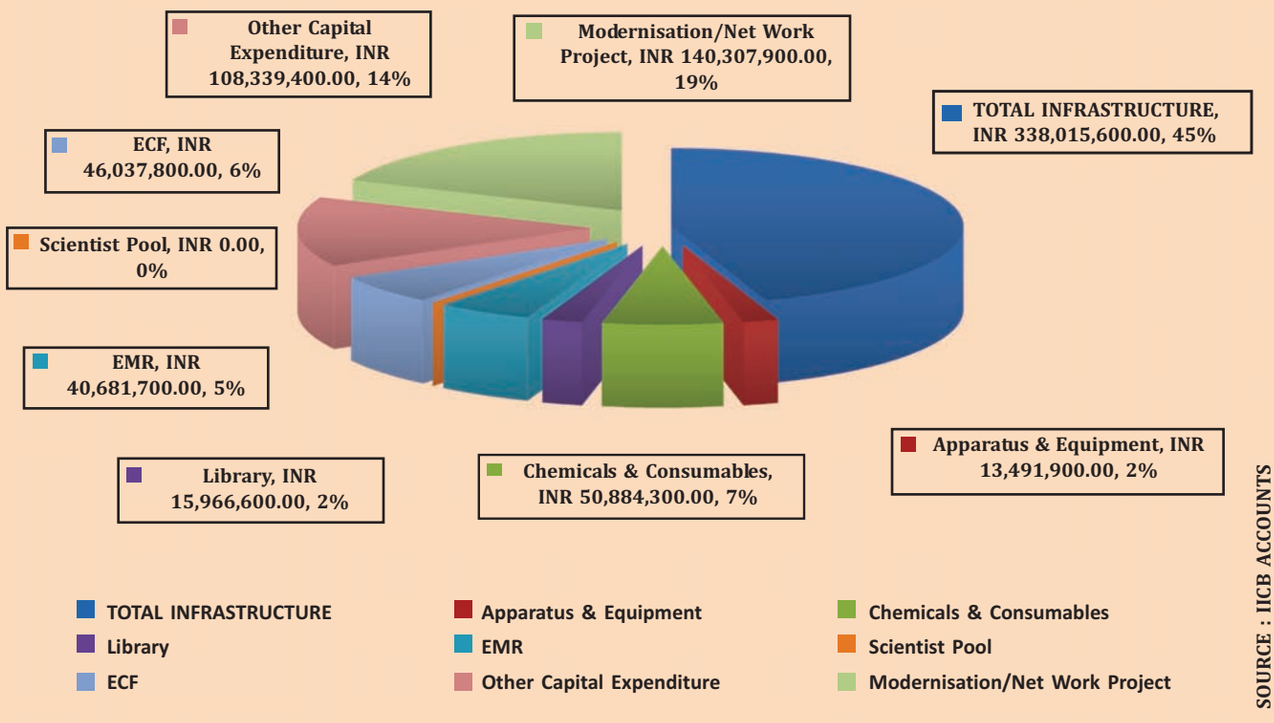
HUMAN RESOURCE DEVELOPMENT

A good number of research scholars carry out their research at Doctoral and Post-doctoral levels every year. Several students from various universities of our country get short-term training in every year. Data for the last five years are presented graphically.



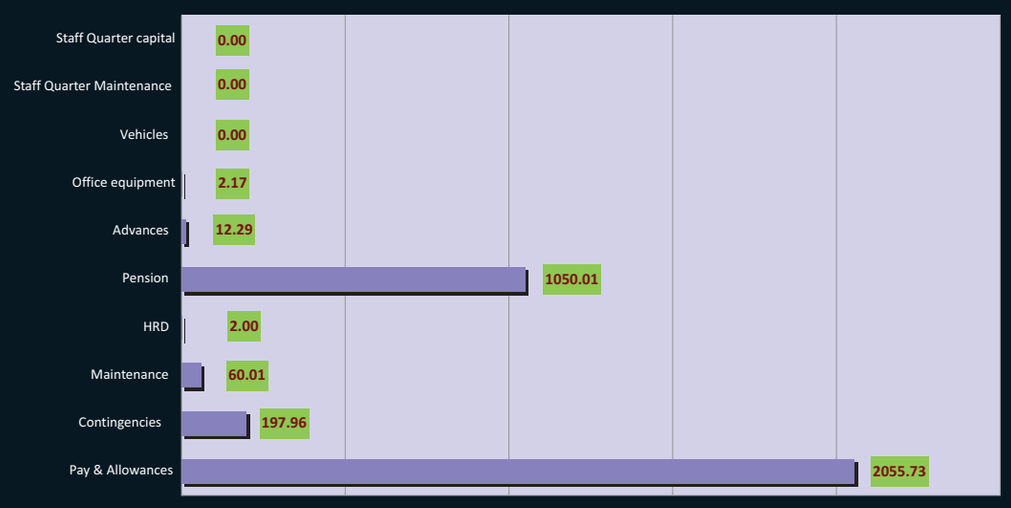
Performance at a Glance

R & D AND TOTAL EXPENDITURE BREAK-UP 2009-10



SOURCE : IICB ACCOUNTS

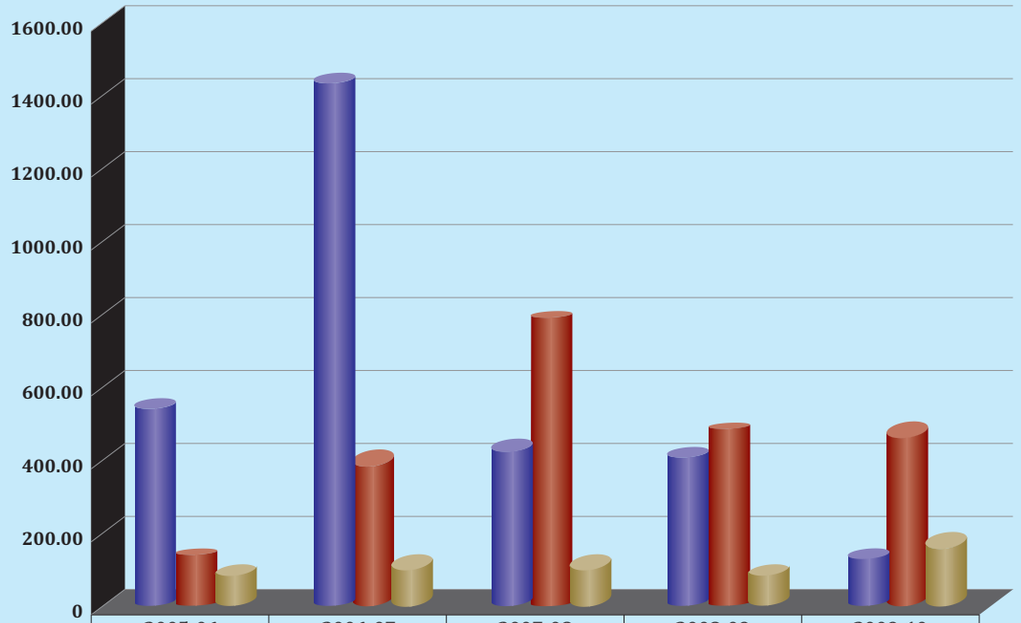
INFRASTRUCTURAL BREAKUP 2009-10



	Pay & Allowances	Contingencies	Maintenance	HRD	Pension	Advances	Office equipment	Vehicles	Staff Quarter Maintenance	Staff Quarter capital
Amount in Lakhs	2055.73	197.96	60.01	2.00	1050.01	12.29	2.17	0.00	0.00	0.00

Performance at a Glance

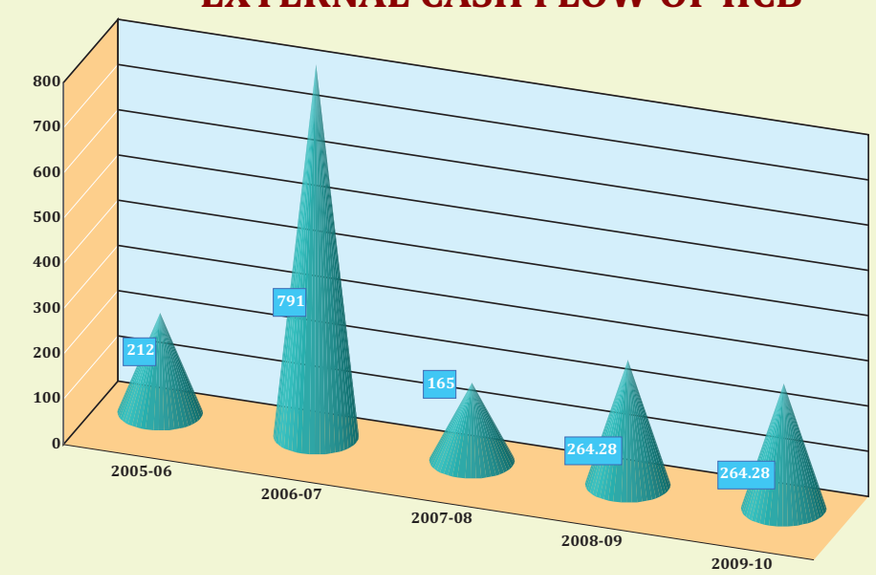
YEARLY EXPENDITURE W.E.F 2005-06 TO 2009-10



	2005-06	2006-07	2007-08	2008-09	2009-10
APPARATUS & EQUIPMENTS	538.50	1432.10	449.84	402.58	134.92
CHEMICALS & CONSUMABLES	129.01	409.15	775.00	509.74	508.84
LIBRARY	86.11	110.10	109.79	99.91	159.67

SOURCE : IICB ACCOUNTS

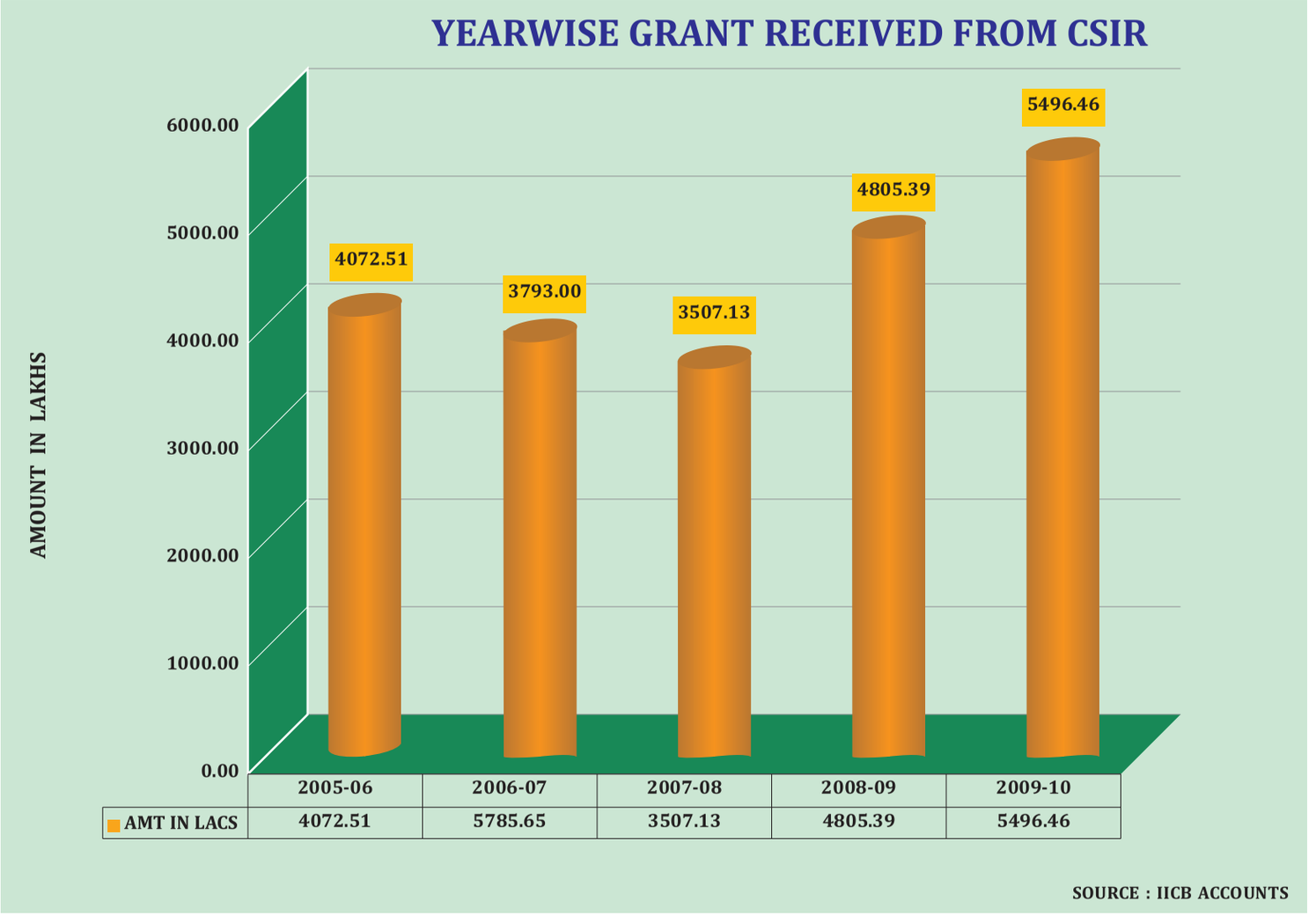
EXTERNAL CASH FLOW OF IICB



	2005-06	2006-07	2007-08	2008-09	2009-10
SERIES 1	212	791	165	264.28	265.28

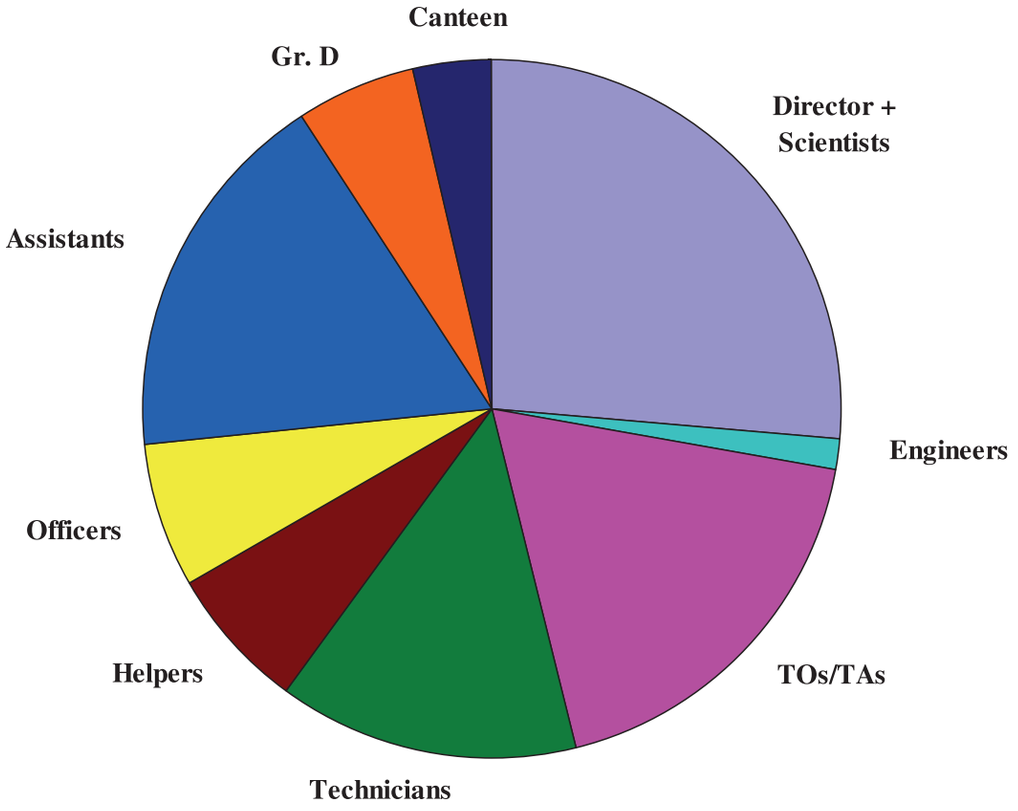
SOURCE : IICB ACCOUNTS

Performance at a Glance



SOURCE : IICB ACCOUNTS

STAFF STRENGTH AS ON MARCH 31, 2010



Total Staff – 273

Scientific & Technical Staff – 182

Director – 1, Scientists – 71, Engineers – 4, Technical Officers & Assistants – 50, Technicians – 38, Helpers – 18

Administrative Staff – 91

Officers – 18, Assistants – 48, Group D – 15, Canteen – 10

Staff Ratio :

Scientist : Technical Staff : Supporting Staff = 1 : 1.5 : 1.3

INFECTIOUS DISEASES AND IMMUNOLOGY

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Research activity of infectious diseases and immunology group involves various fields of biological sciences with special interest to *Leishmania, Malaria* and *Cholera*.

Dr. H. K. Majumder and group

Identification of tyrosyl DNA phosphodiesterase 1 (Tdp 1), a DNA repair enzyme

Tyrosyl DNA phosphodiesterase 1 (Tdp1) is a member of phospholipase D superfamily, conserved from yeast to humans, which cleaves a broad range of 3′ DNA adducts, the best characterized of which is the phosphodiester bond formed between DNA and topoisomerase IB. This study describes for the first time the cloning and functional characterization of the enzyme in DNA damage repair pathway in kinetoplast parasite *Leishmania donovani*. The protein is termed as LdTdp1. Sequence analysis study confirmed conservation of the active site motifs typical for Tdp1 family. Transcriptional down regulation of the gene was observed during CPT and H_2O_2 mediated apoptotic death of the parasites indicating a regulatory role, played by the gene. Enforced expression of the active enzyme protected the parasites against CPT and H_2O_2 mediated cytotoxicity. Overproduced Tdp1 reduced the DNA damage mediated by CPT inside the cells whereas its down regulation rendered the parasites hypersensitive to CPT. LdTdp1 activity was identified inside the nucleus as well as in the kinetoplast of *Leishmania* parasites. The protein harbors the nuclear localization signal (NLS) at its C-terminus. The active site residues of LdTdp1 have been identified by site directed mutagenesis. LdTdp1 transcripts and protein levels were observed to be higher during non-dividing and oxidative stress resistant stationary phase of *L. donovani* parasites compared to proliferative logarithmic phase suggesting a role of LdTdp1 in handling DNA damage repair in highly oxidative environment. Recombinant LdTdp1 was found to be active in vitro on 3′-tyrosine linked oligonucleotide substrate that mimicked the in vivo substrate of the enzyme. Altogether, this study reports for the first time, a tyrosyl DNA phosphodiesterase 1 protein in kinetoplastid parasites, which actively participate in removing trapped topoisomerase 1 from topo I-DNA dead end complexes generated from endogenous or exogenous sources, enabling the parasites to gain resistance against topoisomerase inhibitors.

Identification of DNA topoisomerase IA and III

DNA topoisomerases of kinetoplastids represent a family of DNA processing enzymes that essentially solve the topological problems not only in nuclear DNA but also in kinetoplastid DNA. Type I topoisomerases are classified in two subfamilies, IA and IB, based on differences in amino acid sequence and reaction mechanisms. Role of IB type of topoisomerase is well studied in *L. donovani*. Apart from this, three type IA topoisomerases are there in the parasite genome, termed as topoisomerase IA, and two topoisomerase III.

Kinetoplastids are ‘living bridges’ in the evolution from prokaryotes to higher eukaryotes. A key member of this foray is DNA topoisomerase IA of *Leishmania* (LdTOPIA), which we have identified and functionally characterized for the first time *in vitro* and *in vivo*. The strong prokaryotic lineage of LdTOPIA is evident from the conservation of active site residues and its ability to complement bacterial TopA null mutant strains. The Mg^{2+} dependent relaxation activity of only negatively supercoiled plasmids and the preference for single stranded substrates exhibited by recombinant LdTOPIA overexpressed in *Leishmania* conclusively establishes

its evolutionary ancestry from prokaryotes. But eukaryotic features include adaptation for the compartmentalized structure wherein the enzyme localizes in the nucleus and kinetoplast and has a codon bias for expression. The enzyme prevents DNA gyrase induced hypernegative supercoiling and thereby inhibits R-loop formation inside the TopA null mutant bacterial strain. All these properties of LdTOPIA make it an attractive molecular target for drug development. Our study on the basic understanding of the properties of LdTOPIA paves a future path in therapeutic interventions against leishmaniasis.

While the function of topoisomerase II and I are quite well established, the role of topoisomerase III in DNA metabolism has remained largely enigmatic. There is more known about its biochemical activities than its role in the cell. Genes encoding topoisomerase III enzymes are highly conserved in evolution from bacteria to human, and the phenotypic consequences of loss of topoisomerase III function are generally quite severe. It has been shown to possess a weak, ATP independent relaxation activity towards negatively supercoiled DNA only and strict dependence on magnesium. We have, for the first time, identified and characterized *L. donovani* homologue of bacterial and eukaryotic topoisomerase III in vivo, in order to get insight into its importance in *Leishmania* biology. The two topoisomerase III genes were cloned and amino acid sequence analysis revealed that one of the two proteins shares 47.84 identity with *H. sapiens* top IIIβ and 45% identity with *D. melanogaster* top IIIβ and termed as LdtopIIIβ. The second topo III showed to be divergent from the first one and shares significant homology with top III of *A. thaliana*, termed as LdtopIIIa. Complementation study of wild type and mutant LdtopIIIβ with slow growing topo3 mutant yeast *S. cerevisiae* revealed the functional conservation of the leishmanial counterpart of topoIIIß enzyme, the 327-tyrosine residue being the active site amino acid. A C-terminal deletion construct of LdtopIIIβ could not suppress the slow growth phenotype of mutant yeast revealing the requirement of C-terminal region for the enzyme function in vivo. Localization study with the LdtopIIIa indicated nuclear specific localization of the protein whereas LdtopIIIβ localized inside the nucleus and kinetoplast both, which indicates organelle specific differential function played by the two proteins in the parasite.

The genes for LdTOP1A, LdtopIIIα and LdtopIIIβ have been successfully expressed in *in vitro* transcription-translation system of *E. coli*. All the proteins are able to show their activities in crude extracts. Purification of the proteins and further characterization are in progress.

Effect of ATP on the ATP independent type IB topoisomerase of L. donovani

Topoisomerases are ubiquitious enzymes that resolve the torsional strain in DNA built up during vital cellular processes such as replication, transcription, recombination etc. The unusual bi-subunit topoisomerase IB of Leishmania is a paradigm shift in the evolution of type IB topoisomerases.

The heterodimeric *L. donovani* topoisomerase I shares mechanistic similarity with other eukaryotic type I topoisomerases with tyrosine as the nucleophile. Type IB topoisomerases are independent of ATP and Mg^{2+}, but presence of Mg^{2+} stimulates the relaxation activity. There have been conflicting reports in the literature regarding the effect of ATP on type IB topoisomerase. It has been shown that ATP stimulates the activity of vaccinia topoisomerase I whereas ATP has been reported to inhibit the activity of human topoisomerase I. With this background, we have evaluated the effect of ATP on the unusual bi-subunit type IB topoisomerase of *L. donovani* (LdTOP1L/S). We have shown that ATP stimulates the relaxation activity of LdTOP1L/S in absence of Mg^{2+} and ATP hydrolysis is not involved in the process. In presence of Mg^{2+}, ATP inhibits the relaxation activity of LdTOP1L/S. The ATP mediated stimulation occurs strictly in the presence of salt. However, in presence of Mg^{2+}, ATP forms complex with Mg^{2+}, which removes free Mg^{2+} or free ATP from solution thus rendering both of them ineffective in eliciting their respective stimulatory effects. Our results confirm that ATP has no effect on the initial cleavage step but it increases the strand passage rate of the enzyme. Using molecular docking, we have identified four amino acid residues on the large subunit as probable candidates for ATP binding. Mutagenesis of these residues to alanine reveals that the R190A mutant is unable to exhibit ATP mediated stimulation of DNA relaxation activity although ATP independent relaxation activity is unaffected.

Studies with fluorescent analogue of ATP provide evidence that ATP binds the enzyme and the binding is rather abolished in the R190A mutant. This study provides strong evidence that ATP can directly bind and stimulate the activity of *L. donovani* type I topoisomerase. This unique phenomenon of ATP mediated stimulation of an ATP independent topoisomerase undoubtedly raises the possibility that the enzyme or its subunits might be involved in some unique physiological processes that requires ATP binding.

Type IB topoisomerase of Leishmania with reference to development of therapeutics

The enormous development of molecular and cellular biology in recent times have provided opportunity for discovering newer molecular targets for drug designing, which form a rational basis for the development of improved anti parasitic therapy. This laboratory has been involved in developing DNA topoisomerase targeted anti-leishmanial agents.

3,3'-Diindolylmethane (DIM), a novel poison targeting *L. donovani* topoisomerase I (LdTOP1LS), induces programmed cell death in *Leishmania* parasites. Forced molecular evolutionary approach revealed that F270L mutation of large subunit confers DIM resistance to parasites. To deal with the problem of future DIM resistance, we have prepared three derivatives of DIM namely DPDIM (2,2'-diphenyl 3,3'-diindolyl methane), DMDIM (2,2'-dimethyl 3,3'-diindolyl methane) and DMODIM (5,5'-dimethoxy 3,3'-diindolyl methane) from parent compound DIM. Interestingly, DPDIM is more potent than the parent compound DIM against parasite growth. All the compounds stabilize the topo I-DNA cleavable complex *in vitro* and can also stabilize the complex formation with the F270L mutant enzyme. The *in vitro* results corroborate with the *in vivo* experiments where higher levels of protein-DNA complexes were detected in *Leishmania* promastigote cells treated with DPDIM than those treated with DIM, DMDIM and DMODIM. Interestingly, DMDIM and DMODIM failed to inhibit the catalytic activity of human topoisomerase I upto a concentration of 200 M, whereas DPDIM has some inhibitory effect at this concentration. Altogether the results suggest that the three derivatives of DIM can act as promising lead molecules for the generation of new anti-leishmanial agents.

Dr. Pijush K. Das and group

The work in my laboratory is centered on studying macrophage biology using visceral leishmaniasis as a model disease of macrophage. It may be broadly divided into two aspects: direct therapeutic approaches in general for macrophage-associated diseases and indirect therapeutic approaches based on unique cellular or metabolic events that may be exploited as targets. In our indirect therapeutic approaches, we first showed that differentiation-coupled induction of resistance of *Leishmania* parasites to macrophage oxidative damage is associated with increased intracellular cAMP and cAMP-mediated response. cAMP pool is dependent on adenylate cyclase, which synthesizes cAMP from ATP and phosphodiesterase, which degrades it to 5'AMP. Of 10 different leishmanial receptor adenylate cyclases (Ldrac), two (LdracA and LdracB) are stage-specific and developmentally regulated. Silencing and other biochemical parameters showed that differentiation-coupled induction of cAMP is regulated by LdracA. We are the first to clone and characterize all five isoforms of PDE from *Leishmania* and showed that the soluble cytosolic isoform, PDEA is heavily down regulated as the parasite is differentiated from promastigotes to amastigotes. Knocking down the enzyme as well as by using specific inhibitors, we found that PDEA-inhibited parasites have markedly higher peroxide degradative capacity. This increased peroxide degradation is not due to increased trypanothione (TSH) biosynthesis or transport; rather it is due to the shifting of TSH pool utilization bias towards peroxide degradation, i.e. antioxidant defense. In our direct therapeutic approaches, we wanted to identify the exact steps of macrophage signal transduction pathway hijacked by *Leishmania* for their successful survival and establishment of infection. Role of phosphatases in the impairment of MAP kinase signaling, which is directly responsible for *Leishmania*-induced macrophage dysfunction, is still poorly understood. Gene expression profiling revealed that *L. donovani* infection markedly upregulated the expression of 3 phosphatases, MAP kinase phosphatase (MKP)1, MKP3 and protein phosphatase 2A (PP2A). Inhibition of these phosphatases prior to infection points towards preferential induction of Th2 response through

deactivation of p38 by MKP1. On the other hand, MKP3 and PP2A might play significant roles in the inhibition of inducible nitric oxide synthase (iNOS) expression through deactivation of ERK1/2. Among various protein kinase C (PKC) isoforms, PKC ζ was associated with induction of MKP3 and PP2A in infected macrophages whereas PKC ε was correlated with MKP1 induction. Inhibition of phosphatases in *L. donovani*-infected BALB/c mice shifted the cytokine balance in favour of host by inducing TNF-α and iNOS expression. This was validated by cystatin, an immunomodulator and curing agent for experimental visceral leishmaniasis, which showed that inhibition of MKPs and PP2A activity may be necessary for favourable T cell response and suppression of organ parasite burden. This study for the first time suggests the possibility of the involvement of MAP kinase-directed phosphatases in the establishment of *L. donovani* infection.

Future plans: (i) For comprehensive understanding of cAMP signaling, we would like to carry out a thorough study of cAMP-metabolizing enzymes such as cAMP synthesizing enzyme, adenylate cyclase, degrading enzyme, phosphodiesterase (PDE), regulating enzyme, pyrophosphatase and functional enzyme, cAMP-dependent protein kinase (PKA). (ii) Sequestering itself inside the cells of the host allows *Leishmania* to hijack host-signalling systems, which primarily involve MAPK as well as TLR signalling cascades. We would like to have a comprehensive understanding of the homeostasis including both positive and negative regulators of these signalling systems.

Dr. (Mrs.) Chitra Mandal and group

Impact of glycosylation of biomoleculs in health and disease

Sialic acids (Sias) and its derivatives are found in nearly all higher animals studied and in certain bacteria and have been recognized to play a pivotal role in modulating various biological and pathological processes such as cell-cell and virus-cell adhesion, signalling, differentiation, immune reactions including apoptosis and malignancy. The main attention of my laboratory is focused on identification of modified sialylated structures, the understanding the importance of modulation of sialylation, its biological role and their utility as potential disease-associated biomarkers in leukemia and visceral leishmaniasis (VL). The following projects are ongoing to address the above points. Additionally, identification of molecular targets and signal cross talking using herbal compounds in cancer are ongoing.

Mahanine mediated apoptosis through crosstalk between Apo-1/Fas signaling and the Bid protein and via mitochondrial pathways in human leukemic cells

Mahanine, purified from the leaves of *Murraya koenigii,* showed apoptosis in a dose- and time-dependent manner in acute lymphoid (MOLT-3) and chronic myeloid (K562) leukemic cell lines and primary cells from leukemic and myeloid patients with minimal effect on normal immune cells. Mahanine-induced apoptosis was mediated by oxidative stress and showed involvement of the mitochondrial pathway (Fig. 1). Cytochrome c release was followed by the activation of caspases and cleavage of PARP in these cells. In MOLT-3, formation of the Fas-FasL-FADD-caspase-8 heterotetramer occurred, leading to the cleavage of Bid to its truncated form, which consequently resulted in formation of the mitochondrial transmembrane pore (Fig. 2). Mahanine was also a potent inhibitor of K562 xenograft growth (Fig. 3). Our results provide evidence for involvement of the death receptor-mediated extrinsic pathway of apoptosis in the mahanine-induced anti-cancer activity in leukemic cells, but not in myeloid cells, which are deficient in Fas/FasL (Fig. 4).

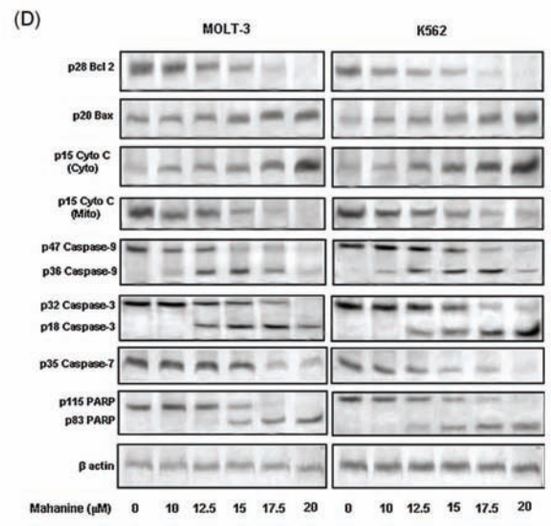

Fig. 1. Mahanine treatment led to - down regulation of Bcl2, upregulation of Bax, translocation of cytochrome c from the mitochondria to the cytosol, activation of caspase-9, caspase-3 and caspase-7 and the cleavage of PARP.

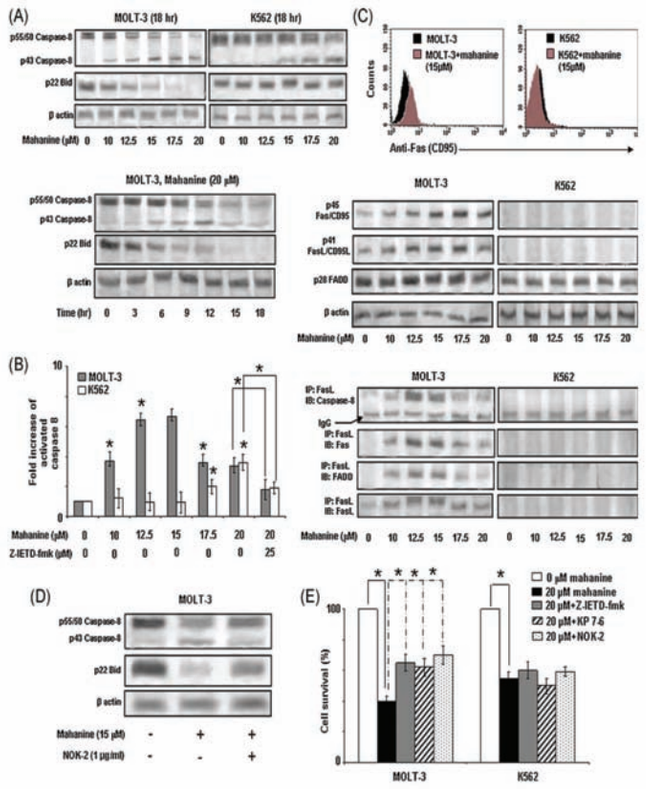

Fig. 2. Mahanine induces differential activation of the death receptor and associated proteins. (A) caspase-8 activation and Bid cleavage. (B) Activated caspase-8 in the absence and presence of the Z-IETD-fmk. (C) over expressed Fas/CD95 in mahanine-treated MOLT-3, but not in K562. Endogenous expression levels of Fas, FasL, FADD. Association between Fas-FasL-FADD-caspase-8 and DISC formation (D) FasL-neutralizing antibody NOK-2-mediated inhibition of caspase-8 activation and Bid cleavage (E) Measurement of cell survival.

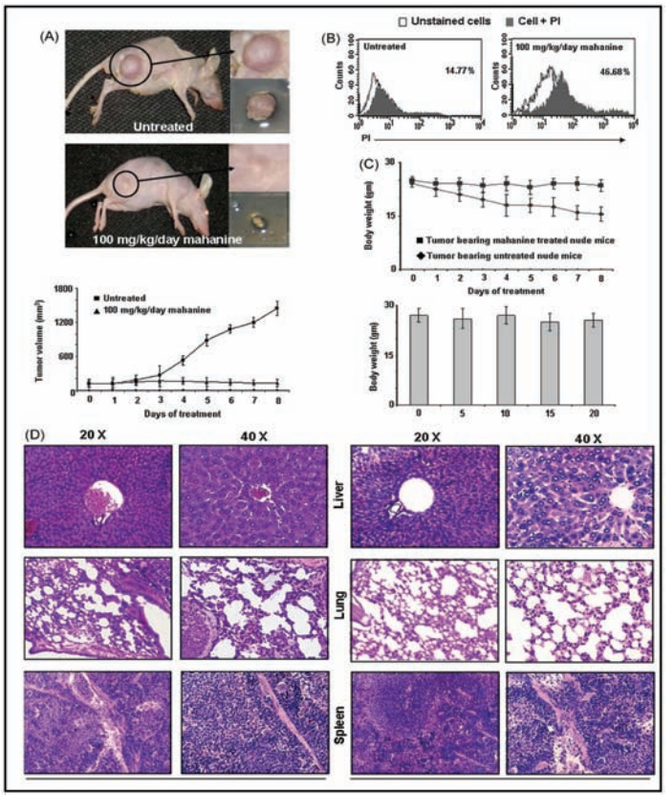

Fig. 3. Mahanine inhibits growth and induces apoptosis in the K562 xenograft in an athymic nude mice model. (A) Mean of tumor volume (B) Status of apoptotic cells in the tumor. (C) Effect on body weight of normal Balb/c mice. (D) Tissue sections of the livers, lungs and spleen.

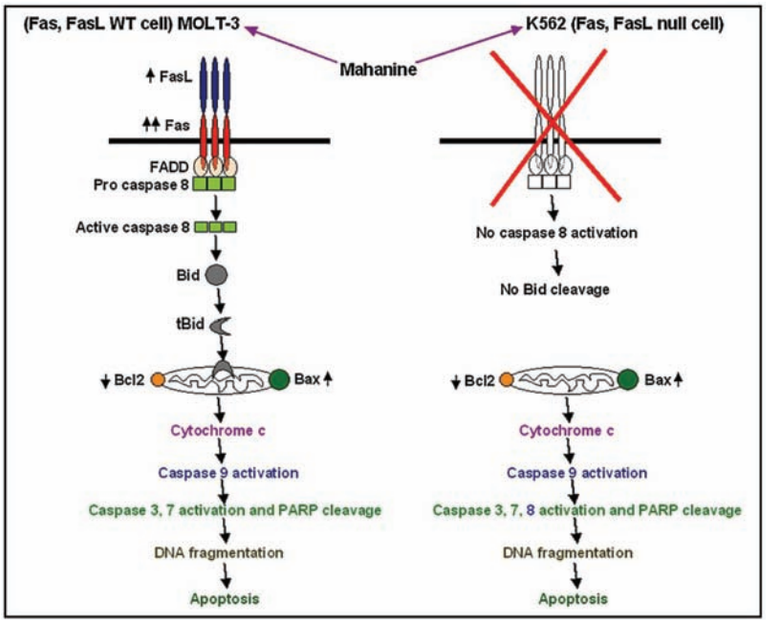

Fig. 4. Schematic representation of the probable apoptotic pathways in the mahanine-induced death.

Modulation of sialic acid regulating enzymes crucially drives the fate of leukemic cells and their correlation with disease status in leukemia

Earlier studies have established an enhanced presence of leukemia-associated 9-O-acetylated sialoglycoproteins (Neu5,9Ac2-GPALL) and gangliosides (9-OAcGD3) on lymphoblasts of ALL but not in corresponding cells of healthy children or in patients with other haematological disorders. We have further demonstrated a link between induction of this sialoglycotope and their role in regulating viability of lymphoblasts suggesting that O-acetylation of sialic acids (Sias) on lymphoblasts might play an additional mechanism that promotes the survival of these cells by escaping apoptosis. Sialate-O-acetyltransferase (SOAT), sialate-O-acetylestarase (SOAE), sialyltransferase (ST) and sialidases are the key enzymes accountable for the quantitation of the O-acetylation of Sias. Therefore, the activity and understanding the regulation of these enzymes involved in the O-acetylation of sias is important.

Recently, we have observed 24.34 fold enhanced SOAT activity capable of transferring acetyl groups to sias of glycoconjugates in the microsomes of lymphoblasts of bone marrow and peripheral blood of B- and T-ALL patients. Membrane bound sialidase (Neu3) is a key enzyme for the extralysosomal catabolism of gangliosides. It regulates pivotal cell surface events, including trans-membrane signaling, and plays an essential role in carcinogenesis. Currently we have demonstrated a marked down-regulation of Neu3 both in gene expression and enzymatic activity. Induced over-expression of Neu3, led to a significant increase of ceramide and decrease of lactosylceramide. These Neu3-transfected lymphoblasts showed apoptosis by maintaining the cellular ceramide below a critical limit. Taken together, the fine-tuning of these enzymes plays a significant role in disease biology and also decides the fate of ALL-cells (Fig. 5&6).

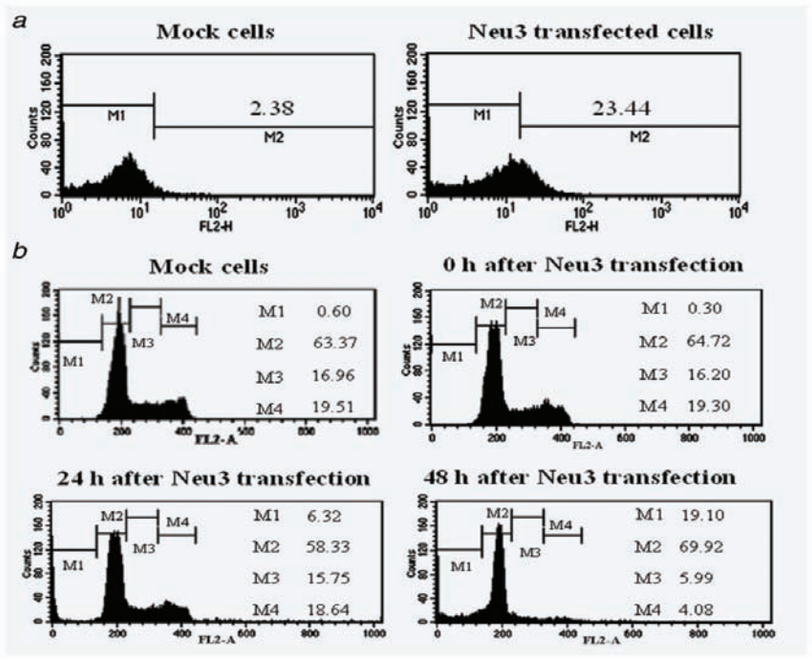

Fig. 5. Transfection of Neu3 in MOLT-4 cells and cell cycle analysis. (a) MOLT-4 cells were transfected with Neu3 cDNA. The transfection efficiency was measured by the expression of Neu3 protein (b) Cell cycle analysis after transfection.

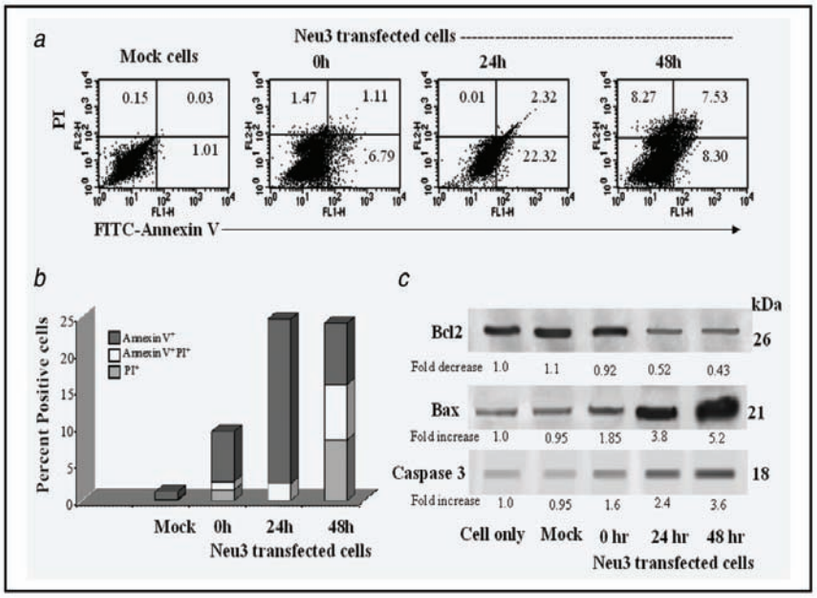

Fig. 6. Analysis of apoptosis-regulating molecules in transfected MOLT-4 cells. The percentage of apoptosis (a-b), expression of Bcl-2, Bax and active caspase3 (c).

Future plan: 1) Modulation of other sialylating enzymes to understand the disease biology in leukemia. **2)** ALL-associated sialoglycans through glycoproteomic approaches. **3)** Search for anti-cancer compounds and identification of molecular targets and signal cross talking. **4)** Sialoglycoprofiling of normal stem cells for their potential application.

Sialic acids in VL

We have earlier established an enhanced presence of 9-O-acetylated sialoglycoconjugates (9-O-AcSGs) on erythrocyte of VL patients (RBC_{VL}) and developed a user friendly, simple blood based assay for the diagnosis by detecting disease-associated antigen. These 9-O-AcSGs trigger the alternate complement pathway in VL. We have also demonstrated the contributory role of these sialoglycotopes as immunomodulatory determinants leading towards a beneficial immune response influencing the disease pathology.

Detection and characterization of a sialoglycosylated ABC-type phosphate transporter protein from patients with VL

Three 9-O-AcSGPs (19, 56 and 65 kDa) were purified from the peripheral blood mononuclear cell (PBMC) of VL patients and biochemically characterized in details. For the 56 kDa protein, N- as well as O-glycosylations were demonstrated and found to account for more than 9 kDa of the protein mass. The protein was identified by mass spectrometry and de novo sequencing of five tryptic fragments as a periplasmic ABC-type phosphate transporter of Pseudomonas aeruginosa (PA). The amino acid sequences of the assigned peptides had 83-100% identity with the NCBI entry for a Pseudomonas transporter protein. Based on the recently reported X-ray structure of a human phosphate-binding protein, we predicted a 3D structural model for the 56 kDa protein using homology and threading methods. The most probable N- and O-glycosylation sites were identified by combinations of sequence motif-searching bioinformatics tools, solvent accessibility calculations, structural environment analyses and mass spectrometric data. This is the first reported glycosylation as well as sialylation of the periplasmic component of an ABC-type phosphate transporter protein and of one of few identified bacterial glycoproteins.

Sias acquired by PA are involved in reduced complement deposition and siglec mediated host-cell recognition

The presence of 56 kDa sialoglycoprotein of PA in immunocompromised VL patients prompted us to explore the potential role of Sias in this phenomenon. Culture of PA in the presence of exogenous Sia resulted in linkage-specific incorporation of Sia (Fig. 7), which was associated with decreased complement deposition on the bacteria (Fig. 8). Sia acquired by PA mediated enhanced binding of bacteria to recombinant-CHO cells expressing human siglec-7 or siglec-9, as well as to human NK-cells and monocytes naturally expressing these siglecs (Fig. 9). Therefore, Sia may be acquired by PA in the host and contribute to bacterial pathogenicity and host-cell interactions via reduction of complement deposition and siglec-dependent recognition.

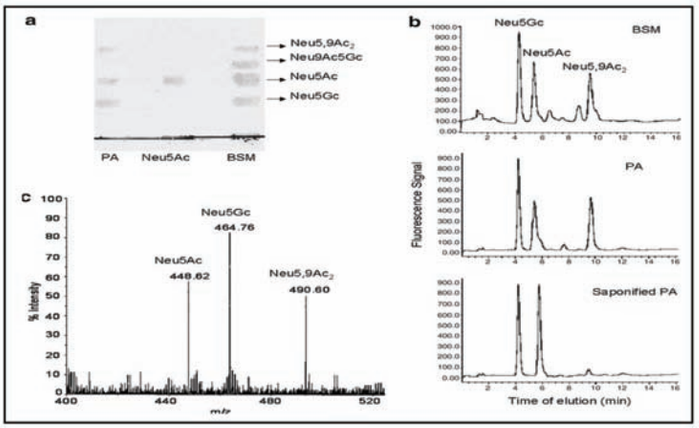

Fig. 7. Identification of Sia on PA by TLC (a), fluorimetric-HPLC (b) and MALDI-TOF-MS (c).

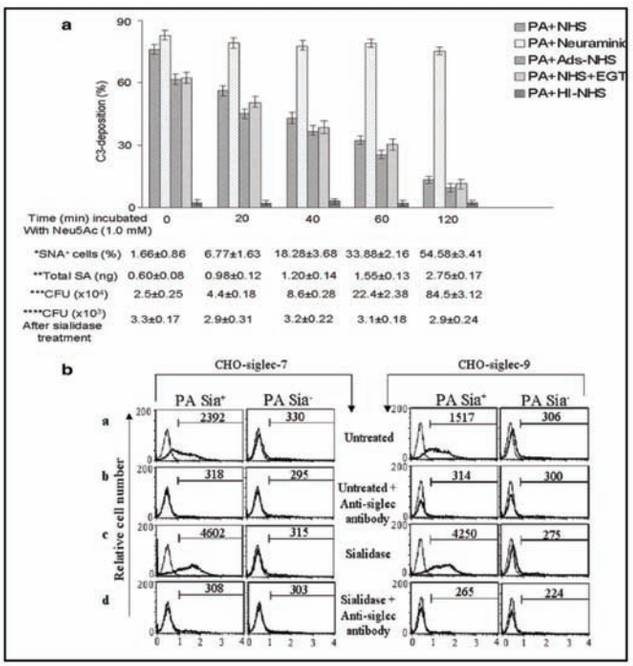

Fig. 8. C3-deposition and Sia-siglec recognition. (a) Increased Sia on PA leads to decreased C3-deposition as supported by enhanced CFU (b) Binding of PASia+ or PASia$^-$, (bold-line) with CHO-siglec-7,-9 compared to only CHO-cells (thin-line). Binding of PASia+ with (a) CHO-siglecs compared to PASia$^-$ (b) preincubated CHO-siglecs with the respective anti-siglec-7,-9 antibodies (c) unmasked CHO-siglecs (d) preincubated sialidase-treated CHO-siglecs with the respective anti-siglecs antibodies.

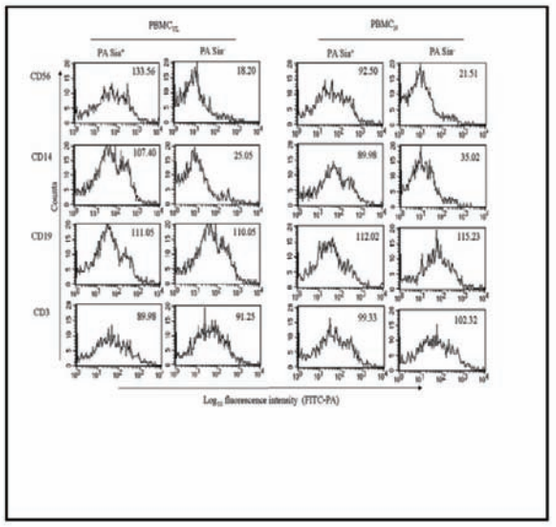

Fig. 9. Sia-dependent recognition of NK-cells and monocytes by PA.

C-reactive protein (CRP_{VL}) showed a protective role towards the clearance of damaged RBC_{VL}

CRP is a clinically important acute phase protein whose level increases upto 1000 folds in acute inflammatory conditions. Human CRP, as a mediator of innate immunity, removed damaged cells by activating the classical complement pathway. Previous studies have successfully demonstrated that CRPs are differentially induced as glycosylated molecular variants in certain pathological conditions including CRP_{VL}. We have also identified a new ligand, Protein A and thus establishing an extended definition of CRP. As anemia is a common manifestation in VL, we assessed the contributory role of glycosylated CRP_{VL} to influence hemolysis via CRP-complement-pathway. The specific binding of affinity-purified glycosylated CRP_{VL} with RBC_{VL} through distinct molecular determinants showed a 7-8-fold more binding compared to deglycosylated CRP_{VL}. Increased fragility, hydrophobicity and decreased rigidity of RBC_{VL} upon binding with glycosylated CRP_{VL} suggested membrane damage. Finally, the RBC_{VL}-CRP_{VL} binding was shown to activate the CRP-complement-cascade causing hemolysis suggesting a protective role towards the clearance of damaged RBC_{VL}.

Sias on parasites are responsible for increased NO resistance and survibility by inhibiting host responses.

We have earlier demonstrated the increased presence of different sets of Sias on promastigotes of virulent as compared to avirulent *Leishmania donovani* and their subsequent role in entry within macrophages. This observation instigated us to investigate their status on six different strains of *Leishmania* sp. causing different forms of VL. Recently we have observed that the strains showed a differential distribution of different derivatives of Sias in spite of their close resemblance in pathogenesis. Interestingly, 9-O-$AcSA^{high}$ promastigotes showed significant viability after exposure to $NaNO_2$ suggesting the involvement of this sialoglycotope in conferring nitric oxide (NO) resistance indicating their contribution in bestowing a survival benefit. Additionally, reduced accumulation of NO, interleukin-12 and interferon- in the supernatant of macrophages infected with such promastigotes indicated suppression of leishmanicidal host responses. However, involvement of other determinants, which may be a function of their inherent parasitic attribute is possible.

Future plan:

- Characterization of sialoglycans induced on immune cells and plasma samples from VL patients through glycoproteomic approaches
- Biological significance of differentially expressed identified sialoglycans

Dr. Syamal Roy and group

Understanding the mechanism of immune suppression in Leishmaniasis

The disease visceral leishmaniasis is characterized by defective cell mediated immunity, the cause of which is still unknown. The parasites replicate within the macrophage, the parasitized macrophages showing inability to stimulate T cells. The kinetic parameters of peptide-MHC complex formation were analyzed on purified membrane by using Surface Plasmon Resonance. It was observed that K_A for peptide-MHC complex formation in the cases of normal, infected and cholesterol-liposome treated infected macrophages were $7.8x10^{10}$, $3.4x10^{7}$ and $6.5x10^{10}$ respectively, and the corresponding K_D values were $1.5x10^{-11}$, $2.3x10^{-8}$ and $4.5x10^{-11}$ respectively. The above kinetic parameters indicated that kinetic stability of peptide-MHC complex formation is compromised on the APC surface under parasitized condition as compared to normal, and this can be corrected by making the membrane rigid through liposomal delivery of the cholesterol. Our study showed that cholesterol may be used, in the form of liposome, as an adjunct in kala-azar treatment.

Development of a DNA vaccine for visceral Leishmaniasis

Until now there is no effective vaccine against Kala-azar. The four immunodominant leishmanial antigens (KMP-11, TSA, A2 and HASPB) have been selected to test the efficacy of the individual candidates or their combination for immunogenicity and subsequent protection against challenge experiments in experimental models. Our study showed that KMP-11, when expressed in MIDGE (Minimalistic Immunogenically Defined Gene Expression) vector, is immunogenic. Similar studies with other antigens are underway. Based on the results of preclinical toxicity and immunogenicity studies, these combinations will be tested for phase-I clinical trial in the field in collaboration RMRI, Patna and other partners.

Dr. Santu Bandopadhyay and group

Role of reactive oxygen species in HCH-induced apoptosis of Bcr-Abl+ CML cells

Many cancer cells have increased levels of ROS compared to their normal counterparts. Redox manipulation is an emerging and feasible approach for possible therapeutic selectivity and overcoming drug resistance. The present investigation was designed to determine the activity of an edible herb-derived natural product hydroxychavicol (HCH) against Bcr-Abl^{+} CML cells and to study the mechanisms of action. HCH causes early but transient increase of intracellular ROS of mitochondrial origin followed by persistent increase of eNOS-mediated NO generation leading to apoptosis and necrosis of CML with minimal cytotoxicity for normal human peripheral blood mononuclear cells. HCH inhibited the key pro-survival PI3-Akt dependent NF-κB pathway by redox-dependent mechanism. Unlike other oxidative stress inducers, HCH-mediated killing of cancer cells did not depend on glutathione depletion. Therapeutic efficacy of HCH was confirmed in nude mice models bearing human cancer xenografts. These data provide a rationale for further developing HCH as an anticancer agent.

Dr. (Mrs.) Nahid Ali and group

Is phenolic glycolipid-I really a specific antigen for leprosy?

Phenolic glycolipid–I (PGL-I) of *Mycobacterium leprae* is a specific antigen for leprosy, and its terminal residue (i.e., 3,6di-O-methyl glucose) has not been found in any other natural molecule. Thus, PGL-I is being employed as a diagnostic tool for the detection of early leprosy. The serum samples obtained from patients with active leprosy cross-reacted with the antigens derived from *Leishmania donovani* (Fig. 10). In an experiment using an enzyme-linked immunosorbent assay, we found that 50% of the VL serum samples showed positivity with

PGL-I. Serum samples obtained from patients with active leprosy also demonstrated a cross-reaction with leishmanial antigens present in the 72, 63, 55, and 51 kDa bands in western blot analysis. Interestingly, we observed 3 distinct bands of 72, 63, and 55 kDa being recognized by the monoclonal antibody specific for PGL-I. These polypeptides were abundantly recognized by serum samples of patients with kala-azar as well. The rabbit polyclonal antibody against PGL-I showed a blotch in the region between 72 and 55 kDa. These 3 distinctly different molecular weight antigens of *Leishmania* somehow share the same exposed antigenic determinants to form the molecular configuration of PGL-I. Our finding therefore reveals that PGL-I is not a specific antigen for *M. leprae*, as claimed by Spencer et al. (J. Immunol. 175:7930-38, 2005) at least in the Indian scenario, because it cross-reacts with leishmanial antigens. This is a very important finding, because many laboratories are trying to establish diagnostic tests using this antigen for detection of early leprosy.

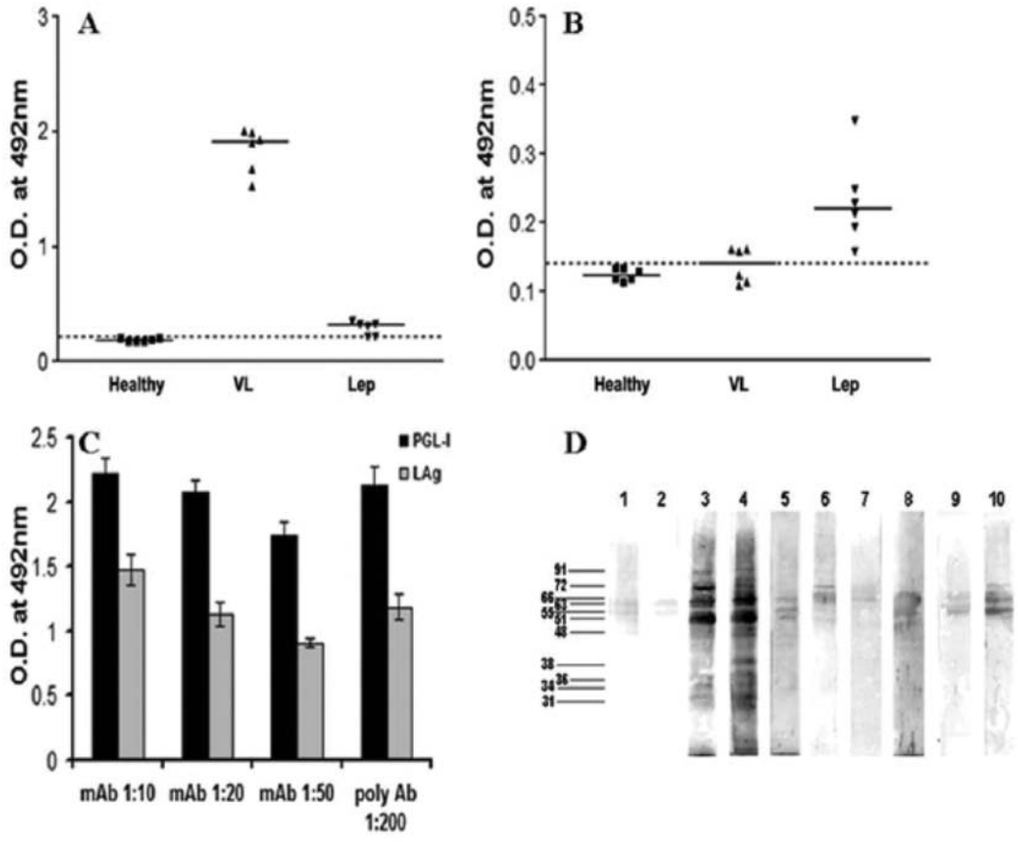

Fig. 10: Recognition of leishmanial antigen and phenolic glycolipid–I (PGL-I) in the serum samples of patients with visceral leishmaniasis (VL) and patients with leprosy (Lep) and in leprosy-specific antibodies. Panels A and B show the reactivity of the serum samples of healthy control subjects, patients with VL, and patients with leprosy (1:500 dilutions) against the *L. donovani* antigen (LAg) and the antigen PGL-I* of *Mycobacterium leprae*, respectively. The dotted lines show the cutoff value (mean of healthy control subjects + [2× standard deviation]), and the solid lines show the median of each group. Panel C shows the optical density (O.D.) (± standard error) of the reactivity of PGL-I and LAg with monoclonal* (mAb) and polyclonal* (poly Ab) antibodies to PGL-I (antibody dilutions are indicated in the figure). Panel D shows recognition of bands of Lag (6 mg/lane) by serum samples diluted to 1:100 from healthy individuals (lanes 1–2), patients with VL (lanes 3–4), patients with leprosy (lanes 5–6), and healthy rabbit and mouse (lanes 7 and 9), a 1:100 dilution of rabbit poly Ab (lane 8), and a 1:500 dilution of mAb to PGL-I (lane 10). *Kind gifts from Dr. P. J. Brennan, Colorado State University.

Comparison of liposome based antigen delivery systems for protection against Leishmania donovani

Liposomes have been widely exploited as antigen delivery systems for a variety of diseases including leishmaniasis. These vesicles can be prepared in various ways, which may affect the immunogenicity of the encapsulated antigens. In this study we compared the vaccine potentiality of three cationic formulations with *Leishmania donovani* promastigote membrane antigens (LAg) and the best vesicle was evaluated for long-term protection against experimental visceral leishmaniasis. We immunized mice with LAg encapsulated in multilamellar vesicles (MLV), dehydration rehydration vesicles (DRV) and reverse-phase evaporation vesicles (REV) and challenged them with parasites ten days after vaccination. LAg in MLV or DRV induced almost complete protection (Fig. 11), while LAg alone or entrapped in REV exhibited partial resistance. Protection observed with antigen incorporated MLV or DRV was predominantly Th1 (Fig. 12) as evidenced by elicitation of significantly high DTH, IgG2a antibodies and IFN-α. MLV encapsulated LAg demonstrated durable cell-mediated immunity and mice challenged ten weeks after vaccination could also resist experimental challenge strongly. Field trials of *L. donovani* vaccine were unsatisfactory mainly due to lack of an appropriate adjuvant. Cationic MLV when used as adjuvant with protein antigens induced sustained Th1 immunity. Adjuvant potential of cationic MLV can be utilized to design subunit vaccines.

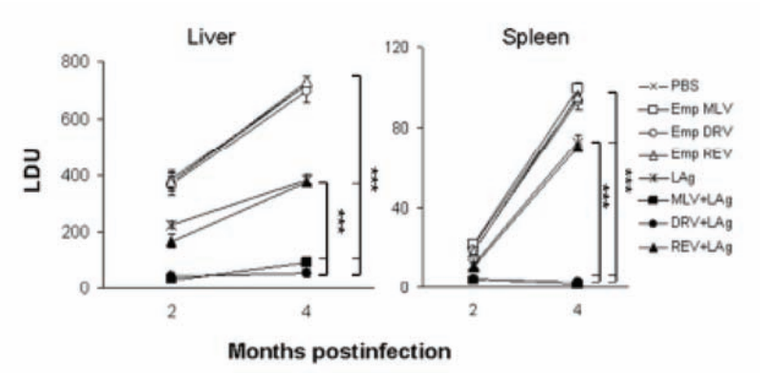

Fig. 11. Comparison of protective immunity of LAg in MLV, DRV and REV in susceptible BALB/c mice. Mice were immunized and boosted twice in two week intervals with PBS, empty REV, DRV or MLV liposomes, LAg alone or encapsulated in REV, DRV or MLV liposomes. Mice were then challenged with *L. donovani* promastigotes 10 days after the final booster, and parasite burden in the liver and spleen were determined 2 and 4 months postinfection. Values are given as mean LDU of four animals; ***, $P<0.001$; significant differences from each other (Tukey post test).

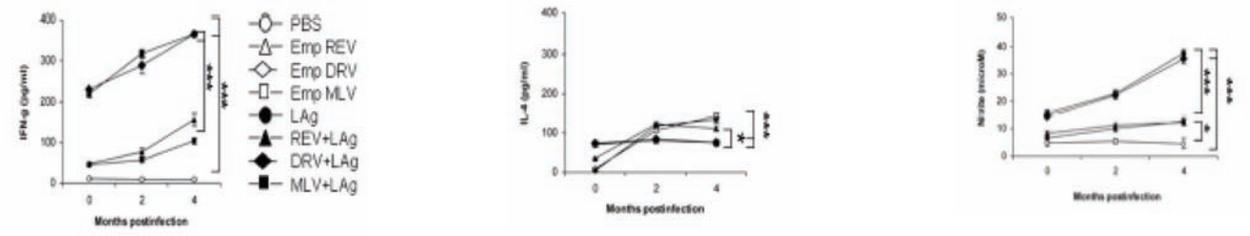

Fig. 12. Comparison of LAg in MLV, DRV and REV to influence the production of Ag-specific cytokines and NO in spleen culture supernatants. Groups of mice were vaccinated and spleens from individual mouse were isolated before or after infection. Single cell suspensions were plated in duplicate wells and pulsed with LAg (10 μg/ml). Seventy two hours later, supernatants were harvested and stored at –70 °C for estimation of IFN-γ, IL-4 and NO. Cytokines and NO were assayed before and after infection. *, $P<0.05$; ***, $P<0.001$; significant differences between groups (Tukey post test).

Vaccination route that induces transforming growth factor β production fails to elicit protective immunity against L. donovani infection

BALB/c mice immunized intraperitoneally (i.p.) and intravenously (i.v.) with *L. donovani* promastigotes membrane antigens (LAg), either free or encapsulated in liposomes, were protected against challenge infection with *L. donovani*, whereas mice immunized by the subcutaneous (s.c.) and intramuscular routes were not protected (Fig. 13). Protected mice showed strong parasite resistance in both the liver and spleen, along with enhanced immunoglobulin G2a and delayed-type hypersensitivity responses. Again, mice vaccinated through the i.p. and i.v. routes showed high levels of NO production after challenge infection. s.c. vaccination resulted in an increased capacity of the spleen cells to produce prechallenge transforming growth factor β (TGF-β) levels during the in vitro antigen recall response, whereas i.p. immunization induced production of prechallenge gamma interferon, interleukin-12 (IL-12), and IL-4 levels, with a Th1 bias. Exposure to antigenstimulated splenocyte supernatants of i.p. but not s.c. immunized mice activated macrophages for in vitro parasite killing. As an enhanced level of TGF-β was detected in supernatants from unprotected s.c. immunized mice, neutralization by anti-TGF-β antibody enhanced in vitro macrophage killing activity. The suppressive role of this cytokine was evaluated in vivo by vaccination with liposomal LAg and anti-TGF-β antibody. Upon parasite challenge, these animals showed significant protection in both the liver and spleen. Moreover, the addition of recombinant TGF-β in splenocyte supernatants of i.p. immunized mice in vitro as well as in vivo inhibited the protective ability of the macrophages by the i.p. route. Thus, the induction of high prechallenge TGF-β limits the efficacy of vaccination by routes that are nonprotective.

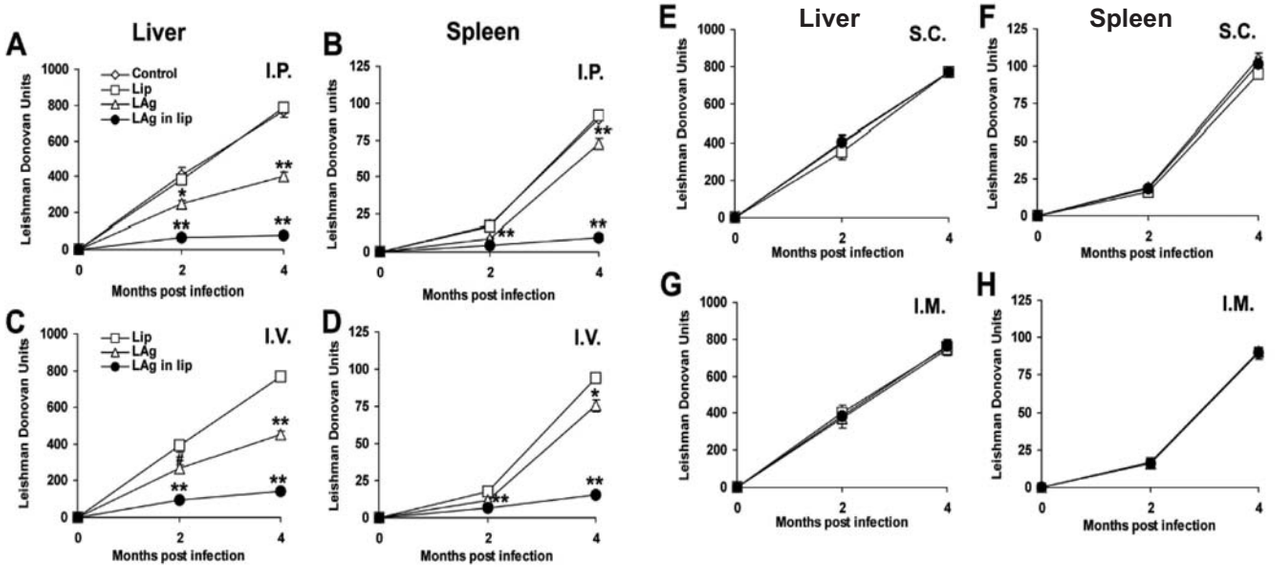

Fig. 13. Clinical outcomes following *L. donovani* challenge in BALB/c mice immunized via four different routes. Mice were immunized three times with 20 g of LAg, alone or entrapped in liposomes, at 2-week intervals through the i.p., i.v., s.c., and i.m. routes. Control groups received nothing or empty liposomes (Lip) through the respective routes. Ten days after the last immunization, the mice were challenged intravenously with 2.5 10^7 promastigotes of *L. donovani*. The parasite loads in the livers and spleens of i.p. (A and B), i.v. (C and D), s.c. (E and F), and i.m. (G and H) immunized animals are expressed in Leishman Donovan units. Data represent mean values standard errors (SE) for five mice per group at the designated timepoints and are representative of two independent experiments with similar results. #, P <0.05; *, P<0.01; **, P<0.001 for comparison to control groups (mice left unimmunized or immunized with empty liposomes by the respective routes).

Identification of novel L. donovani antigens that help define correlates of vaccine-mediated protection in visceral leishmaniasis

Visceral leishmaniasis (VL), caused by the intracellular parasite *Leishmania donovani* is a major public health problem in the developing world. But there is no effective and safe vaccine approved for clinical use against any form of leishmaniasis. Through reactivity with kala-azar patient and cured sera, polypeptides ranging from 91 to 31 kDa from *L. donovani* promastigotes were previously identified as potential protective vaccine candidates. In this study, four polypeptides 91(LD91), 72 (LD72), 51(LD51) and 31 (LD31)-kDa were purified using sodium dodecyl sulphate polyacrylamide gel electrophoresis followed by electroelution. We compared the vaccine efficacy of these antigens encapsulated in cationic liposomes in BALB/c mice against challenge infection with *L. donovani*. Our results demonstrated that liposomal LD31 (74%– 77%) and LD51 (72%–75%) vaccination reduced parasite burden to the greatest degree followed by liposomal LD72 (65%– 67%) and LD91 (46%–49%) (Fig. 14). Analysis of the cytokine responses in immunized mice revealed that all the vaccinated groups produced prechallenge interferon-γ, interleukin-12 and interleukin-4. Interestingly, the degree of reduction in parasite load could be predicted by the magnitude of the cytokine responses, which correlated inversely with the parasite burden both in liver and spleen. The 31, 51 and 72-kDa bands were identified as ATP synthase α chain, β-tubulin and heat shock 70-related protein 1 precursor of *L. major*, respectively using matrix-assisted laser desorption ionization–time of flight (MALDI-TOF/TOF) mass spectrometry (Table 1). These three leishmanial antigens have not been described before as successful vaccine candidates examined against in vivo VL model. Thus, these antigens can be potential components of future antileishmaniasis vaccines.

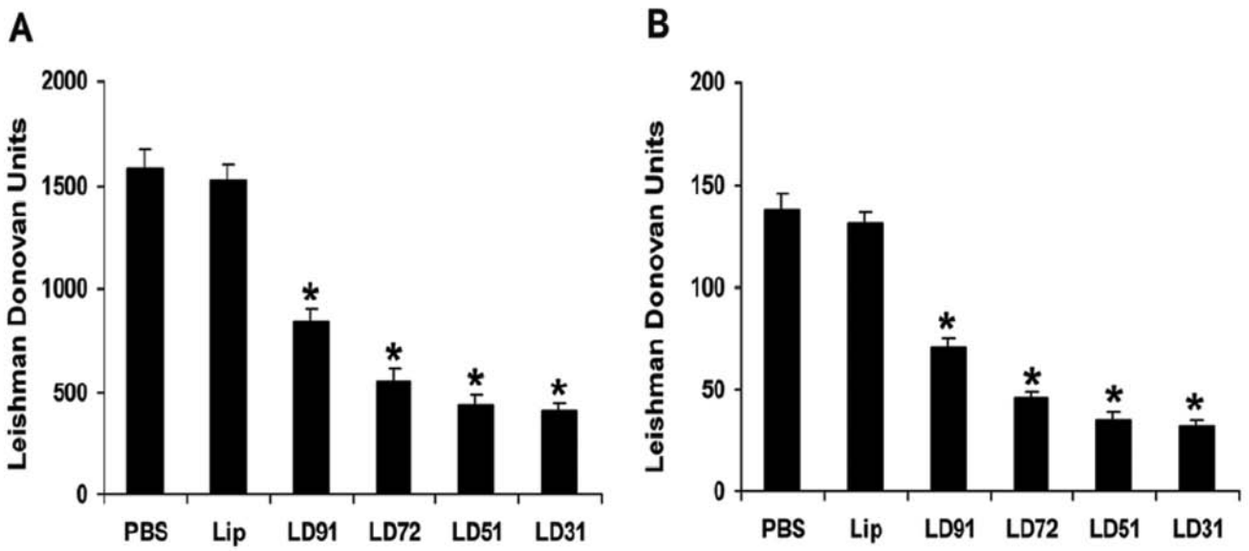

Fig. 14. Parasite burdens in BALB/c mice vaccinated with cationic liposomal antigens after L. donovani challenge infection. Mice were vaccinated intraperitoneally 3 times with 2.5 mg of each antigen entrapped in cationic liposomes at 2-week intervals. Control groups received PBS or empty liposomes (Lip). At 10 days after the last immunization, the mice were challenged intravenously with 2.510^7 promastigotes of L. donovani. Liver (A) and spleen (B) parasite burden were measured 3 months after challenge as Leishman Donovan Units (LDU). The results are mean LDUS.E. of five individual mice per group, representative of two independent experiments with similar results. * $p<0.001$ in comparison to control groups as assessed by one-way ANOVA and Tukey's multiple comparison test.

Table 1: Proteins identified by MALDI-TOF/TOF mass spectrometry.

Band	Protein name	Accession Number[a]	Matching Peptides	Probability-based Mowse score	% Sequence coverage
LD31	ATP synthase α chain (*L. major*)	68223738	18	324	20
LD51	β-tubulin (*L. major*)	68224035	18	223	27
LD72	Heat shock 70-related protein 1 mitochondrial precursor (*L. major*)	57015345	11	71	18
LD91	β-tubulin (*L. major*)	68224035	6	57	14

Dr. (Mrs.) Rukhsana Chowdhury and group

Host-pathogen interaction

Vibrio cholerae, a gram negative, non-invasive enteric bacterium is the causative agent of the diarrheal disease cholera. Cholera continues to be a major public health concern especially in developing countries, in many of which it exists in endemic form and frequently assumes epidemic proportions. For successful infection of its human host, *V. cholerae* must colonize the intestinal epithelium, and secrete cholera toxin (CT), a potent enterotoxin that causes the severe fluid loss characteristic of the disease. A toxin-coregulated pilus (TCP), coordinately expressed with CT, greatly enhances colonization of the intestinal epithelium by the bacterium. A subset of virulence factors including CT and TCP is coordinately regulated by the hierarchical expression of regulatory proteins comprising the ToxR regulon. Although many studies have described the effects of a variety of environmental parameters on the expression of the virulence genes of *V. cholerae*, the effect of contact with host cells has not been investigated. As this is of primary importance in host-pathogen interaction leading to disease, expression of the virulence genes was examined in *V. cholerae* following adherence to the intestinal epithelial cell lines. Adherence of .*V. cholerae* to the intestinal epithelial cell line INT407 strongly induces expression of the major virulence genes *ctxAB* and *tcpA* coding for CT and TCP. Expression of *toxT* encoding the transcriptional activator of *ctxAB* and *tcpA* was also significantly increased in the adhered bacteria. Adherence to INT 407 cells could also, overcome the repressive effect exerted by bile on the expression of virulence genes. Evidence has been obtained of a role of the second messenger cyclic di-GMP in the induction of *toxT*. The *vieA* gene encoding a c-di-GMP phosphodiesterase is induced in the early stages of adherence. A *vieA* mutant has been constructed and the induction of *toxT* has been shown to decrease in the *vieA* mutant following adherence.

In the gastric pathogen *Helicobacter pylori*, also, host cell contact induces expression of virulence genes including *cagA, vacA, urease* etc. The virulence genes were induced to different extents in cell-associated bacteria. The induction was not due to host cell components secreted from AGS but requires direct contact of the bacteria with the host cells. A proteomic analysis has indicated that several proteins are altered in the adhered *H. pylori*

Regulation of the virulence cascade of V. cholerae.

Unsaturated fatty acids present in the intestine exert multiple effects on virulence gene expression and also toxin in *V. cholerae.* A mutation has been constructed in the *fadD* gene that is involved in converting fatty acids to fatty acyl-CoA and simultaneous uptake into the cytosol. The *fadD* mutant exhibited decreased expression

of virulence factors including CT and TCP and also the regulatory gene *toxT*. The molecular basis of *fadD* mediated regulation of *toxT* expression has been elucidated. It has been demonstrated that membrane localization of the regulatory protein Tcp is altered in a *fadD* mutant thereby impairing the function of TcpP in activating *toxT* expression.

Competitive exclusion of classical biotype by El Tor biotype of V. cholerae.

V. cholerae strains of the O1 serogroup that typically cause epidemic cholera can be classified into two biotypes, classical and El Tor. The El Tor biotype emerged in 1961 and subsequently displaced the classical biotype as a cause of cholera throughout the world. When strains of the El Tor and classical biotypes were cocultured in standard LB medium, the El Tor strain could eventually take over the population. Transposon mutagenesis of a population of classical *V. cholerae* indicated that a mutation in the *rpoS* gene encoding the stationary phase sigma factor delayed the population takeover by the El Tor biotype.

Dr. Rupak K. Bhadra and group

V. cholerae is a major human diarrhoeal pathogen causing frequent epidemics in most developing countries including India. The situation is further complicated by frequent emergence of new pathogenic clones with multiple drug resistance. In this regard recent spread of the hybrid *V. cholerae* El Tor strains carrying classical type CTX phages in Africa and Indian Subcontinent is noteworthy. However, recent progress in bacterial genomics and proteomics has dramatically altered the study of bacterial pathogenesis and designing of experiments for complete understanding the virulence mechanism, growth, survival and persistence of the pathogens in various environmental niches. As a result new genes and regulatory circuits of the above pathogens are identified. It is also necessary to understand the role played by various mobile genetic elements in the evolution of new pathogenic clones. Different physico-chemical stress signals including nutrition deprivation received by pathogens in environmental reservoirs as well as under in vivo situations are quite dissimilar and probably play critical roles in adaptation through genetic mutation and help a pathogen to evolve further. In this regard, role of quorum sensing and biofilm formation also appears to be important for survival and growth of *V. cholerae*.

Evolution of hybrid Vibrio cholerae O1 biotype El Tor

The *ctxAB* operon, encoding cholera toxin (CT) in *V. cholerae*, is carried by the genome of a filamentous phage CTX. Usually, specific CTX infects each of the two important biotypes, classical and El Tor, of epidemic *V. cholerae* strains belonging to serogroup O1, which are called CTX^{class} and CTX^{ET}, respectively. However, an unusual hybrid El Tor strain carrying CTX^{class} caused cholera epidemic in Mozambique in 2004. To understand its evolution, we have further analyzed some representative hybrid El Tor strains isolated in Kolkata, India in 1992 and the results indicate that both the Mozambique and Indian strains are infected with a unique CTX^{class} having only 4 copies of tandem heptamer repeat sequence, 5'-TTTTGAT-3', present in the *ctxAB* promoter (P_{ctxAB}) region, like in CTX^{ET}. Usually the P_{ctxAB} of classical biotype contains 7-8 copies of such sequences. However, sequence analyses of the P_{ctxAB} regions of several classical strains indicated that the copy number of heptamer repeat sequences might vary from 4-8 copies, which was previously unknown. Since the hybrid strains analyzed in this study carry 4 copies of the heptamer sequences it may thus serve as a marker to trace the strain in future. Interestingly, while the Mozambique strain is devoid of El Tor specific free RS1 element or pre-CTX prophage, the Indian hybrid strains carried such elements. The free RS1 has been mapped, cloned and sequenced. Like pre-CTX and CTX prophages, multiple copies of free RS1 elements were found to be integrated in tandem in the large chromosomal *dif* site. Since Indian hybrid El Tor strains carry either free RS1 or pre-CTX prophage in their large chromosomes, it may be possible that the Mozambique hybrid El Tor strain has evolved from these progenitor strains by step-wise deletion of CTX genetic elements from their large chromosomes.

Molecular basis of survival of V. cholerae under nutritional stress

RelA and SpoT enzymes of Gram-negative organisms critically regulate cellular levels of (p)ppGpp, the cellular alarmone. We have dissected the *spoT* gene function of the cholera pathogen *Vibrio cholerae* by extensive genetic analysis. Unlike *Escherichia coli*, *V. cholerae relA spoT* cells accumulated (p)ppGpp upon fatty acid or glucose starvation. The result strongly suggested RelA-SpoT independent (p)ppGpp synthesis in *V. cholerae*. We have isolated by repeated subculturing a suppressor strain with (p)ppGpp^0 phenotype using *V. cholerae relA spoT* mutants. Bioinformatics analysis of *V. cholerae* whole genome sequence allowed identification of a hypothetical gene (*VC1224*), which codes for a small protein (~29-kDa) with only Rel_Spo domain and the gene is found to be highly conserved in vibrios; hence it has been named *relV*. Using *E. coli relA* or *relA spoT* mutant we showed that *relV* indeed codes for a novel (p)ppGpp synthetase. Further analysis indicated that *relV* gene of the suppressor strain carries a point mutation at nucleotide position 676 of its coding region (*relA spoT relV676*), which seems to be responsible for the (p)ppGpp^0 phenotype. Analysis of a *V. cholerae relA spoT relV* triple mutant confirmed that apart from canonical *relA* and *spoT* genes, *relV* is a novel gene in *V. cholerae* responsible for (p)ppGpp synthesis. The results also suggest that (p)ppGpp metabolism is quite complex in *V. cholerae.* Stringent response in bacteria is also regulated by a factor, called DksA (product of the gene *dksA*). We have generated several *dksA* mutants of *V. cholerae* and characterization of those mutants revealed that the DksA protein apart from its role in stringent response may control motility, biofilm formation etc. Role of stringent response genes *relA*, *spoT* and *dksA* will be further explored for their involvement, if any, in quorum sensing, biofilm formation, long-term starvation survival and relation with stationary phase sigma factor gene (*rpoS*) expression. We are also working on the essential GTP binding protein *cgtA* and further work has been carried out on this aspect, which is as follows. The protein sequence alignment of CgtA$_{Vc}$ with other organisms revealed some unique facts. The first five amino acids at the start of the CgtA$_{Vc}$ ORF was absent not only in other relative organisms but also in other species of *Vibrio* whose sequences could be found in existing database (www. biocyc.org, www.ncbi.nlm.gov). We also found that these five amino acids are quite conserved among various *V. cholerae* strains. So, to understand the importance of these five amino acids at the N-terminal of CgtA$_{Vc}$, we deleted this 15-bp region coding for five amino acids in the start of the 5' region of the *cgtA* ORF and the 15-bp deleted ORF was cloned under an arabinose inducible promoter in pBAD. The authenticity of the protein was confirmed by Western blot analysis using anti-CgtA$_{Vc}$ antibody. Overexpression of this recombinant protein in *E. coli* caused slowing in growth compared to the control strain. However, the growth difference was insignificant in the case of *V. cholerae*. The results indicate that extra five amino acids present in the N-terminal of the CgtA of *V. cholerae* probably required for normal functioning of the protein.

Dr. (Mrs.) Tripti De and group

CD1d mediated T cell recognition of Leishmanial glycosphingophospholipid

CD1d-restricted natural killer Tcells (NKT cells) possess a wide range of effector and regulatory activities that are related to their ability to secrete a variety of proinflammatory and immunomodulatory cytokines leading to potent activation of a variety of innate and adaptive immune cells. Through a combination of these and other activities, NKT cells can exert major effects on the immunity to a wide variety of infectious pathogens. The binding groove of the CD1d molecules is hydrophobic and enfolds alkyl chains of lipid antigens, thereby allowing interactions of polar chains with the T cell receptors. Different kinds of glycolipids including glycosphingolipids presented by CD1d have been identified.

An immunomodulatory glycosphingophospholipid (GSPL) was purified from *Leishmania donovani* promastigotes. Besides reactive oxygen and nitrogen species, GSPL also induced interferon gama and interleukine 12 in human peripheral blood monocytes. GSPL also induced blood cells to proliferate. The stimulatory properties of GSPL were also studied by using a mouse NKT cell hybridoma. iGb3 (iso globotriosyl ceramide) was taken as a

positive control and Gb3(globotriosyl ceramide) as the negative control of NKT cell stimulation. The response of NKT cells to presentation of GSPL by APC was studied. GSPL induced IL-2 in NKT cells. Surface antigens of infected macrophages are obvious targets in immunoprophylsxis for leishmania infection. These data suggested that this functionaly important antigen of *L. donovani* may be used as a candidate vaccine. At a dose of 5 mg/Kg body weight, GSPL induces sterile protection in an animal model of visceral leishmaniasis. Resolution of the disease required the presence of T cells and the recovered animals remained immune to re-challenge. GSL mediated protection is controlled by the CD1d/NKT cell pathway.

The host protective purified leishmanial glycoprotein (LGP)

A glycoprotein was isolated from avirulent *L. donovani* clonal parasites. The purified protein induces sterile protection against subsequent challenge and during active infection. The role of pattern recognizing receptors in controlling parasite growth in the protected mice is under investigation.

Mrs. Neeta V. M. Khalkho

To study the localization of UMSBP1 and UMSBP2 from *L. donovani*, the antibody raised in rabbit against UMSBP1 revealed the localization of UMSBP1 in mitochondria, but nothing could be said conclusively regarding localization of UMSBP2 as the antibody raised against UMSBP1 in rabbit cross reacted with UMSBP2 because of total homology of UMSBP1 with UMSBP2 with an extra stretch of sixty amino acids at the N–terminal region of UMSBP2. Thus keeping this point of cross reactivity, C-Terminally His-tagged protein of UMSBP1 and UMSBP2 from *L.donovani* were cloned at N-terminal site of pXG-GFP+2 with a stop codon before GFP and was transfected in AG83 cells. Cells were selected under drug pressure of 200 mM with G418 at 22°C. The cells so cultured were immunostained and seen under confocal microscope for localization. The study revealed that both UMSBP1 and UMSBP2 are located at mitrochondria. The PSort search for localization signal revealed theoretical N-terminally located mitochondrial localization signal in first fifteen amino acids of UMSBP2, hence primers were designed for N-terminal localization signal deleted UMSBP2 with the idea that if the signal is removed the localization should get altered. But immunocytochemistry of $\triangle N_{15}$UMSBP2 transfected cells revealed that the localization of $\triangle$N15UMSBP2 doesn't get disturbed and is still present in mitochondria. The EMSA of UMSBP1 with labeled ligant universal minicircle sequence (UMS) at different temperature for the same time interval show differential level of binding. The amount of nucleo-protein complex formation is found to be directly proportional to the temperature. Down regulation of UMSBP1 co-operatively down regulates UMSBP2 and vice versa.

Dr. Uday Bandyopadhyay and group

Vicinal cysteines 3 and 4 are essential for oxidoreductase activity of Plasmodium falciparum macrophage migration inhibitory factor

Among macrophage migration inhibitory factors (MIF), only *Plasmodial* MIF, including *Plasmodium falciparum* MIF (*Pf*MIF) contains a sequence of typical CC chemokine (CC–C–C) family. *Pf*MIF possesses typical oxidoreductase and tautomerase activities. The N-terminal proline is assigned for tautomerase activity, which is conserved in all MIFs; however, CXXC motif which is responsible for oxidoreductase activity in human MIF is absent in MIF of malaria and other parasites, but they demonstrate oxidoreductase activity. *Pf*MIF contains four cysteines, of which two N-terminal vicinal residues (Cys 3 and 4) are highly conserved across the species of malaria parasites. Thiols and vicinal thiol modifiers were used to evaluate the role of thiols and vicinal thiols in oxidoreductase activity of *Pf*MIF. Site directed mutagenesis were used to confirm the chemical modification result. Thiol-reactive *N*-ethylmaleimide inhibits the oxidoreductase but not the tautomerase activity of *Pf*MIF. Furthermore, vicinal thiol modifiers such as diamide and phenylarsine oxide specifically inhibit the oxidoreductase sparing tautomerase activity and thiol compounds protect against inhibition by vicinal thiol

modifiers. Mutation of either cysteine 3 or 4 abolished the oxidoreductase activity keeping the tautomerase activity intact. Interestingly, mutation at 59 or 103 did not affect either the oxidoreductase or the tautomerase activity. Only vicinal thiols (Cys 3 and 4) are essential for oxidoreductase activity. Identification of active site motif of *Pf*MIF responsible for enzymatic activity with a view to design specific inhibitor to explore its possible role in *P. falciparum* metabolic pathways and in the induction of host pathology.

Indomethacin, a non-steroidal anti-inflammatory drug, develops gastropathy by inducing reactive oxygen species-mediated mitochondrial pathology and associated apoptosis in gastric mucosa: A novel role of mitochondrial aconitase oxidation

We have investigated the role of mitochondria on the development of indomethacin (a non-steroidal anti-inflammatory drug)-induced gastric mucosal apoptosis and associated gastropathy in rat. Transmission electron microscopic studies indicate that indomethacin damages mitochondrial ultrastructure and causes mitochondrial dysfunction as evident from decreased stage-3 respiration, dehydrogenase activity and transmembrane potential (m). Mitochondrial pathology is associated with increased generation of intramitochondrial reactive oxygen species, such as $O_2^{\bullet-}$, H_2O_2 and OH leading to oxidative stress. $O_2^{\bullet-}$ is the most effective to damage mitochondrial aconitase, leading to the release of iron from its iron-sulfur cluster. The released iron, by interacting with intramitochondrial H_2O_2 forms $^{\bullet}OH$. Immunoprecipitation of mitochondrial aconitase and subsequent westernimmunoblotting indicate carbonylation of aconitase along with the loss of activity *in vivo* after indomethacin treatment. The release of iron has been documented by fluorescence imaging of mucosal cells by using Phen Green SK, a specific probe for chelatable iron. Interestingly, intra-mitochondrial $^{\bullet}OH$ generation is crucial for the development of mitochondrial pathology and activation of mitochondrial death pathway by indomethacin. Scavenging of $^{\bullet}OH$ by dimethyl sulfoxide or α-phenyl-n-tert-butyl-nitrone, a spin-trap, prevents indomethacin-induced mitochondrial ultrastructural changes, oxidative stress, collapse of $\triangle\psi m$, and mitochondrial dysfunction. The scavengers also restore indomethacin-induced activation of caspase-9 and caspase-3 to block mitochondrial pathway of apoptosis and gastric mucosal damage. This study thus reveals the critical role of O_2-mediated mitochondrial aconitase inactivation to release intra-mitochondrial iron, which by generating $^{\bullet}OH$ promotes gastric mucosal cell apoptosis and gastropathy during indomethacin treatment.

Dr. (Mrs.) Malini Sen

Role of Wnt5A signaling in inflammatory disorders, role of WISP3 (Wnt induced secreted protein, in the maintenance of chondrocyte/cartilage integrity

We are interested in understanding the molecular basis of WNT5A and WISP3 mediated regulatory networks in health and disease. Our primary focus is on two aspects of signal transduction: (i) the role of WNT5A, a member of the WNT family of growth regulators in immune response, and (ii) the role of WISP3, a connective tissue growth modulator in sustaining chondrocyte / cartilage integrity.

Our experimental results suggest that WNT5A signaling contributes to macrophage growth / differentiation and phagocytosis. This aspect of WNT5A signaling can be both beneficial for innate immunity and also enhance context dependent chronic inflammation. We also propose that WISP3 sustains chondrocyte / cartilage integrity by inducing collagen II and modulating IGF1 mediated effects, for example, cellular hypertrophy.

Dr. (Mrs.) Mridula Misra and group

Tyr3 octreotide derivatives: synthesis, radiolabelling and application as tumor targeted radiopharmaceuticals

Peptides are important regulators of growth and cellular functions not only in normal tissue but also in tumors. Peptides are becoming of increasing interest in nuclear oncology for targeted tumor diagnosis and therapy.

[(^{111}In-diethylenetriaminepentaacetic acid°)] labelled Octreotide (Octreoscan; Mallinckrodt / Inc.) [(^{111}In-DTPA°] was the first routinely used tracer in nuclear medicine for the localization and staging of somatostatin receptor positive tumors. Stable somatostatin derivatives such as octreotide / lantrotide are the most frequently used radiopharmaceuticals acting through specific binding to somatostatin receptors however they do not bind with high affinity to all five receptor subtypes. [(^{111}InDTPA°)]-OC] based imaging served as a sensitive and specific technique for somatostatin receptor scintigraphy that can detect *in-vivo* somatostatin receptors in various tumors mainly of endocrine origin. ([^{111}In-DTPA°]-OC) is commercially available for imaging, however the use of ^{111}In as a radioisotope results in high cost, limited availability, suboptimal image quality and a high radiation burden to the patient. These disadvantages were overcome by the use of ^{99m}Tc labeled somatostatin analogs. Thus newly developed somatostatin analogs labelled with ^{99m}Tc will be intensively studied in the proposed research work.

Tyr^{3}Octreotide and derivatives were semi-automatically synthesized on a peptide synthesizer by standard Fmoc solid phase synthesis. The peptide was purified semi-preparative HPLC and characterized by MALDI mass, 1H NMR, 13C NMR and HPLC. Peptides were radiolabeled by ^{99m}Tc. The complexation efficiency and radiochemical purity of radiolabelled peptide complexes were analysed by ITLC and HPLC. Stability study was performed at different time intervals. Further in future pharmacokinetics, scintigraphic imaging and biological study will be performed with the peptide radiopharmaceuticals.

Dr. Mita Chatterjee Debnath and group

Preparation, characterization and biodistribution of letozole loaded PLGA nanoparticles in Ehrlich ascites tumor bearing mice

In recent years nanotechnology, as applied to medicine, has brought significant advances in the diagnosis and treatment of diseases. Nanoparticles (NPs) are considered to be the best drug delivery system, have considerable potential for drug targeting and exhibit several advantages over conventional delivery systems. These are: high stability conferring long shelf lives, high carrier capacity, feasibility of incorporation of both hydrophilic and hydrophobic substances, and possibility of administration through variable routes and can also be designed to allow controlled drug release from the matrix. All these properties enable improvement of drug bioavailability producing high level of pharmacological action and reduction of the dosing frequency. Breast cancer is the most common non-cutaneous cancer among women. The antiestrogen tamoxifen has long been used in the treatment of pre and postmenopausal breast cancer. However some breast cancer became resistant to tamoxifen, and in some cases the drug increases the risk of endometrial cancer. Nowadays the aromatase inhibitors, representing a new class of agents are considered as more effective than tamoxifen in the treatment of breast cancer. Letrozole (LTZ) is an oral nonsteroidal aromatase inhibitor approved by United States FDA and has been introduced for the adjuvant treatment of hormonally-responsive local or metastatic breast cancer.

We have tried to develop LTZ loaded nanoparticulate to facilitate controlled release and targeted delivery of drugs thereby enhancing its therapeutic efficacy. LTZ loaded PLGA NPs were prepared by solvent displacement technique using poloxamer-188 as stabilizer To prevent aggregation, the internal phase, acetone from the nano dispersion was evaporated by slow stirring at room temperature instead of quick rotative evaporation under partial vacuum. Which yielded spherical powder particles (Fig. 15) with diameter of 15-100 nm and poly dispersity index of 0.087 0.019. The value of polydispersity index indicates the narrow distribution profile of particles. Particle size distribution profile as analysed by Master sizer (Fig. 16) reveals the size distribution by intensity. The yield, loading as well as drug entrapment efficiency of LTZ loaded PLGA NPs were 77.44 0.24%, 14.34 1.95% and 43.03 2 .20% respectively. The zeta potential values of LTZ loaded PLGA NPs w ere found to be negative, -12 to –19.50 mV. The free drug (LTZ), and the LTZ–loaded PLGA NPs were r adiolabeled with technetium-99m by direct radiolabeling approach using stannous chloride dihydrate as r eductant. evaluated. The labeled complex showed good in vitro stability as verified by DTPA challenge test.

The labeled complexes also showed significant in vivo stability when incubated in rat serum for 24 hour. Biodistribution studies of ^{99m}Tc labeled complexes were performed after intravenous administration in normal mice and Ehrlich Ascites tumor bearing mice. Compared to free LTZ, LTZ loaded PLGA NPs exhibited significantly lower uptake by the organs of RES. Drug loaded nanoparticles exhibited much better tumor to muscle ratio than that of free letrozole, which was remarkably high, 3.73 at 4 h. The above value in case of free drug was 1.65. Scintigraphic images were obtained at 4 h after injecting ^{99m}Tc labeled LTZ and LTZ loaded PLGA NPs in tumor bearing mice. The uptake in tumor site was observable more predominantly in case of LTZ loaded PLGA NPs (Fig. 17), however in both formulation significant amount of radioactivity was associated with urinary bladder and liver. Bladder activity cleared gradually with the increase of post injection time period. All these are in concurrence with the results obtained from biodistribution studies. Further investigations regarding the influence of administration route on the biodistribution and tumor uptake of LTZ loaded PLGA NPs in tumor bearing mice model are in progress.

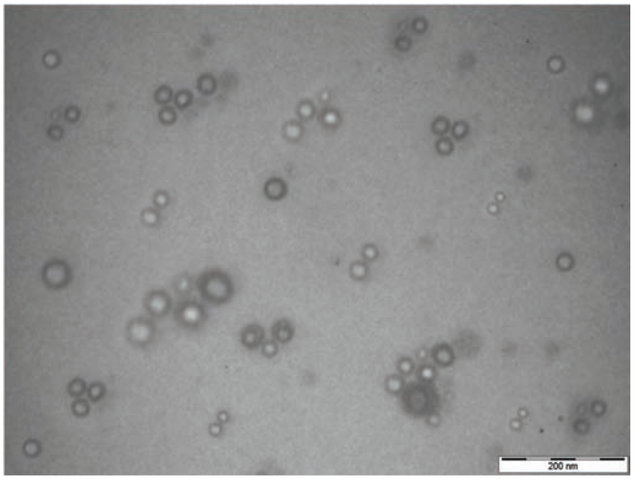

Fig. 15. Transmission electron micrograph of letrozole loaded nanoparticles.

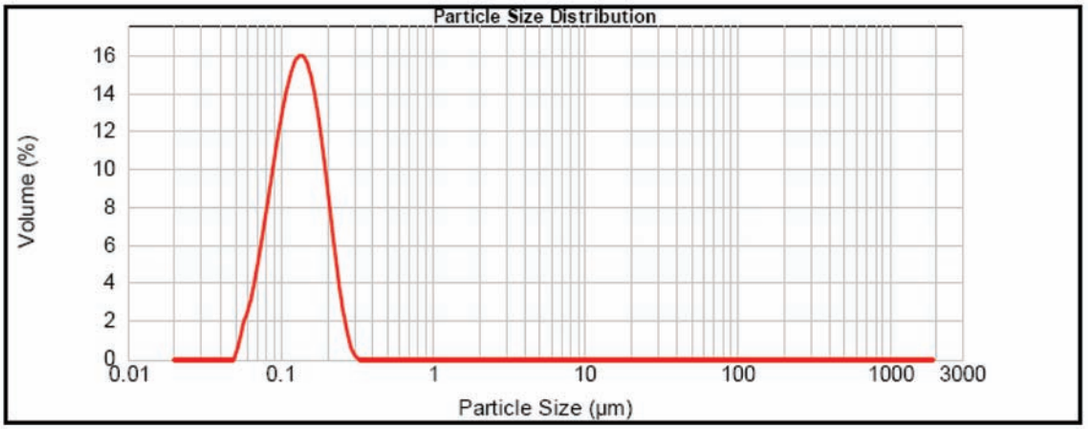

Fig. 16. A plot of particle size distribution against intensity.

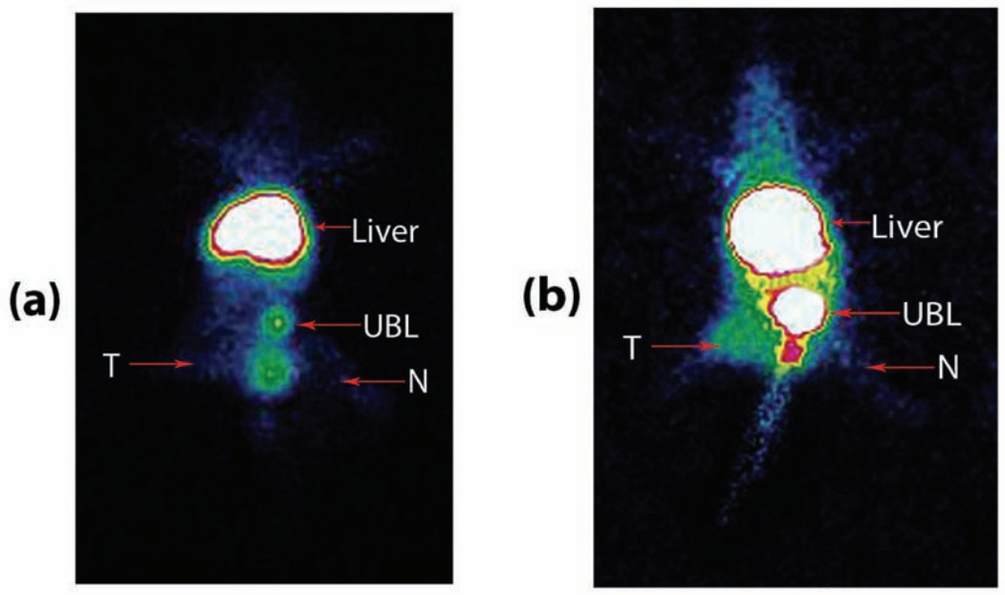

Fig. 17. Scintigraphic images of (a) normal and (b) Ehrlich Ascites tumor bearing mice at 4 h post-injection (i.v.) of ^{99m}Tc labeled LTZ loaded PLGA NPs. T= tumor cell implanted in right hind leg of mice, N= normal left hind leg.

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Preamble

Cell Biology and Physiology Division, a team of cell biologists, physiologists and molecular biologists have a common goal of understanding the pathophysiology of certain metabolic and degenerative diseases, cancer and regenerative therapy. Cancer, stem cell biology, cardiac hypertrophy, diabetes, drug addiction, neurodegenerative diseases, utero-ovarian dysfunction and responses to pathogens in hematopoietic system are dealt with by the group. This division has developed and tested a number of models for various human diseases, and foresees immense benefit to all who want to initiate cooperative collaborative program of mutual interest. The members of the division actively participate in postgraduate teaching at various Universities, PhD mentoring, and summer training programs. Regular biweekly seminars on the latest developments in the field, strong inter-institutional multidisciplinary collaborations, and regular organizations of workshops and symposia in the area of cellular physiology are other activities of the Division. This Division is planning to start a Research Festival of the Division from the next financial year onwards to get all the new and old students, and the Faculty to come together and present their research work once in a year, and get a review from selected reviewers. The young researchers present their work in front of invited peers in the filed, and three prizes are planned to be awarded, in form of latest text books in the field. The research highlights from the Division are: protection of cardiomyocyte death via peroxiredoxin II and melatonin mediation, sperm ecto-protein kinase as novel regulators of membrane fusion during acrosome reaction and detection of an endogenous neurotoxin, 6-hydroxydopamine that causes dopaminergic cell death in the brain due to long-term L-DOPA administration.

NEUROSCIENCE

Dr. K. P. Mohanakumar and group

Endogenous neurotoxins generated to the chronic administration of the antiparkinsonian drug, L-DOPA has been extensively investigated during the current year. It has been discovered that chronic pharmacological doses of L-DOPA caused a dose- and time-dependent production of a neurotoxic molecule, 6-hydroxydopamine (6-OHDA) in the striatum, and aggravated syndromes of Parkinson's disease (PD) in mice and rats. Studies led to the fact that 6-OHDA production is sensitive to a denervated, but not innervated striatum, and that the generation of this dopaminergic neurotoxin in the brain is dependent on hydroxyl radical (.OH) production and 'freely' available dopamine in the synapse or in the neurons. Salicylic acid, melatonin and selegiline showed remarkable protective effects against the increased production of 6-OHDA, and therefore validated the hypothesis that these antiparkinsonian drugs should be used in conjunction with L-DOPA, and suggested that such mode of treatment would the most ideal therapy for PD for slowing the progression of the disease.

Production of a potent neurotoxin in the brain following chronic L-DOPA administration

6-OHDA production in the mouse brain is dependent on the levels of free dopamine and hydroxyl radical

On the hypothesis that excessive unregulated dopamine in the otherwise dopamine rich brain areas would cause autoxidation of the molecule to produce highly toxic 6-OHDA, we estimated its content in the striatum of mice daily treated with L-DOPA systemically for seven days. We have reported that prolonged L-DOPA treatment in mice causes significant elevation in 6-OHDA production from 1-6 h after the drug treatment, which is dependent on the dopamine present in the brain (Fig. 1).

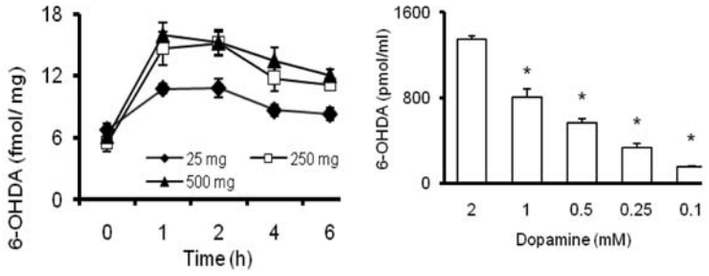

Fig. 1: 6-OHDA production in mouse striatum: Balb/c mice treated with L-DOPA (25, 250 and 500 mg/kg, p.o) for 7 days caused significant time -and dose-dependent production of 6-OHDA, which was dependent on concentration of dopamine. The study used a novel, sensitive HPLC-electrochemical detection procedure. *p ≤ 0.05; n = 8.

6-OHDA production in the striatum of mice is suggested to be resulting from the oxidation of excessive dopamine formed from L-DOPA due to the production of reactive oxygen species, since incubation of dopamine with ferrous-ascorbate (FAD) system *in vitro* was found to cause generation of .OH and 6-OHDA, both of which were sensitive to presence of catalase, superoxide dismutase and reduced glutathione (Fig. 2).

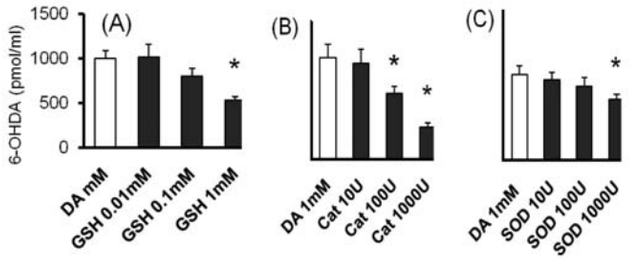

Fig. 2: Antioxidants attenuate *in vitro* 6-OHDA generation: DA (1 mM) was incubated with 1 mM ascorbate, 240 µM EDTA, 200 µM ferrous sulfate and 50 mM phosphate buffer at pH 7.2. 6-OHDA production was sensitive to GSH, catalase (Cat) and (C) superoxide dismutase (SOD). Mean±SEM. *p ≤ 0.05 as compared to 6-OHDA produced by 1 mM DA (n=8).

Dopamine utilization was evident from the reduced levels of its presence in the FAD system following 6-OHDA production. These results point to an inherent hazard of long-term administration of L-DOPA in PD patients.

L-DOPA-induced 6-hydroxydopamine production in the striata of rodents is sensitive to degree of nigrostriatal denervation.

We examined the production of 6-OHDA in the brain of innervated and denervated rodents to find the relevance of chronic L-DOPA treatment in PD. Mice were treated 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP; 30 mg/kg, i.p., twice, 16 h apart) (Fig. 3) and rats received methyl-4-phenylpyridinium ion [MPP(+); 16 nmol in 1 l] unilaterally in median forebrain bundle, and measured 6-OHDA in the striatum using the sensitive HPLC-electrochemical detection procedure.

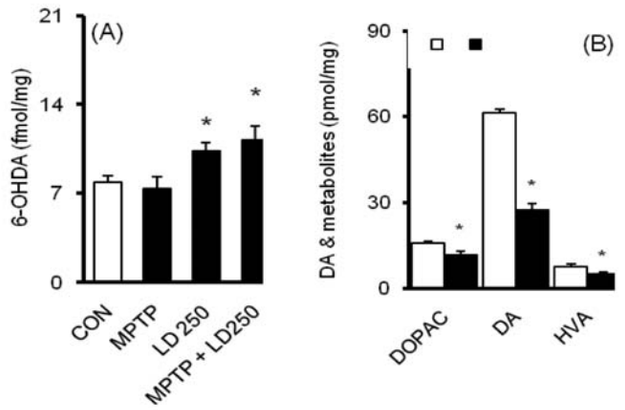

Fig. 3. L-DOPA causes production of 6-OHDA levels in mouse striatum. The animals were administered with L-DOPA for 3 consecutive days and sacrificed at 2 h after the last dose of the drug. **(A)**. 6-OHDA levels are expressed as mean±SEM. *$p \leq 0.05$ (ANOVA followed with Dunnett test) and as compared to control (n=6; t-test, unpaired). In MPTP mouse model of PD striatal levels of DA, DOPAC and HVA were measured on 4th day **(B)**. Mean±SEM. *p≤0.05 and as compared to control (t-test, unpaired; n=6).

While the contralateral innervated striatum of rats showed no difference, a significant increase in 6-OHDA level in the denervated (>85% dopamine depletion) ipsilateral striatum was observed. Partial nigrostriatal denervation with a lower dose of MPP^+ (8 nmol in 1l) in rats or following sub-acute MPTP treatment in mice failed to cause any significant change in 6-OHDA level following several doses of L-DOPA administration (Fig. 4). A single dose of MPTP (30 mg/kg, i.p.) or L-deprenyl (0.25 mg/kg, i.p.) in L-DOPA primed (250 mg/kg daily for 7 days) mice caused significant increase in 6-OHDA in the striatum (Fig. 5). An augmentation of .OH production concomitant to excessive dopamine concentration in this region is proposed to be the basis of this effect. These results suggest creation of potential pro-toxic environment in the brain due to the long-term administration of L-DOPA, which may get further sensitized by the treatment of monoamine oxidase inhibitors.

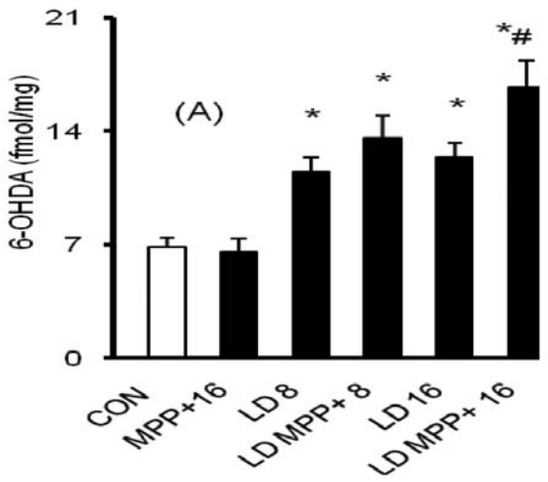

Fig. 4. 6-OHDA levels in MPP^+ rat model of hemiparkinsonism: Sprague Dawley rats infused with MPP^+ (8 or 16 nmol in 1 ìl) into the right median forebrain bundle were treated with L-DOPA (250 mg/kg, p.o.) or the vehicle for 30 days and sacrificed following 2 h after the last dose of the drug. L-DOPA was administered in the animal from the 7th day post-infusion. The striatal levels of 6-OHDA levels are expressed as mean ± SEM. *$p \leq 0.05$ (ANOVA followed with Dunnett's test) and $^{\#}p \leq 0.05$ (t-test; unpaired) as compared to L-DOPA naive parkinsonian control (contralateral striata) and L-DOPA treated parkinsonian striata (contralateral) respectively (n = 6).

Melatonin inhibits 6-hydroxydopamine production in the brain to protect against experimental parkinsonism in rodents

Since melatonin is a potent .OH scavenger, we thought it prudent to check if administration of this pineal hormone provides any beneficial effect in MPTP-induced increased 6-OHDA production in chronically L-DOPA treated mice

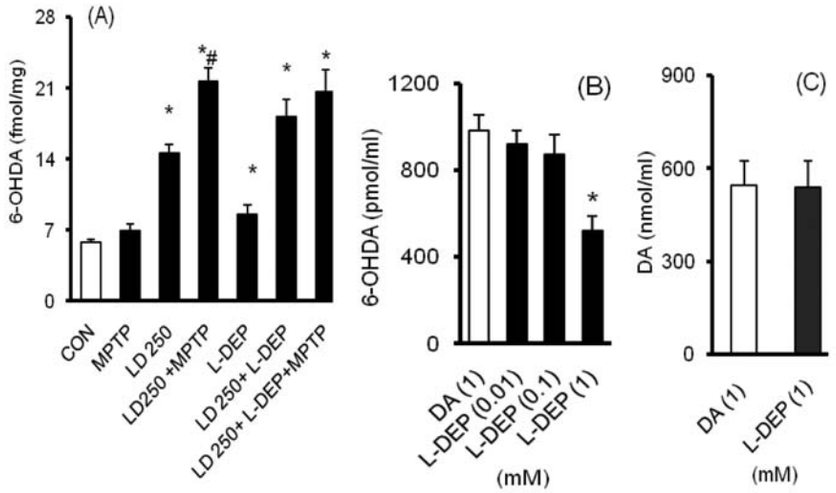

Fig. 5. Effect of L-deprenyl on L-DOPA- and/or MPTP-induced 6-OHDA production in the brain: Mice were administered with saline (CON) or L-DOPA/carbidopa (LD250) (250/25 mg/kg, p.o.) and L-deprenyl (0.25 mg/kg, i.p) (L-DEP) daily for 7 days. A single dose of MPTP (30 mg/kg) was administered 30 min after the last dose of L-DOPA (MPTP). Striatal 6-OHDA levels **(A)** are mean±SEM. *p=0.05 (ANOVA followed with Dunnett's test), $^{\#}$p = 0.05 (t-test) respectively are compared to control and L-DOPA treated group (n=6). Effect of L-deprenyl on *in vitro* 6-OHDA generation from ferrous ascorbate system was measured employing HPLC-electrochemistry **(B).** L-Deprenyl (0.01-1.0 mM) was incubated with FAD to test if this monoamine oxidase inhibitor affects the yield of 6-OHDA from DA. Results are expressed as pmol/ml of the reaction mixture and the values are mean±SEM. *p = 0.05 (ANOVA followed with Dunnett's test and t-test) as compared to 6-OHDA produced by 1 mM DA (n = 8). The remaining concentration of DA after 2 h incubation with FAD system was monitored with and without L-deprenyl **(C)**. Results are expressed as nmol/ml of the reaction mixture (n = 8).

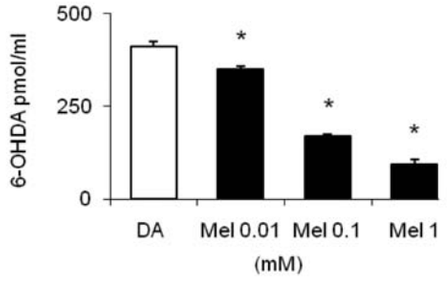

Fig. 6. Melatonin attenuates 6-OHDA generation from FAD system: Melatonin was added to FAD to test the protective effect of this antioxidant on the yield of 6-OHDA from DA. The reaction mixture was incubated at 37°C in dark for 120 min. Ten µl of the sample was injected into HPLC system for the analysis of 6-OHDA. Results are pmol/ml of the reaction mixture and are mean ± SEM. *p ≤ 0.05 as compared to 6-OHDA produced by 1 mM DA (n = 8).

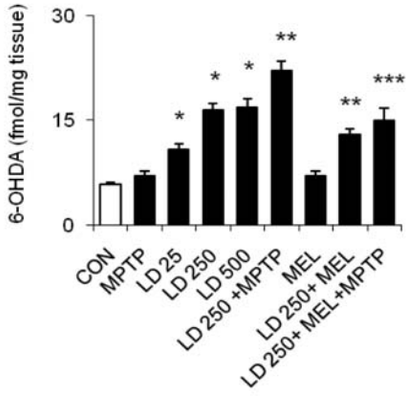

Fig. 7. Melatonin attenuates 6-OHDA levels in the mouse striatum: Mice administered with L-DOPA and melatonin daily for 7 days and a single dose of MPTP (30 mg/kg) were sacrificed 2 h after the last dose of L-DOPA. Striatal levels of 6-OHDA were measured. Results are mean ± SEM. *p ≤ 0.05, $^{\#}$p ≤ 0.05, $^{@}$p ≤ 0.05 as compared to control, L-DOPA and L-DOPA plus MPTP group respectively (n=8).

In vitro generation of 6-OHDA in the FAD system was significantly reduced by melatonin (Fig. 6). Per-oral administration of L-DOPA for 7 days caused a dose-dependent increase in the formation of 6-OHDA in the mouse striatum, which was increased synergistically by the systemic administration of the parkinsonian neurotoxin, 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) on the 7th day of L-DOPA treatment. Melatonin treatment significantly attenuated both the L-DOPA and MPTP-induced increases in the levels of striatal 6-OHDA (Fig. 7), and protected against striatal dopamine depletion caused by the neurotoxin.

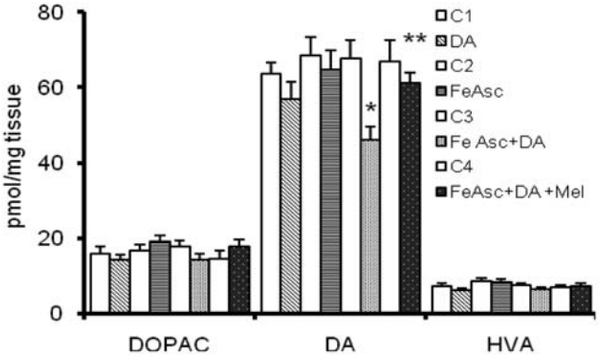

Fig. 8. Effect of melatonin on striatal monoamine levels following intra-MFB infusion of incubated FAD mixture. Rats were sacrificed on the 19th day following intra-MFB infusion of 4 µl of the 120 min incubated FAD mixture with or without melatonin (1 mM). DA and its metabolites levels in the striata, contra- and ipsilateral to the infused side were analyzed. Results are mean ± SEM. *p ≤ 0.05 and $^{\#}$p ≤ 0.05 as compared to control (contralateral striata) and ipsilateral striata from the animal infused with Fe^{2+}- EDTA-ascorbate plus DA respectively (n = 6).

These observations suggest a novel mode of melatonin-induced dopaminergic neuroprotection in two models of PD, and suggest the possible therapeutic use of this well known antioxidant indoleamine neurohormone in parkinsonism.

Contribution of dopamine in the neuropathology of Huntington's disease

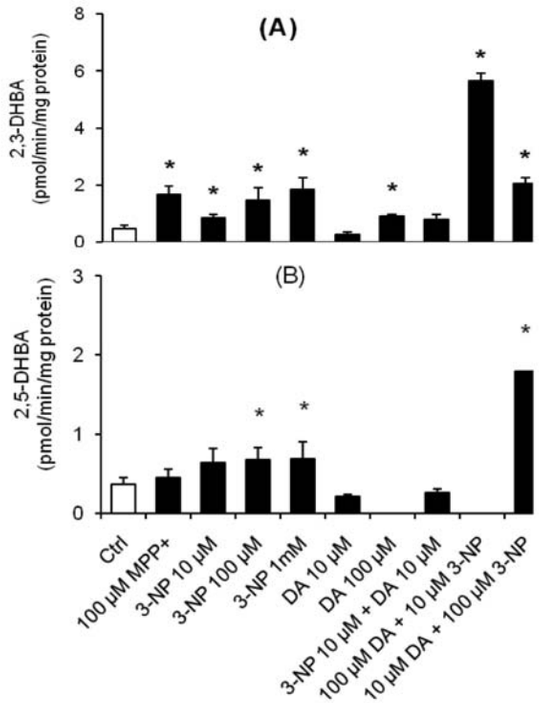

Fig. 9. Effect of dopamine (DA) and 3-NP on hydroxyl radical (.OH) generation in mitochondrial P_2 fraction: Mitochondrial P_2 fraction was prepared from rat forebrain and incubated with different concentrations of 3-NP (10 to 100 µM) and/or DA (10 to 100 µM) for 30 min in presence of sodium salicylate (100 M). The reaction was stopped with perchloric acid, the samples were centrifuged and 10 il of the supernatant was injected into the HPLC-ECD for detection of the salicylate adduct (A) 2,3-DHBA and (B) 2,5-DHBA. The 2,3- and 2,5-DHBA control values were respectively 0.46 ± 0.11 and 0.368 ± 0.083 pmol/min/mg protein. Data are represented as Mean ± SEM, * $p \leq 0.05$ as compared to control (n = 4).

We tested the hypothesis that dopamine contributes significantly to the hydroxyl radical (.OH)-induced striatal neurotoxicity caused by 3-nitropropionic acid (3-NP) in a rat model of Huntington's disease. Dopamine (10-100 µM) or 3-NP (10-1000 µM) individually caused a significant increase in the generation of hydroxyl radical (.OH) in the mitochondria (Fig. 9), which was synergistically enhanced when the lowest dose of the neurotoxin (10 µM) and dopamine (100 µM) were present together.

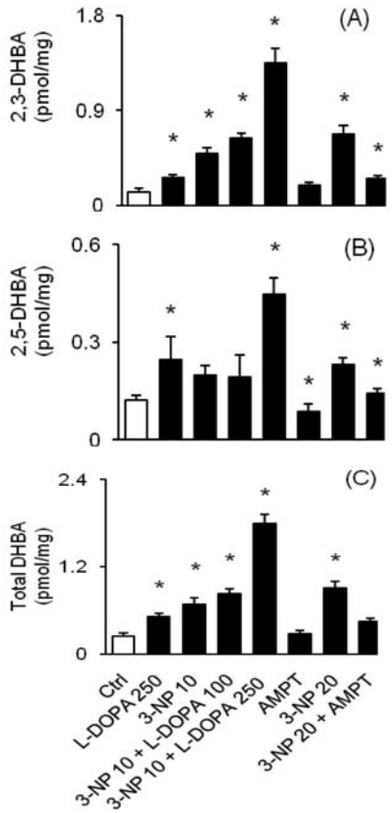

Fig. 10. Intrastriatal levels of hydroxyl radicals are dependent on free dopamine in the striatum: Animals were treated in 2 batches. In the first batch, animals received L-DOPA (100 or 250 mg/kg for 8 days), and those that were treated with 3-NP (10 mg/kg) or saline received the dose on the last 4 days of L-DOPA administration. In the second batch, animals were treated with 3-NP (20 mg/kg) with/without -methyl-p-tyrosine (AMPT) or AMPT alone for 4 days. Sixty min after the last 3-NP treatment, animals were injected with 100 mg/kg sodium salicylate i.p. and 60 min later were sacrificed and the brains were dissected out. Striata were micropunched, sonicated in perchloric acid, the samples were centrifuged and 10 ìl of the supernatant was injected in the HPLC-ECD for the detection of (A) 2,3-DHBA, (B) 2,5-DHBA and (C) total DHBA. Data are represented as Mean ± SEM, * $p \leq 0.05$ as compared to control. n = 3-5.

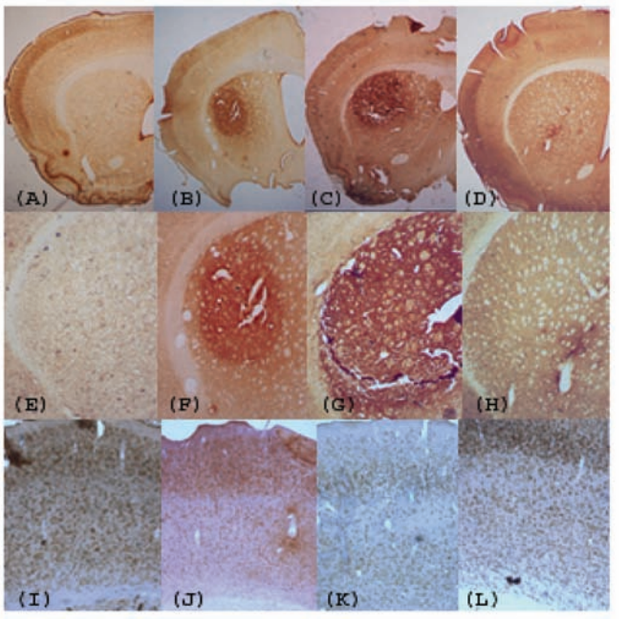

Fig. 11. Increase in striatal dopamine aggravates, and decrease in striatal dopamine protects against 3-NP neurotoxicity: Coronal sections passing through the striatum were stained for NeuN, a marker of mature neurons immunohistochemistry. The first (A,E,I), second (B,F,J), third (C,G,K) and the fourth (D,H,L) columns contain brain sections passing through mid striatal region respectively from control, 3-NP (20 mg/kg) alone, L-DOPA (250 mg/kg) + 3-NP (10 mg/kg), and the AMPT (a dopamine synthesis inhibitor; 80 mg/kg) + 3-NP (20 mg/kg).

Similarly, systemic administration of L-DOPA (100-250 mg/kg) and a low dose of 3-NP (10 mg/kg) potentiated .OH generation in the striatum (Fig. 10), and exhibited significant decrease in stride length in rats, a direct indication of neuropathology. The pathology was also evident in striatal sections subjected to NeuN immunohistochemistry (Fig. 11). The significant changes in stride length, the production of striatal .OH and neuropathological features due to administration of a toxic dose of 3-NP (20 mg/kg) were significantly attenuated by treating the rats with tyrosine hydroxylase inhibitor -methyl-*p*-tyrosine prior to 3-NP administration (Figs. 9-12). These results strongly implicate a major contributory role of striatal dopamine in increased generation of •OH, which leads to striatal neurodegeneration and accompanied behavioral changes, in 3-NP model of Huntington's disease.

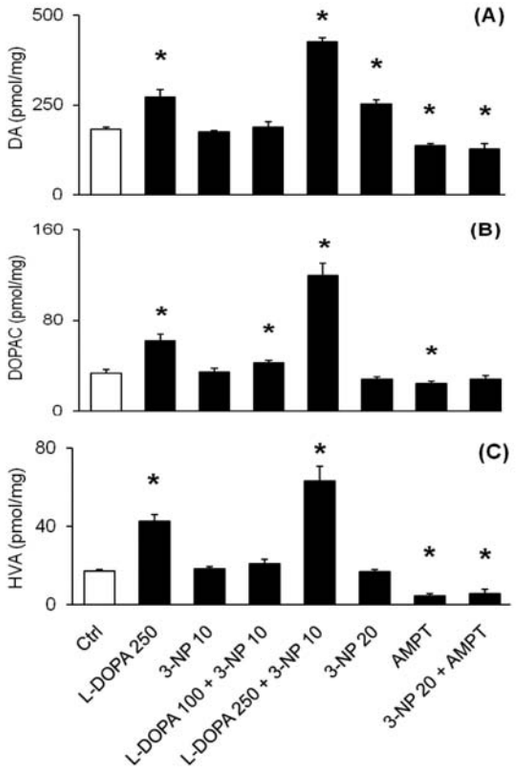

Fig. 12. Dopamine cause neurodegeneration in Huntington's disease: Animals were treated in 2 batches. In the first batch, animals were treated with L-DOPA (100 or 250 mg/kg for 8 days), and those that were treated with 3-NP (10 mg/kg) or saline received the dose on the last 4 days of L-DOPA administration. In the second batch, animals were treated with 3-NP (20 mg/kg) with/without the dopamine synthesis inhibitor, -methyl-p-tyrosine (AMPT) or AMPT alone for 4 days. Striata were analyzed for the detection of (A) dopamine (DA), (B) DOPAC, (C) HVA. DA - Control values of DA, DOPAC and HVA were respectively 182.3 ± 5.86, 33.46 ± 2.92 and 17.36 ± 0.55. Data are represented as Mean ± SEM, * $p \leq 0.05$ as compared to control. n = 3-5.

Dr. Sumantra Das and group

Treatment and understanding of narcotic addiction

As a part of the ongoing program in our laboratory, we have been trying to screen novel anti-addictive drugs. Based on established 3D pharmacophore, we had previously demonstrated a series of quinoline derivatives having varying degree of activities at the κ and μ opioid receptors with negligible interactions at the δ receptor. One such compound successfully inhibited two most prominent quantitative features of naloxone precipitated withdrawal symptoms: stereotyped jumping and body weight loss. We have now tested the compound in alcohol addiction and found it to attenuate alcohol seeking behavior in alcohol dependent mice. The work was in collaboration with Synthetic, Biophysical and Natural Product Chemistry group of the institute and we are presently investigating a new series of quinolines for their anti-addictive properties. In another collaboration with the Chemistry group to study putative κ-opioidergic activity in the eight-member ring compounds, dibenz [*b*,*f*]1,5-oxazocines, it was found that one such derivative showed significant agonistic activity at the kappa receptor. The compound appears to be the first example of a non-peptidic κ-agonist lacking positively charged nitrogen.

Ongoing collaborative projects with a psychiatric clinic, Baulmon, Kolkata as well as Chittaranjan National Medical College, Kolkata are underway to carry out genetic epidemiological studies on opioid addiction by investigating the possible association of specific SNPs of certain candidate genes like nNOS, CREB, μ-opioid receptor, etc. in addiction using PCR based RFLP as well as DNA sequencing analysis. The work has resulted in identifying some novel SNPs, some of which show high degree of association with development of addiction.

Using high throughput proteomic approaches, identifying of target molecules involved in relapse in narcotic addicts are underway. Our studies suggest persistent dysregulation of cytoskeletal actin assembly involving various actin regulatory molecules much after the removal of morphine in chronic morphinised animals. The significance of these findings is being understood.

Limbal stem cell culture

This is a collaborative project with Regional Institute of Ophthalmology, Kolkata. Limbal stem cells from cadaver eyes were successfully expanded on amniotic membrane. Two such preparations have been transplanted in two patients suffering from damaged cornea.

Nano vesicles for effective transport of biomolecules within cells

A collaborative project with Indian Association for the Cultivation of Science, Kolkata was undertaken to develop anionic dipeptide based nontoxic vesicles as carriers for drugs and other biologically important molecules. It was observed that these self-assembling water-soluble synthetic dipeptides could form vesicles having multivesicular architectures wherein it was capable of encapsulating the fluorescent dye, eosin B. The dye loaded vesicles not only enter into the cells but also can successfully release the entrapped molecules within the cells, possibly through calcium ion dependent mechanisms (Fig. 13A). Cellular uptake study using vesicles loaded with the biologically important molecule, cyclic adenosine monophosphate (cAMP), which by itself is unable to enter the cell, demonstrates that these vesicles not only enter into the cells but also can successfully release the entrapped molecules within the cells causing differentiation into process bearing cells (Fig. 13 B). Thus, these peptide based vesicles offer a fascinating opportunity of being used as a cargo for delivering drugs and other biologically important molecules inside the cells.

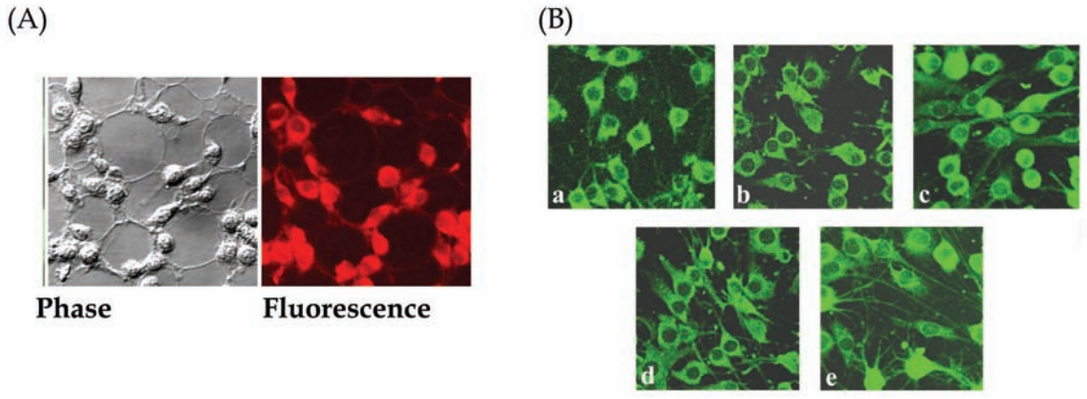

Fig. 13 A & B. Internalization of Eosin B loaded dipeptide vesicles within the cytosolic compartment of cells. Photomicrographs represent confocal fluorescence microscopic image and the corresponding bright field image. B. Effect of vesicles loaded with cAMP on the morphology of C_6 glioma cells. Cells were cultured in DMEM containing 10% serum on coverslips until 50% confluency. Cells were then grown in DMEM containing 0.2% serum for 24 hr followed by treatment with same medium for an additional 24 h in absence (a) and presence (c) of vesicles loaded with cAMP. In (b) the C_6 glioma cells were instead incubated with media containing 1 mM cAMP for 24 h and served as controls. Additionally, instead of treatment with vesicles, cells were cultured for a further period of 24 h in DMEM containing 10% serum (d) or DMEM containing 0.2% serum and 1mM dibutyryl cAMP in (e). Following treatment, the C6 glioma cells were immnnofluorescent stained for GFAP and examined by confocal microscopy. Magnification, X 400.

Dr. Subhas C Biswas and group

Molecular basis of neurodegeneration in Alzheimer's disease

The mechanism of neurodegeneration in Alzheimer's disease (AD) is not clearly understood. Beside classical pathological hallmarks such as beta-amyloid plaques and neurofibrillary tangles, aberrant expression of cell cycle markers in non-proliferating neurons is well documented in AD patients. Activation of cyclin dependent kinase 4 (Cdk4) and their downstream molecules are reported in cellular models of AD. While in proliferating cells, Cdk4 is activated by cell division cycle 25A (Cdc25A) phosphatase, how Cdk4 is activated in degenerating neurons is unclear. One of the objectives of this laboratory is to study whether Cdc25A is required for activation of Cdk4 and subsequent apoptotic cascade that leads to neuron death in AD.

Cdc25A is required for neuron death induced by NGF deprivation

Among multiple possible etiologies in sporadic late onset AD, one of the reasons is loss of trophic support such as nerve growth factor (NGF). We employ primary culture of sympathetic neurons, survival of these neurons is dependent on NGF, for this purpose. Our preliminary studies indicate that Cdc25A plays a necessary role in neuron death in response to NGF deprivation. We found that a shRNA against Cdc25A protects sympathetic neurons from death induced by NGF deprivation. Moreover, inhibition of Cdc25A maintains overall neuronal morphology of sympathetic neurons.

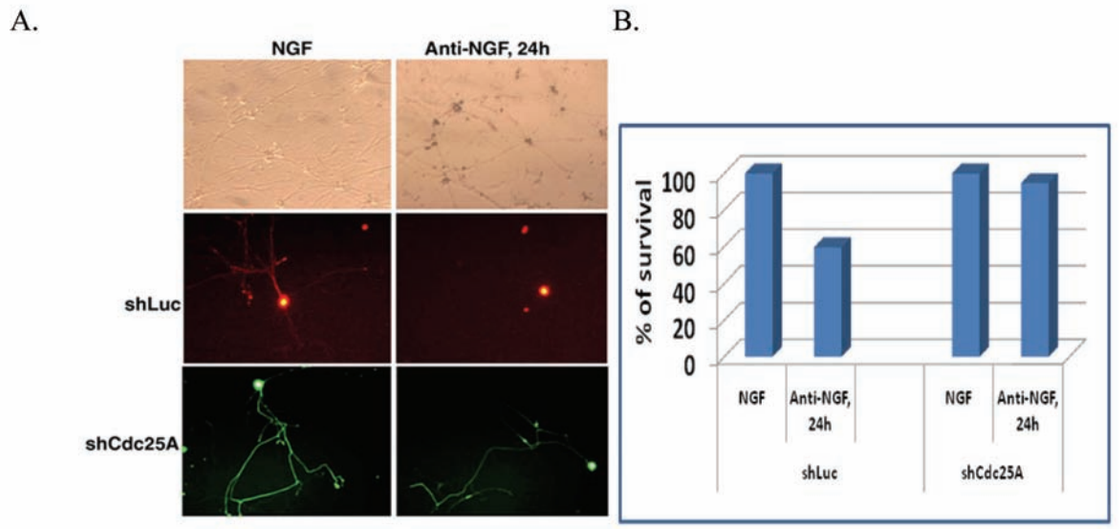

Fig. 14 A & B. Cdc25A knockdown by RNAi blocks neurodegeneration in response to NGF deprivation. Sympathetic neurons were isolated from superior cervical ganglia of 1 day old rat pups and then cultured in collagen coated petridishes in presence of 10% donor horse serum and 100 ng/ml NGF. At day 4, neurons were transfected with pSIREN-Luc-shRNA-dsRed (shLuc) and pSIREN-shCdc25A-zsGreen (shCdc25A) vectors that express siRNA against Luciferase and Cdc25A respectively and maintained for 2 days, then subjected to NGF withdrawal (Ani-NGF treatment). Figure A shows the phase contrast as well as fluorescence photograph of neurons with or without NGF. Note the degeneration of neurons after NGF withdrawal. shLuc (control) expressing neurons are degenerated, where as shCdc25A expressing neurons look healthy after NGF deprivation. B. Numbers of surviving transfected (red or green) cells were counted after 1 day of NGF deprivation using an inverted fluorescence microscope.

TOXICOLOGY

Dr. Tuli Biswas and group

4-Hydroxynonenal-mediated erythrocyte death during chronic exposure to arsenic

Chronic exposure to arsenic through consumption of contaminated drinking water has taken an epidemic form in Bangladesh and West Bengal (India). Our previous study had shown morphological alterations of erythrocytes leading to their premature destruction in human population suffering from chronic arsenic exposure. Here, we report some of the events involved in arsenic induced abbreviated lifespan of erythrocytes in an animal model. Chronic exposure to arsenic in rats led to gradual accumulation of the toxicant in erythrocytes, causing oxidative stress in these cells. 4-Hydroxynonenal (4-HNE), an alpha, beta-unsaturated hydroxyalkenal formed during oxidative stress, interacted with cytosolic proteins and formed hybrid compounds called adducts. Our results confirmed the presence of HNE-cytosolic protein adduct of molecular mass 25kDa, during first and second month. With increase in the duration of arsenic exposure, 40 kDa and 55 kDa protein bands were found along with 25 kDa protein bands (inset of Fig.15). Densitometric analysis of the Western blot revealed progressive increase in the accumulation of HNE protein adducts in cystosol during chronic exposure to arsenic (Fig. 15).

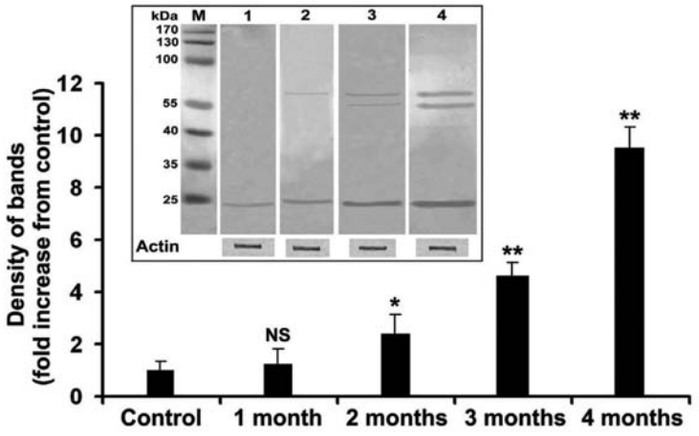

Fig. 15. HNE-protein adduct formation in erythrocytes during arsenic exposure. Densitometric quantification of HNE modified protein bands detected by Western blot analysis. Inset: Representative blots at different time points of exposure period. NS, Nonsignificant; *P <0.05 and **P <0.001 vs respective controls

Mass spectrometric analysis revealed absence of any detectable GSH – HNE adduct in control erythrocytes (Fig. 16A). Erythrocytes incubated in presence of HNE showed formation of GSH – HNE adducts at m/z 317, 446 and 464 (Fig. 16B). HNE-protein adduct formation led to depletion of cytosolic GSH content, while disturbances in GSH homeostasis resulted in the failure of the antioxidant defense, followed by increased generation of reactive oxygen species (ROS). Imbalance between the increased ROS generation and the scavenging capacity of cellular antioxidants, eventually caused activation of caspase 3 in erythrocytes during arsenic exposure. Attenuation of HNE-mediated activation of caspase 3 in presence of N-acetylcysteine indicated the involvement of GSH in the process. Results indicate the effect of arsenic exposure on the changes in HNE that modulated erythrocyte death in arsenic exposed animals.

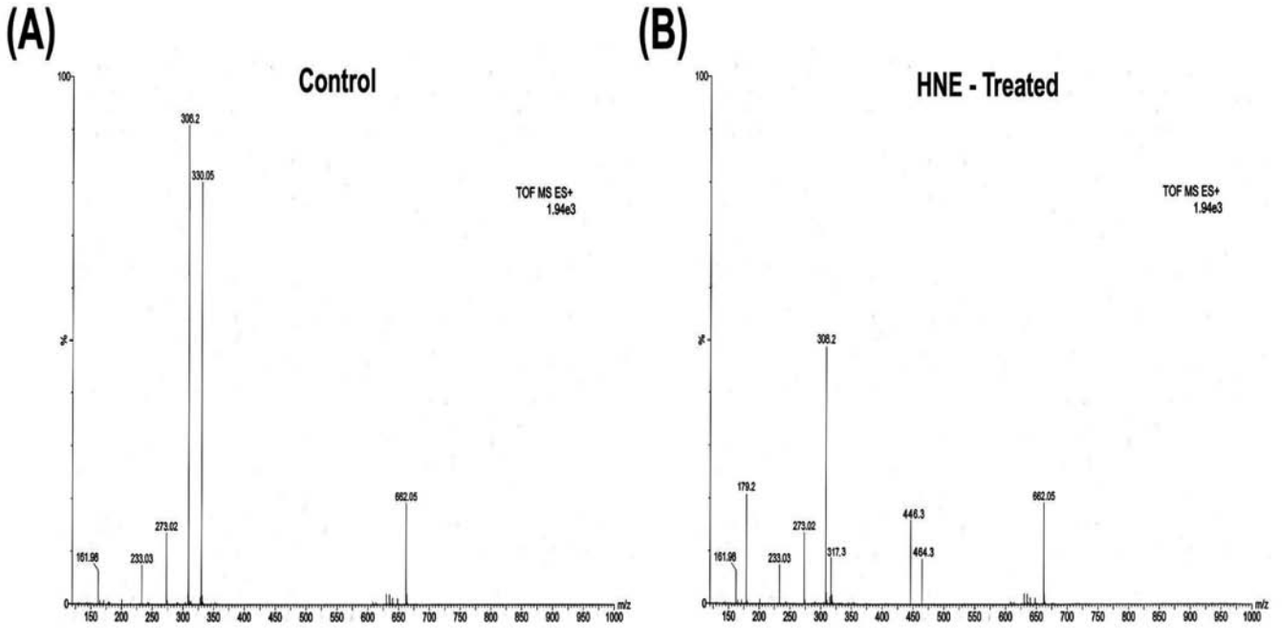

Fig. 16. Mass spectrometric analysis of HNE-GSH adduct formation. (A) Spectrum of GSH (m/z at 308) in control erythrocytes. (B) Major fragments of HNE-GSH adduct (m/z at 317,446,464) after incubation of erythrocytes with HNE

Superoxide anion mediated mitochondrial dysfunction leads to hepatocyte apoptosis during copper toxicity

Copper is an essential transition metal which functions as a cofactor for several mammalian enzymes. Hepatocellular copper homeostasis involves copper uptake into hepatocytes followed by its incorporation into major copper containing proteins and excretion through bile. When copper accumulation surpasses the normal storage capacity of the liver, it causes hepatocellular injury and cell death. Enhanced production of ROS with predominance of $O_2^{\cdot -}$ indicates the contribution of redox imbalance in the process. Down regulation of Cu-Zn SOD in consequence of the degradation of this enzyme, causes decreased dismutation of $O_2^{\cdot -}$, that contributes to the enhanced level of $O_2^{\cdot -}$ in the hepatocytes. Decreased functioning of Mn SOD activity, reduction in mitochondrial thiol/disulfide ratio and generation of $O_2^{\cdot -}$ were high in mitochondria, which point to the involvement of this organelle in the hepatotoxicity observed during copper exposure. This was supported by copper mediated enhanced mitochondrial dysfunction as evident from ATP depletion, collapse of mitochondrial membrane potential ($\Delta\psi m$) and induction of mitochondrial permeability transition. Metal-catalyzed thiol depletion with the generation of $O_2^{\cdot -}$ appears to be a possible reason for copper-mediated enhanced liver cell apoptosis under *in vivo* conditions. This observation was further strengthened in an *in vitro* experiment, where oxidation of GSH in presence of GPx and H_2O_2, was effective in restricting copper-induced $O_2^{\cdot -}$ generation (Fig. 17A) and dissipation of $\Delta\psi m$ (Fig. 17B) to the basal level, thereby emphasizing the importance of cytosolic GSH in the reaction. Results suggest active participation of $O_2^{\cdot -}$ in inducing mitochondrial dysfunction that eventually leads to the development of hepatotoxicity due to chronic exposure to copper in rats.

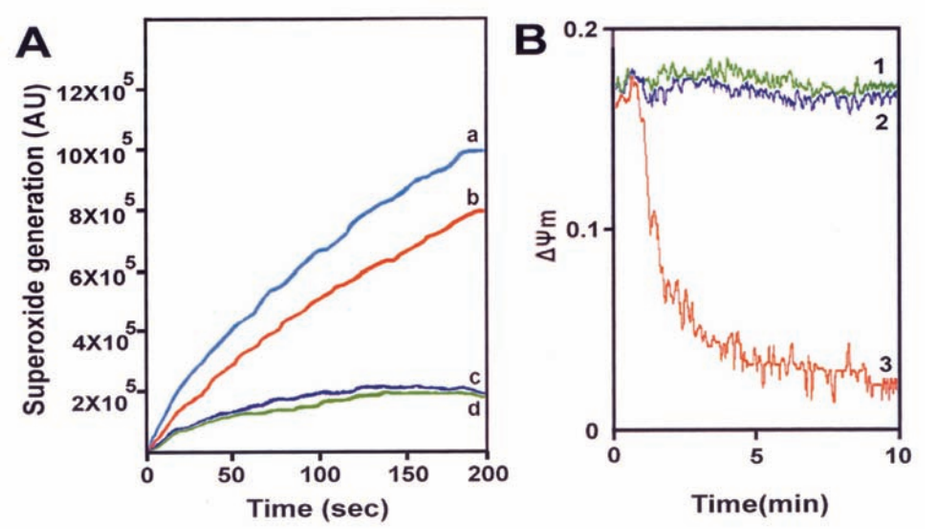

Fig. 17. copper induced $O2^{\cdot-}$ generation and dissipation of $\Delta\psi m$ in hepatocytes. (A) $O2^{\cdot-}$ generation was monitored in presence of : (a) Cytosol (GSH source) + DETC (SOD inhibitor) [Light blue], (b) Cytosol + Copper [Red], (c) Cytosol + H_2O_2 + GPx + Copper [Dark blue] and (d) Cytosol [Green]. (B)Changes in $\Delta\psi m$ was estimated in presence of: (1) Lysate (mitochondrial source) [Green], (2) Lysate + H_2O_2 + GPx + Copper [Dark blue] and (3) Lysate + Copper [Red].

MOLECULAR ENDOCRINOLOGY

Dr. Arun Bandyopadhyay and group

Interaction of annexin A6 with alpha actinin in cardiomyocytes

Annexin A6 (AnxA6), a member of the Ca^{2+} dependent phospholipid binding protein family, is a major isoform expressed in the heart. Localization and functions of AnxA6 in cardiomyocytes is not known till date. To identify the possible-binding partners of AnxA6 in the heart, the whole homogenate (WHH) of the ventricular extracts were subjected to GST-AnxA6 pull down and the GST-AnxA6 bound proteins were identified by mass spectrometry. The GST-AnxA6 pull down fraction displays the presence of α actinin in the interactome (Fig 18A). To validate the interaction of AnxA6 with α actinin in cardiac myocytes, immunoblotting analysis of GST-AnxA6 pull-down fraction with anti α actinin antibody was conducted. As shown in Fig. 18(B), the GST-AnxA6 pull-down fraction of the WHH showed the presence of α actinin. Since AnxA6 is a phospholipid binding protein and α actinin is known to bind with phosphatidylinositol bisphosphate (PIP2), we examined whether binding of AnxA6 with α actinin in heart homogenate depends on PIP2. In vitro binding assay clearly demonstrates that delipidation of heart homogenate does not influence interaction of AnxA6 with α actinin (Fig. 18C).

To further validate the interaction of AnxA6 with α actinin, WHH was directly subjected to immunoprecipitation with α actinin antibody followed by western blotting with AnxA6 antibody. As shown in Fig. 18(D), AnxA6 was present in the immunoprecipitate indicating that these two proteins interact *in vivo.* To search for the domains of AnxA6 that could serve for the interaction with α actinin, *in vitro* binding assay was conducted using various deletion mutants of GST-AnxA6 fusion proteins (Fig. 19). As shown in Fig. 19, SDS-PAGE analysis followed by *in vitro* binding experiment with GST fused proteins exhibited significant binding to α actinin with AnxA6 (lane 1) or mutants lacking domains C1-C3 (GST-AnxA6 ΔC1 – GST-AnxA6 ΔC3; lanes 8-10). However, the interaction between AnxA6 and α actinin was completely abolished in the AnxA6 mutants lacking domains N1-N3 (GST-AnxA6 ΔN1- GST-AnxA6 ΔN3; lanes 3-5, Fig. 2).

Localization of GFP-AnxA6 and its deletion mutants in cardiac myocytes

To examine the subcellular localization of AnxA6 in cardiomyocytes, GFP-AnxA6 was introduced into NRVM and visualized under fluorescence microscope after 48 hrs. As shown in Fig. 20, GFP-AnxA6 was localized to the cytoskeletal structure, which closely resembles the Z discs typically seen in cardiomyocytes. However, GFP-AnxA6 ΔN1 was mostly localized to the nucleus whereas GFP-AnxA6 ΔC1 was localized to the cytosol and appeared to be large aggregates or vesicles. Though, *in vitro* binding experiment showed that GST-AnxA6 C1 could interact with α actinin, however, it did not localize to the Z discs *in vivo*. It is likely that over-expression of this mutant induces cellular toxicity and cardiomyocytes did not survive after 48 hrs of transfection.

The interaction of AnxA6 with α actinin was further validated by immunofluorescence microscopy. The pattern of AnxA6 localization was similar to α actinin and both displayed striated distribution similar to Z discs of actin-myosin complex (Fig. 21). The extent of co-localization for AnxA6 and actinin was enumerated by generating the line profiles of fluorescence intensities of TRITC and FITC images (Fig. 21 lower panel). These fluorescence profiles demonstrates (through randomly chosen line over the merged images) the parallel pattern of spatial distribution of AnxA6 and actinin signals, indicating a high degree of co-localization of these two proteins, which was further strengthened by Pearson's correlation coefficient as high as 0.898 ±0.014, obtained from co-localization analysis.

The present study demonstrates AnxA6 to be a member of the actin-myosin cross bridge. Therefore, altered level of AnxA6 might impair cardiac excitation and contraction, which could explain the contractile abnormality in AnxA6 transgenic as well as knockout mice.

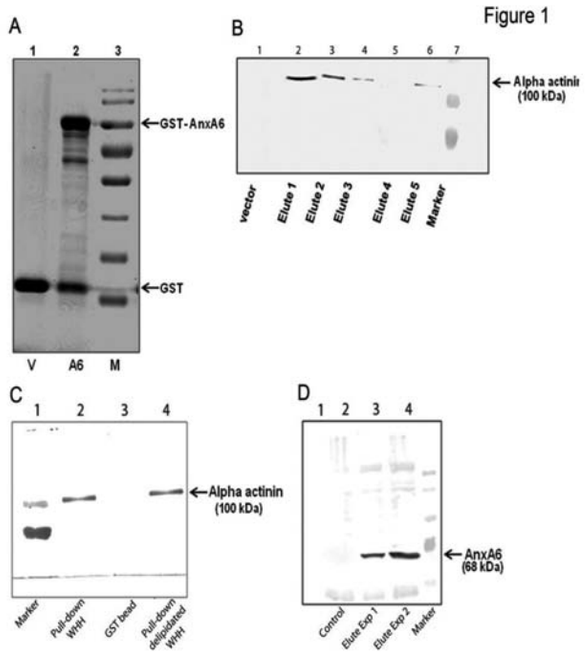

Fig. 18. Identification of putative AnxA6 binding partner(s) in heart. (A). Purified GST-AnxA6 (A6) affinity beads or GST affinity beads (V) were incubated with NP-40 solubilised WHH (1.5 mg) and the bound proteins (interactome) were separated in 12% SDS-PAGE, stained with Coomassie (lane 2) and analysed via LC MS/MS. (B). In vitro binding assay: Solubilised whole heart homogenates (WHH) were incubated with GST affinity beads (vector) or AnxA6-GST affinity beads and the bound proteins collected in the elute were separated by 10 % SDS-PAGE followed by immunoblotting analysis with anti á actinin antibody. (C). In vitro binding assay with lipid depleted WHH: Solubilised WHH or delipidated WHH incubated either with GST-AnxA6 affinity beads or GST (vector) affinity beads and the bound proteins in the elute were separated by 10 % SDS-PAGE followed by immunoblotting analysis with anti á actinin antibody. (D). Immunoprecipitation: The whole heart homogenate (300 µg) was subjected to immunoprecipitation with anti- α actinin antibody followed by western blotting with anti-AnxA6 antibody.

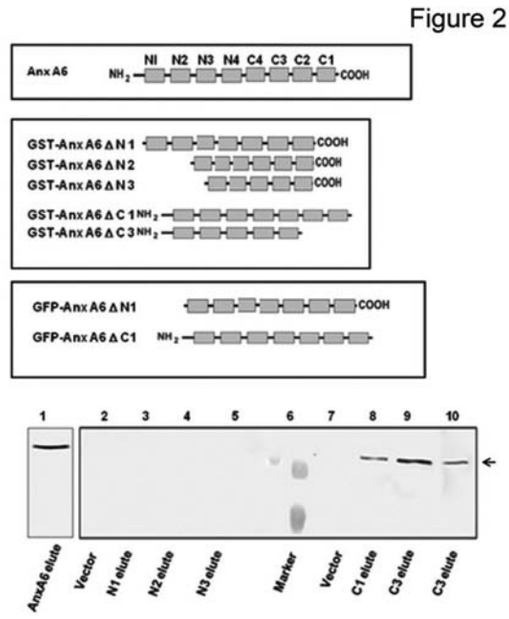

Fig. 19. N-terminus of AnxA6 mediates binding with α actinin. Scheme of AnxA6 deletion mutants**.** The full length AnxA6 contains eight repeat domains and associated linker residues (residues 1-673). Deletion mutants GST-AnxA6 N1 lacks N terminal tail and repeat domain 1 (residues 1–89); GST-AnxA6 N2 lacks N terminal tail, repeat domains N1 and N2 (residues 1–163); GST-AnxA6 N3 lacks N terminal tail, repeat domains N1, N2 and N3 (residues 1–250); GST-AnxA6 C1 lacks C terminal tail and repeat domain C1 (residues 600–673); GST-AnxA6 C3 lacks C terminal tail and repeat domains C1, C2 and C3 (residues 435-673). GFP-AnxA6 N1 lacks N terminal tail and repeat domain 1 (residues 1–89) and GFP-AnxA6 C1 lacks C terminal tail and repeat domain C1 (residues 600–673). Solubilised WHH was incubated with GST affinity beads (vector) or various mutants of AnxA6 lacking domains N1-N3 (GST-AnxA6 N1- GST-AnxA6 N3) or mutants lacking domains C1-C3 (GST-AnxA6 C1 and GST-AnxA6 C3). The presence of α actinin in the bound fractions was detected by immunoblotting analysis with anti α actinin antibody (arrow head).

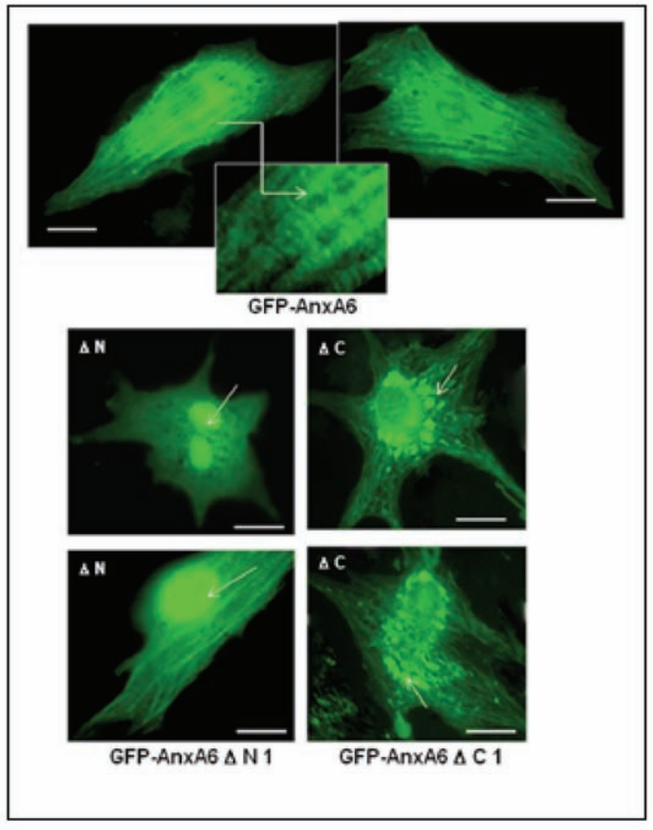

Fig. 20. Sub-cellular localizations of GFP-AnxA6 fusion protein in cardiomyocytes. The representative images showing expression of AnxA6 and its mutants in NRVM. The GFP expression was examined under Olympus (IX71) microscope after 96 hrs of transfection. The GFP-AnxA6 appears to be localized to sarcomeric Z lines (arrow), GFP-AnxA6 N1 is localized to the nucleus (arrow) and GFP-AnxA6 C1 is expressed as aggregate like structures in cytosol (arrow), The experiment was repeated with three different batches of myocytes preparation (n=3). Scale bar represents 5μM.

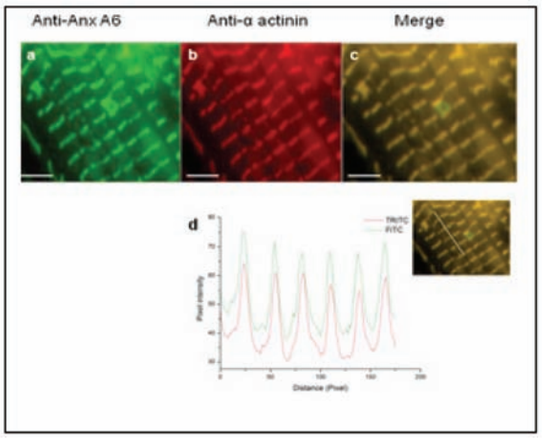

Fig. 21. Co-localization of AnxA6 (a) and actinin (b) in cardiomyocytes. Representative images shown are endogenous expression of AnxA6 (a) and α actinin (b) in the same cell and their co- localization pattern (c). The line profile for quantification of co-localization (d) was done using the merged image (inset) of AnxA6 and cardiac α actinin. The images represent results of three different experiments with separate batches of myocyte preparation. Scale bar represents 10 μM.

Dr. Sib Sankar Roy and group

Pitx2 homeodomain transcription factor and gonadal development and function

We have identified different gene promoters by ChIP-chip method that is probable targets of Pitx2. The Pitx2-associated cofactors are found important for regulation of expression of Pitx2 target genes in ovary. We have shown the temporal and spatial expression pattern and localization of Pitx2 throughout the embryonic development as well as in neonatal and adult gonads of both sexes. Two predominant isoforms of Pitx2 has been shown to express in a criss-cross manner in male and female gonads during embryonic development and in post-natal Stages (Fig. 22). Another transcription factor, GCMa, co-localizes with PITX2 in testis during developmental stages and co-immunoprecipitation data suggests that the PITX2 and GCMa interact with each other during gonadal development in a sex-specific manner (Fig. 23). Presently we are pursuing our study to explore the role of Pitx2 in controlling different vital genes that are essential for gonadal development and function.

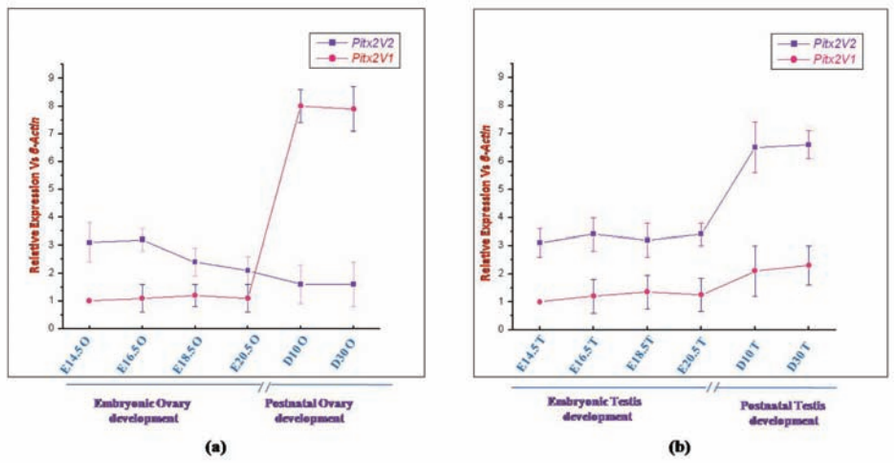

Fig. 22. Comparative gene expression profile of *Pitx2v1 and -v2* in rat gonads at embryonic and postnatal stages. Total RNAs from ovary (O) and testis (T) were isolated at embryonic days, E14.5, -16.5, -18.5, -20.5 and postnatal days, D10 and D30 followed by Taqman Q-PCR using rat *Pitx2v1 and Pitx2v2* gene-specific primers and probes. The Fig (a) and (b) show the Q-PCR results of two variants with ovarian and testicular RNAs respectively. The data are represented by relative gene expression in fold change calculated by $2^{-\Delta\Delta C_T}$ method. The C_T -value of *Pitx2* gene are normalized from the C_T -value of the housekeeping gene β-Actin. The gene expression level of Pitx2v1 at E14.5 ovary and testis was considered as 1. The embryonic and the postnatal developmental days of ovary and testis have been mentioned. The experiments were performed three times and the mean ± SE value have been shown, *, $P<0.05$.)

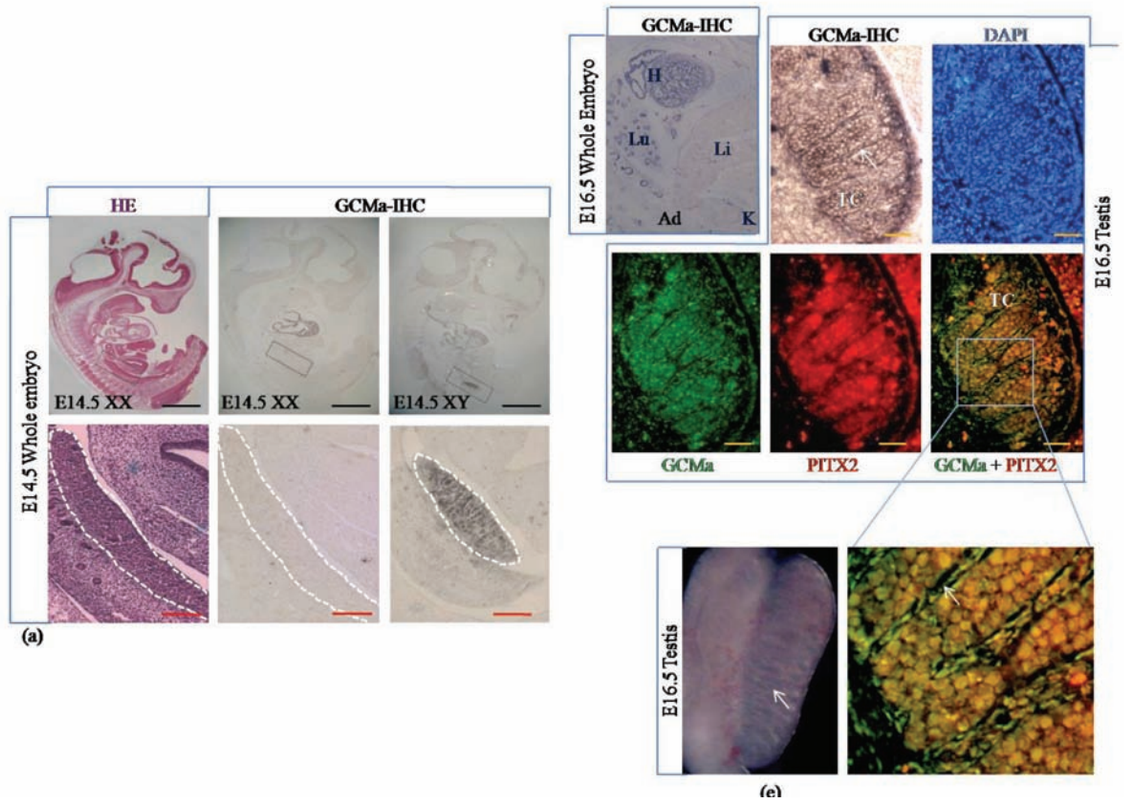

Fig. 23. Localization of GCMa in the ovary and testis at E14.5 has been shown by IHC using GCMa-specific antibody. In the upper panel, localization of GCMa has been shown in whole embryonic section (a). The marked area shows the presumptive ovary and testis respectively and the lower panel shows the magnified view of the same section. Localization of GCMa at different cell types of E16.5 testicular cords, heart and lungs has been shown by IHC and IF using GCMa-specific antibody whereas, no expression was detected in adrenal, kidney and liver (Fig.b). Further, GCMa has been shown to co-localize with Pitx2 in the nucleus of PGCs as shown by dual IF (yellow color) and DAPI staining. The vascular tissue surrounding the testicular cords show specific expression of GCMa at this stage (Fig. b and e, white arrow), where Pitx2 expression was not significant. For the sake of brevity, images of the selected days are furnished to highlight the pattern of developmental expression. The GCMa expression is designated as green fluorescence (FITC), red fluorescent for Pitx2 (TRITC) and blue fluorescence for DAPI. O, Ovary, T, Testis, TC, Testicular cord; H, Heart; K, Kidney; Ad, Adrenal; Lu, Lungs; Li, Liver; M, Mesonephros; T, Testis. Scale bars: black, 1mm; red, 100µm; yellow, 50 µm.

Regulation of collagen metabolism in ovary in normal and diseased condition

In our earlier studies, we showed the role of hypothyroidism in regulation of Plod2 and in turn malfunction in collagen metabolism. We have shown the regulation of Plod2 gene expression in ovary by Pitx2 homeodomain transcription factor and showed that it binds to bicoid element of Plod2 promoter and that it is an upstream activator of Plod2 gene. The involvement of MMPs and TIMPs were also studied in connection with hypothyroidism-associated ovarian dysfunction. Some MMPs are found to be differentially expressed in ovarian cancer. Ets-related transcription factors including PEA3 regulate different MMP gene expression in many tissues. We have investigated the role of VEGF and T3 in regulating the Ets gene expression in ovarian cancer cell line. We showed that these factors influence the differential expression and nuclear translocation of Ets1 and Ets2 transcription factors in this cell line. By applying different inhibitors of several key pathways, we could show how these factors activate Ets1 and Ets2 and regulate key MMP gene expression in ovarian cancer cells.

Mitochondrial dysfunction and type 2 Diabetes

The involvement of mitochondria and mitochondrial proteins is well established in insulin resistance and diabetes type 2. There is an established connection between free fatty acid induced insulin resistance and mitochondrial dysfunction in adipocyte and muscle cells, but the exact mechanism of this involvement is still unclear. We showed the mitochondrial structural and functional disorders in diabetic model system and in insulin target cell lines. These includes mitochondrial membrane fluidity isolated from skeletal muscles of STZ-induced diabetic rat, mitochondrial membrane potential measurement in high insulin and high glucose treatment in muscle cell line, expression profile of different genes in muscle and adipose tissues of diabetic model, which are either mitochondrial genes or the proteins act in mitochondria. We have found that the mitochondrial membrane fluidity at hypothyroid condition as well as in diabetic condition is increased. By using array that is specific for mitochondrial and associated genes, we could show the differential expression of some genes in free fatty acid-treated cells and that may be involved in mitochondrial biogenesis and dysfunction and our future study will be focused on this aspect to decipher the exact mechanism. Work is also being progressed to screen and identify the antidiabetic compounds and their respective molecular mechanism of action as a part of CSIR network project. In another aspect of Diabetes research, we have found unusual type of mutations in MODY genes in some families we have studied.

REPRODUCTIVE BIOLOGY

Dr. Syed N. Kabir and group

Physiological and pathophysiological aspects of female reproduction

Animal model for premature ovarian failure

Ovary is a major target of galactose toxicity. Premature ovarian failure is a frequent finding in women with galactosemia. We have earlier demonstrated that experimental galactose toxicity in rats induced by pre- and early postnatal exposure to high galactose, produces a sequel of ovarian dysfunction including increased rate of follicular atresia. Recent studies suggest that p53-mediated death pathways may be central in the induction of follicular atresia. We have earlier reported that galactose significantly down regulates ovarian growth differentiation factor-9 (GDF-9), an oocyte-specific factor that plays pivotal role in maintaining oocyte-granulosa-theca cell communications to promote follicular differentiation and maturation. There are reports that galactose up-regulates the expression of p53 that inversely correlates with GDF-9 expression. We explored if ovarian toxic effects of galactose are mediated by p53-mediated GDF-9 down regulation pathway. Galactose toxicity was evaluated *in vitro* in ovarian carcinoma cell line SKOV3, breast carcinoma cell line MCF7, and isolated rat granulosa cells or intact follicles. The 2 cancer cell lines were selected because unlike normal ovarian surface epithelial cells, both of these neoplastic cells express GDF-9, while SKOV3 cells are p53 null. Cells were harvested and cultured under optimised conditions in the presence or absence of D-galactose at concentrations ranging between 50mM and 200mM. The effects of galactose on cell cycle was analysed by fluorescence-activated cell sorting (FACS). The effects on cellular expression of GDF-9 and p53 were analyzed by western blot analyses. Flow cytometric analysis of mitochondrial membrane potential was done using JC-1 staining. Cellular apoptosis was evaluated by confocal microscopy using annexin V-affinity assay. Effect of galactose on granulosa cell apoptosis was studied also in the presence recombinant GDF-9. Like in the cell lines, most of the study parameters were investigated in isolated granulosa cells, however, the expression of p53 and GDF-9 was evaluated following culture of intact follicles.

In the cultured follicles and MCF 7 cells, galactose up-regulated p53 and down-regulated GDF-9 expressions in a dose-dependent manner, but no impact was demonstrated in the expression of GDF-9 in the p53-null SKOV3 cells. However, in all cell types the cell cycles were arrested at G1 and G2/M phase. Observation of annexin V-affinity assay demonstrated that galactose triggered apoptosis in all cell types at lower

concentrations, but was lethal at higher dose level. Results on loss of mitochondrial transmembrane potential also corroborated this observation. Supplementation of recombinant GDF-9 in culture failed to prevent galactose-mediated apoptosis in the granulosa cells. We conclude that galactose represses GDF-9 possibly by way of p53 activation, but perhaps an extra-P53-GDF-9 pathway is operative in mediating the apoptotic effects of galactose in follicular atresia.

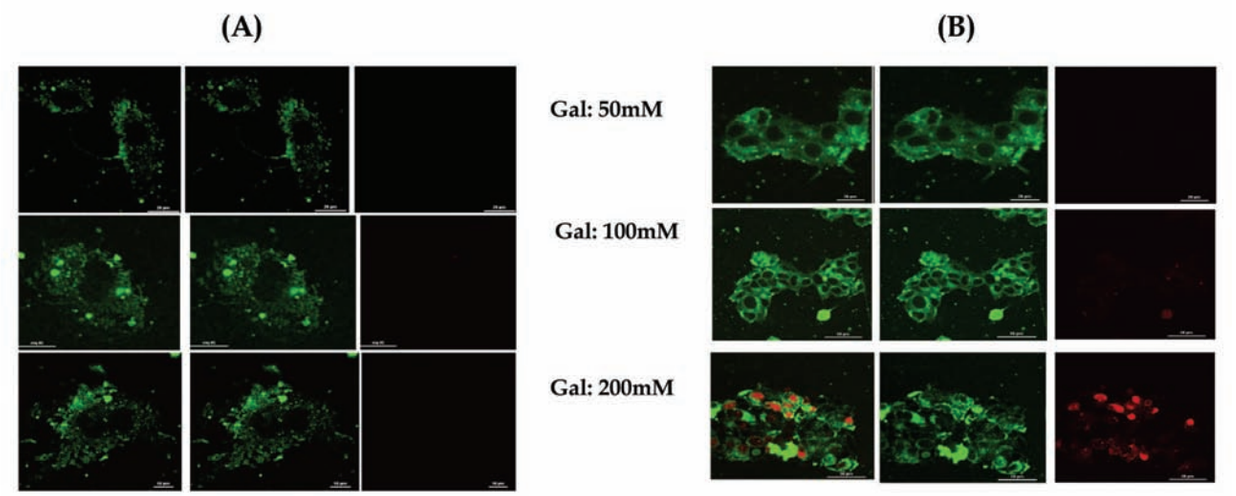

Fig. 24. Confocal micrograph of Annexin V-affinity binding demonstrating that galactose triggers apoptosis in SKOV3 (panel A) and MCF-7 (Panel B) cells.

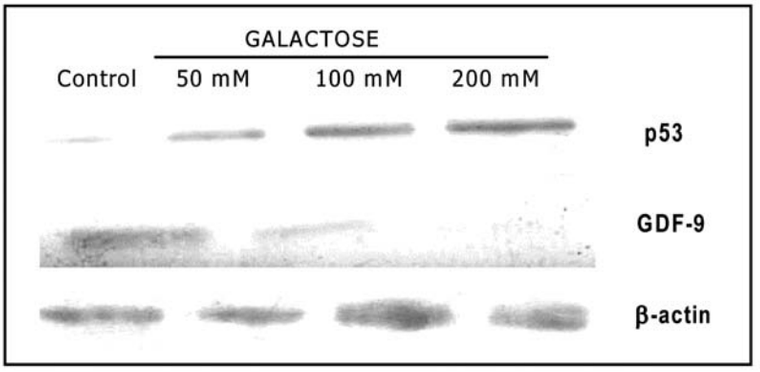

Fig. 25. Galactose dose-dependently up-regulates p53 and down regulates GDF-9 expression in breast carcinoma cell line MCF-7

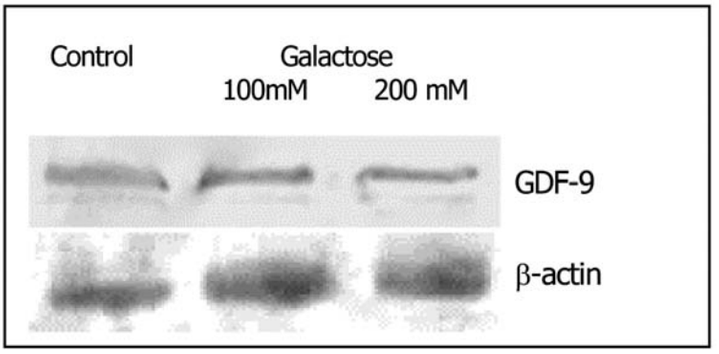

Fig. 26. Galactose does not impact GDF-9 expression in ovarian surface epithelial cell line SKOV3

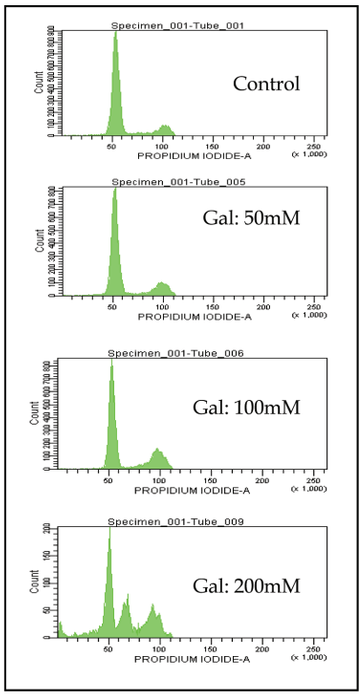

Fig. 27. FACS analysis of cell cycles in SKOV3 cell line showing galactose-induced arrest of cycle at G2/M phase at moderate dose and at S-phase at higher concentration.

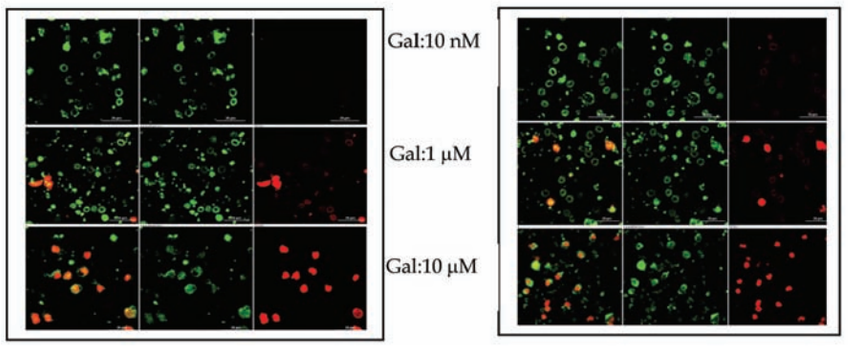

Fig. 28. Confocal micrograph of Annexin V affinity binding in galactose-exposed granulosa cells treated with **(panel A)** and without GDF-9 **(panel B)** showing failure of GDF-9 to prevent galactose-mediated apoptosis.

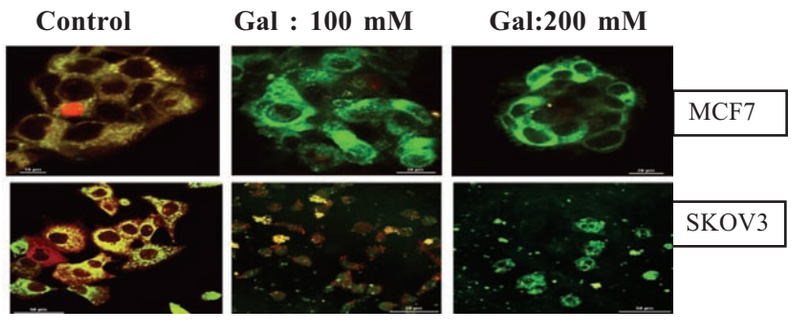

Fig. 29. JC-1 analysis of mitochondrial transmembrane potential in SKOV3 & MCF-7 cells

Search for anti-fertility molecules of plant origin

Antifertility effects of puerarin

Emergency contraception is one of the most widely accepted contraceptive options today. However, the untoward effects attributed to the proliferative actions of estrogenic component of the pill, or higher failure rate and menstrual abnormalities associated with progestogen-only pills demands the search for a safe and effective estrogen-free contraceptive formulation. In many tissues including uterus estrogen mediates its proliferative effects by estrogen receptor-α (Erα), while anti-proliferative effects are mediated by ERβ; and ER-β has an inhibitory effect on ERα. Isoflavones have oestrogenic and/or anti-oestrogenic activity, though they preferentially trigger ER-β transcriptional pathways. We have demonstrated that puerarin, an isoflavone glycoside isolated from *Pueraria tuberosa*, effectively prevents establishment of pregnancy in rats following administration once a day for two consecutive days after mating. Electrospray ionization mass spectrophotometry analysis demonstrates comparatively higher endometrial accumulation of puerarin in mated rats. This effect parallels with disruption of the downstream estrogen-signaling pathway as characterized by adverse alteration of endometrial expression of leukemia inhibitory factor (LIF), cycloxygenase-2 and vascular endothelial growth factor - the three most important molecules known for their significant roles in signaling the process of implantation. As compared to increased expression of LIF in the luminal epithelia and decreased expression of LIF in glandular epithelia of the control receptive uterus, the treated horn exhibited higher expression of LIF in the glandular epithelia. On day 5, the uterine expression of ERα decreased while that

of ERβ increased in the treated group. The blastcysts remain in dormant state. Luteal function, as evaluated by circulating progesterone levels, however remains undisturbed. This characteristic estrogenic/antiestrogenic potential of puerarin at endometrial level makes it worthy to be investigated for development of emergency contraceptive.

Spermicidal & anti-HIV effects of Acaciaside-B (Ac-B) and Ac-B-enriched fraction (Ac-B-en)

The population explosion coupled with steer rise in the incidence of HIV infection through heterosexual contacts has regenerated our interest to develop topical microbicides with discerning spermicidal property. We have demonstrated earlier that isolates of the extracts of *A.*

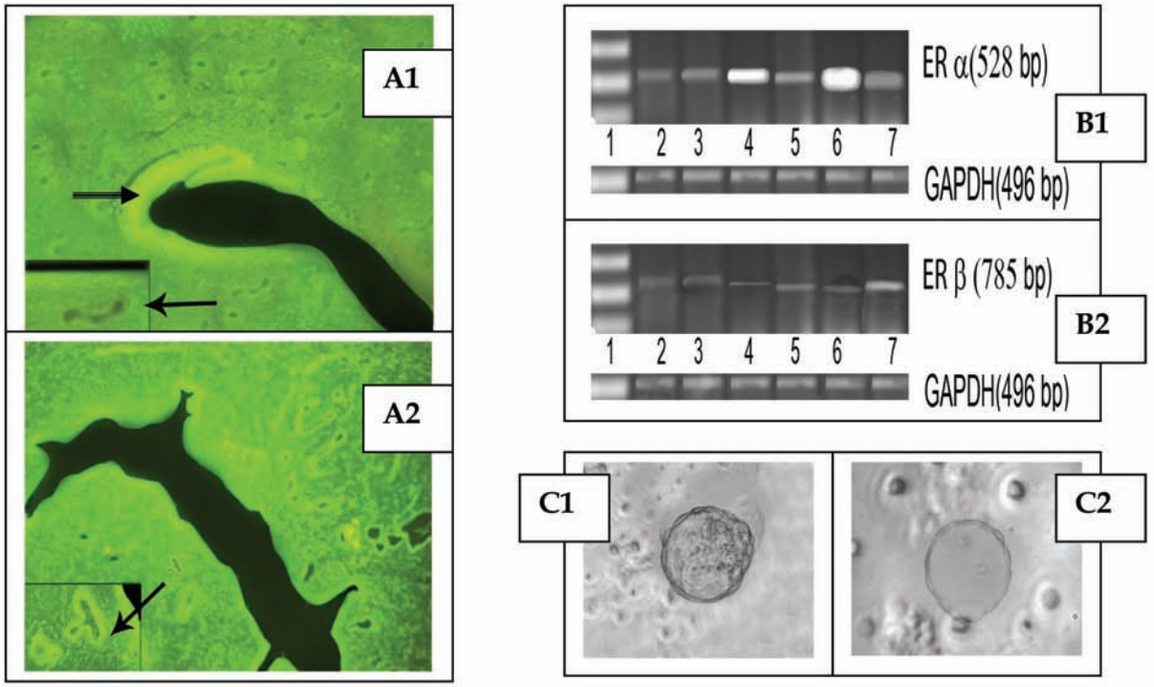

Fig. 30. A. Overlaid fluorescence images of control (A1) and puerarin-treated (A2) rat uterus (x400) showing differential LIF expression. Control uterus shows increased luminal epithelial expression of LIF at the anti-mesometrial site, while treated uterus exhibits higher LIF expression specifically at glandular epithelia. **B.** RT-PCR data of Erα **(B1)** and ERβ **(B2)** expression in the control (lane 2,4,6) and puerarin treated (lane 3,5,7) rat uteri during days 3 (lane 2 & 3), 4 (lane 4 & 5), and 5 (lane 6 & 7) of gestation. **C.** Phase contrast micrograph of implantation-competent **(C1)** and dormant **(C2)** blastocysts collected from the control **(C1)** and puerarine-treated **(C2)** rat uterus

auriculiformis seeds, Acaciaside-B (Ac-B) and an Ac-B-enriched fraction (Ac-B-en), offer spermicidal activity and attenuate HIV-1 transmission in vitro at significantly lower concentrations. As a part of safety studies we evaluated the cytoxic effects of Ac-B and Ac-B-en in cervico vaginal cell lines.

Cytotoxic effects on cervico-vaginal cell lines

Cells of cervicovaginal origin (vaginal keratinocyte cell line: Vk2/E6E7; ecto-cervical cell line: Ect1/E6E7; and endo-cervical cell line: End1/E6E7) were assessed for their sensitivity to Ac-B, Ac-B-en by a colorimetric cell viability assay, which is based on the principle that viable cells reduce a tetrazolium compound [3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium] to a formazan product that is soluble in tissue culture medium. Cells were seeded overnight in a 96-well plate at a density of 5000

cells per well. After 24 hours, culture medium was replaced with fresh medium containing serial dilutions of Ac-B as well as Ac-B-en and incubated for another 24 hours. Positive control wells contained an equal concentration of N-9. The absorbance of formazan was measured directly at 490 nm in 96-well assay plates by using automated microplate reader (Qualigen, India). At least two independent experiments were conducted in which each concentration was examined in triplicate for each experiment. The results are presented in the following figure. Considering the earlier demonstrated IC 50 doses of 0.035 and 0.15 mcg/ml of Ac-B and Ac-B-en for their anti-HIV activity in vitro, the present results suggest for a wide margin of safety index (HIV part of the investigation was done in collaboration with Dr. D. Mitra, NCCS, Pune).

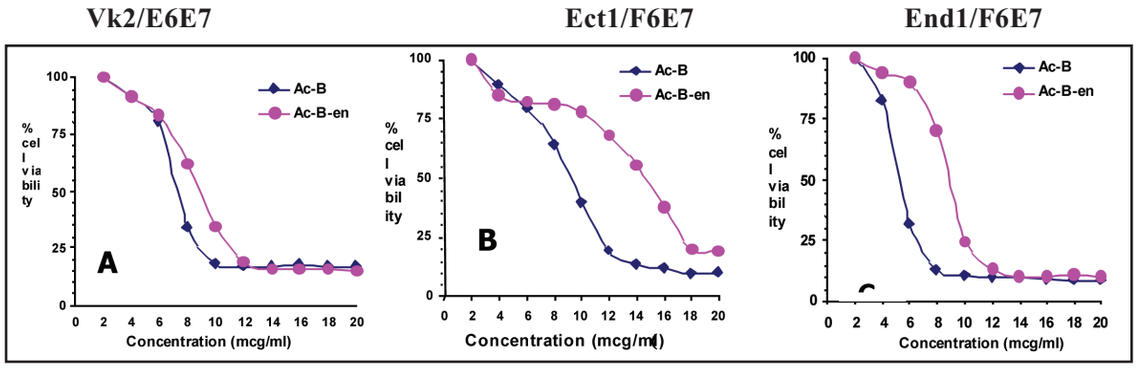

Fig. 31. Dose-response curve of MTT-based cytotoxicity of Ac-B and Ac-B-en in cervico-vaginal cell lines. The respective IC50 values (mcg/ml) of Ac-B and Ac-B-en are calculated to be 7.66 & 8.91 for vaginal keratinocytes (Vk2/E6E7), 8.83 & 13.9 for ectocervical cell (Ect1/E6E7) and 5.41 & 8.84 for endocervical cells (End1/E6E7).

Dr Smritinath Chakraborty and group

Search for fertility regulating agents from natural resources

The explosive growth of the global population added with the relentless spread of sexually transmitted diseases (STD), especially human immunodeficiency virus (HIV) through sexual contacts has instigated us to identify topical microbicides with desired spermicidal activity that could prevent undesired pregnancies and can limit HIV infection. We have reported earlier that compound isolated from *S. sesban* root extracts, oleanolic acid 3-α–D glucuronide (OAG) possess spermicidal activity at appreciably very lower concentration in rats. That was tested positive in human sperm also. Mutagenicity of OAG was assayed by using the Muta-chrome Amees' principle that uses *Salmonella typhimurium*, carrying mutation/s in the operon coding for histidine biosynthesis with reversion property. The assay was performed with or without metabolic activities by cofactor-supplemented post-mitochondrial fraction of (S9). The sample was tested five times in independent experiments. The number of revertant of OAG-treated groups did not differ significantly to negative control.

Biocompatibility studies of polymer composites

Wound healing is a complex process and is promoted by dressings that maintain a moist environment but allow excess fluid to escape without permitting wound desiccation. Being biodegradable, biocompatible, non-toxic, antithrombogenic, stable, sterilizable, chitosan acts as a potential biomaterial for wound management, space filling implants etc. This study aims at the development of chitosan-poly vinyl alcohol blended membrane and chitosan-hydroxyapatite composite membrane, characterization and comparison of results, along with in vivo assessment of the membranes for their effectiveness as wound healing material. The membranes were characterized for their strength, swelling properties and blood compatibility. These membranes did not elicit adverse reactions and were biodegradable. Chitosan-hydroxyapatite membrane promoted better healing, with faster and orderly reorganization of wounded area into healthy new skin in rats and rabbit. Analyses done

with various membranes yielded favorable results for the chitosan-hydroxyapatite membrane as a wound healing material. The features observed in the membrane make it a significant and effective resorbable wound healing material.

Active targeting of nanoparticles grafted with ligands to cells of reticuloendothelial system by receptor-mediated endocytosis and their application against macrophage associated disorder

Poly-(DL-lactide-co-glycolide)(PLGA) nanoparticles have been prepared by an emulsification solvent evaporation method. For targeting macrophages, the PLGA nanoparticles have been modified by incorporating mannose ligands. Characterization of morphology of the mannose-grafted nanoparticles by scanning electron microscopy and atomic force microscopy and of composition by FT-IR and 1H-NMR have been carried out. Uptake of fluorescein-incorporated nanoparticles is being studied by fluorescence spectrophotometry and confocal microscopy in in-vitro culture of isolated mouse peritoneal macrophages Studies on the *in vivo* biodistribution of the ligand-grafted nanoparticles quantitatively by fluorescence pectrophotometry and qualitatively by fluorescence microscopy after cryo-sectioning, was carried out which indicates that the PLGA nanoparticles are being transported inside the body and incorporated by macrophages in the reticulo endothelial organs. We thus have established a new method of preparing ligand-grafted PLGA nanoparticles for targeting macrophage associated diseases as well as we are trying to develop a useful tool for new targeted drug-nanoparticle formulations for potential clinical application against macrophage-associated diseases.

Search for controlling agent(s) for breast cancer

In our effort to find some drug that could be effective against breast cancer, previously it was reported that PH-DIM reduces tumor in *in-vivo* model and worked excellently in *in-vitro* system also Genotoxicity test and mutagenecity test gave negative results that confirmed its anti-carcinogenic activity. The drug reduce tumor by inducing cell cycle arrest and apoptosis which was proved by tunnel assay, western blot with apoptosis indicator protein from tissue and breast cancer cell line. To find out the mode of action of this drug, estrogenic /antiestrogenic test, variability of different steroid receptor were measured by IHC method. The drug has a high potential to prevent breast cancer.

Dr. Padma Das and group

Evaluation of anti-cancer activity of the Andrographolide derivative

Andrographolide derivatives are very active and possess a number of medicinal activities. In our study we have found that growth of U937 cells was affected in the presence of Andrographolide derivative (BD43) with an IC_{50} of 5.4 μM after 48h treatment. In our earlier studies we have demonstrated that Andrographolide derivative (BD43) induced apoptosis in U937 cells and which was accompanied by loss of mitochondrial transmembrane potential, phosphatidyl serine externalization and cell cycle arrest at sub G0/G1 phase, which is considered as a hall mark of apoptosis. In our present study we have assessed ROS, TUNEL, laddering and confocal microscopy. Intracellular ROS level was measured in U937 cells. Cells were incubated with an IC_{50} concentration of Andrographolide derivative BD43 (5.47 μM) and demonstrated a time-dependent increase in the generation of ROS, maximum being at 3 h. We concluded that Andrographolide derivative BD43 induced an oxidative burst, the observed fluorescence being specifically attributed to enhanced generation of ROS. To confirm whether the oxidative burst induced by Andrographolide derivative BD43 was a major contributory factor towards its anti proliferative activity, U937 cells were co-incubated with Andrographolide derivative BD43 and a non-toxic concentration of N-acetyl-L-cysteine (NAC, 2.5 mM), an established antioxidant. With the addition of NAC, the IC_{50} of Andrographolide derivative BD43 increased from 5.47 μM to greater than 50.0 μM, substantiating that induction of oxidative burst is a key factor triggering the anti proliferative activity of Andrographolide derivative. In order to assess the morphology of the cell death induced by andrographolide derivative BD43, we performed confocal microscopy. Following treatment of

U937 cells with an IC_{90} dose of Andrographolide (IC_{90}=16.69 µM; 24h) showed nuclear fragmentation and marginalization of fragmented nuclei towards the membrane after staining with Hoechst 33258. Apoptosis thus appeared to be the primary mode of cell death induced by BD43. To evaluate the endonuclease activity of Andrographolide derivative BD43, in situ TUNEL staining was performed. Microscopic evaluation of U937 cell treated with Andrographolide derivative BD43 for 24hr, brown deposits representing incorporated TdT-labeled nuclei were observed, indicating nicking of the DNA. One of the hallmarks of apoptotic cell death is internucleosomal DNA digestion by endogenous nucleases that yields a characteristic laddering pattern. Accordingly, oligonucleosomal DNA fragmentation following treatment of U937 cells with Andrographolide derivative BD43 (IC_{50}=5.47 µM, IC_{90}=16.69 µM; 48 h) was studied; a degree of smearing was observed. Collectively, Andrographolide derivative (BD43) induces apoptosis which was accompanied by generation of ROS, nuclear fragmentation and marginalization of fragmented nuclei towards the membrane, nicking of the DNA and a degree of smearing.

Evaluation of the anti-proliferative activity of Sesbania grandiflora

In the indigenous system of medicine in India, the plant *Sesbania grandiflora* is claimed to be useful for various ailments, and one such use is for the treatment of cancer. The present investigation was undertaken to evaluate the anti-proliferation and apoptosis of crude methanolic flower extract (CMFE) from *Sesbania grandiflora* using different types of leukemic cell line such as U937 and K562 as well as normal cell line L132 and NIH3T3. Growth of U937 cells was affected in the presence of crude extract of *Sesbania grandiflora* (SG) with an IC_{50} of 19.8 µg/ml after 48 h treatment. The result established that the anti-proliferative effect of CMFE of *Sesbania grandiflora* was associated with apoptosis on leukemic cell line by determinations of Phosphatidylserine externalization and confocal microscopy. In addition, CMFE at various concentrations and incubation times were also found to generate ROS. Thus, it indicates that this substance can show apoptosis and has potential for cancer chemoprevention which was dose dependent as well as exposure time dependent. The overall results obtained in this study provide evidence for the efficacy of the methanolic extract of *Sesbania grandiflora* flower as potent anti-proliferative agent. That may further be explored for its future study.

Evaluation of Anti proliferative Activity of Regioselective One pot Synthesis of bioactive 3, 3'-diindolylethylene derivatives (DIE)

Indole and its derivatives possess a wide range of biological activities with interesting chemistry. Bis(indolyl)methanes are most active substances from cruciferous vegetables for promoting beneficial estrogen metabolism and inducing apoptosis in human cancer cells. In our study we have evaluated the cytotoxic activity of DIE derivatives (IC_{50}, 13.06 µM in U937 cell) against human leukaemic cell lines U937 and K562 in using MTS-PMS assay and indicate that the Novel synthetic compound has potent anti-proliferative activity. Flow cytometric data indicates that in untreated cells, the degree of binding of annexin V at 8 h was 16.08 %. Following treatment of U937 cells with 3g derivative of DIE with its IC_{50} value of 13.06 µM for 8 h, the percentage of annexin V-positive cells increased to 51.87% at 8 h. Collectively the study of cytotoxic activities of DIE derivatives against human leukemic cell lines U937 and K562 revealed that Novel synthetic compound 3g was first evaluated for its antiproliferative activity in U937 and K562 cells using MTS-PMS assay and the cell death through apoptosis. Experiments are in progress and results are yet to be obtained.

Dr. Sandhya R. Dungdung and group

Isolation and characterization of a sperm motility inhibiting factor from caprine epididymal plasma

Recently we have identified and purified a sperm motility inhibiting protein factor (MIF) from caprine epididymal plasma to apparent homogeneity. The factor was purified about 770 fold with 55% recovery. The motility inhibiting activity of MIF increased linearly up to 6.5 units at the concentration of 1 µg/ml (6.25

nM). The inhibitory effects of the factor showed maximal activity (approx. 92%) at 2 µg/ml (12.5 nM) concentration of MIF (Fig. 32). The factor showed a single protein band on staining with silver nitrate when examined by polyacrylamide gel electrophoresis (PAGE) under non-denaturing condition. The MIF activity co-migrated with the protein band (Fig.33 A&B). The molecular weight of the purified MIF was approx. 160 kDa as estimated by Sephacryl S-300 gel filtration. Further characterization is under progress.

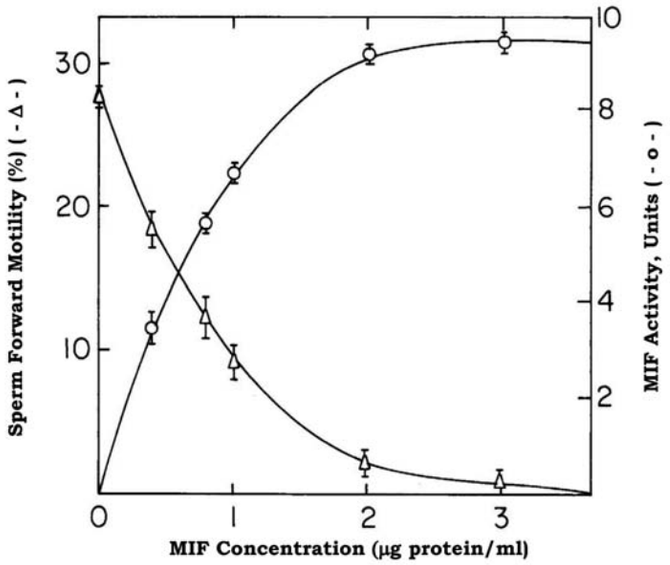

Fig. 32. Dose course of action of purified MIF under the standard assay conditions

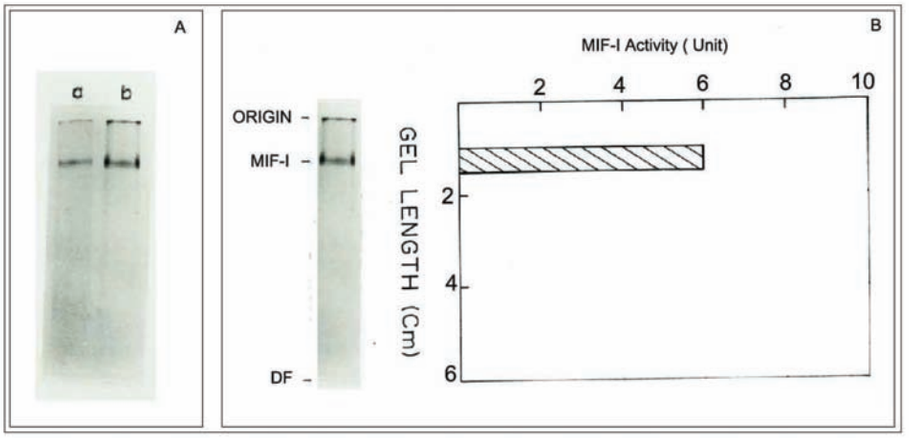

Fig. 33. (A) Native PAGE of the purified MIF on 5% gel. Lane a: 15 µg; Lane b: 30 µg (B) Co-migratin of MIF activity with the protein band

Physiological characterization of forward motility stimulating factor (FMSF)

In our previous report we have discussed about the isolation of a 66 kDa forward motility stimulating factor (FMSF) from goat blood serum. Further physiological characterization of FMSF showed that papain digested FMSF monovalent antibody treatment of goat cauda sperm prevent the sperm agglutination due to antibody treatment and to determine the exact effect of the antibody molecules. It was observed with 1:50 dilution of FMSF monovalent antibody decreased the 50% (approx.) of the forward motility from the control value. The

intrasperm cAMP level was estimated before and after treatment with FMSF antibody to determine the dependency of FMSF action on the cAMP. There was no significant lowering or increase of intrasperm cAMP level even after antibody treatment. This shows that the FMSF activity is not dependent on cAMP and there must be some other pathway through which the FMSF activity is mediated. So, much more research is required to elucidate the pathway by which the action of FMSF takes place.

Further studies on upgrading the recently developed computerized spectrophotometric sperm motility analyzer (SPERMA)

Calibration and Standardization of the SPERMA has been done with sperm cells of different species, like, Goat, Bull, Rat, Hamster and Human. The comparative tests have been conducted using phase contrast microscope, spectrophotometer, SPERMA and CASA.
To elucidate the correlation of the vertical velocity and other available parameters with the fertilizing ability of spermatozoa, tests such as capacitation, acrosome-reaction, egg-penetration, and sperm-egg-interaction are under progress. Modification / alteration / addition of the associated software for the existing mathematical model and data analysis of the instrumental system are completed. The new modification for the development of multi-cuvette (multi-sample) and multi-height exposure of the sample is under progress with the collaboration with Indian Association of Cultivation of Science (IACS), Kolkata and ELICO Ltd. Hyderabad.

GENE REGULATION & METAGENOMICS

Dr. Tushar Chakraborty and group

Metal Microbiome and Metagenomics

A large numbers of different genera of microorganisms can interact with varieties of metals presented in diverse chemical forms in nature. The often exist as communities. Mining areas are the rich source of such communities. Diversity is also manifest within a genus, and also at the level of individual species. These organisms have developed elaborate strategies to transact metals. Some are metal oxidizing and some are metal reducing organism. Some accumulate them, and some exclude or secrets metals. Activities are often related biogeochemical cycling. In contrast to the great amount of information concerning metal resistance, absorption and sequestration by individual model microorganism – little is known about the microbial communities associated with ores and metal rich environments and nature of their interactions. Our aim is to it in a systematic way – and to ultimately model such community.

The microbial community we are analyzing mostly comes from copper and uranium mines. We have analyzed a large numbers of iron and metal reducing bacteria which can concentrate, sediment out, or fix toxic heavy metals. One Interesting isolate is a eubacteria that secrete redox mediator ligand in high amount, and found only in contaminated areas has been identified and cultured. The ligand has been purified and its mass-spectral characterization has been carried out. We found these bacteria to be capable of reducing U (VI) to U (IV).It is easily culturable in soil and can form biofilm. It is potentially useful for bioremediation of toxic and hazardous radioactive metals.

Overall, microorganisms of 17 genera and 278 species has been characterized with the help of 16s rDNA phylogeny. Preliminary analysis revealed 8 types of cohorts, each defined by a characteristic core-group of microorganisms.

Towards Epigenetics of Arsenic Exposure and Toxicity through Genome Wide Methylation Study

In collaboration with Dr Sarmishtha Chanda (Presidency College) & Prof Debendranath Guha Mazumder (DNGMRF), this study is a cross sectional study in the population of West Bengal suffering from chronic

arsenic exposure through their drinking water. People taking arsenic contaminated water for years for drinking and cooking purpose have shown discreet differences in the clinical manifestations.

Epigenetic modifications of chromosomes by Cytosine-5 methylation at the CpG islands in the regulatory sequence of a gene one of the key mechanisms of gene inactivation.DNA Methylation/demethylation affects numerous key biological processes involving transcription, differentiation, development, DNA repair, recombination, and chromosome organization. Perturbation of DNA methylation has been correlated with many cases of cancer incidence and progression. The hypothesis that arsenic perturbs DNA methylation has been tested successfully on tissue culture cells. We probing these now in arsenic exposed population. These studies are in progress. We are also investigating the association of GSTMITI and Cytochrome P450 polymorphism with arsenic induced skin Lesions among Arsenic exposed populations.

Exploitation of Soil Microorganisms for Biodegradation of Nanomaterials in Collaboration with Dr Arindam Bandyopadhyay (IACS)

We have made unusual dipeptide based nanomaterials which can act as organozeolites . This material has potential industrial application. However, one major concern regarding development and use of these novel materials are their toxicity and their environmental impacts. Hence, we have developed a novel strategy to biodegrade these organozeolite nanomaterials – which forms stable nanostructures even in solution state. This material was previously shown to be refractory towards Proteinase K digestion. When we first tested their impact on selected laboratory strains of *E Coli* and *Pseudomonus species*, we found these materials to be detrimental to their growth. However, using a novel selection strategy we have been able to select a group of soil microorganisms which can biodegrade and use these peptide based nanomaterials as carbon and nitrogen source. Characterization of these organisms and the mechanisms involved in such biodegradation are being investigated.

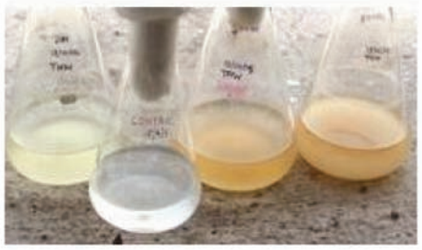

Fig. 34. Metal Oxidizing Autolithotrophic Bacteria from Copper mines Grown without any C or N Source

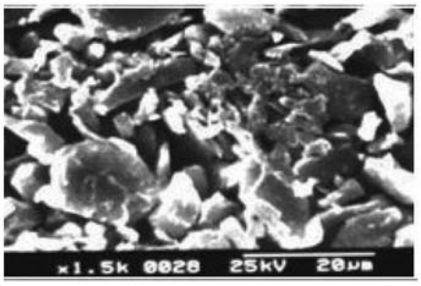

Fig. 35. Scanning EM of Biominerals known as Jarosites produced by Bacteria isolated from mine sediments

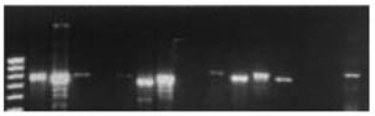

Fig. 36. 16s rDNA phylogeny of Selected Isolates from metal microbiome. The leftmost lane represents DNA size markers and the rest of the lanes contain PCR amplified rDNA spacer region from individual isolates picked up from a single cohort.

SIGNAL TRANSDUCTION IN CANCER & STEM CELLS

Dr. Mrinal K. Ghosh and group

Cancer is one of the major health issues in all developed countries and the molecular mechanisms that directly control the initiation and progression of cancer remains uncharacterized. Our research group is involved in studying the functional role of important molecular factors like Stat3, MAPK, Akt, and β-catenin. We will try to elucidate the molecular signaling pathways responsible for initiation and progression of cancers. This is very important because these proteins are highly oncogenic and involved as major players in most of the human cancer. This is to be done by studying the differential role of these molecular factors and their mechanism of activation in different cancers. This would lead to the identification of potential molecular targets in cancer chemo-prevention.

We have tried to establish a relation between STAT3 activation pathway and Wnt/ β-catenin signaling in glioblastoma and prostate cancer. During characterization of the various, we found that a positive correlation between the presence of Stat3 and β-catenin exists i.e. a cell line having higher level of Stat3 also expressed higher level of β-catenin. We are trying to elucidate how this feedback loop is regulated. Hence, our objective in this project is to elucidate the molecular mechanisms involved in these two pathways and possible crosstalks. The interdependent mechanism of regulation by these pathways on the cell cycle profile is under investigation. The results are being analyzed by Western blot, immunocytochemistry, EMSA and quantitative Real Time PCR.

We are also investigating the role of p68 in cancer. p68 (Ddx5), a member of the DEAD box family RNA helicases, has been implicated in growth regulation and has been shown to be involved in both pre-mRNA and pre-rRNA processing. More recently, this protein has been reported to act as transcriptional co-activators for several transcriptional factors and to interact with co-activators p300/CBP and the RNA polymerase II holoenzyme. We are interested in finding Wnt/β-catenin signalling regulation on p68 expression. We found that upon exogenous expression of WT-TCF4 there was an increase in p68 mRNA levels, indicating regulation of p68 by Wnt signaling. It was also observed that p68 knockdown decreases the TCF4 expression. Indications suggest p68 may be involved in regulating the expression of TCF4 and â-catenin and also TCF4 dependent gene expression through TCF4 expression.

The chaperone/proteasome system of a cell, supervises the global protein turnover rates and quality control. These machineries can contribute to the altered protein levels observed in cancer cells, probably because of altered disposal rates and specificities of the faulty proteins. However, the decision of which proteins are kept and which are degraded includes partially known mechanisms, one of the central players of it being NY-CO-7. The main theme of this project is to understand how this E3 ubiquitin ligase is involved in the progression and survival/maintenance of cancer cells. Here we focus on understanding whether β-catenin signaling and NY-CO-7 cross-talk with each other. Our preliminary results show that NY-CO-7 may be a transcriptional target of this pathway and the fact that it destabilizes β-catenin, suggesting the existence of a feedback loop between the two players.

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MOLECULAR & HUMAN GENETICS

Dr. Samit Adhya, Dr. Keya Chaudhury, Dr. Kunal Ray, Dr. Ashok Kumar Giri, Dr. Susanta Roychaudhury and Suvendra Nath Bhattacharya

Brief Preamble:

The broad aims of the division are to understand the molecular genetic basis of diseases common in Indian populations, to study gene expression and function in pathogenic microorganisms.

The specific objectives are : to decipher the molecular basis of the genomic instabilities in head and neck cancer (HNSCC) and to identify the putative tumor suppressor genes involved in the development of this cancer: to identify susceptibility alleles in *Helicobacter pylori* associated gastroduodenal diseases: to study the molecular pathogenesis of oral submucous fibrosis: to understand the molecular genetics of haemophilia, glaucoma, Wilson disease, and oculo-cutaneous albinism: to assess the health effects, genetic damage and genetic variants in populations exposed to arsenic through drinking water in West Bengal: to test the antimutagenic and anicarcinogenic effects of black tea polyphenols theaflavins and thearubigins: to identify differentially expressed *V. cholerae* genes following infection to host and their role in pathogenesis, and to study the response of human intestinal epithelial cells to *V. cholerae* infection: to study the molecular basis of the import of nuclear-encoded tRNAs into the mitochondria of the kinetoplastid protozoon *Leishmania* using a combination of biochemical and reverse genetic approaches; to develop gene delivery protocols for mammalian and also to undustand the mechanism of miRNA mediated gene regulation in mammalian cells.

Dr. S. Adhya and Group

Necessary and sufficient factors for import of tRNA into the kinetoplast-mitochondrion

Mitochondrial (mt) dysfunction is associated with numerous disorders including aging. Mutations and deletions in mtDNA have been observed in these situations, but their relative contribution to a particular disorder is unknown, because of the lack of an efficient method for targeting of correctional nucleic acids to the organelle. In work done under the XI Plan Suprainstitutional Project on Evaluation and Correction of Mitochondrial Dysfunction in Disease, a major advance was made on the development of a novel protocol for mitochondrial gene therapy.

We investigated the ability of a multiprotein RNA transport complex derived from the protozoal parasite *Leishmania tropica* to deliver tagged RNAs of at least 6.7 kb to the mitochondria of cultured mammalian cells. As indicated by confocal microscopy and subcellular fractionation experiments, the ribonucleoprotein complex, after binding to the plasma membrane, was internalized in a membrane-bound compartment(s) and delivered within hours to the mitochondrial surface, following which the RNA was separated from the carrier and imported into the matrix. RNAs of various shapes and sizes were thus transported. Mitochondrial expression of tagged Green Fluorescent Protein (GFP) RNA, as well as of a polycistronic (pc) RNA1 transcript containing the COI, COII, COIII, ATP6/8, mttRNALys, mttRNASer and mttRNAAsp genes, was observed. pcRNA1 was rapidly processed to form polyadenylated mRNAs and aminoacylated mttRNAs. Additionally, the carrier complex, bound to the mitochondrial membrane, induced the import of several cytosolic tRNAs. The mRNAs were translated on membrane-bound ribosomes, resulting in assembly of active cytochrome c oxidase. Thus delivered, pcRNA1 boosted the respiration of a cybrid carrying a 1.9-kb mtDNA deletion from a patient with Kearns-Sayre syndrome. The findings have implications for therapeutic correction of mitochondrial mutations and for basic studies of mitochondrial.

Dr. Keya Chowdhury and group

***Host-Vibrio cholerae interaction*:**

Vibrio cholerae, the etiological agent of cholera, colonizes the small intestine, produces an enterotoxin and causes acute inflammatory response at intestinal epithelial surface. Chemotaxis and motility greatly influence the infectivity of *V. cholerae* although the role of chemotaxis genes in *V. cholerae* pathogenesis is less well understood. Four *cheY* genes are present in three clusters in the complete genome sequence of *V. cholerae*. A less motile and less adherent mutant was generated by inactivation of *cheY-3* (O395Y3N) or *cheY-4* (O395Y4N) whereas alterations in motility or adherence were not observed for *cheY-1* (O395Y1N) or *cheY-2* (O395Y2N) insertional mutants. In contrast to O395Y1N and O395Y2N, O395Y3N and O395Y4N showed reduced cholera toxin production compared to wild-type in vitro. Infection of the human intestinal epithelial cell line Int407 with O395Y3N and O395Y4N caused reduced secretion of interleukin (IL)-1a, IL-6, tumor necrosis factor (TNF-α) and monocyte chemotactic protein-1 (MCP-1) compared to wild-type and was associated with delayed activation of nuclear factor kappa B (NF-kappaB) p65 and its co-activator cAMP response element binding protein (CREB). Further, the absence of nuclear translocation of NF-kappaB p50 subunit upon infection with O395Y3N or O395Y4N and its reversal upon complementation indicates the involvement of *cheY-3* and *cheY-4* in *V. cholerae*-induced pro-inflammatory response in the INT407 cell line.

V. cholerae activates proinflammatory response in cultured intestinal epithelial cells. In another study, we have demonstrated that *V. cholerae* O395 infection of intestinal epithelial cells results in the activation of Akt. Inhibition of Akt significantly decreases IL-1α, IL-6, and TNF-alpha production in *V. cholerae* infected Int407 cells. Analysis of the mechanisms of Akt influences on cytokine response demonstrates that Akt promotes NF-κB activation. We have extended these findings to show that Akt activation may be regulated by bacterial genes associated with virulence, adherence, or motility. Insertion mutants in the virulence genes coding for CtxA, ToxT, and OmpU of *V. cholerae* modulate the activation of PI3K/Akt signaling pathway, whereas an aflagellate non-motile mutant (O395FLAN) and an adherent and less motile mutant (O395Y3N/O395Y4N) of *V. cholerae* both show very significant down-regulation of Akt activity in Int407 cells. Together, these observations indicate that Akt promotes proinflammatory cytokine production by *V. cholerae* infected human intestinal epithelial cells through its influences on NF-κB.

Bioinformatics studies: Analysis of tRNA composition and folding in psychrophilic, mesophilic and thermophilic genomes: indications for thermal adaptation

Comparative genomic studies on several thermophilic archaea and bacteria revealed that a set of coordinated changes are associated with organisms adapted to a higher temperature, among which the dinucleotide composition of genomic DNA, pattern of codon usage and amino acid composition of the proteomes reveal subtle differences between thermophilic and mesophilic organisms. In this context, we have analyzed all tRNA sequences present in the complete genome sequences of 57 organisms belonging to psychrophiles, meophiles, thermophiles and hyperthermophiles. The presence of distinct selective constraints was revealed in the number and distribution of tRNAs and in their folding patterns, which could be correlated with the optimal growth temperature. The tRNA contents of thermophiles were found to be significantly less compared with the two other groups, whereas the tRNA genes of thermophiles exhibit a much higher guanine plus cytosine content.Analysis of the entire data set revealed that tRNAs from thermophiles showed greater structural stability at higher temperatures compared with the other two groups. Repeated cluster analysis applied to two sets of data from tRNA folding, the free energy of folding (dG) and the melting temperature (Tm), indicated that the thermophiles always had a tendency to cluster together.

Isolation of Arsenic-resistant bacteria from arsenic-infested areas of West Bengal

An arsenic-resistant bacterium, strain KRPC10YT, was isolated from arsenic-infested bore-well of West Bengal, India. The bacterium was resistant to exceeding concentrations of arsenate (30 mM) and arsenite (20 mM).

The bacterium was Gram-positive, rod-shaped, motile and yellowish to orange-pigmented. The major fatty acids were anteiso-C15:0, iso-C15:0. The DNA G+C content was 49 mol %. Based on its phenotypic, chemotaxonomic and phylogenetic characteristics, it was identified as a member of the genus *Planococcus* and is the first known *Planococcus* resistant to arsenic. KRPC10YT was positive for indole, catalase, tolerated up to 12.0% NaCl and exhibited phenotypic differences with other type strains of genus *Planococcus*. Strain KRPC10YT thus could be a novel species of the genus *Planococcus*. The type strain is KRPC10YT (= MTCC 7758T, = JCM 13947T).

***Biology of Oral Cancer and precancer:*Repeat number variation in the promoter region of XRCC5 gene associated with increased susceptibility to oral cancer**

XRCC5 or Ku80 gene known for its various functions like role in DNA non homologous end joining (NHEJ) required for double-strand break repair, V(D)J recombination and telomere end capping is related to different cancers and autoimmune diseases. We have studied different polymorphisms in Ku80 gene present in normal Indian population and also their association with the disease phenotype in oral cancer and pre cancer patients. We prepared genomic DNA from the peripheral blood of Indian population and patients suffering from cancer and precancerous lesions and conditions. By use of PCR, we amplified the exons and flanking regions of the XRCC5 gene followed by sequencing to identify the nucleotide variants. We genotyped the SNPs in 1871 individuals (normal population) by use of the Sequenom mass array system. We made linkage disequilibrium plots using Haploview software. In addition to SNPs, a novel variation in repeat number at the promoter region [-267 to -120] of Ku80 gene has been found to be particularly important for the predisposition of oral cancer. The repeat sequence is composed of a near perfect palindrome of 21 bps repeated 5, 6, 7 or 8 times with small base changes and controls sp1 binding dependent Ku80 expression level. We have found that increase in repeat number is a risk factor. Repeat number 5 is protective and higher repeat number 7 is associated with increased risk of oral cancer. Possible functional consequences of repeat number variation will be studied in future.

Dr. Kunal Ray & group

Molecular Genetic Studies on Human Diseases

A few genetic diseases that are common in India are being studied. These are eye disorders (primary open angle glaucoma, POAG & oculocutaneous albinism, OCA), neurological disorders (Wilson disease & Parkinson's disease), and bleeding disorder (Haemophilia). The intent of the study is to understand the molecular basis of these diseases.

Eye Disorders: We are interested to understand the molecular bases of (a) primary open angle glaucoma (POAG), a major cause of restricted vision and blindness worldwide; and (b) Oculo-cutaneous albinism (OCA) an inherited disorder characterized by deficient synthesis of melanin pigment affecting skin, hair and eye.

(a) Glaucoma is a heterogeneous group of optic neuropathies with a complex genetic basis. Primary Open Angle Glaucoma (POAG) is the most common form of the disease, affecting 33 million people worldwide, where loss of vision is progressive and often silent. In POAG, characteristic acquired loss of retinal ganglion cells (RGC) and atrophy of the optic nerve have been observed. The tissue hypoxia found in glaucomatous retina can potentially give rise to excessive generation of free radical, known to cause mitochondrial dysfunction. This free radical injury constitutes a caspase independent mitochondrial cell death pathway in RGCs. Recent evidences revealed a spectrum of mitochondrial abnormalities in patients with POAG, implicating oxidative stress in POAG. Thus, mitochondria dysfunction being a risk factor for POAG could open up new experimental and therapeutic opportunities. We are investigating alterations in mitochondrial genes and proteins in primary open angle glaucoma (POAG), using POAG DNA samples and ocular cell models. We have collected blood samples from 150 primary open angle glaucoma patients and 100 control subjects with detail clinical

characterization. The Phase I data, that is 48 patients and 48 controls is being analyzed which led to identification of a few rare variants in patients along with some polymorphisms in both patients and controls using a software SNPscore, developed by CSIR scientist at IGIB, which scores each variants based on its functional impact. The study is in progress to decipher the changes identified.

(b) OCA is one of the major causes of childhood blindness in India. Our observations suggest that among Indian OCA patients Tyrosinase defect is responsible for the disorder in >50% cases. Nonsynonymous mutations identified in our OCA cohort were introduced in normal TYR cDNA clone by site-directed mutagenesis, expressed in HEK293 cells and their enzymatic activities (both tyrosine-hydroxylase and DOPA-oxidase) were measured. The mutant proteins were assayed by western blot and compared with the wild type. The processing defect of TYR mutants at the subcellular level were explored by immunohistochemical studies with appropriate ER and Golgi markers. Biochemical assays revealed that, compared to the wildtype protein, all the mutants were almost devoid of any enzymatic activity. However, western blot analysis detected similar protein levels in wildtype as well as mutants. Immunohistochemical studies suggested ER retention of three TYR mutants.

Neurological Disorders: Among neurological disorders studies on (a) Wilson's disease (WD), (b) Parkinson's disease (PD) and (c) dystonia is being carried out. The focus of the study is to identify the molecular basis of the disease among Indians. The studies are conducted in collaboration with Bangur Institute of Neurology & Psychiatry for clinical areas of the study. While our group is focused primarily on Wilson disease, studies on PD and dystonia are done in collaboration with the Prof. Jharna Ray (SN Pradhan Centre of Neurosciences, Calcutta University).

(a) Wilson's disease is an inborn error of copper metabolism due to mutation in the copper-transporting gene *ATP7B* and characterized by excessive copper deposition predominantly in the liver and brain. Symptoms of WD can be reversed and the quality of life may improve if detected at a presymptomatic stage. We have over 200 unrelated patients in our cohort which contains patient samples largely from eastern India and some from western India. We are analyzing markers in the affected families and screening for defects in the causal gene (*ATP7B*) in patients to identify the carriers of mutant allele. In addition we are studying other genes in copper homeostasis pathway as potential modifier loci in an attempt to genotype-phenotype correlation.

(b) Parkinson's disease (PD) is the second most common neurodegenerative disorder. The prevalence of PD varies significantly around the world. A recent study on a heterogeneous population from Kolkata has recorded a prevalence rate of Parkinsonism to be 3.3 per 1000 for subjects above 60 years of age. There is evidence that genetic factors also play a major role in the etiology of some cases of PD. We are studying the underlying genetic variants in the potential candidate genes for association with PD as mentioned below:

We identified mutations in PINK1 in familial and sporadic cases of early onset Parkinson's disease (PD). To our knowledge it is the first report on molecular genetic studies on Indian PD using PINK1 as a candidate gene. To determine the contribution of PINK1 variants in Indian PD patients, the gene was screened in 250 patients and 205 ethnically matched controls. Two potentially pathogenic variants (Arg246Gln & Arg276Gln) were detected in the heterozygous state in 5 patients; none of the patients carried homozygous or compound heterozygous mutations. In addition, 13 other variants were identified, including a known polymorphism (Ala340Thr), a few synonymous or intronic changes, none of which are likely to be pathogenic. Unlike the Chinese population, the Ala340Thr variant did not show any association with PD in Indian population. Six single nucleotide polymorphisms (SNPs) selected from dbSNP were genotyped in 531 normal, healthy individuals representing different ethnic groups of India. Most of the SNP markers were observed to be highly heterozygous among Indians, which could be used for segregation analysis of PINK1 alleles in familial PD cases.

In addition, microtubule-associated protein tau (MAPT), a neuronal protein is involved in the pathogenesis of several neurodegenerative diseases including PD. To determine the broader significance of this association with PD, replicative studies in distinct ethnic populations are required. In this study, we investigated *MAPT* for its potential association with PD using five haplotype-tagging SNPs and the *del-In9* polymorphism of *MAPT* in PD patients and healthy controls from eastern India. Our case–control analysis did not show a significant

association with any of the markers and PD. However, a risk haplotype [GAC +G] for PD was identified. In addition, haplotype AAC +A was strongly associated with early onset PD (age at onset≤40 years). This is the first association study from India conducted on *MAPT* among PD patients and provides valuable information for comparison with other ethnic groups.

Bleeding disorder: Currently our lab is engaged in molecular genetic studies on Haemophilia. This X-linked disease is caused independently by defects in Factor VIII and Factor IX genes resulting in Haemophilia A and Haemophilia B, respectively. Usually females carry and males are affected with the disease. At present the most practical approach to contain haemophilia relates to strategies for carrier detection and prenatal diagnosis. We are investigating to identify a set of common informative markers for efficient carrier detection. Also, studies are in progress to determine functional aberration of mutant factor IX protein causing haemophilia B.

Dr. A. K. Giri & group

Genetic variants are expected to play an important role in arsenic susceptibility, as only 15 -20% of exposed individuals develop arsenic-induced skin lesions. A case-control study was conducted in West Bengal, India, involving 206 cases with arsenic-induced skin lesions and 215 controls without arsenic-induced skin lesions. Data revealed that possession of at least one Met allele (Met/Met and Thr/Met) imparts significant protection towards the development of arsenic-induced skin lesions. A significant correlation was observed between protective genotype and decreased frequencies of chromosomal aberrations. The genotype-phenotype correlation data also suggest that presence of Met allele even at single dose is sufficient enough to provide protection towards arsenic-related peripheral neuropathy and conjunctivitis, further strengthening the plausible protective role of the variant allele towards arsenicism. We have also studied the polymophrisms in the promoter regions of the cytokine genes to find out whether polymorphisms in the cytokines genes could contribute to arsenic susceptibility. We had found that -308 G>A SNP in the TNF-α gene promoter and -3573 T>A polymorphism in the IL10 gene promoter contributed significantly to arsenic susceptibility.

In our recent study, we looked into the effects of chronic arsenic exposure on the macrophages which happen to be one of the most important components of our immune defense system. In macrophages of exposed individuals when compared to unexposed group, there was cell rounding accompanied with a significant loss of cell adhesion capacity, decrease in nitric oxide production, impaired phagocytic capacity and decreased CD54 and F-actin expression. Additionally chronic arsenic exposure affected RhoA-ROCK pathway which in turn impaired macrophage functions. These altogether could contribute significantly to arsenic-induced immunosupression observed in the arsenic exposed individuals.

Antimutagenic and Anticancer Activities of Black Tea Polyphenols Theaflavins and Thearubigins and the Fractions of Thearubigins.

Tea (*Camellia sinensis*), the second most popular beverage in the world constituted with different polyphenols exerts its potent anticancerous activity, which appears to be an ideal agent for chemoprevention. During the fermentation process, tea catechins are polymerized by polyphenols oxidase (released from crushed tea-leaves) to form theaflavins (TF) and thearubigins (TR). Earlier we have found that TF and TR can inhibit proliferation of A375 and A431 cells in dose dependent manner. Significant inhibition of cell proliferation was observed in case of A375 cells after treatment. In this cell line our compounds have induced higher expression of proapoptotic protein Bax and have hindered the expression of antiapoptotic protein Bcl2, which indicates these two compounds are able to induce apoptotic signals in human malignant melanoma cells. We have observed that TF and TR treatment can inhibit the kinetics of cell cycle in A375 cells. To study the molecular mechanism of this event we examined the expression level of two proteins viz. p53 and p21 and found that these two proteins play a significant role in induction of growth inhibition in the selected cell line. The loss of mitochondrial membrane potential (MMP) is a hallmark for apoptosis. It is an early event preceding phosphotidylserine externalization and coinciding with caspases activation. So we next determined the loss of MMP after the treatment of TF and TR. All those observations indicated that TF and TR can work against human skin cancer by inducing

apoptogenic signals via mitochondria mediated pathway. Further we have found that activation of JNK and p38 is dependent on the production of intracellular ROS. ASK1 protein is playing a key regulatory role in ROS induced activation of JNK and p38 which are acting upstream of the mitochondria-mediated death cascade in A375 cell.

Arsenic-attributable risks from exposure through rice:

It has been found that rice was the most important exposure route for areas with low or no arsenic in drinking water in a study conducted over the arsenic exposed population of Chakdha in our UKIERI funded PRAMA project. Bearing this in mind our key objective was to collect rice samples from contrasting areas with both high and low arsenic in and determine the relative risks attributable from water and rice intake. For the exposure assessment study raw and cooked rice samples along with drinking and/or cooking water samples were collected from Bhawangola-I block of Murshidabad district, Chakdha block of Nadia district and Khejuri-I block of Midnapur district and analysed at the University of Manchester. The risk from rice intake was assessed using the USEPA One hit model.

The arsenic concentration in cooking and drinking water of Murshidabad district is significantly higher than that of Nadia district while there is no significant difference in the raw rice concentrations between the two areas. Results show that rice is a major potential source of arsenic exposure when arsenic concentration in drinking water is low as in Chakdha block while drinking water is the dominant exposure route as long as arsenic concentration in it is high as in Bhawangola I block of Murshidabad district.

Dr. Susanta Roychowdhury and group

The Spindle Assembly Checkpoint (SAC) is one of the surveillance mechanisms that protect cells from genomic instability and prevents mis- Transcrpitional control of spindle assembly checkpoint genes:

Segregation of chromosomes during mitosis and meiosis. It is executed by the Bub-Mad group of proteins which prevents ubiquitin (Ub) -mediated degradation of regulators of sister chromatid cohesion by Anaphase Promoting Complex (APC/C). This pathway involves the *Mad1, Mad2, Mad3, Bub1, Bub3, BubR1, CDC20* and *Mps1* gene products. Defects in the spindle assembly checkpoint are thought to be responsible for an increased rate of aneuploidization during tumorigenesis.

CDC20 is a critical molecule in the SAC. It activates the APC/C and helps a dividing cell to proceed towards Anaphase. CDC20 is overexpressed in many tumor cells which cause chromosomal instability. There have been limited reports on the mechanism of SAC's response to genotoxic stress. We show that ectopically expressed p53 or DNA damage induced endogenous p53 can downregulate Cdc20 transcriptionally. We have identified a consensus p53-binding site on the Cdc20 promoter and have shown that it is being used by p53 to bind the promoter and bring about chromatin remodeling thereby repressing Cdc20 (Fig.). Additionally, p53 also downregulates Cdc20 promoter through CDE/CHR element, but in a p21 independent manner. This CDE/CHR element-mediated downregulation occurs only under p53 overexpressed condition but not in the context of DNA damage. The present results suggest that the two CCAAT elements in the Cdc20 promoter are not used by p53 to downregulate its activity, as reported earlier.

Deciphering host-susceptibility to Helicobacter pylori associated human diseases:

It is important to dissect the effect of the alternative alleles of a functional SNP on the entire biochemical pathway for the complete understanding of the mechanism of the manifestation of complex diseases. IL1β-511C>T and -31C>T promoter polymorphisms have been suggested as potential susceptibility loci for *Helicobacter pylori* associated gastroduodenal diseases. We report that altered expression of IL1β due to a specific

polymorphism in its promoter modulates the expression of gastrin, an acid regulating hormone. Treatment of gastric carcinoma cells, AGS, with IL1β resulted in a 20-fold reduction in gastrin expression. Gastrin promoter assay showed that IL1β inhibits gastrin expression at the transcriptional level and part of this inhibitory process is mediated via activation of NFκβ and involvement of HDACs. An almost 3-fold increase in IL1β expression was observed when AGS cells were transfected with -31TIL1β expression plasmid in comparison to -31CIL1β. The -31TIL1β induced a 2-fold greater repression of the gastrin luciferase activity compared to -31CIL1β. This signaling of the -31TIL1β variant allele driven IL1β revealed an almost 1.5-fold greater expression of NFκβ. Thus, this study showed that a single base substitution at the -31 position of the IL1β promoter brought about differential expression of IL1β which differentially altered both NFκβ activation and gastrin expression.

Dr. Suvendra Nath Bhattacharyya and group

MiRNAs are ~21-nt-long regulatory RNAs expressed in eukaryotes. Expression of many miRNAs is tissue or development stage specific and major changes in miRNA expression are observed in human pathologies. MiRNAs regulate gene expression post-transcriptionally, by imperfectly base-pairing to 3'UTR of mRNAs, what results in translational repression or mRNA degradation. Repressed mRNAs are localized to P-bodies, cellular structures involved in storage and degradation of mRNAs. Present data provided evidence that P-bodies function in storage of miRNA-repressed mRNAs and demonstrated that miRNA-mediated repression is a reversible process. Decipher the mechanism of miRNA-mediated gene regulation process in mammalian cells is one of the target of our research group.

Mecanism of miRNA mediated gene regulation in mammalian cells:

We have used HeLa cells cultured to different cell density in 2-D culture. Density of the cells in a culture can alter cellular microenvironment and affects gene expression. Non-transformed and contact inhibited mammalian cells cease to proliferate while cancerous or transformed cells continue to proliferate after reaching confluence state. Interestingly miRNA-122 level in transformed liver cells and in liver tumors is significantly lower than primary hepatic cells. It has been hypothesized that miRNAs regulate number of oncogenes in non-proliferating cells. It would be very interesting to know how miRNA level and activity changes with cell density. To test the effects the cellular density on miRNA expression, hepatoma cells Huh7 which express miR-122 were cultured to different confluency and level of miRNA was measured. The miRNA-122 found to be upregulated in cell culture to high density. Interestingly the upregulation of miRNA with cell density is a post-transcriptionally regulated process and miRNA precursor level does not alter with cell density. Interestingly, similar observations have been documented in HeLa cells for another miRNA let-7.

Interestingly, we have observed that miRNA becoming more stable with cell density in cell culture. Additionally we observed that the increased miRNA level did not reflect in higher miRNA activity in confluent cells. We speculate that the increased miRNA level is due to low turnover of miRNA engaged in translation repression in confluent cells. We have performed experiments to test miRNA half life and our data suggest that miRNA level showed a rapid decrease in non confluent cells than what in confluent cells in presence of transcription inhibitor. Interestingly localization of miRNP to P-bodies gets impaired in confluent cells with a reduction in P-body number in mammalian cells. That can account for low efficiency of repression level in cells grown to higher confluence (Fig.1 and 2).

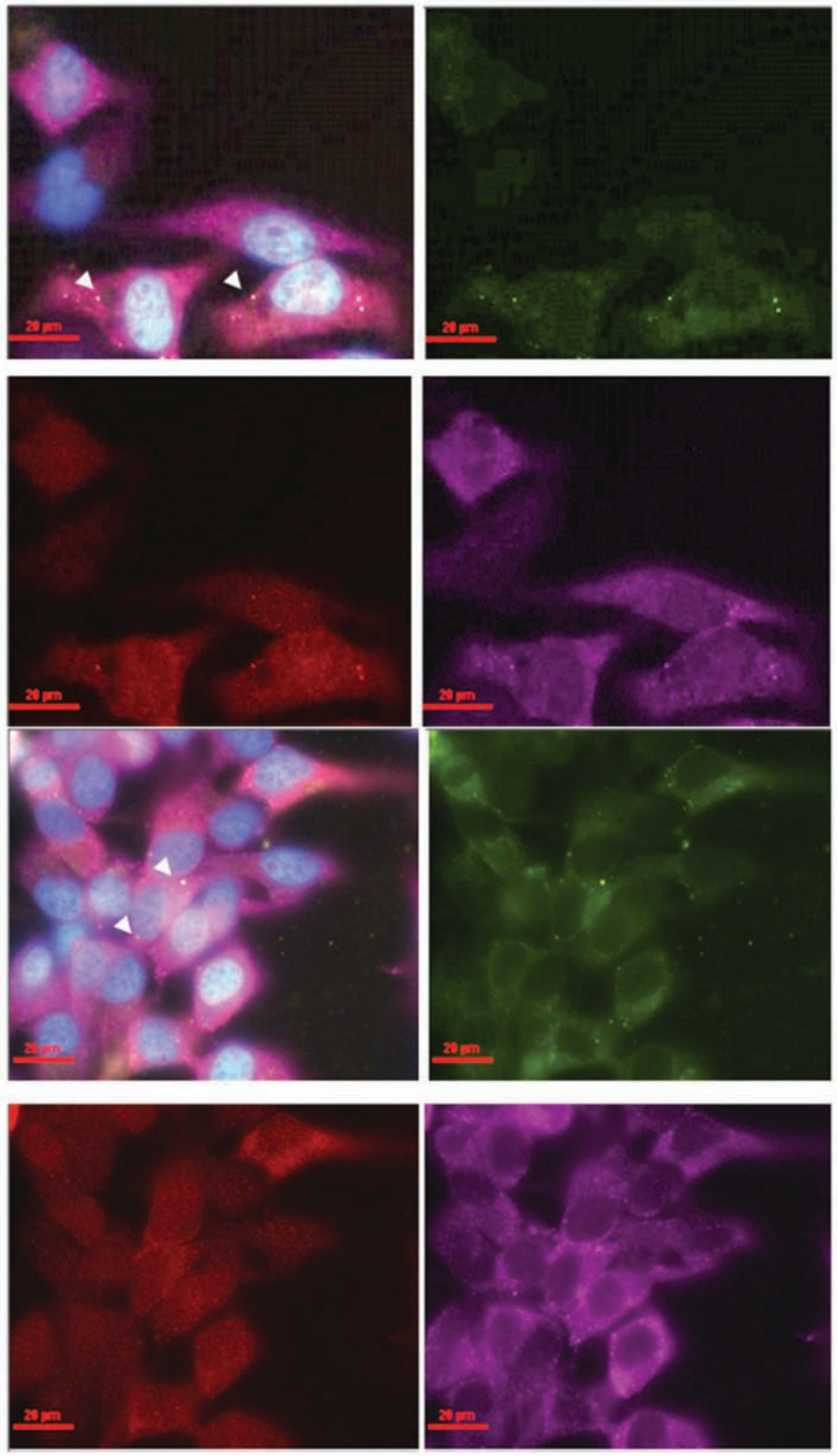

Figure 1. Effect of cell confluency on P-bodies. Impaired localization of Ago protein in HeLa cells co-transfected with GFP-Dcp1a (green) and Myc-Ago2 (Red) constructs. The P body structures were observed with specific antibodies against c-Myc (Santa Cruz) and endogenous Xrn1 (purple). Nucleus is shown in blue (DAPI). P-bodies are marked by white arrowhead showing colocalization of Xrn1 and GFP-Dcp1. Upper four panels are for cells from sub confluent culture while cells grown at higher confluency are shown in the lower four panels.

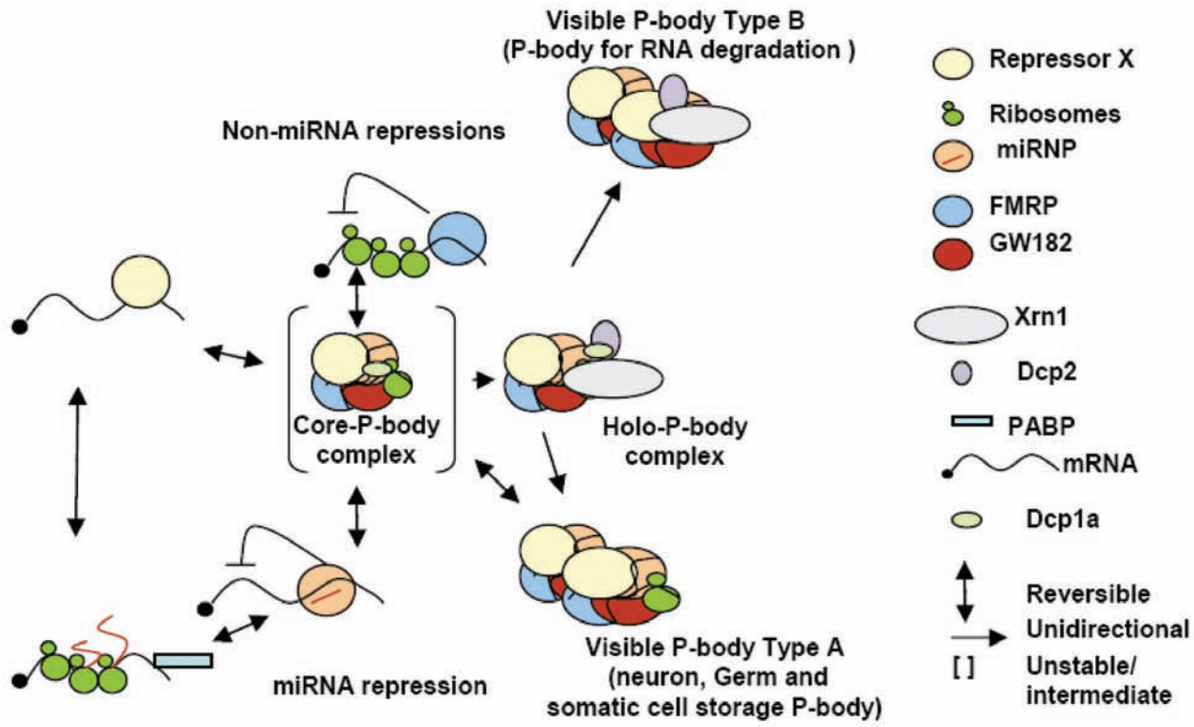

Fig. 2. A model of stepwise formation of P-bodies in mammalian cells. According to this model, translational repression by a miRNA-dependent or independent mechanism can reversibly forms core-P-body complexes that by interacting RNA catabolizing proteins generate holo-P-body complexes. Holo-P-body formation can leads to appearance of visible P-bodies. Alternatively core-P-bodies may also form visible RNA storage granules or a separate types of P-bodies in somatic or germ cells and also in neurons.

3-D and co-culture of hepatic cells and its effect on miRNA activity

We are using hydrogel that provide flexibility to culture cells in 3-D. This has been the attractive models to test the effects of microenvironment. It has advantages over the animal model due to its flexibility for genetic manipulation and biochemical studies. Stable transfectants of human hepatoma cells Huh7 expressing miR-122 reporter mRNAs has been generated and are now being used to establish a 3-D culture of Huh7 cells using hydrogel and had been used to test the effect of different ECM components (laminins, collagens and fibronectins in combinations) in a 3-D context on cell growth and peoliferation. We have found that Huh7 cells are growing to form colonies when grown in gel using Matrigel. Reciprocally, Huh7 on gel growth on Matrigel does not result colony formation and estimation of miRNA suggest changes in miRNA activity under these two different growth conditions. We are exploring the mechanism of this phenomenon.

Effect of Leishmania donovani infection on miRNA activity in mammalian macrophage:

To study the effects of microenvironment composed of parasite infected macrophages on gene expression in neighboring mammalian cell, we have planned to use Leishmania donovani infection of macrophage as model system. Leishmania donovani is a protozoan parasite cause visceral Leishmaniasis in human. We have established the conditions of co-culture of infected macrophage with non-infected cells and doing subsequent isolation of RNA from non-infected cells to perform gene expression analysis and miRNA profiling. Interestingly after Leishmania infection miRNA let-7 showed increased level in Leishmania infected mammalian macrophage.

The importance of miRNA activity changes in Leishmania infected macrophage is not apparent. We are currently investigating that aspect.

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DRUG DEVELOPMENT, DIAGNOSTICS & BIOTECHNOLOGY

Drs. Tarun Kumar Dhar, Anil Ghosh, Nirmalendu Das, Aparna Gomes, Pratap K. Das, Suman Khowala, Samir Kr. Dutta, Sharmila Chattopadhyay, Snehasikta Swarnakar

Bioactive molecules from natural sources are well known for their therapeutic, diagnostic and industrial importance. This group is involved in studies on bioactive compounds for improving health and quality of life, as also for promoting future economic growth through innovation in biotechnology. The major field of activity includes – isolation of lead bioactive compounds from plants microbe or venom for useful pharmacological activity; mechanism of gastric ulceration; engineer plant genes for improved production of pharmaceuticals / nutraceuticales; immunoconjugate preparation strategies; nanocapsulated drug delivery in combating cerebral oxidative damage; molecular mechanisms of trehalose metabolism and microbial gycosidase enzymes.

Dr. (Mrs.) Aparna Gomes and group.

Development of drugs from plant materials, animal products and synthetic agents

The main objective is to identify and develop new antihyperglycemic, antineoplastic, prokinetic, anti-inflammatory and antioxidant agents.

Studies with Scorpion venom

Scorpion venom possesses protein toxins having numerous biological activities, some of which are potentially anticancerous. Previously we had reported antiproliferative activity of the venom of Indian black scorpion, *Heterometrus bengalensis* Koch. Here we have isolated and purified a novel protein named Bengalin (72kD) from the venom, responsible for antiproliferative and apoptogenic activities against human leukemic cells U937 (histiocytic lymphoma) and K562 (chronic myelogenous leukemia). N-terminal sequence of first 20 amino acids of Bengalin was G-P-L-T-I-L-H-I-N-D-V-H-A-A/R-F-E-Q/G-F/G-N-T. Bengalin induced cell growth inhibition at IC50 values of 3.7μg/ml and 4.1μg/ml for U937 and K562 cells respectively did not significantly affect normal human lymphocytes. Inhibition of U937 and K562 cell proliferation occurred by apoptosis as evidenced from damaged nuclei, cell cycle arrest at sub G1 phase, increase of early apoptotic cells, augmentation of DNA fragmentation and also a reduction of telomerase activity. Further insights revealed that Bax:Bcl2 ratio was elevated after Bengalin treatment. Moreover Bengalin elicited loss of mitochondrial membrane potential (MMP) which commenced cytochrome c release in cytosol, decreased heat shock protein (HSP) 70 and 90 expression, activated caspase-9, caspase-3 and induced poly (ADP-ribose) polymerase (PARP) cleavage (Fig. 1 & 2). We have also determined that HSP70 and 90 inhibitions correlated with Bengalin induced antiproliferation, caspase-3 upregulation, apoptogenesis and increased DNA fragmentation. These results hypothesize that Bengalin might provide a putative molecular mechanism for their anticancer effect on human leukemic cells which might be mediated by mitochondrial death cascade. Inhibition of HSPs might also play a crucial role in induction of apoptosis.

Studies with arial parts of Corchorus acutangulus Lam

In the present study, the anti-leukemic activity of the methanol extract of aerial parts (ME) of *C. acutangulus* has been investigated, and efforts have been made to identify the active ingredient responsible for this activity. The anti-leukemic activity of ME, its fractions and corchorusin-D (COR-D), the active ingredient, was investigated in leukemic cell lines U937 and HL-60 using cell viability and MTT assays. The molecular pathways leading to the activity of COR-D were examined by confocal microscopy, flow-cytometry, caspase and Western blot assays. ME, its n-butanolic fraction and COR-D inhibited cell growth and produced significant cytotoxicity

in leukemic cell lines U937 and HL-60. COR-D produced apoptotic cell death via mitochondrial disfunction and was found to pursue the intrinsic pathway by inciting the release of apoptosis-inducing factors (AIFs) from mitochondria. COR-D-induced translocation of Bax from cytosol to mitochondria facilitating caspase-9 activation and up regulation of downstream pathways leading to caspase-3 activation and PARP cleavage, which resulted in the subsequent accumulation of cells in the sub-G0 phase followed by DNA fragmentation. COR-D possesses

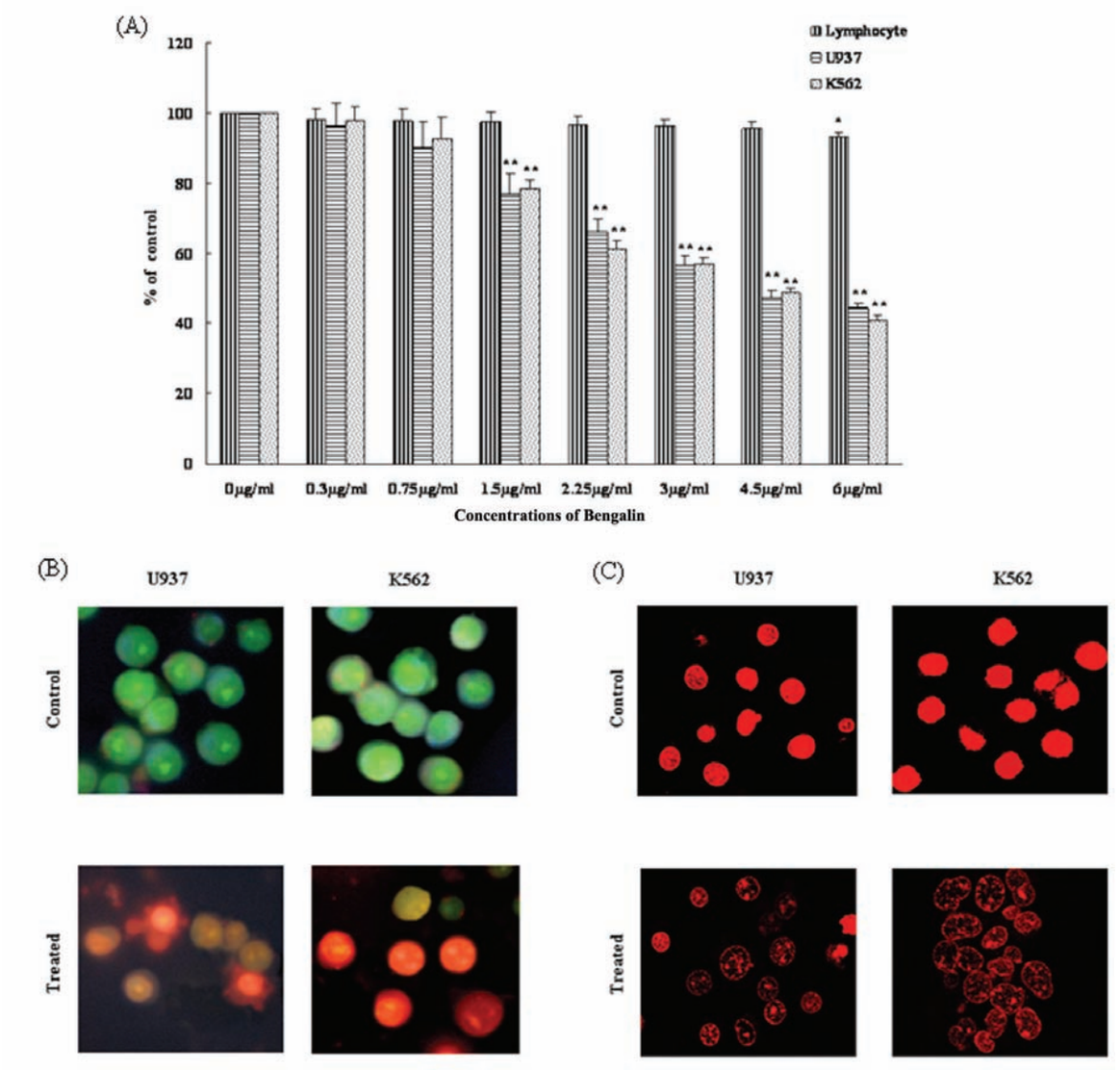


Fig. 1. Effects of Bengalin on the viability of normal human lymphocytes, U937 and K562 cells and representative fluorescence and confocal micrograph of Bengalin induced apoptotic cells. (A) Bengalin treatments were done for 48 h in U937 cells at 1.85 and 3.7μg/ml while K562 cells at 2.05 and 4.1μg/ml, respectively. Changes in cell viability were measured by MTT assay. Each value is expressed as mean±S.D. (n = 3). *$p < 0.05$ and **$p < 0.01$ are the Bengalin treated groups compared to the control (0μg/ml). (B) Bengalin treatments were done for 24 h in U937 cells at 1.85 and 3.7μg/ml while K562 cells at 2.05 and 4.1μg/ml respectively and morphology observed under fluorescence microscope using AO/EtBr (100× magnification). Representative figures are the U937 and K562 cells treated at 3.7 and 4.1μg/ml of Bengalin, respectively. (C) After treatment with Bengalin at respective cells were seen under a confocal microscope using PI (1000× magnification). Representative figures are the U937 and K562 cells treated with Bengalin at 3.7 and 4.1μg/ml, respectively. Data shown here are from one of the three repeated experiments with similar results.

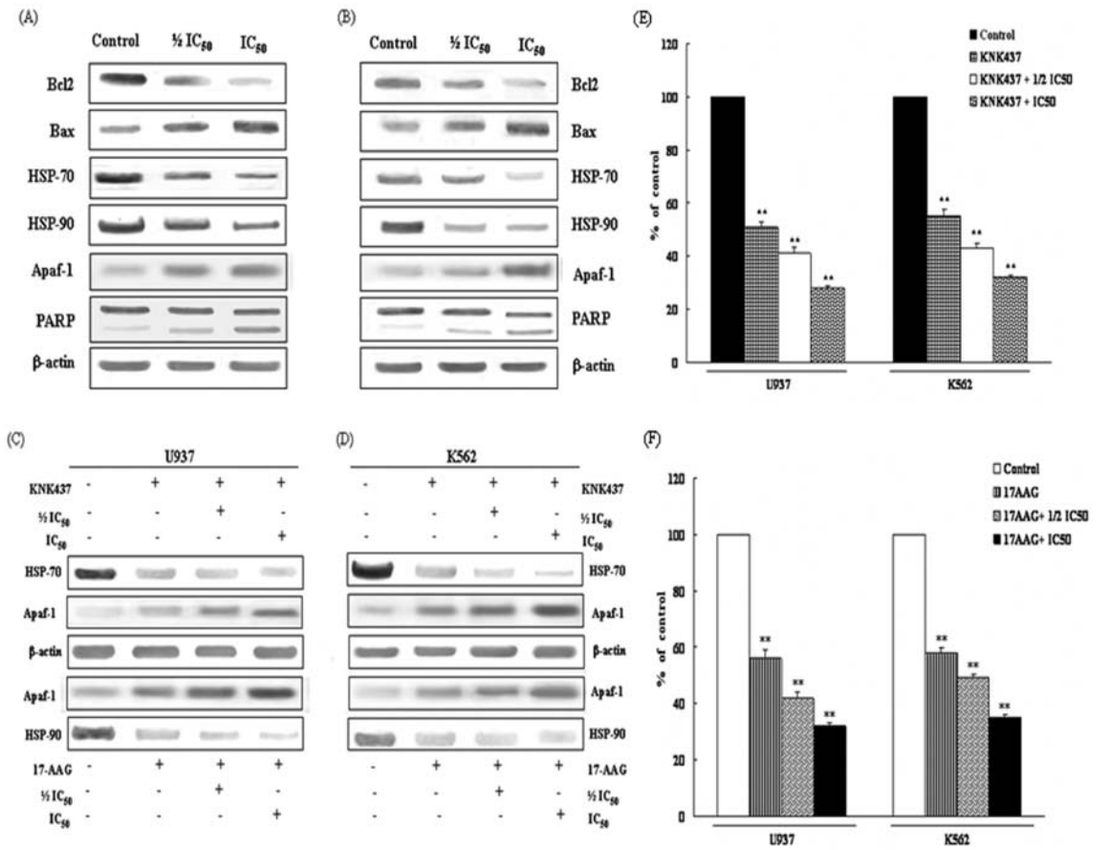


Fig. 2. Effect of Bengalin on apoptosis associated proteins and cell proliferations in presence or absence of HSP inhibitors. (A and B) Bengalin treatment was done for 24 h in U937 cells at 1.85 and 3.7µg/ml and K562 cells at 2.05 and 4.1µg/ml. Protein from the total cell lysate was subjected to SDS-PAGE and western blot using Bcl2, Bax, PARP, HSP70, HSP90, Apaf-1 and β-actin antibody. Representative blots from three independent experiments gave identical results. (C and D) U937 and K562 cells were incubated with KNK437 (100µM) or 17AAG (500 nM) alone or in combination with Bengalin for 24 h. The blot was incubated with primary HSP70, HSP90 and β-actin antibodies. Representative blots from three different experiments showed identical results. The relative intensity of each band was measured after normalization with the intensity of β-actin in a blot (given below each Western blot). Here control served as group with no Bengalin treatment. (E and F) U937 and K562 cells were treated with KNK437 or 17AAG alone or in combination with Bengalin for 48 h. MTT assay was performed to detect the inhibition of cell proliferation. Each value is expressed as mean±S.D (n = 3). **p < 0.01 are the Bengalin treated groups as compared to control (0µg/ml of Bengalin).

significant anti-leukemic activity in U937 and HL-60 cell lines by acting on the mitochondrial apoptotic pathways. Since the necrotic body formation is low after COR-D treatment, the occurrence of inflammation in in vivo systems could be reduced, which represents a positive indication in view of therapeutic application.

Studies with leaves of Litchi chinensis

The aqueous methanolic extract of leaves of Litchi chinensis was evaluated experimentally for its in-vivo anti-cancer/tumor activity .The aqueous methanolic leaf extract Litchi-chinensis (LCLE) was produced significant anti-tumor effect in 3-methylcholanthrene (3MC) induced solid tumor model in mice (Fig. 3). The estimation of tumor weight and biochemical parameters in serum and liver was studied. Tumor growth was markedly reduced in the LCLE and 5-FU treated mice compared to that of the untreated control mice and biochemical parameters also suggest that treatment with LCLE produces anti-carcinogenic activity against 3-MC induced solid tumor model in mice by maintaining the appropriate balance between free radical production and accumulation and free radical scavenging property.

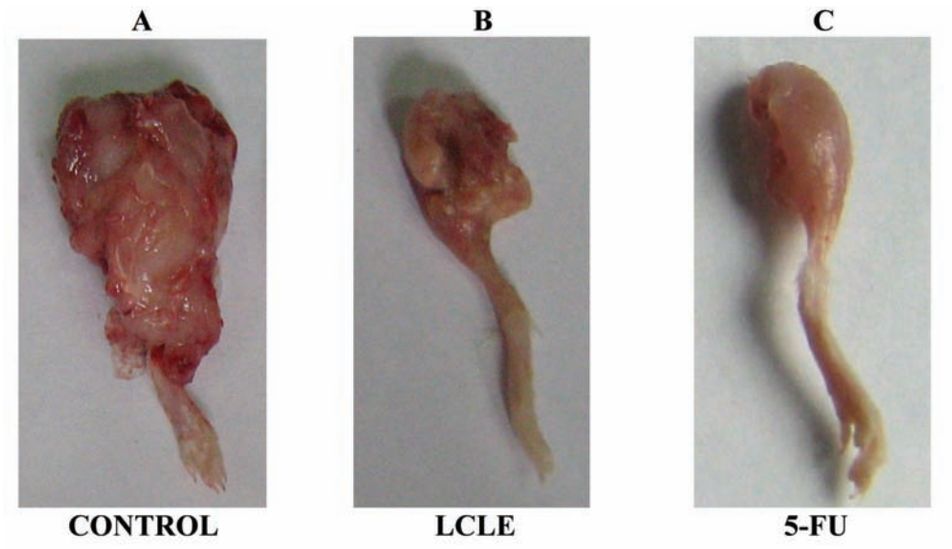


Fig. 3. 3-MC induced solid tumor bearing, (A) untreated control mouse, (B) LCLE (100 mg/kg) treated mouse, (C) 5-FU(5 mg/kg) treated mouse. The solid tumors are dissected out from calf muscle of respective animals.

Dr. Pratap K. Das and group

Screening of Indian biodiversity and Indian Systems of medicine for anti gastric ulcer principle(s)

The central objective of this research has been to develop appropriate strategy and protocol(s) for effective screening of Indian biodiversity with a view to examining their efficacy against peptic ulcer diseases in preclinical experimental models. Two of the major etiologies, namely the acid HCl and the bug *H. pylori*, are being targeted for lead discovery. Large-scale screening followed by revalidation experiments generates identified leads for further investigations around drug discovery. During the period under consideration, we have screened about 1400 samples of plant, bacterial and fungal origin, and a few single molecules of natural product origin in gastric antisecretory and anti-*H. pylori* models. Two anti-*H. pylori* samples obtained through screening during preceeding year were revalidated for future consideration.

During screening, the leaf extract of the plant *Tricosanthes dioica* exhibited gastric antisecretory potential. Since this plant and its aerial parts have traditional use in various stomach ailments, it was of interest to investigate this observation in further details. When examined in Ussing chamber model using alcoholic, hydroalcoholic and aqueous extracts and their fractions, the water extract and its aqueous fraction showed greater activity. Both inhibited basal acid secretion to some extent, dose-dependently inhibited histamine-stimulated acid secretion significantly, and were also effective against pentagastrin- and forskolin-stimulated acid secretion (Figs. 4&5).

The flowers of the plant *Woodfordia fruticosa* demonstrated both gastric antisecretory as well as anti-*H. pyloi* activity. The active principle isolated through bio-assay-guided fractionations (Fig. 6) helped delineate such contention through series of experimental evidence. The structure of the lead molecule was elucidated to be a monomeric ellagitannin, oenothein C, which showed very strong gastric anti proton pump activity and specific anti-*H. pylori* activity. Since the yield of the active molecule through isolation is painstakingly low, and since the complexity of the compound is beyond the scope of commercially viable synthetic strategy, we have developed an enriched herbal extract according to WHO guidelines for clinical trial and commercialization (ICB-014-P04-A002). Simultaneously, we are working on building structural analogues of the isolated molecules, an ellagitannin, so as to bring out New Chemical Entities (NCEs) that could be synthesized as commercially viable Active Pharmaceutical Ingredient (API). NCEs are being synthesized based on the furanose and pyranose sugar structures using di-, tri and poly hydroxylated aryl methanols and acids, and small ring heterocycles around

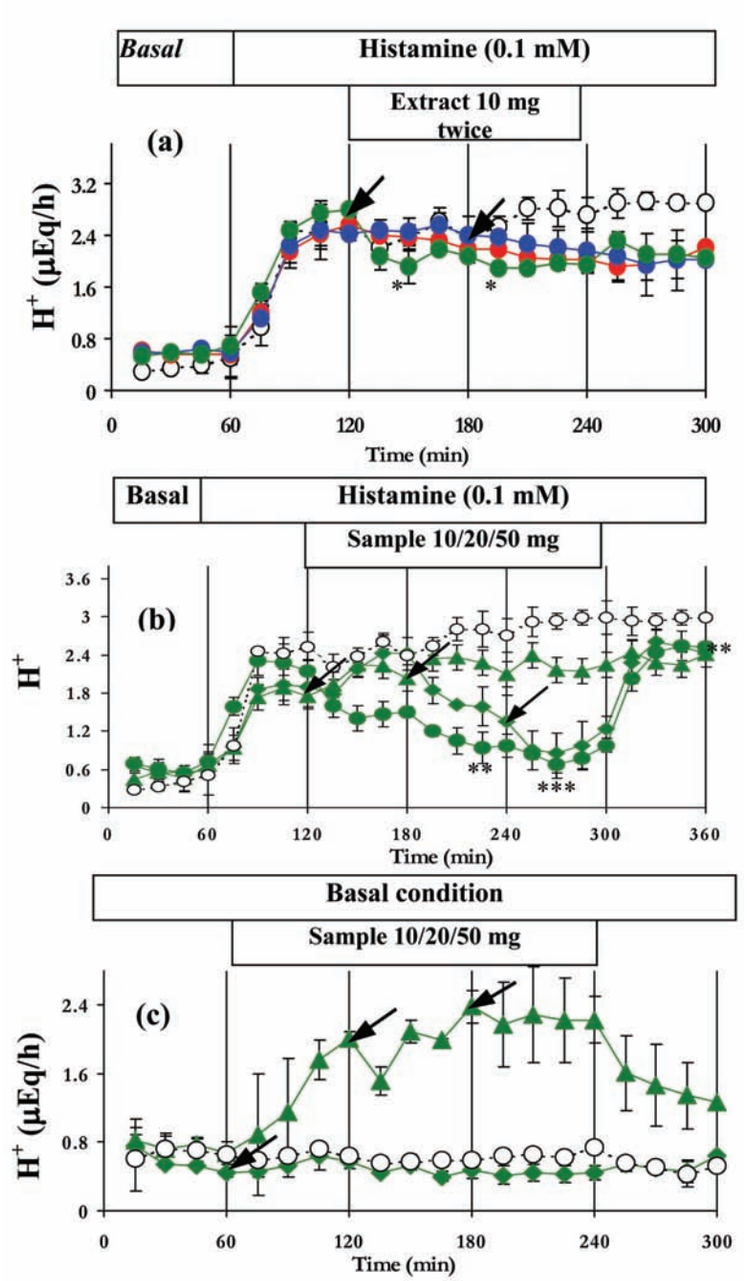


Fig. 4. Gastric antisecretory activity of alcoholic, hydroalcoholic and aqueous extracts of the leaves of *Trichosanthes dioica*. The rate and extent of proton secretion in the presence of different extracts are shown by symbols: alcoholic (-•-), hydroalcoholic (-•-), aqueous (-•-) and control (-o-). Arrows indicate the time point of addition of the samples in individual chambers. Panel a represents the effects of three extracts on the histamine-stimulated acid secretion. The data are mean ± SEM (n = 6, 3, 3 and 4 respectively for control, alcoholic, hydroalcoholic and aqueous extracts). The asterisks indicate statistically significant difference from the maximum stimulated value (*p<0.005). Panel b represents dose-response profile of the aqueous extract (-•-) and its *n*-butanol (-▲-) and water (-◆-) fractions on histamine-stimulated acid secretion. The data are mean ± SEM (n = 4, 2, 2 and 4 respectively for control, *n*-butanol and water fractions, and aqueous extract). The asterisks indicate statistically significant difference from the maximum stimulated values (**p≤ 0.001, **p≤0.0001). Panel c exhibits dose-dependent effect of the fractions on basal acid secretion. The data in panel c are presented as mean ± SEM (n = 2 for both the fractions).

the sugar core structure with or without the aryl groups to create diversity. This latter part of the investigation is being carried out in collaboration with Dr. GVM Sharma and his group at IICT, Hyderabad. A patent for the herbal extract has been secured and another one for the molecule is now under examination.

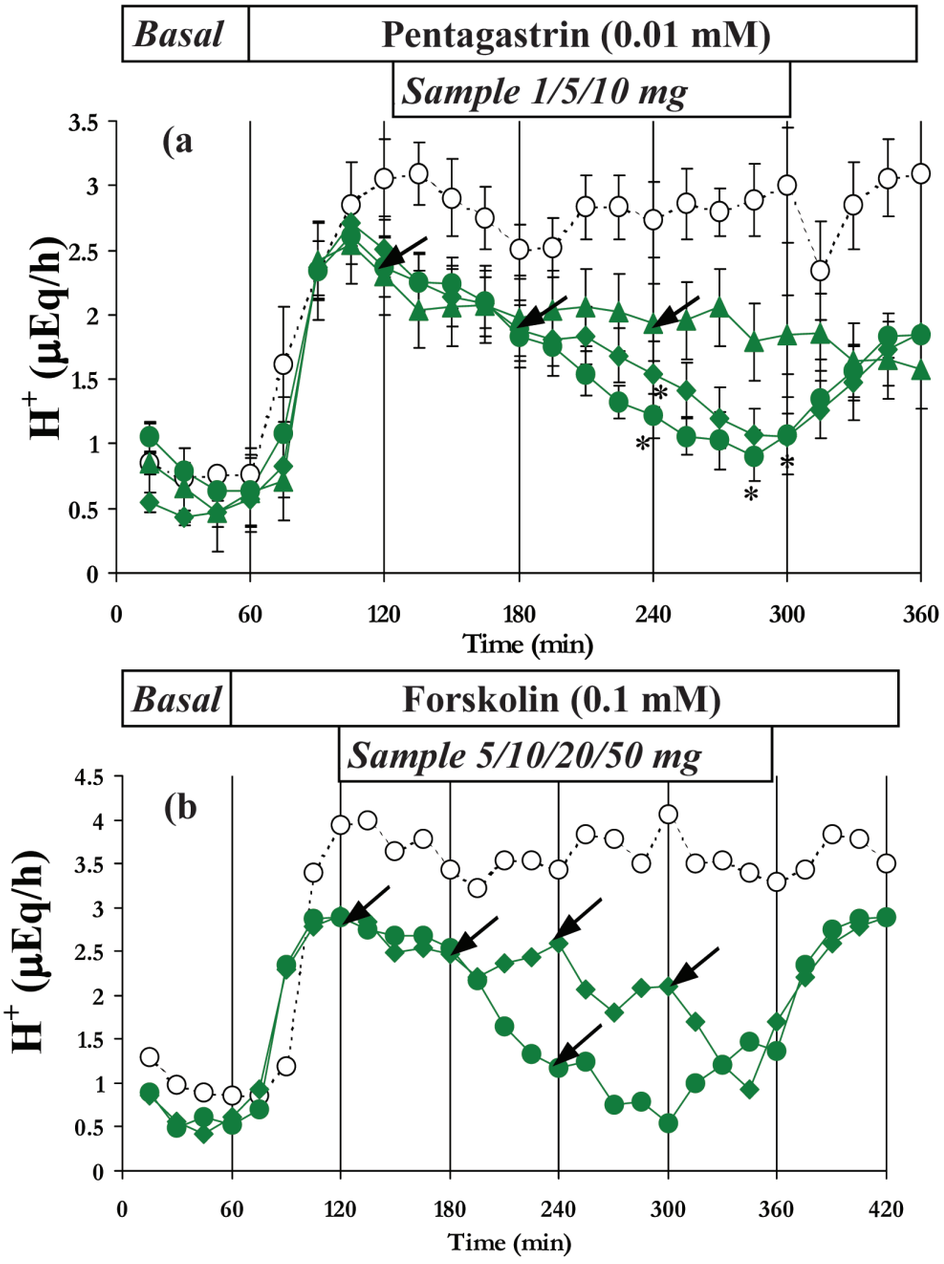


Fig. 5. Effect of aqueous extract and its fractions on pentagastrin- and forskolin-stimulated acid secretion. Arrows indicate the time point of addition of the samples in individual chambers. Panel a exhibits dose-response profile of the extract (-●-) and the two fractions, *n*-butanol (-▲-) and aqueous (-◆-), on pentagastrin (0.01 mM) stimulated acid secretion. The data are mean ± SEM (n = 5, 4, 4 and 2 respectively for control, water extract, butanol fraction and aqueous fraction. The asterisks indicate statistically significant difference from the maximum stimulated values (*$p < 0.005$, **$p \leq 0.001$). Panel b represents dose-dependent effect of the extract and the aqueous fraction on forskolin (0.1 M) stimulated acid secretion and is representative outcome of different experiments where the extract was examined at 5–20 mg and fraction at 5–50 mg dose range.

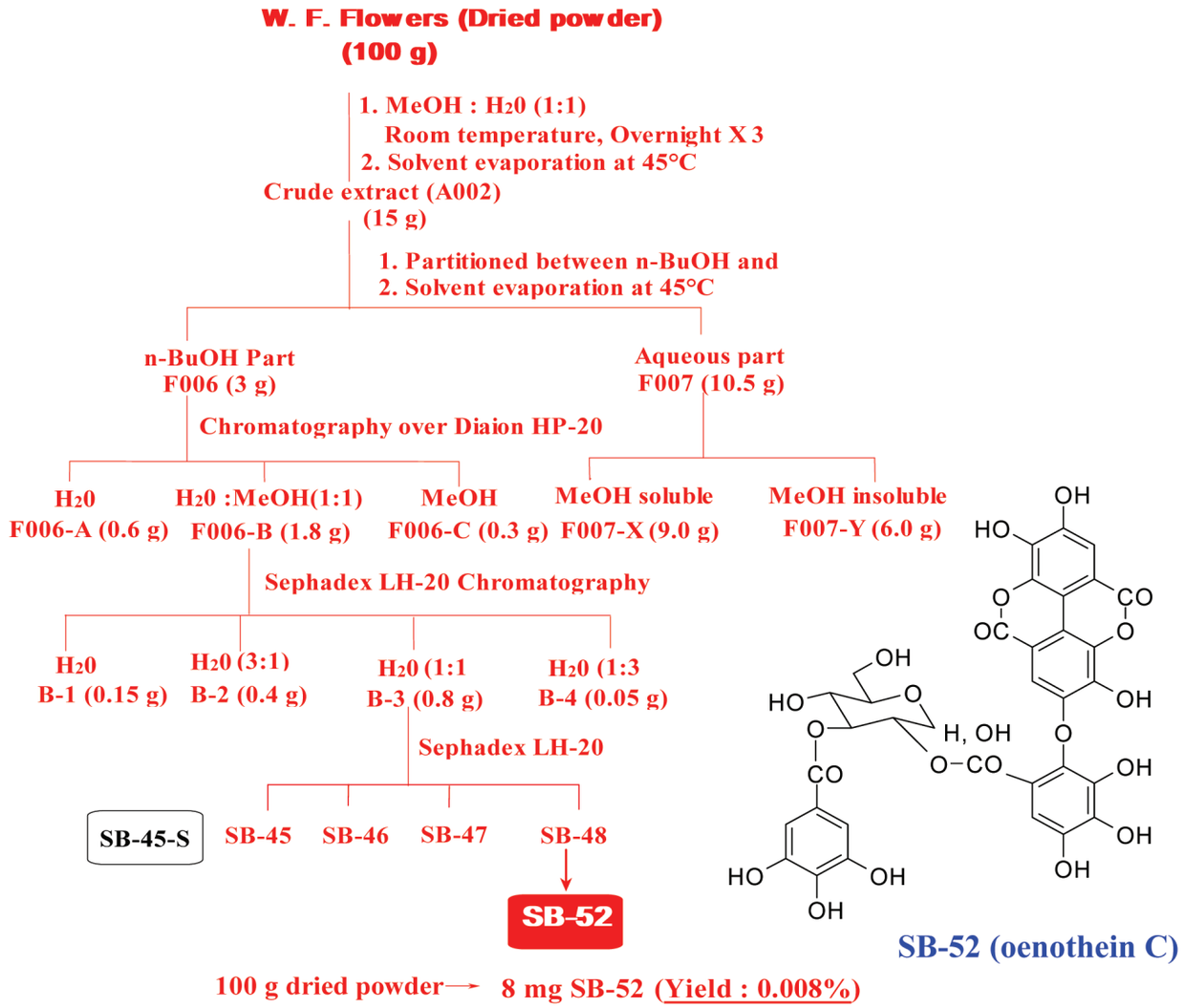


Fig. 6. Bioassay-guided fractionation of *Woodfordia fruticosa* flowers and isolation of the active principle oenothein C. Another isolated molecule SB-45-S (methyl gallate) was found to be inactive.

Post-revalidation drug discovery was being initiated with two plant extracts for gastric antisecretory activity. Fractions and sub-fractions when examined under different experimental conditions indicated reasonable potential of these two samples. In case of the plant sample IHB-630-P02, the non-polar fractions of the alcoholic extract exhibited highest potential. However, in case of the other plant sample IHB-646-P03, the chloroform fraction of the hydroalcoholic extract and the aqueous fraction of the water extract showed better antisecretory activity. Further mechanistic examinations of the more potent antisecretory sample, IHB-630-P02, revealed that the non-polar fractions are strong inhibitor of gastric H^+,K^+-ATPase (Fig. 7). The work is being actively collaborated with Dr. Bikram Singh *et al*. of IHBT, Palampur.

A long-standing interest on the multi-functional role of membrane lipids particularly phospholipids in gastric acid secretion has recently been reviewed based on earlier studies around proton translocating potassium stimulated H^+,K^+-ATPase, its cytosolic activator factor and the cations that modulate tubulovesicular and apical membrane ATPase(s).

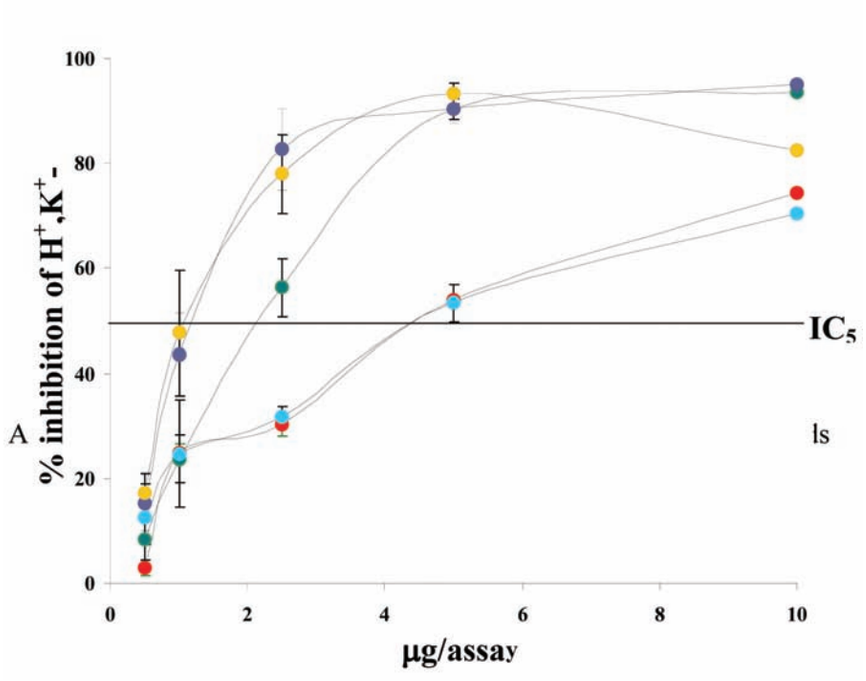


Fig. 7. Gastric anti proton pump activity of IHB-630-P02 alcoholic extract and fractions. Percent inhibition of H^+,K^+-ATPase activity in the presence of different doses (110 g) of the extract and fractions are shown by symbols : extract (-•-), *n*-hexane fraction (-•-), chloroform (-•-), *n*-butanol (-•-), and aqueous (-•-). Gastric H^+,K^+-ATPase-rich membranes were prepared from pig stomach and used for the assay. H^+,K^+-ATPase activity was measured at 37°C in 1-ml reaction mixture containing 10 mM PIPES (pH 6.8), 2 mM each of $MgCl_2$ and ATP, 20 mM KCl and 10 µg membrane protein. The data are mean ± SEM (n = 3 except 10 µg assay where n = 2). Omeprazole, under the present experimental conditions produced ~ 20% inhibition at 1 µg and ~ 80% inhibition at 10 µg concentration.

Dr. Snehasikta Swarnakar and group

Role of matrix metalloproteinase (MMP)-2 on angiogenesis and prevention of gastric ulcer: Regulation by melatonin

Matrix metalloproteinases (MMP)s are extracellular matrix-degrading endopeptidases that can influence physiological and pathological situations, such as tissue development, atherosclerosis, ovarian function, arthritis, osteoarthritis, cancer, angiogenesis, and wound healing. Gastric ulcer healing is a complex process involving enzymatic activities that converge towards damage repair. The aim of the present study was to evaluate MMP-2 activity on angiogenesis during gastric ulcer healing and effect of melatonin (N-acetyl-5 methoxy tryptamine) thereon. Angiogenesis, the growth of new blood capillaries from the existing vessels, is the key physiologic process and is controlled by signals from pro- and anti-angiogenic molecules in the gastric mucosa. Some MMPs regulate wound healing by removal of damaged tissues and thus may facilitate migration of different cell types during neovascularization and collagenization. MMPs also release ECM bound proangiogenic factors, viz. VEGF, transforming growth factor (TGF)β and basic fibroblast growth factor (bFGF). Lower expression or absence of these growth factors or receptors may limit angiogenesis and thereby decelerate the healing process of gastric ulcer.

Using rat corneal micropocket assay we evaluated angiogenic potential of MMP-2. MMPs herein digest the basement membrane and ECM to allow cell proliferation and angiogenesis. Gelatin zymographic as well Western blot analysis revealed that MMP-2 activity and expression reduced along with angiogenesis significantly in indomethacin treated cornea. (Fig.8a-f). Herein, the studies on angiogenesis using rat corneal micropocket assays

revealed that melatonin showed significant pro-angiogenic activities. In support, gastric wound in rat was prevented significantly by melatonin and MMP-2 expression increased while pretreatment with melatonin was made on indomethacin-induced gastric wound. (Fig.8g-n). The study reveals for the first time a mechanistic basis of angiogenesis via MMP-2 expression and activity during prevention of indomethacin-induced acute gastric ulcer.

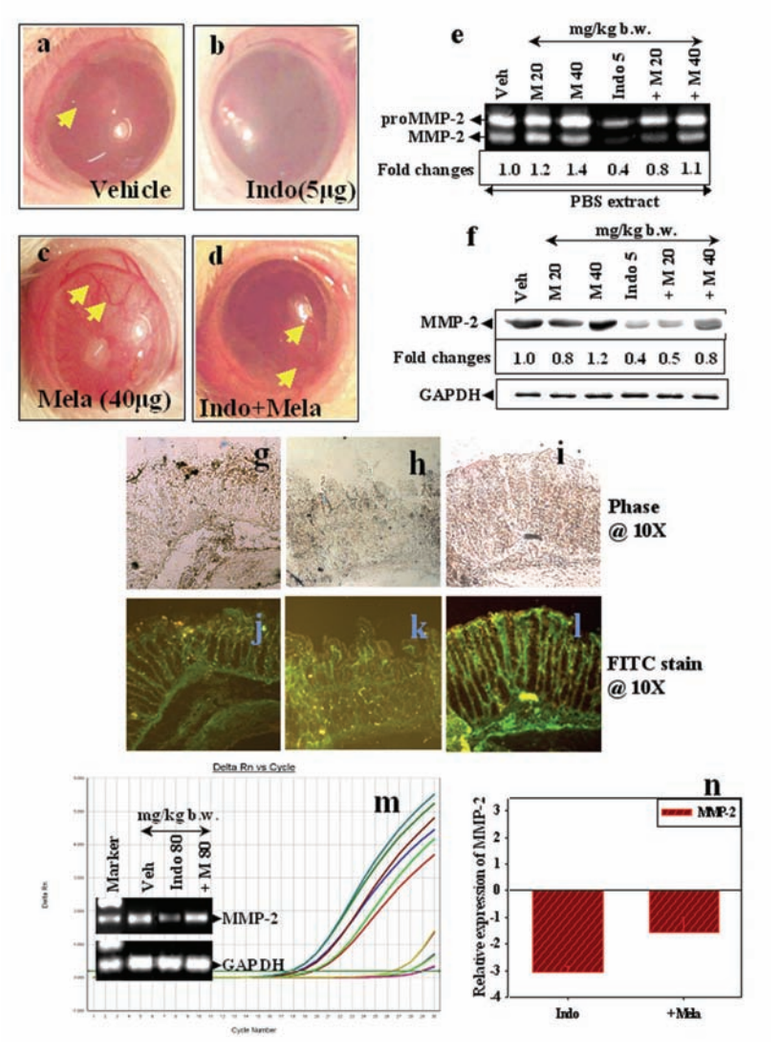


Fig. 8. Regulation in MMP-2 expression in rat cornea and mouse gastric tissues: Angiogenic effect of melatonin during ulcer prevention. The experiments were conducted by implanting molecules impregnated in carboxymethayl cellulose disc in rat cornea. Picture of new blood vessels in rat eye treated with vehicle (a), 5µg/mm^2 indomethacin (b), 40µg/mm^2 melatonin (c), indomethacin plus 40µg/mm^2 melatonin (d). In order to monitor the secreted MMP-2 activities, PBS extracts (80µg) of rat cornea were subjected to gelatin zymography (e). PBS extracts (120µg) of rat cornea were subjected to Western blot and probed separately with anti-MMP-2 and anti-GAPDH antibodies (f). Fold changes in individual bands were measured by Lab Image based designed densitometry program and the values were given below respective gel picture and Western blot.

Gastric ulcer was induced in mice by indomethacin administration and melatonin were administered intraperitoneally prior to indomethacin. After 4h, mice were sacrificed and stomachs were processed and immunofluorescence slides were prepared. The phase contrast picture and FITC immunofluorescence of MMP-2 slides at 10X magnifications of vehicle (g) and j), indomethacin treated (h and k) and melatonin pretreated

indomethacin treated (i and l) gastric tissues respectively. cDNA was prepared from different tissues and equal amount was used for real time-PCR analysis of MMP-2 and GAPDH mRNA. Graphical representation of linear amplification plot of MMP-2 (m) and GAPDH mRNA specific products of control, ulcerated and melatonin pretreated gastric tissues where ÄRn values were plotted against cycle number. Inset showing the MMP-2 and GAPDH mRNA specific products from real-time PCR.. Histographic representation of relative expression of MMP-2 specific transcript in different tissues (n).

Role of MMPs in hepatic tissue damage during ethanol consumption:

Alcohol drinking is a major etiological factor in liver damage, both acute and chronic, worldwide causing fatty liver, alcoholic hepatitis, cirrhosis and hepatocellular carcinoma. Factors involved that linked ethanol intake to the onset and progression of liver injury are poorly understood. The aim our study was to understand the molecular mechanism of underlying alcoholic liver injury in mouse model. Alcohol induced liver injury is well associated with the generation of reactive oxygen species (ROS) as well as tissue injury and the remodeling of extracellular matrix (ECM). We generated alcohol induced chronic liver damage in Balb/c mouse by oral administration of 40% ethanol for 20 days. Liver injury was assessed by measuring alanine amino transferase (ALT) and aspartate amino transferase (AST) enzymes and their ratios in serum.

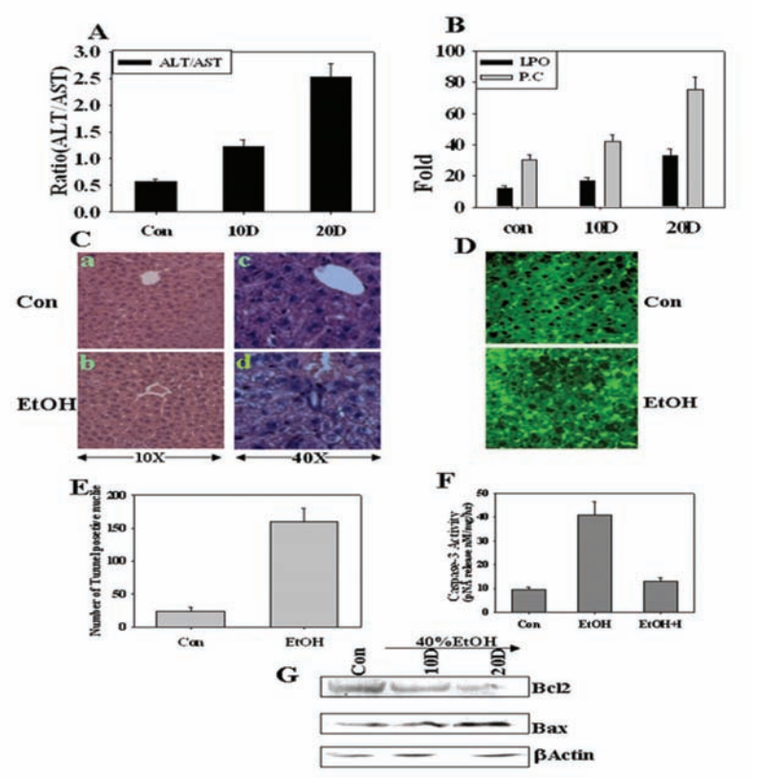


Fig. 9. Chronic ethanol consumption leads changes in liver function and tissue damage. The ratio of ALT vs AST and, protein carbonylation (PC) lipid peroxidation (LPO) were plotted with the duration of ethanol administration in histogram (A) and (B) respectively. H&E staining of liver tissue section of control and ethanol treated (C). Tunnel assay of the tissue section from control (upper panel) and ethanol treated (lower panel) liver tissue (D). Histographic representation of Tunnel positive cells (E) and caspase-3 activity (F) in liver tissues under different condition. Western blot analysis with liver tissue extract of control and ethanol treated liver mice (G).

Time dependent increased in lipid peroxide and protein carbonyl level in liver tissues suggest the etiological role of reactive oxygen species (ROS) for tissue damage (Fig. 9B). Histological as well as biochemical analysis of liver tissue revealed that severe steatosis in pericentral to mid zonal region and, inflammation and necrosis in ethanol treated tissue section (Fig. 9C). We also further checked the hepatic cell death due to chronic ethanol consumption more detailed by TUNNEL assay as well as Caspase-3 activity assay. Tissue section from the

ethanol treated group exhibited ~15 fold higher number of tunnel positive cell as compared to the control group (Fig. 9D,E). Furthermore, the expression of pro apoptotic molecule (Bax) decreased and anti apoptotic molecule Bcl2 increased in ethanol treated liver tissue extract (Fig. 9G).

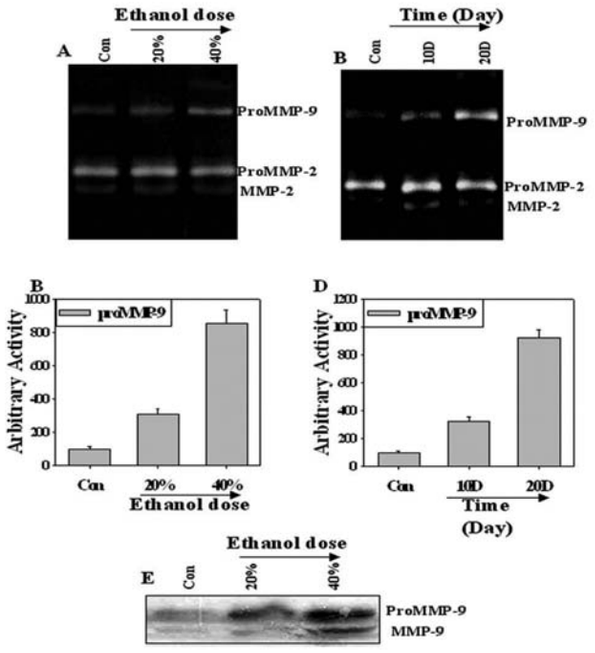


Fig. 10. Induction of MMP-9 activity and expression in mouse liver after chronic ethanol consumption. Zymograpic representation of proMMP-9 activity in the PBS extract of liver tissue from mouse treated with different doses of ethanol (A). Histographic representation of proMMP-9 with different dose of ethano l(B). Zymograpic representation of proMMP-9 activity in the PBS extract of liver tissues from mice treated with ethanol for different time(C). Histographic representation of proMMP-9 with the duration of ethanol administration on mice (D). ProMMP-9 and active MMP-9 expression in mouse liver following treatment with different doses of ethanol (E).

MMP-9 activity in liver tissue extract was assayed by gelatin zymoraphy. ProMMP-9 activity increased with the dose and duration of ethanol administration (Fig. 10A, C). Liver tissue extract exhibited higher proMMP-9 activity of ~ 3.5 fold in low dose (20%) ethanol, and of ~8 fold in high dose (40%) ethanol as compared control group of mouse (Fig. 10D). In time course study, we found proMMP-9 activity increased significantly as compared to control on 10 day and 20 day by ~3 fold and ~8 fold respectively (Fig. 10D). Consistent with the zymographic study MMP-9 expression also increased with the dose of ethanol consumption. Interestingly, activation of MMP-9 is observed in case of high dose of ethanol administration (Fig. 10E).

Dr. T. K. Dhar and group

Rapid preparation of hapten-protein conjugate

The covalent conjugation of small molecules (hapten) to proteins to form bioconjugates is an extremely important process in the field of immunology. During the past two decades, several procedures using various coupling reagents have been described for the preparation of hapten-protein conjugates. Despite the complexity of protein structure, including composition and sequence, haptens have been linked to various proteins without protein inactivation. For example, immunoconjugates comprised of haptens linked to carrier protein are useful for eliciting the production of specific antibodies for use in immunoassays, and hapten-modified enzymes form the basis of many types of enzyme immunoassay.

The current most widely used approach for the preparation of hapten-protein conjugate involves stirring a mixture of N-hydroxysuccinimide ester of hapten (NHS-hapten) and protein in an aqueous alkaline solution (pH 7.5 to 8.5) for 4-6 hrs. This procedure though simple is problematic due to the prolonged reaction time (4-6 hrs) and the NHS-esters hydrolyse at alkaline pH resulting in less conjugation of hapten to the proteins. We explored the possibility of accelerating the reaction kinetics of NHS ester method by filtration through a membrane. Using biotin as a model hapten, a solution of BSA and biotin-NHS ester at alkaline pH was allowed to pass thrice through a filtration unit containing nitrocellulose membrane. The results showed moderate degree of hapten conjugation compared to conjugate prepared by standard method. We thought the degree of hapten conjugation might be increased further if the reaction mixture can be passed multiple times through a membrane filter. We assembled a highly practicable filtration device and used for passing the reaction mixture multiple times by pressing two ends of the syringe plunger one at time. Compared with the current standard method, the new approach reduces total incubation time from 4-6 hrs to 5 min and also increases the amount of conjugated hapten to protein by 40-60%. The number of biotin conjugated in different biotin - BSA conjugates by both the methods were determined by the TNBS method. The results showed filtration method of conjugation yielded better conjugation than the conventional method (around 30-50% increase in number of biotin conjugated to BSA). We systemically studied the effect of protein, biotin-NHS ester concentration and buffer strength on the filtration-based conjugation technique. The results showed by the present method 50 to 0.5 mg of protein may be used for conjugate preparation.

The qualities of the present synthesized conjugates were compared to those prepared by standard methods by an AFB1 ELISA. Biotin-anti-AFB1 antibody prepared by both the methods were tested by an indirect ELISA. Dose-response curves (Fig. 11) obtained by using biotinylated antibody prepared by filtration method produced much higher intensity and sensitivity than that obtained by standard method.

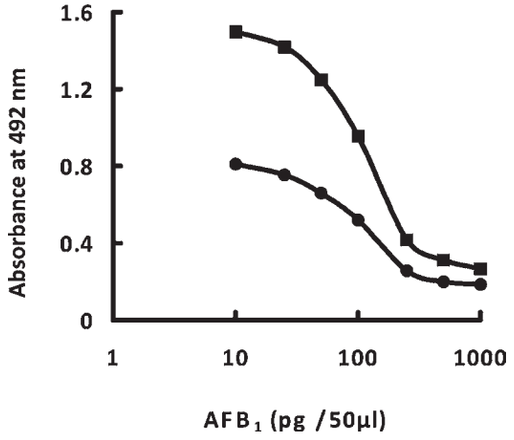


Fig. 11. Comparison of AFB1 dose-response curve obtained by using biotin-anti-AFB1 antibody conjugate prepared by standard (-•-) and filtration (-■-) methods.

Thus the utility of conjugation through the filtration method is broad. It can probably be applied beneficially in many other conjugations in organic synthesis.

Dr. Nirmalendu Das and group

Vesicular flavonoid in combating diethylnitrosamine induced hepatocarcinoma in rat model

Oxygen free radicals generating from cerebral ischemia/ reperfusion exert a potential threat on neuronal mitochondria and cellular antioxidant defence and hence accelerate the aging process and age dependent neuropathology. Thirty minutes of transient global ischemia and subsequent 30 minutes reperfusion resulted

neuronal mitochondrial damage with significant decrease in antioxidants level of normal young (2 months old) and normal aged (20 months old) Swiss albino rat brain. Cytidine 5' diphosphocholine (Citicoline) is a known drug mostly employed in the treatment of stroke. Owing to its hydrophilic nature the compound hardly circumvent Blood- Brain Barrier.

Mannosylated Liposomal CDP choline treatment when compared to free or liposomal CDP-choline treatment prevented global transient cerebral ischemia-reperfusion induced mitochondrial damage as evident ultra structurally and release of cytochrome c from mitochondria into cytosol and protected mitochondria to restore its normal structure and functions.

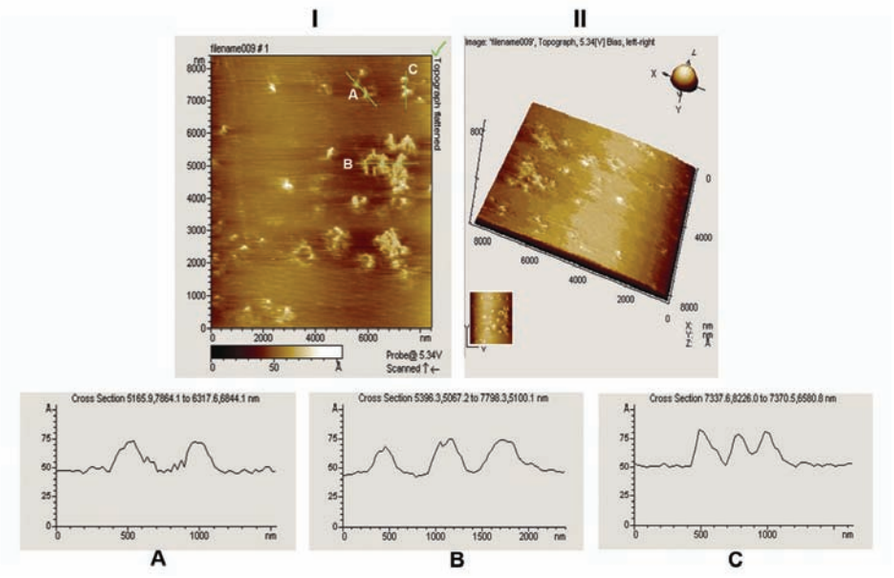


Fig. 12. AFM images of liposomes under water obtained 30 min after the deposition on mica support. (I) Topography flattened and (II) 3D- view. A, B and C indicate height of liposomes from the substratum i.e. the mica sheet.

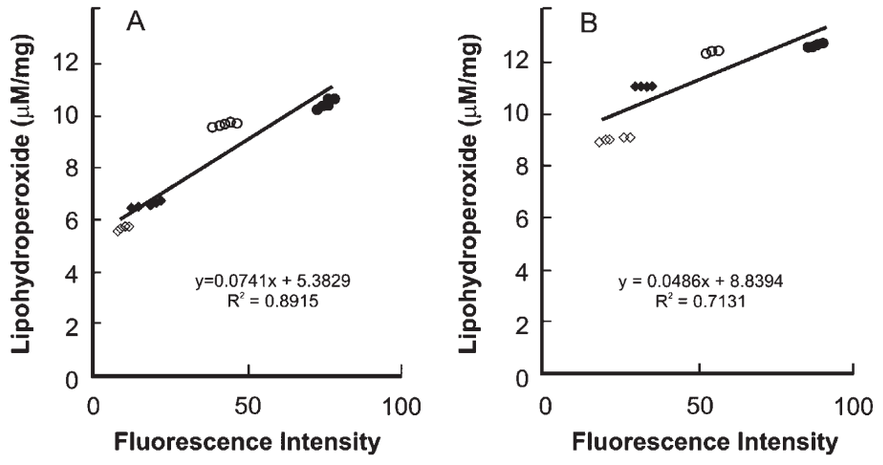


Fig 13. Correlation between ROS generation and conjugated diene level in mitochondria membrane in rat brain. X axis indicates ROS in terms of DCH2FDA fluorescence and Y axis indicates amount of lipohydroperoxide generated in µmol/mgProtein. A: Young group, B: Aged group. □ Sham operated, • cerebral ischemia reperfused (CI), o CI + LCDP, ♦CI +MLCDP.

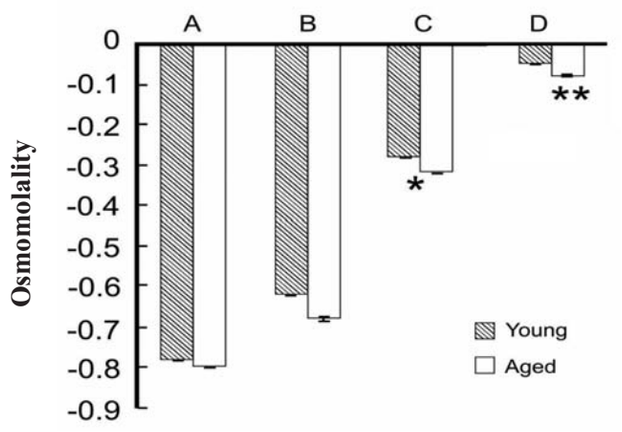


Fig. 14. Osmomolality difference between cerebral ischemia-reperfused (CI). (A) free CDP-Choline + CI (B), CI + LCDP (3), CI + MLP (C), and CI + MLCDP (D) treated rat brain. Osmomolality differences in osmol per cm^3 of brain tissue are presented in case of ischemic reperfused. Values shown as mean differences of osmols/cm^3 of brain tissue .Values are mean ± SD for 5 rats. * indicates $p<0.05$ significantly different from sham operated normal, ** indicates $p<0.001$ significantly different from ischemia-reperfused groups.

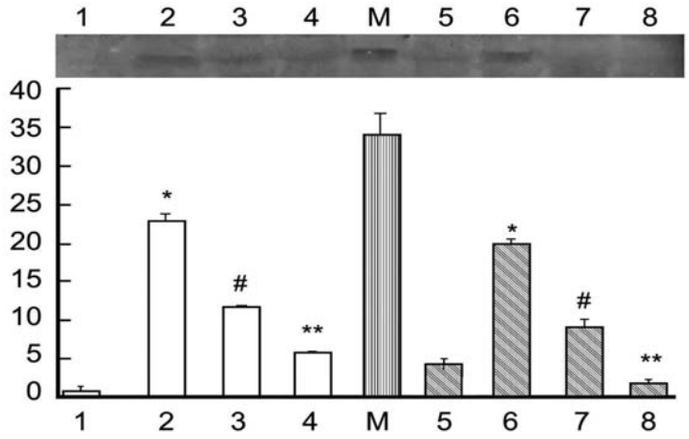


Fig. 15. Western Blot analysis of cytochrome c protein expression in brain tissues of experimental rats. **1**. Young sham operated. **2**. Young cerebral ischemia reperfusion induced (A). **3**. (A) + LCDP-Choline treated. **4**. (A) + MLCDP treated. **M**. Protein marker (12 kD) **5**. Aged sham operated. **6**. Aged cerebral ischemia reperfusion induced (B) **7.** (B) + LCDP. **8.** (B) + MLCDP treated. Histogram showing representative pixel intensities (arbitrary units of densitometric analysis using Image J software) of the immunoblot performed with different individual rats. * indicates $p<0.001$ significantly different from sham operated normal. #, indicates $p<0.05$ significantly different from ischemia-reperfused groups, **, indicates $p<0.001$ significantly different from ischemia-reperfused groups.

Dr. Anil K. Ghosh and group

Characterization of trehalose-6-phosphate synthase from Saccharomyces cerevisiae

The current study was undertaken to correlate post translational protein modification by methylation with the functionality of enzymes involved in trehalose metabolism in *Saccharomyces cerevisiae*. Trehalose is an economically important disaccharide providing protection against various kinds of stresses. It also acts as a source of cellular energy by storing glucose. Methyl group donor S-adenosyl L-methionine (AdoMet) and

methylation inhibitor oxidized adenosine (AdOx) were used for the methylation study. AdoMet delayed initial growth of the cells but the overall growth rate remained same suggesting its interference in G1 phase of the cell cycle. Metabolic altered enzyme activities of acid trehalase (AT), neutral trehalase (NT) and trehalose-6-phosphate synthase (TPS) were observed when treated with AdOx and AdoMet separately. A positive effect of methylation was observed in TPS, hence, it was purified in three different conditions, using AdoMet, AdOx and control. Differences in mobility of methylated, methylation inhibited and control TPS during acidic native gel electrophoresis confirmed the occurrence of induced methylation. Hydrolysis under alkaline pH conditions revealed that methylation of TPS was different than O-methylation. MALDI-TOF analysis of trypsin digested samples of purified methylated, methylation inhibited and control TPS revealed that an increase of 18Da mass in methylated peptides suggesting the introduction of methyl ester in TPS. Results of amino acid analysis corroborated the presence of methyl cysteine. The data presented here strongly suggests that trehalose production was enhanced due to methylation of TPS arising from carboxymethylation of cysteine residues.

***Purification and characterization of neutral trehalase-invertase activity from Candida utilis*.:**

Sucrose and trehalose, the two most important non-reducing disaccharides known for their anti-stress role, are catabolized by invertase and neutral trehalase respectively. Previously a dimeric protein (112 KDa) was purified from mid logarithmic cells (O.D-15) of *Candida utilis* strain having both invertase and neutral trehalase activity, but heavy loss of both activities probably due to presence of protease activity was unavoidable throughout purification scheme. This resulted in very low yield of enzyme activity (10%) as well as low purification fold (11 fold). To solve this, both enzymes were now co-purified to electrophoretic homogeneity from the same yeast strain but using cells from early logarithmic phase of growth (O.D.-10). The protein purified from these cells has almost 3 times more enzyme yield (30%) and purification fold (35 fold) in case of both invertase and neutral trehalase. Molecular weight of the single peak in HPGPLC was 174 KDa, while the single band SDS-PAGE was of 58 KDa. HPRPLC also showed only one protein peak. So it may be hypothesized that the functional form of the enzyme is a trimeric protein composed of three identical subunits.

Various physiochemical characteristics of the purified protein were studied. Both were found in the same fractions throughout the purification protocol. Specific activity of invertase was always around 3.5 times higher than neutral trehalase. Effect of common enzyme modifiers, thermal and pH stress also revealed that both activities are shown by same protein. Multisubstrate specificity of the purified protein showed highest activity against sucrose followed by trehalose. Km values of the purified enzyme against the two sugars were very similar while Vmax followed the same ratio (3.5) confirming that same protein is responsible for both activities. Purification table, biochemical characterization and enzyme kinetics proved that both activities are shown by a single protein complex with 3 identical monomeric units. Invertase and neutral trehalase have been purified separately before but this is the first report to inform the purification of a single protein showing both activities. The study also enlightens about the physicochemical properties of the enzyme.

Purification and characterization of a low molecular weight endoxylanase from mushroom Termitomyces clypeatus.

Xylan, the most abundant of the hemicelluloses in terrestrial plant cell walls has a linear â-1, 4-linked xylopyranosidic back bone with side chain glucose, arabinose, glucuronic acids and arabinoglucuronic acid residues on its D-xylose backbone. Larch wood xylan also contains similar backbone of â-1, 4- linked D-xylopyranosyl residues with every fifth or sixth xylose residue substituted at C2 with 4-Ï-methyl-D-glucuronic acid and at C3 with arabinofuranosyl units, where none of the xylosyl residue have more than one branch.

An endoxylanase was purified from an edible mushroom *Termitomyces clypeatus* grown in submerged medium with oat spelt xylan. Production of the enzyme peaked in the presence of 1% Xylan reveal that it is an inducible enzyme. Effect of pH on either production or liberation into culture filtrate has been found to play a significant

role. Omeprazole, a fungal proton pump inhibitor has been found to alter enzyme production. Xylanase was purified to electrophoretic homogeneity by ammonium sulfate fractionation and gel filtration chromatography. Gel filtration chromatography and SDS-PAGE estimated the molecular weight of the protein to be 12 kDa. The optimum conditions for enzyme activity was found to be at 50 °C and pH 5.0, being most stable at ph 6.5. The Km for oat spelt xylan was determined to be 10.4 mg/ml. The specificities of the enzyme was observed to be highly specific towards oat spelt xylan and was inhibited by Mercuric chloride (HgCl2), N-bromosuccinimide (NBS) and trans-1,2-diaminocyclohexane-N', N', N', N'- tetraacetic acid (CDTA) strongly. The inhibitory action of N-bromosuccinimide on enzyme confirmed the presence of one tryptophan residue in its substrate binding site. Amino acid analysis for xylanase showed the presence of high amount of hydrophobic Serine, Glycine, Threonine and Alanine residues. The N-terminal sequencing study for the previously purified and characterized 56 kDa xylanolytic amyloglucosidase reveal the presence of 33.30 % identity with glucoamylase chain A from *Aspergillus awamori*. The N-terminal sequence analysis of present 12 kDa enzyme showed highest similarity (72.22 % identity) towards xylanase from *Neurospora crassa*.

Dr. Suman Khowala and group

Molecular mechanisms regulating production and secretion of carbohydrases in the fungus Termitomyces clypeatus.

The main objective of the project are to study the regulatory mechanisms of production, secretion and properties of cellobiase from filamentous fungus *Termitomyces clypeatus* influenced by intracellular processing and translocation of the enzymes by post-translational modification in presence of glycosylation inhibitors.

Regulatory effects of glycosylation inhibition on activity and secretion of glycosidases.

Intracellular post-translational modification by glycosylation affects biochemical and biophysical properties of glucosidases in *Termitomyces clypeatus*, a filamentous fungus. The fungus produced a number of carbohydrases and majority of them are glycosylated. In presence of the glycosylation inhibitor 2-deoxy-D-Glucose biochemical properties of the enzymes were influenced. The enzyme produced under restricted glycosylation showed better activity towards lignocellulose and also had better stability towards salts and detergents. In this context the extra and intracellular cellobiase (β-glucosidase: EC 3.2.1.21) were purified and characterized.

Enhanced activity and stability of extracellular cellobiase (β-glucosidase: EC 3.2.1.21) produced and purified in presence of 2-deoxy D-glucose from the fungus Termitomyces clypeatus

Glycosylation is known to influence activity, stability of enzymes. Generally less glycosylation or deglycosylation has detrimental effect on the enzyme activity and stability. Increased production and secretion of cellobiase (β-glucosidase: EC 3.2.1.21) was earlier obtained in presence of the different glycosylation inhibitors 2-deoxy D-glucose, tunicamycin, 1-deoxynojirimycin and D-glucono-δ-lactone in filamentous fungus *Termitomyces clypeatus*, where presence of 2-deoxy D-glucose in the growth medium resulted in unprecedented increase in cellobiase production and secretion. In this study the enzyme was purified from the culture medium by ultrafiltration and gel permeation, ion exchange & high performance liquid chromatography. The catalytic activity of the purified enzyme was 6 times higher as compared to the control enzyme. K_m and V_{max} of the purified enzyme were measured as 0.187 mM and 0.018 U/mg respectively using *p*NPG as substrate (Table 1). Substrate affinity of the enzyme increased by 25 times leading to overall increase of catalytic activity by 6 times, which was due to restricted glycosylation in presence of DG.

Table 1. Kinetic parameters of purified extracellular cellobiase

Cellobiase (purifed)	Km (mM)	Vmax (U mg^{-1})	Vmax Km^{-1} (U mg^{-1} mM^{-1})
Cg	0.187	0.018	0.096
C	4.762	0.076	0.016

Cg: underglycosylated cellobiase; C: native cellobiase; Substrate (*p*NPG) concentrations were used 0.01-2 mM.

The enzyme had optimum temperature and pH values at 45ºC and 5.4 respectively and showed full activity between pH range of 5-8 and temperatures 30-60ºC. Due to underglycosylation the pH optimum of Cg changed to 5.4, which was earlier observed at 5.0 in absence of DG for C. Purified Cg was most stable at pH 5.4 and retained around 68-71 % residual activity between pH 4.0-9.0 after 24 h of incubation at 30°C (Figure 16A). Only 8% activity was lost at pH 6.0 but residual activity was 5% at pH 10.4. Earlier purified C was found to be inactive at pH 3.5 and 8.0. The enzyme showed more than 80% residual activity during 1 h incubation in the temperature range 30-53°C and 42% activity at 60°C (Figure 16B) and became inactive at 70°C in 30 min, whereas C had temperature optima at 47°C and showed no activity at 60°C.

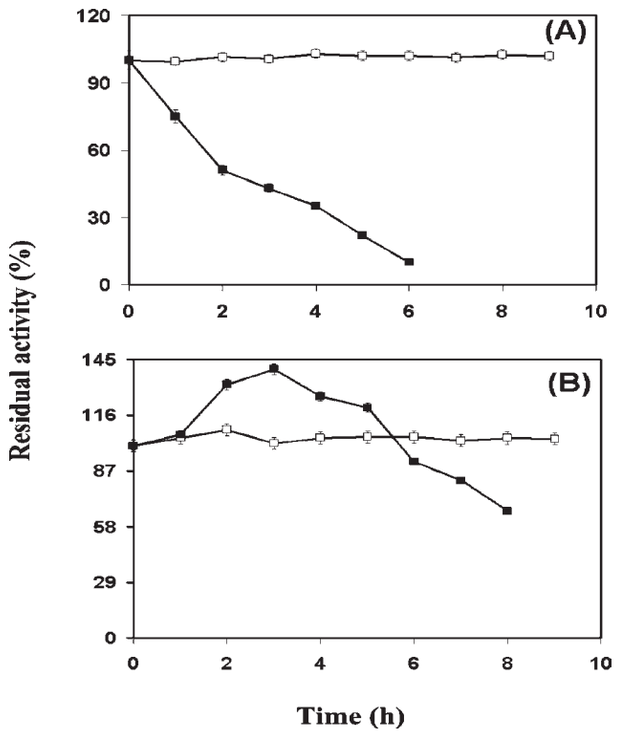


Fig. 16. pH (A) and temperature (B) stability of extracellular cellobiase. pH (A) and temperature (B) stability of extracellular cellobiase**.** Residual enzyme activities were measured at different temperatures and pH for purified Cg (-■-) and C (-■-).

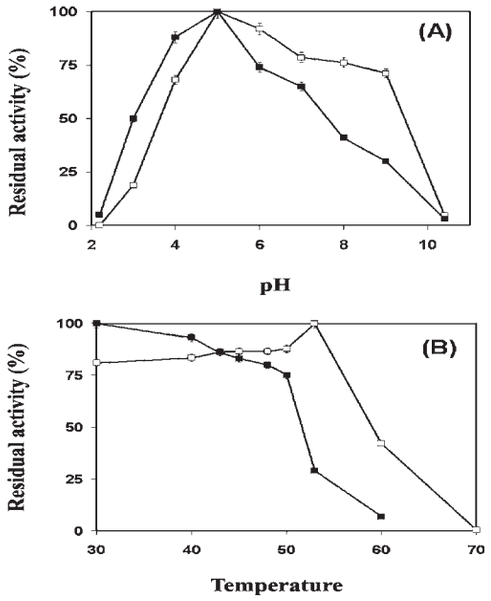


Fig. 17. Susceptibility of extracellular beta-glucosidase to Trypsin (A) and Endo-H (B) digestion. 50mU of purified Cg (-■-) and C (-■-) were incubated with trypsin (5 µg) and endo-H (0.3 mU/µg enzyme) and residual activities were measured.

The enzyme also showed higher stability compared to the native enzyme and was found to be less susceptible towards Mg^{2+}, sodium azide, PCMB, Gdn.HCl, urea, DTT, 2-mercaptoethanol and 2-deoxy D-glucose, moreover it showed higher specific activity in presence of cellobiose and *p*NPG than the native control enzyme. Contrary to the characteristics of any less/deglycosylated enzyme reported so far Cg was not at all susceptible towards hydrolytic action of trypsin and endo-H until 36 h whereas C gradually lost activity respectively after 30 min and 5 h in presence of trypsin (Figure 17A) and endo-H (Figure 17B). Stability to trypsin and endo-H may be attributed to the increased aggregation property of Cg after restricted glycosylation.

Novelty of the work lied on high activity and stability of underglycosylated cellobiase produced in presence of the glycosylation inhibitor due to high aggregation of the enzyme. The observations altogether was quite an exception to the general trend where restricted glycosylation led to loss in enzyme activity and stability. The amino acid sequences and N-terminal analysis revealed that the enzyme was novel, which appeared as an interesting model for study of glycosylation and for aggregation of proteins from filamentous fungi. The beta-glucosidase can be exploited as a potential enzyme in various food processing, pharmaceutical and fermentation industries.

Purification and characterization of a thermostable intracellular beta-glucosidase with transglycosylation properties from filamentous fungus Termitomyces clypeatus

Finding applications for enzymes in industry is a great challenge and dependent on the development of novel enzymes with desirable activities and properties. Many glycosidase have saccharification ability but recent studies created the interest in the enzymes having the ability to catalyze the transglycosylation reactions. Glycosidase-catalyzed transglycosylation is a promising alternative to classical chemical glycosylation methods. In comparison with chemical methods, enzymatic glycosylation is particularly useful for the modification of complex biologically active substances, when generally harsh conditions or use of toxic (heavy metals) catalysts are undesirable. Enzymes possessing transglycosylation properties are in high demand for the production of bioactive compounds.

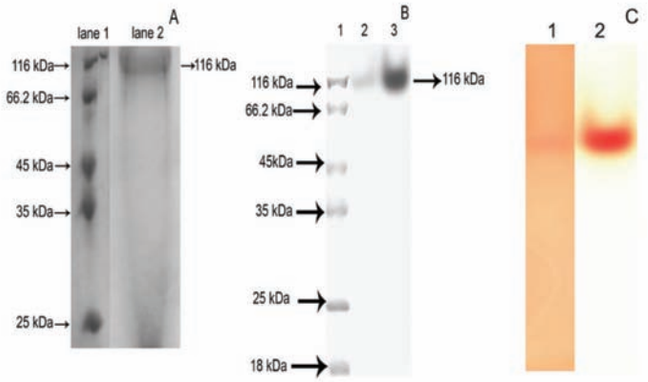


Fig. 18. Electrophoretic analyses of purified intracellular β-glucosidase. Purified β-glucosidase from HPGPLC (*Lane2*) and protein marker (*Lane 1*) were loaded on SDS-PAGE (A). In western blotting (B) purified intracellular β-glucosidase from HPGPLC peak 1 (*Lane 3*), peak 2 (*Lane 2*) and protein marker (*lane 1*) were loaded. In activity staining (C) purified intracellular β-glucosidase from HPGPLC peak 1 (*lane 2*) and mycelial extract (*lane 1*) were loaded.

The intracellular β-glucosidase was purified to homogeneity by gel filtration, ion exchange chromatography and HPGPLC from mycelial extract of *Termitomyces clypeatus* in the presence of the glycosylation inhibitor 2-deoxy-D-glucose (DG). The size of the enzyme was identified as 6688 daltons by MALDI-TOF, but SDS-PAGE and immunoblotting indicating that the enzyme was highly aggregated (Figure 18). The enzyme also showed unique properties of co-aggregation with sucrase in the fungus. CD spectroscopy demonstrated that the purified enzyme exhibited α-helical conformation, but in presence of sucrase showed random coil structure (Figure 19).

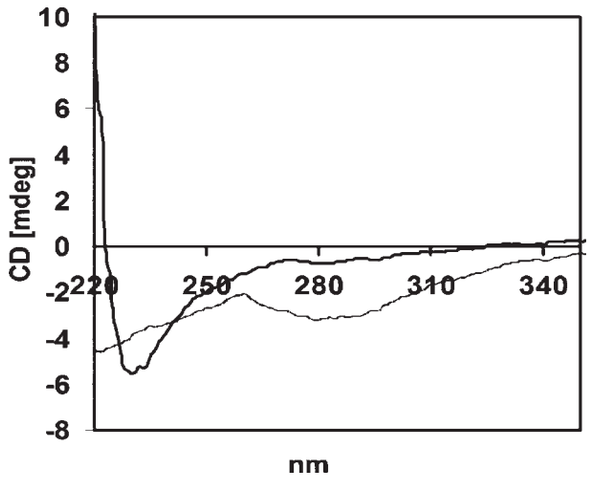


Figure 19: Circular dichroic spectra of intracellular β-glucosidase. The circular dichroic (CD) spectra of purified intracellular beta-glucosidase (–) and co-aggregated enzyme with sucrase (–) were measured in a JASCO J-720 spectropolarimeter.

The enzyme showed around 80% stability up to 60ºC and residual activity was 80-100% between pH ranges 5-8. The enzyme had higher specific activity against *p*-nitrophenyl-D-glucopyranoside than cellobiose and possessed transglycosylation activity as confirmed by synthesis of cello-oligosaccharides by addition of glucose (Figure 20). The transglycosylation activity was due to underglycosylation of the enzyme in presence of DG.

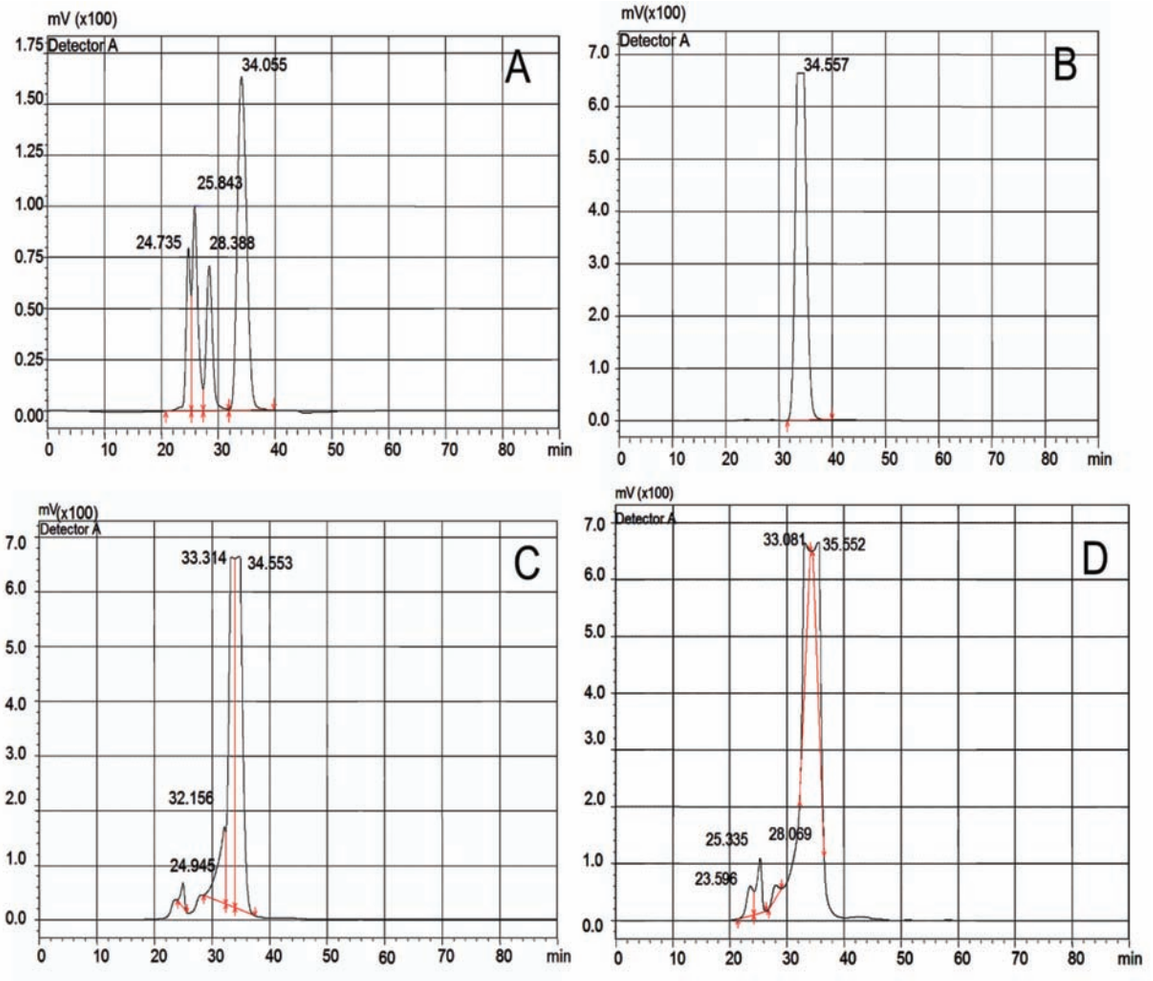


Fig. 20. Transglycosylation activity of Intracellular beta-glucosidase of *T. clypeatus*. Transglycosylation reaction was carried out by incubating the intracellular enzyme for 0h (B), 3h (C) and 6h (D) by using glucose as the substrate. Standards samples of glucose (34 min), cellobiose (28.3 min), cellotriose (25.8 min) and cellotetraose (24.7 min) were run as control (A). Reaction products were analyzed by Rezex polymer based HPLC carbohydrate column (Shimadzu).

This is the first report of a beta-glucosidase enzyme with transglycosylation activity with such low size monomeric units from any source. The enzyme was different from other enzymes the category from the same fungus (Table 2). The enzyme by virtue of low size may serve as an interesting model to study protein-protein interaction, protein aggregation and for biomedical as well as biotechnological applications.

Co-aggregation of cellobiase and sucrase in the fungus T. clypeatus

The sucrase in co-aggregation with cellobiase (β-glucosidase: EC 3.2.1.21) in the secretory pathway affected the activity, stability and conformation of the enzymes. It was observed that after restricted glycosylation also the same observation was observed. Due to co-aggregation catalytic activities of extra and intracellular glucosidases increased significantly. Presence of sucrase also rendered the intracellular beta-glucosidase enzyme more susceptible to urea, Triton X-100, 2-mercaptoethanol and DTT as compared to the mycelia extract enzyme.

Table 2: Comparison of purified intracellular β-glucosidase with purified extra and intracellular enzymes in presence and absence of DG from *T. clypeatus*.

Characters	IG	IFC	EG (Cg)	EFC (C)
Molecular weight	6688 Da	ND	ND	14000 Da
*p*NPG (U/mg)	0.539	2.32	17.9	2.41
Cellobiose (U/mg)	0.148	2.06	21.43	2.35
pH optima	5.0	5.0	5.4	5.0
Temperature optima (°C)	45°C	47°C	45°C	47°C
Thermal stability 70°C	64%	60%	ND	ND
K_m (mM)	0.148 (0.131)*	3.448	0.187	4.762
V_{max} (U/mg)	0.07 (77.51)*	0.076	0.018	0.076
K_{cat} (U/mg/mM)	0.52 (591.67)*	0.022	0.096	0.016
Conformation	Alpha helical	Beta sheet	ND	Random coil

IG- Intracellular enzyme in presence of DG; EG- Extracellular enzyme in presence of DG
EFC- Extracellular enzyme in absence of DG; IFC- Intracellular enzyme in absence of DG
*, Values in brackets correspond to enzyme in mycelial extract; ND, not determined.

Biotechnology of conversion of lignocellulose for production of bioethanol

Depletion of world's petroleum supply and green house effects have resulted in a growing interest in alternative fuels as bioethanol. Earlier in search of new agro-residues Tamarind kernel powder (TKP) was introduced in the lab as a soluble and renewable source of energy for use as substrate for production of lignocellulolytic enzymes. TKP was used without any pretreatment for the study. The raw material supported excellent growth of the fungus and had promising capability to produce the range of cellulolytic and hemicellulolytic enzymes in appreciable titers in submerged fermentation. Production of enzymes were tried by solid state fermentation to save down stream processing and other running costs for the process using TKP with polyurethan foam. Significant increment of specific activities of enzyme like xylanases and Filter paper activity, carboxy methyl cellulose and cellobiase was observed in SSF. In future the method would be employed to use other agrowastes for the purpose.

Dr. Sharmila Chattopadhyay and group

Medicinal plants and metabolic engineering

Podophyllum hexandrum, is a critically endangered medicinal plant. Basically, the rhizomes of this plant is rich in podophyllotoxin, the diarylnapthelene group of lignan, the predominating compound and the active ingredient used as the starting compound for the chemical synthesis of etoposide (VP-16-213), and teniposide (VM-26) and ethophos that are used for the treatment of lung and testicular cancers.

This endangered *Himalayan* plant is inherently slow growing. Micropropagation is one of the best choices for large-scale multiplication of this medicinal herb. Furthermore, successful in vitro regeneration technology is an essential prerequisite condition to obtain genetic manipulation of desired trait of the plant itself or its constituents. Here, an efficient method for in vitro regeneration and callus formation from rhizome and leaf explants of *P. hexandrum* of freshly collected plants was established. Rhizome explants were noted as the best explants for in vitro multiplication through direct organogenesis. MS medium supplemented with various growth regulators like BAP, NAA, Kn, 2,4-D and IAA either singly and/or in combination, at different concentrations was used for shoot regeneration and callus formation. Highest rate of multiple shoot formation was noted with 11.42 µM IAA within three months followed by a synergistic effect of 2.68 µM NAA and 11.1 µM BAP (Fig. 21a, b). The ½ MS liquid medium supplemented with µ100 µM IBA was most suitable for rooting of in vitro regenerated shoots. Leaf explants were resulted in callus only (Fig. 21c).

Phyllanthus amarus popularly known, as "Bhumyamlaki" is a well-known hepatoprotective Indian herb along with a wide range of other therapeutic properties. Dibenzylbutane group of lignans like phyllanthin and hypophyllanthin are primarily responsible for the hepatoprotective activity of the genus. In this investigation the transformation of *P. amarus* with *LuPLR* gene with a view to obtain enhanced phyllanthin content was established. Shoot tips of *P. amarus* were used for *Agrobacterium tumefaciens* LBA 4404 mediated transformation as standardized in our laboratory before. Recombinant *A. tumefaciens* LBA 4404 harboring 35S:*LuPLR* gene in pCAMBIA2301 backbone was used here. The kanamycin resistant (K^R) independent transgenic lines (Fig. 22a) were selected by *GSU* analysis (Fig. 22b) as well as PCR analysis of neomycin phosphotransferase (*npt* II) and *LuPLR* gene. Efficient and effective rooting of K^R plantlets was achieved by culturing the in vitro regenerated shoots on liquid ½ MS medium supplemented with 0.7 mg l^{-1} of indole 3-butyric acid (IBA) and 5 mg l^{-1} of kanamycin (Fig. 22c,d). Rooted plants were acclimatized in the mixtures of vermiculite and soil. Southern blot and RT-PCR analysis confirmed the integration and expression of *LuPLR* gene in transgenic lines. HPLC analysis demonstrated that phyllanthin content was enhanced upto two folds in comparison to that of wild plant. This study demonstrated that metabolic engineering play a significant role in the genetic manipulation of plant natural products that have a beneficial biological effect. To the best of our knowledge, this is the first report of enhanced production of phyllanthin in transgenic *P. amarus*, which in turn will be helpful to improve the therapeutic potential of this popular medicinal herb.

Fig. 21A

Fig. 21B

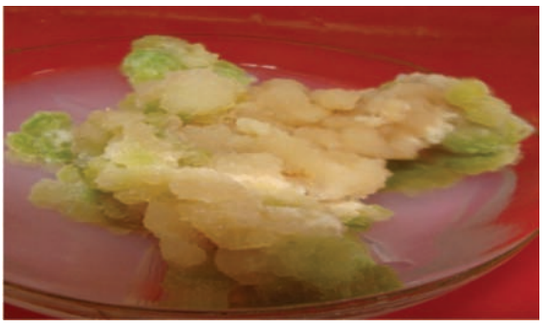


Fig. 21C

Fig. 21. In vitro regeneration and callus formation from rhizome and leaf explants of *Podophyllum hexandrum.*

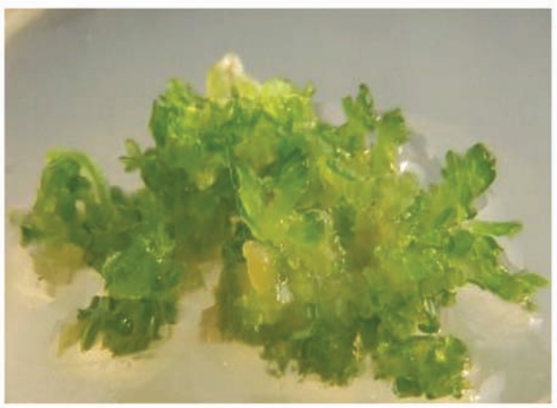


Fig. 22A

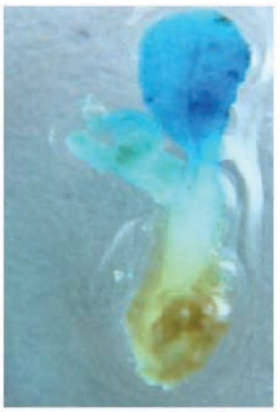


Fig. 22B

Fig. 22C

Fig. 22D

Fig. 22. Metabolically engineered *Phyllanthus amarus*

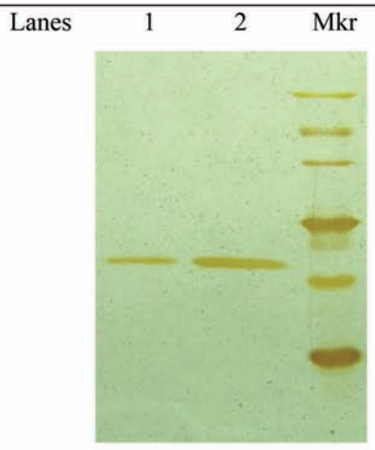
Herbal and traditional plant medicines have been emerged as antioxidant-containing products in our study. Results showed that selected herbs used in traditional and folk medicine with variable content of polyphenols and flavonoids, demonstrate significant free radical scavenging activity by $ABTS^{+}$, $^{\circ}OH$ and $NO\cdot$ scavenging assay, which can be corroborated with their extensive age-old use in this sub-continent.

Dr. Samir K Dutta and Group

Cloning, expression, and characterization of Plant Protease Inhibitors–plausible biotechnological application and Biotransformation of Plant Secondary Products for increased therapeutic value

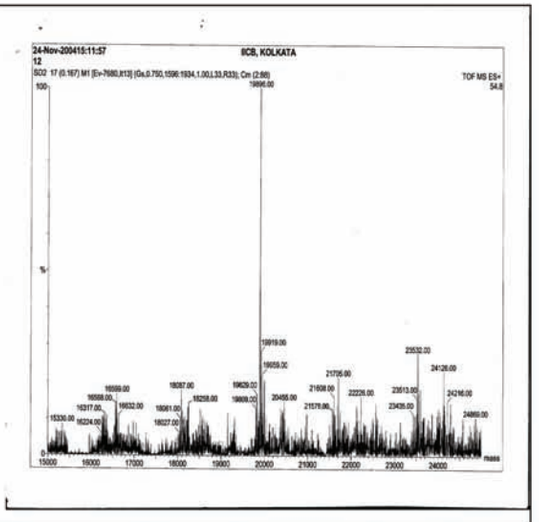
Earlier we reported cloning, expression, mutations and characterizations of a protease inhibitor from a leguminous plant, winged bean (*Psophocarpus tetragonolobus*) that inhibits both trypsin and chymotrypsin (WbTI-1A), but not simultaneously, which means the same Reactive Site Loop (RSL) is some what flexible. Specific point mutations converted this chymotrypsin/ trypsin inhibitor from winged bean specifically to a chymotrypsin inhibitor and a trypsin inhibitor. Since it can kill the *Hellicoverpa armigera* larvae, the clones are supposed to become useful for producing pest resistant transgenic plants. Subsequently, we purified another trypsin inhibitor from winged bean (WbTI-2) seeds using immunoaffinity column (Fig. 23) and the molecular mass was identified from the Mass Spectrum analysis done at the institute using Q-TOF-MS/ MS facility (Fig. 24).

Further characterization of the primary structure was done using CNBr fragmentation and separation of the fragments using SDS-PAGE for understanding the size of each fragment (Fig. 25). Western blot analysis showed that only one of the CNBr fragments was recognized by the antibody raised against the seed purified WbTI-2 (Fig. 26).



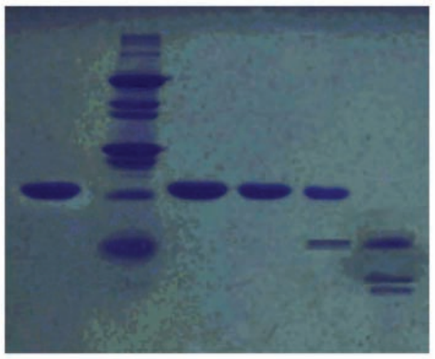
Lane 1 and 2 of showing 1.5 and 2.5 µg of protein respectively from immunoaffinity column and lane 3 showing marker proteins (4 µg)

Fig. 23: Silver stained SDS-PAGE showing homogeneity of seed purified WbTI-2



The mass of the single major peak was close to 20 kD

Fig. 24. Mass-spectrum of purified WbTI2



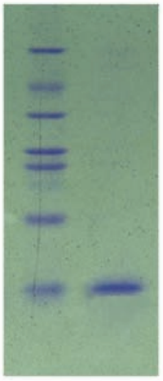
Lane 1: Undigested WbTI-2 (7 µg), lane 2: marker(20 µg of total protein), lane 3-6: 0 h, 6 h , 12 h and 24 h CNBr digested WbTI-2 (7 µg of protein in each lane). *Fragment III (17 amino acid residue), and the 146th methionine could not be resolved in SDS-PAGE

Fig. 25: SDS-PAGE analysis of CNBr-fragmented WbTI-2

Lane 1: Undigested protein (5 µg), lane 2 colored markers (Sigma, 5 µg), and lane 3: 24 h CNBr-digested WbTI-2.

Fig. 26: Western blot of CNBr fragmented WbTI-2

CNBr fragmented peptides were separated and isolated using a FPLC peptide gel filtration column, (from the size it was identified as the RSL containing fragment) (Fig. 27) showed trypsin inhibitory activity,



Lane 1: Molecular wt. markers (Lysozyme at the lowest position) and Lane-2: FPLC peptide gel filtration column eluant.

Fig. 27: CNBr digested fragment II separated by FPLC peptide gel filtration column

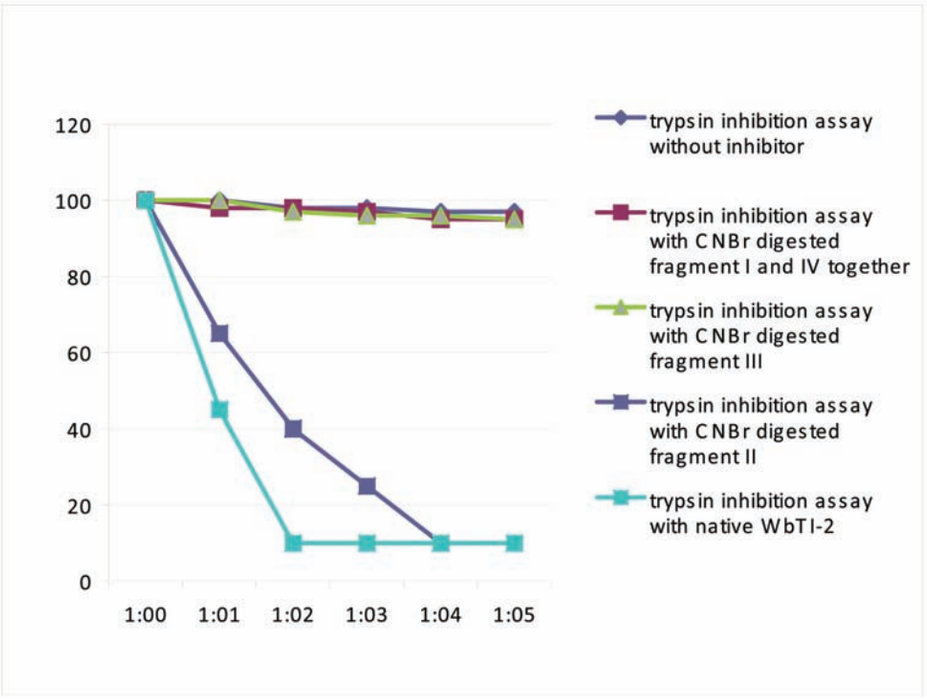
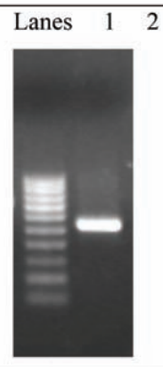


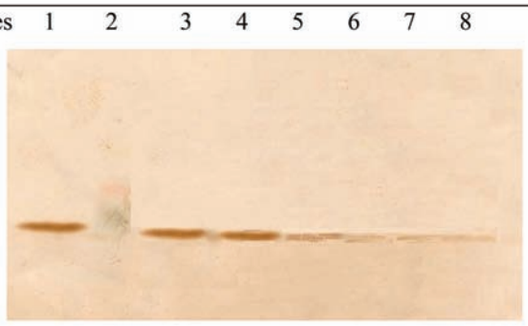
Fig. 28: Trypsin inhibition assay with CNBr digested fragments against native WbTI-2 (Fragments I and IV were assayed together as they co-eluted through FPLC gel filtration column)

although to a lesser extent (Fig. 28). The gene for WBTI-2 has been cloned (GenBank Accession No. DQ363437), using the PCR product (Fig. 29) and IPTG dependent expression was checked from Western blot analysis (Fig. 30), mutated and characterized for understanding its structure-function relationship. Thus, the seed purified WbTI-2 and the recombinant WbTI-2 (rWbTI-2) against molecular wt. markers. WbTI-2 is highly effective against the K-562 cell line, which undergoes apoptotic death, as was revealed from Annexin-V FITC Kit assay.



Lane 1: marker, lane2 PCR product.

Fig. 29: PCR product obtained from cDNA with unique primer set.



Lane 1: native protein purified from winged bean seeds, lane2: marker, lane 3 to lane7 expressed protein with 0.6mM, 0.5mM, 0.4mM, 0.2mM and 0.1mM IPTG inductions respectively, lane 8: expressed protein without IPTG.

Fig. 30: Western blot-analysis of native protein and expressed protein with varying amount of IPTG induction using Anti-WbTI-2-antibody.

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Visit of Dr. K Kasturirangan, Member, Planning Commission

CHEMISTRY

S. B. Mandal, Asish K. Sen, B. C. Pal, A. K. Sen (Sr.), S. Mukhopadhyay, P. Chattopadhyay, G. Suresh Kumar, S. Bandyopadhyay, N. B. Mondal, P. Jaisankar, R. Mukhopadhyay, Asish K. Banerjee, R. C. Yadav, Chinmay Chowdhury, Biswadip Banerji and S. Garai

Despite rapid expansion of the allopathic system of medical treatment in India, commercial demand for pharmacopoeial drugs and products from medicinal plants is continually increasing for the treatment of various diseases. Based on the rich heritage of knowledge on the use of plants of medicinal values, the current research activity of the chemistry division has been focused on the isolation of bioactive natural products from medicinal plants to determine their efficacies as well as on the formulation of herbal preparations for treatment of some major ailments. Synthesis of bioactive natural products or natural product like molecules in large amount, which includes synthesis of novel nucleosides/nucleotides, chiral/achiral heterocycles, anti-leishmanial compounds etc are the major areas of research in this division. Besides, the division is also working on bacterial cell surface antigens, plant polysaccharides and neoglycoproteins, and on nucleic acid binding properties of natural products. The department has also been involved in teaching and providing guidance to research fellows.

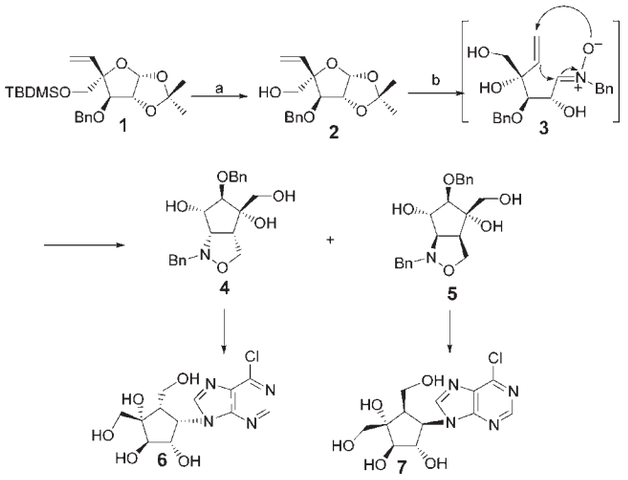
Dr. S. B. Mandal and group

Synthetic approaches to structurally novel nucleosides and analogues from D-glucose

The objective of the subproject is to develop synthetic routes to structurally unique carbocyclic and conformationally locked bicyclic nucleosides based on oxabicyclo[3.2.1]octane and oxabicyclo[2.2.1]heptane skeletons through manipulation of D-glucose derived precursors.

Synthesis of chiral carbanucleoside analogues with cyclopentane rings derived from carbohydrate precursors: The importance of the carbanucleosides has been realized after the isolation of (-)-aristeromycin and (-)-neplanocin A, both displaying antibiotic and antitumor activity, from natural sources. By modifying these biologically active compounds, structurally similar but non-natural synthetic carbanucleoside analogues are generated where the molecular complexity is kept to a minimum whilst improvements are realized in regard to the desired pharmacological activity. Among such nucleosides, carbovir, abacavir, (-) BCA, carba-5-bromovinyl-2'-deoxyuridine, and carba-2-*ara*-fluoroguanosine are important due to their potent anti-HIV activity *in vitro*. Based on these observations, we feel that we should develop a method to synthesize more analogues of such nucleosides. We describe herein an approach to the synthesis of fully substituted and more crowded cyclopentyl amine derivatives, precursors of carbanucleosides, from an appropriate sugar derived substrate having requisite functionalities at the proper positions.

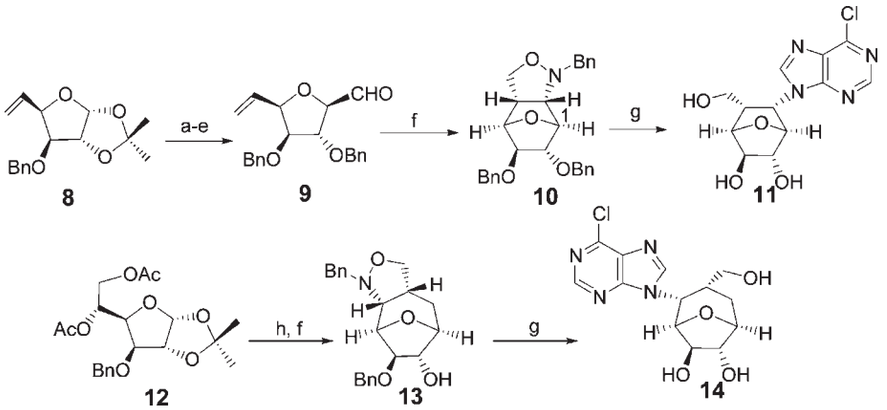
Towards this goal, removal of silyl protection from D-glucose derived substrate **1** afforded **2**, which upon acetonide deprotection followed by reaction with N-benzyl hydroxylamine furnished two isomeric isoxazolidinocyclopentane derivatives **4** and **5** via spontaneous cyclization of an in situ generated nitrone **3** (Scheme 1). Hydrogenolytic cleavage of the isoxazolidine rings of the purified products furnished pentahydroxy aminocyclopentanes, which upon insertion of 5-amino-4-chloropyrimidine moiety and purine ring construction



Scheme 1. Reagemts and Conditions: (a) Bu_4NF, THF, rt, 12 h; (b) (i) H_2SO_4 (4%) CH_3CN-H_2O (3:1), rt 12 h (ii) BnNHOH, reflux, 5 h; (c) Pd/C (10%), H_2 (1 atm), EtOH, rt, 12 h; (d) (i) 5-Amino-4,6-dichloro-pyrimidine, dry Et3N, *n*-butanol, reflux, 30 h, N_2; (ii) $HC(OEt)_3$, *p*-TSA, 10 °C, 16 h, N_2

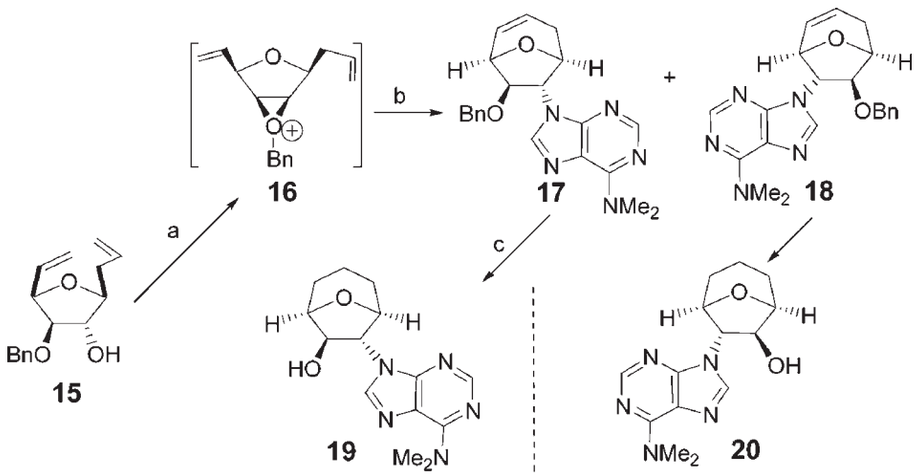
smoothly afforded structurally unique carbanucleoside analogues **6** and **7**. Application of various spectroscopic methods on the synthesized compounds and X-ray analysis on one important intermediate were used to assign the structures and stereochemistry of the products.

Locked nucleosides based on oxabicyclo[3.2.1]octane and oxabicyclo[2.2.1]heptane skeletons: Aiming at the generation of nucleoside analogues for which both solution and solid-state conformations could be very similar, various conformationally locked bicyclic nucleosides (1',2'–linked, 1',3'–linked, 2',3'–linked, 2',4'–linked, 3',4'–linked, and 3',5'–linked) have been targeted for synthesis. As a part our program to construct a new class of C (1)→C (5)-linked bicycles, we carried out the intramolecular nitrone cycloaddition (INC) reaction on a D-glucose derived substrate carrying an aldehyde-nitrone at C-1 and vinyl group at C-4 (**9** derived from **8**) or an allyl group at C-1 and an enose-nitrone at C-5 (derived from **12**) to furnish a tricyclo[5.2.1.$0^{2,6}$]decane **10** or a tricyclo[6.2.1.$0^{2,6}$]undecane ring structure **13**. These tricycles were converted to bicylic nucleosides with oxabicyclo[2.2.1]heptane **11** and oxabicyclo[3.2.1]octane rings **14** in three steps (Scheme 2). An oxabicyclo[3.2.1]octane ring compound could alternatively be formed by RCM reaction between C-1–allyl and C-4–vinyl moieties and transformed to nucleoside analogues through a nucleophilic substitution reaction. Participation of a neighbouring benzyl ether substituent in one case paved the way for an enantiodivergent synthesis. For this, attempted nucleosidation on the triflate derivative (derived from **15**) and subsequent RCM



Scheme 2. (a) (i) 80% AcOH, (ii) Ac_2O, DMAP, Py; (b) TMSCN, BF_3, Et_2O, CH_3CN; (c) K_2CO_3 MeOH; (d) BnBr, Ag_2O; (e) (i) DIBL-H, DCM, (ii) Sodium Potassium tartrate, rt, 1h; (f) BnNHOH, EtOH; (g) (i) Pd/C (10%), MeOH, cyclohexene, (ii) 5/amino-4,6-dichloro-pyrimidine, n-BuOH, Et_3N, (iii) HC (OEt), p-TSA, DMF; (h) (i) AllyITMS, $BF_3.Et_2O$, DCM K_2CO_3, MeOH, (ii) $NaIO_4$, MeOH, H_2O

reaction between the olefins provided the bicyclic nucleosides **17** and **18** via the intermediate **16**. Hydrogenation of these molecules produced enantiomeric nucleosides **19** and **20** (Scheme 3).



Scheme 3. (a) (i) Tf_2O, Et_3N, DCM, (ii) 6-chloropurine, K_2CO_3,18-Crown-6, DMF; (b) Grubbs catalyst, Benzene; (c) Pd/C, H_2, EtOH

Synthesis of new classes of bioactive nucleosides by the application of our methodology on carbohydrate-based precursors is in progress.

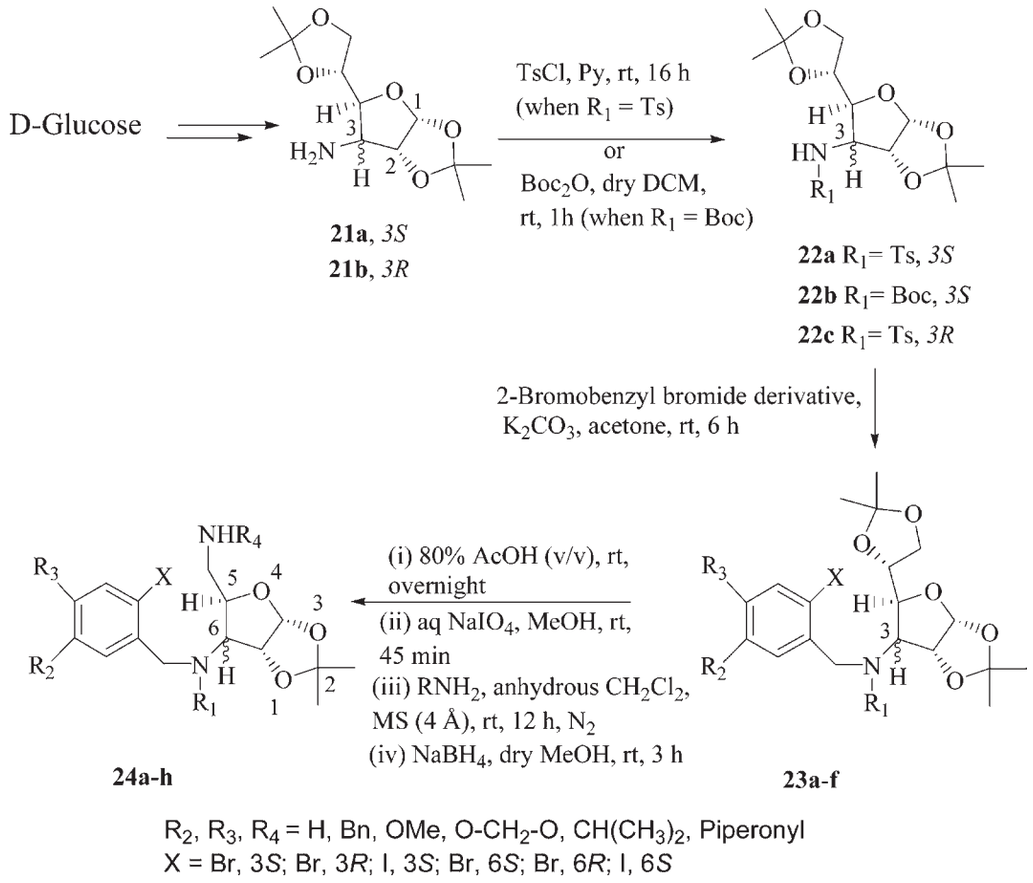
Dr Partha Chattopadhyay and group

Synthesis of annulated medium ring heterocycles

The principal objective of the subproject is to develop synthetic methodology for medium-sized ring ethers and analogues possessing diverse biological properties.

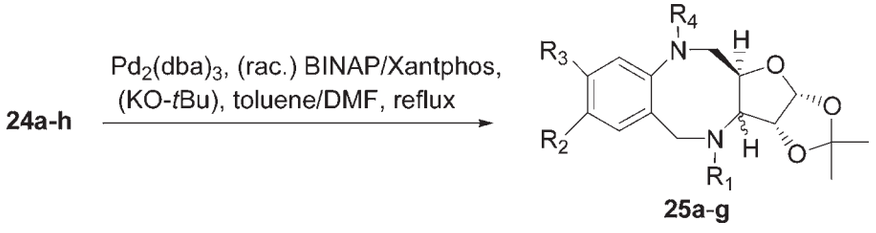
Here, we report an intramolecular aryl amination strategy, which when applied to D-glucose derived sugar amines furnished chiral tricyclic furobenzodiazocine derivatives. Cleavage of the sugar ring of one of these tricyclic derivatives provided chiral, functionalized benzodiazocines. The strategy has also been extended to synthesize a dibenzodiazocine derivative.

The starting material 1,2:5,6-di-O-isopropylidene-α-glucofuranose was converted to amino derivatives **21a** and **21b** according to the reported procedure. N-Alkylation of the corresponding tosyl amides (**22a, 22c**) and Boc amide (**22b**, derived from **21a**) with appropriately substituted 2-bromobenzyl bromides afforded (Scheme 4) the respective 3-N-(2-bromobenzyl)-N-tosyl glucofuranoses **23a-d** and 3-N-(2-bromobenzyl)-N-tert-butoxycarbonyl glucofuranoses **23e-f** in excellent yields. Selective removal of the 5,6-O-isopropylidene moiety from **23a-f** was smoothly effected with 80% aqueous HOAc at 25°C, and the resulting diol on NaIO4 oxidation, imine formation with aliphatic amines, and subsequent NaBH4 reduction in MeOH afforded the desired amines **24a-h** in good yields (68-78 %). The structures of **24a-h** were derived from spectral data and comparison with data for similar compounds prepared by us.



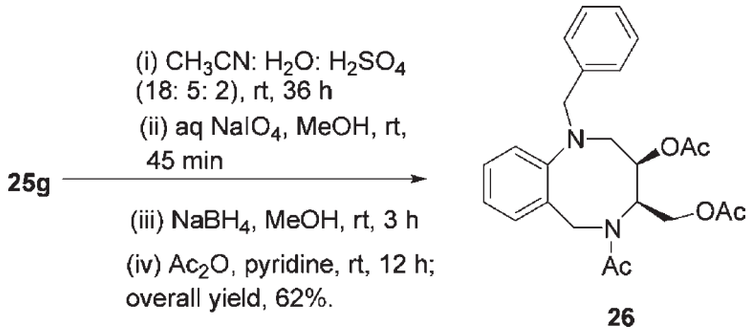
Scheme 4. N-alkylation of aminosugar derivatives with substituted benzyl bromide.

Our initial goal was to explore the synthesis of benzodiazocine-annulated furanose derivatives **25** from **24** through Pd-catalyzed intramolecular cycloamination reaction in the presence of different bases and ligands (Scheme 5). The yields of **25a-g** varied from 60-70 %. The structures of **25a-g** were determined by spectroscopic data and supported by single crystal X-ray analysis of **25e**.



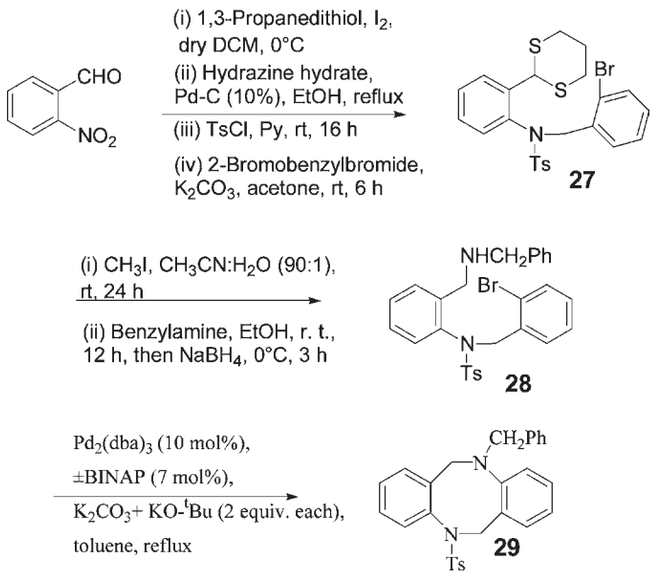
Scheme 5. Cyclization reaction to synthesize benzodiazocine derivative.

As an application of our methodology, the feasibility of synthesizing chiral functionalized benzodiazocines from the annulated sugar derivatives thus obtained could be demonstrated using **25g**. Thus, subjecting **25g** to a sequence of reactions involving removal of the 1,2-O-isopropylidine group as well as the tert-butoxycarbonyl group with H2SO4 in MeCN-H2O (2:18:5), NaIO4 cleavage of the diol, NaBH4 reduction of the generated carbonyl group, and acetylation of the resulting diol with acetic anhydride and pyridine furnished the benzodiazocine derivative **26** (Scheme 6).



Scheme 6. Cleavage of furanose rings by four step reaction.

We next focused our attention on extending our methodology to the synthesis of dibenzodiazocine derivatives. For this, we synthesized compound **27** through a sequence of reactions such as reduction of the nitro group with Pd/C and hydrazine hydrate, tosylation of the resulting amino group, arylation of the tosyl amide with 2-bromobenzyl bromide, and dethioacetalization in the presence of MeI/aq. MeCN. Compound **27** was then cyclised to **28** via imine formation with benzylamine in EtOH and subsequent NaBH4 reduction. The compound **28** when heated at reflux under the standard conditions for bromo derivatives afforded the desired cyclised product **29** in 72% yield (Scheme 7). The spectral data and single crystal X-ray analysis of **29** are in excellent agreement with the assigned structure.



Scheme 7. An approach to the synthesis of dibenzodiazocine derivative

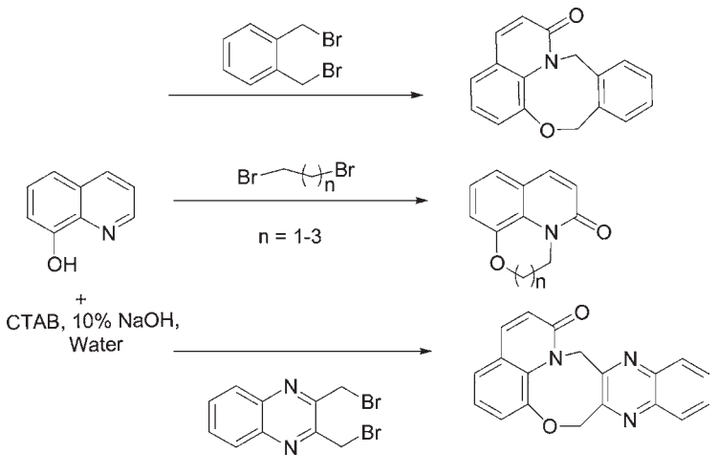
Dr. Nirup Bikash Mondal, Dr. Sukdeb Bandyopadhyay and group

Synthesis of structurally unique bioactive heterocycles

The extensive use of heterocyclic compounds in the pharmaceutical industry is perhaps for the ample range of reaction types that facilitate subtle structural modifications in the heterocyclic compounds. Thus investigations

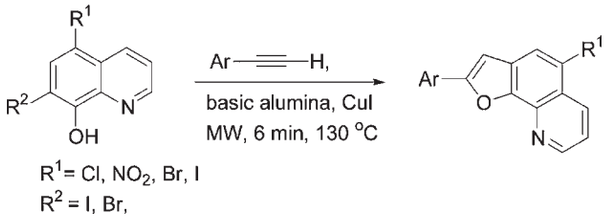
towards the understanding of reactivity of heterocyclic compounds are gaining significance now a days, especially expedient syntheses leading to N-heteroaromatic cations as they often form the framework of DNA intercalating agents. In this perspective, molecules containing quinolinium core constitute one of the important subsets of heteroaromatic cations.

A high yielding green protocol has been developed to synthesize tri-, tetra-, and pentacyclic fused 2-quinolones in micellar medium. The environmentally benign method is more effective compared to phase-transfer catalytic (PTC) one (Scheme 8).



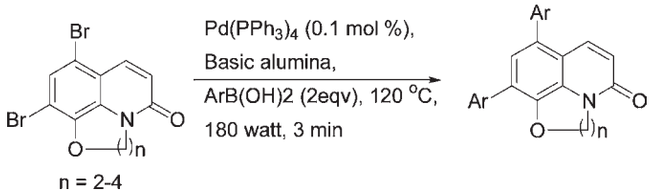
Scheme 8. Synthesis of polycyclic fused 2-quinolones in aqueous micellar system

Acetylenic 8-quinolinols generated in situ by the Sonogashira cross-coupling reaction are efficiently converted into furo[3,2-h]quinolines by microwave-assisted and copper-catalyzed intramolecular cyclization in the presence of basic alumina (Scheme 9).



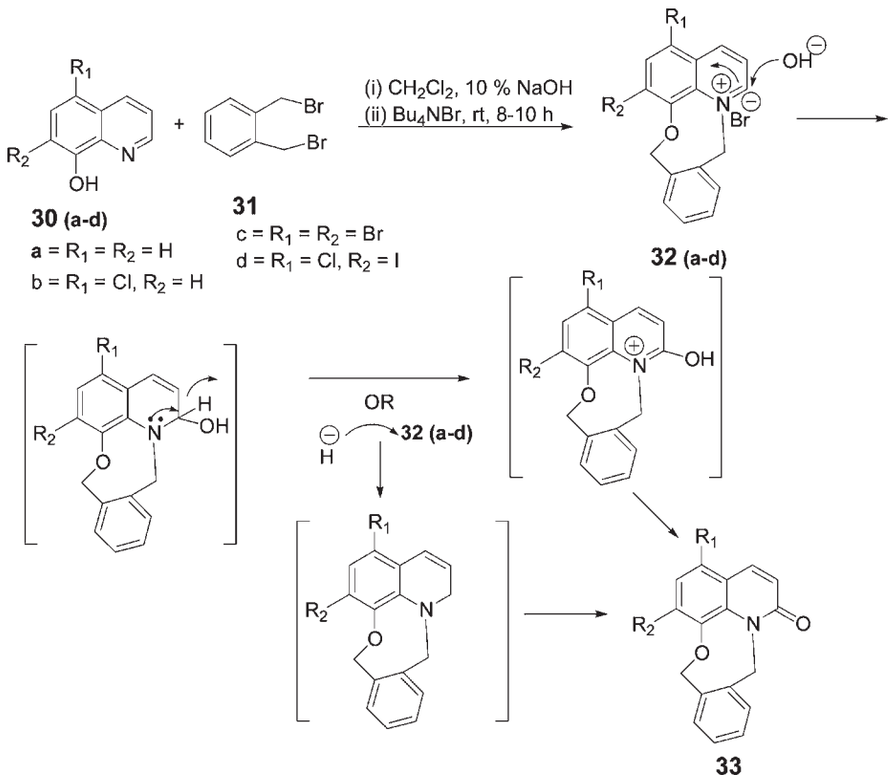
Scheme 9. Microwave-assisted Sonogashira cross-coupling reaction and subsequent intramolecular cyclization

Basic alumina used in lieu of traditional mineral bases efficiently promotes a solvent free and Pd(PPh3)4 catalyzed Suzuki–Miyaura cross-coupling reaction of 5,7-dibromoquinolone under microwave irradiation (Scheme 10).



Scheme 10. Suzuki cross coupling reaction under microwave irradiation

A general and highly efficient synthetic protocol under phase transfer catalytic condition has been established for the synthesis of fused tetracyclic oxazocinoquinolone analogues, which serve as the precursors for novel biaryl quinolones using microwave assisted Suzuki cross coupling reaction (Scheme 11) (Figures 1 and 2).



Scheme 11. Plausible reaction pathway leading to fused quinolone analogues **(33a–d)**

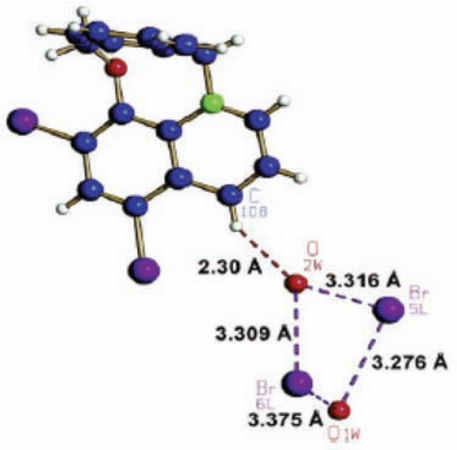


Figure 1. Short contacts in the crystal lattice of **32c** with contributions of molecule 1 of **32c**, the counter ions and the water molecules as illustrated here.

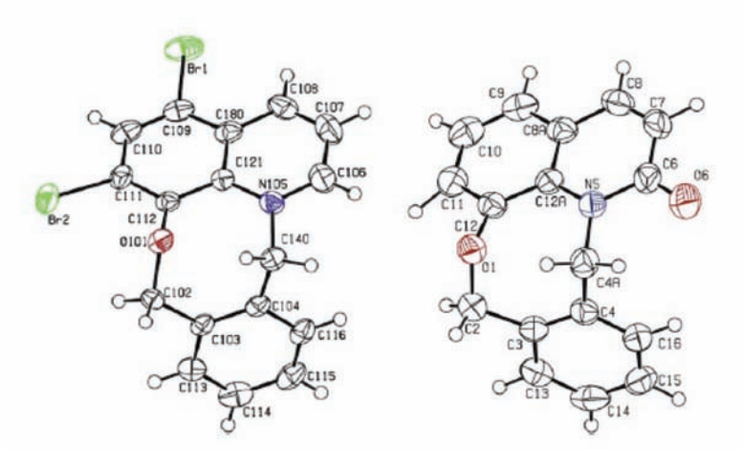
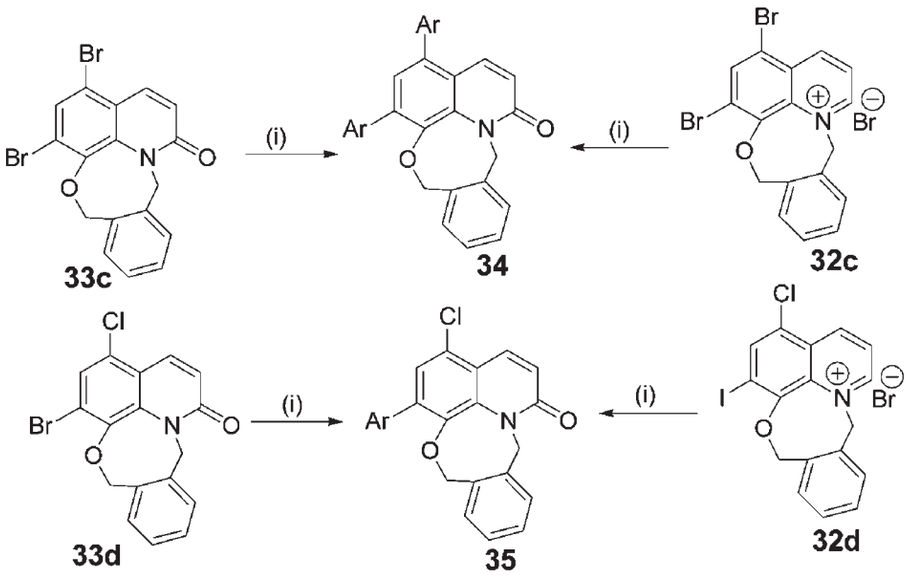


Figure 2. ORTEP representations of compounds **32c** (cationic part, left) and **33a** (quinolone part, right), the displacement ellipsoids are drawn at a probability of 50%.

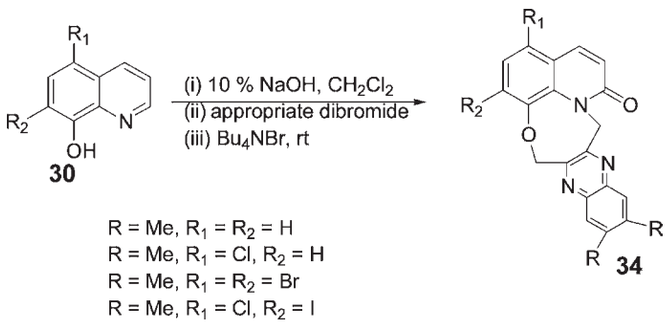
Our next attempt was to apply Suzuki reaction upon the compounds **32c**, **32d** and **33c**, **33d** to produce **34** and **35** as shown in Scheme 12.



(i) Ar $B(OH)_2$, 3 mol%$Pd(PPh_3)_4$, Na_2CO_3,Mw

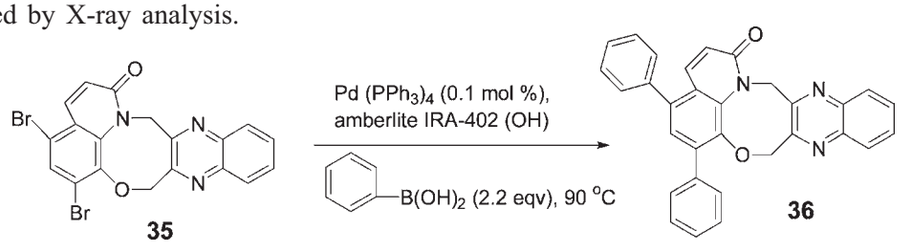
Scheme 12. Suzuki reaction of quinoliniums (**32c/32d**) and quinolones (**33c/33d**) with aryl boronic acid.

An efficient and simple synthesis of pentacyclic quinolonoquinoxalinooxazocines in a one-pot sequence has been performed by unique application of phase transfer catalysis (Scheme 13). Preparative simplicity and conceptual novelty of the methodology suggest an attractive general application for the synthesis of novel quinoline antibiotics. The structure of one of the products was confirmed by X-ray analyses.



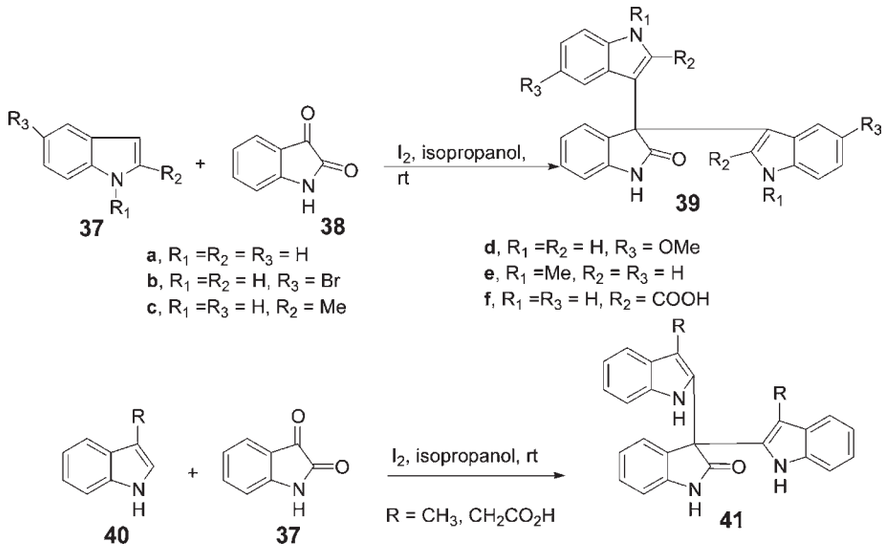
Scheme 13. Synthesis of pentacyclic quinolonoquinoxalinooxazocines

Amberlite IRA 402(OH) effectively mediated biarylation via Suzuki–Miyaura cross coupling reaction on complex systems such as dihalo quinolonoquinoxalinoxazocines **35** in water (Scheme 14). The structure of the product **36** was confirmed by X-ray analysis.



Scheme 14. Suzuki–Miyaura cross-coupling reaction using dibromoquinolonoquino-xalinoxazocine and benzene boronic acid in aqueous medium

Syntheses of 3,3-diheteroaromatic oxindole derivatives **39** have been achieved by coupling indole-2,3-dione **38** (isatin) with differently substituted indoles **37** in presence of I_2 in i-PrOH. The reactions of 3-substituted indoles **40** and isatin **38** led to 3,3-di(2-indolyl)-2-oxindoles **41** (Scheme 15).



Scheme 15. Reactions between 2,3-disubstituted indoles and isatin

The in vitro spermicidal potentials and the mode of spermicidal action of the synthesized analogues were evaluated and the derivative, 3,3-bis (5-methoxy-1H-indol-3-yl) indolin-2-one **39d** exhibited most significant activity (Figure 3). TEM results are shown (Figure 4).

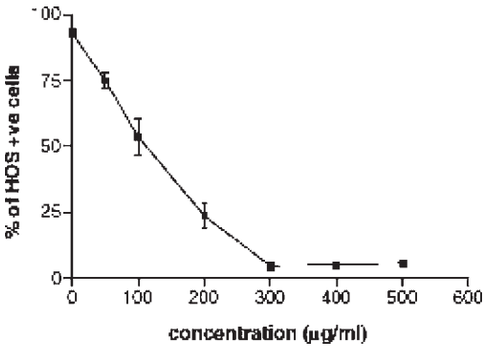


Figure 3. Dose dependent HOS reactivity of spermatozoa exposed to different concentrations of compound **39d**. The number of HOS positive cells exhibiting typical tail coiling was counted under a phase contrast microscope (40x). Each point represents mean ± SEM of at least six observations.

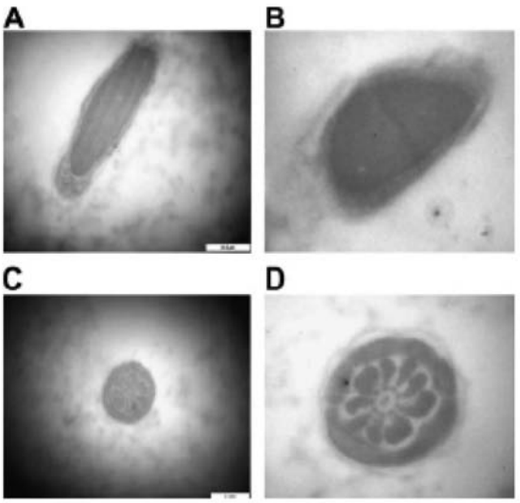
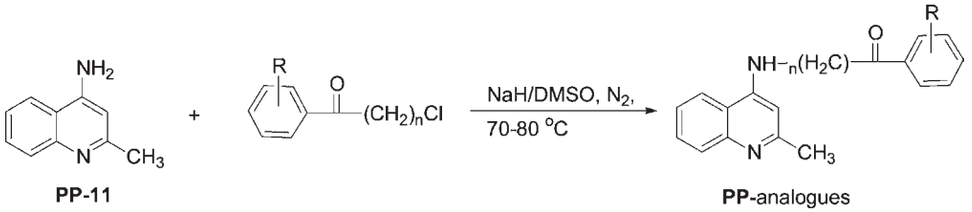


Figure 4. Transmission electron microscopic observation of sperm sample treated with compound **39d** at MEC. (A) Control spermatozoa with intact acrosome covering the sperm head; (B) **39d** treated spermatozoa with disintegrated sperm acrosomal cap indicating membrane damage; (C) (9+1) axoneme doublet of control sperm showed intactness of the sperm membrane in tail portion; (D) (9+1) axoneme structure of the **39d** treated sperm showed loss of membrane coverage.

Based on an established 3D pharmacophore, a series of quinoline derivatives were synthesized. The opioidergic properties of these compounds were determined by a competitive binding assay using ^{125}I-Dynorphine, 3H-DAMGO and ^{125}I-DADLE for j, l, and d receptors, respectively. Results showed varying degree of activities



Scheme 16. General reaction procedure for preparation of PP-analogues

of the compounds to j and l opioid receptors with negligible interactions at the d receptor. The compound, S4 was the most successful in inhibiting the two most prominent quantitative features of naloxone precipitated withdrawal symptoms-stereotyped jumping and body weight loss. Determination of IC_{50} of S4 revealed a greater affinity towards l compared to j receptor. In conclusion, quinoline derivatives of S4 like structure offer potential tool for treatment of narcotic addictions. The results are shown in Figures 5-8.

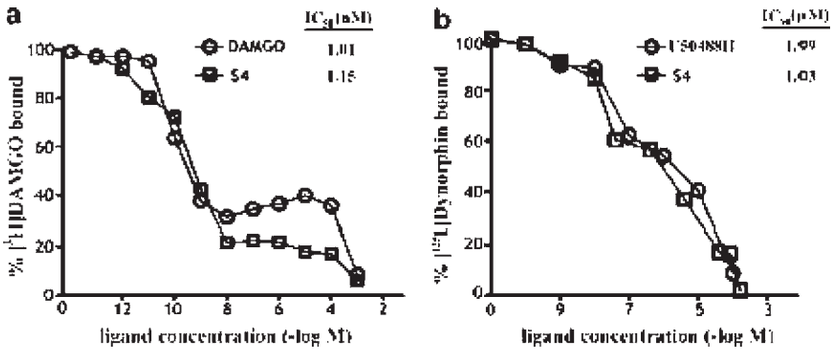


Figure 5. Competitive inhibition of specific (a) [^{3}H]DAMGO and (b) [^{125}I]Dynorphin binding to brain membrane by S-4. Corresponding displacement curves by selective agonists, DAMGO (a) and U50488H (b) were also carried out for comparison. Each point represents mean of three individual determinations. Non-linear regression lines were determined by Graph prism 5 and IC_{50} concentrations calculated.

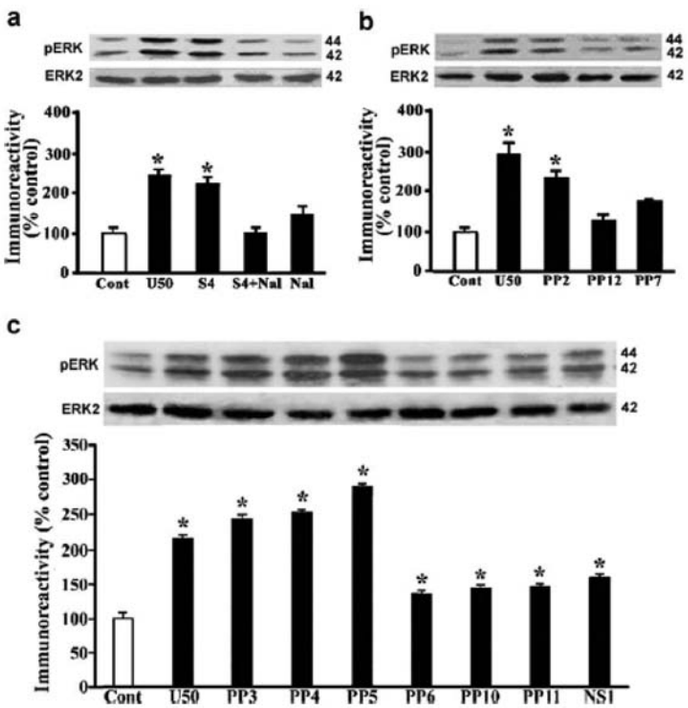


Figure 6. Effect of test compounds on induction of pERK activity in primary cultures of astrocytes. Ten-day-old cultures were serum starved for 48 h. The stimulatory effect of opioid agonist such as j-opioid receptor agonist, U50488H (1 lM) and the test compounds (40 lM) were evaluated by treating cells for 10 min with the drugs and quantitating pERK1/2 by western blot analysis. a) Shows stimulation of pERK by S-4, which was antagonized by co-treatment with naloxone (10 lM). The effect of other test compounds on pERK activation includes PP2, PP12, PP7 in (b) and PP3, PP4, PP5, PP6, PP10, PP11, NS1 in (c). Same blots were probed with ERK2, which served as a loading control. The relative intensities of the pERK bands, indicated in the graph, were obtained by densitometric scanning and pERK levels were quantitated after normalizing against ERK2. Results are mean ± SEM of at least 3 blots. *P <0.05 versus untreated control.

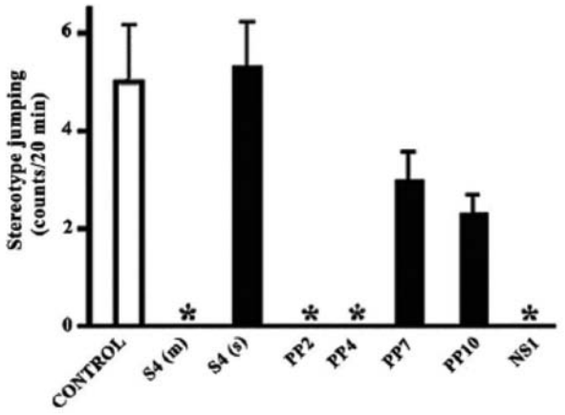


Figure 7. Demonstration of physical dependence by naloxone-precipitated stereotype jumping. Mice (seven per group) in each experiment were treated with chronic morphine regime. Treatment protocol for test compounds induction of precipitated withdrawal by naloxone is described in Methods. S-4 (S) denotes S-4 injected singly after the last dose of morphine. Otherwise, test drugs were given once daily for 6 days. Stereotype jumping in each mouse was scored within a 20-min period after each injection. Data are expressed as mean ± SE of stereotyped jumping in counts per 20 min of three individual experiments indicates significantly different ($p < 0.001$) from control.

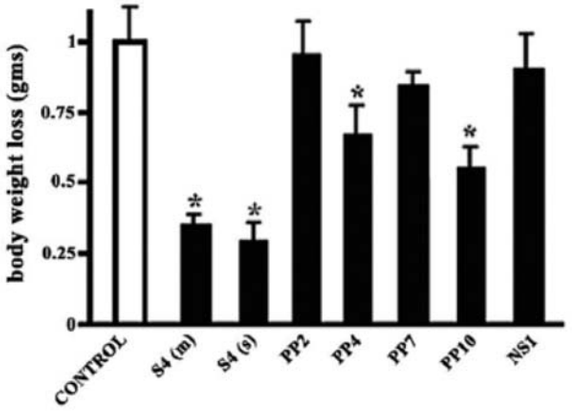


Figure 8. Effect of naloxone precipitated withdrawal on body weight of mice. Mice (seven per group) in each experiment were treated with chronic morphine regime. Treatment protocol for test compounds and induction of precipitated withdrawal by naloxone are described in Methods. S-4 (S) denotes S-4 injected singly after the last dose of morphine. Otherwise, test drugs were given once daily for 6 days. Data are expressed as mean ± SE of Body weight loss before naloxone injection and 4 h after of three individual experiments * indicates significantly different ($p < 0.05$) from control.

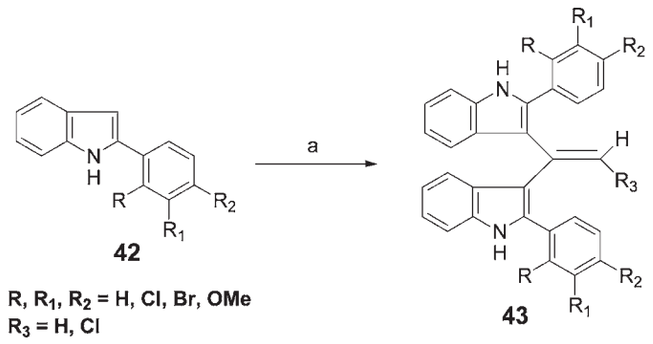
Dr. Parasuraman Jaisankar and group

Synthetic studies in heterocyclic chemistry using catalysts

Synthetic organic chemistry will continue to play a pivotal role in the field of medicinal sciences in the 21st century through the efficient synthesis of medicines and the creation of leading compounds for new pharmaceuticals and chemical probes for life science research. To comply with requests to speed up and diversify

research as well as the need for environmentally benign synthesis, further improvement of synthetic organic chemistry with innovative ideas is desired. Expected to play a leadership role in achieving this goal, the synthetic chemists are seeking breakthroughs. Synthesis of heterocyclic compounds both in chiral and achiral forms have become part and parcel of synthetic chemists due to their wider applications as drug candidates for various diseases. The uses of catalysts not only result in the specific and desired skeletons but also unexpected and completely new compounds.

Regioselective one pot synthesis of 3, 3'-Diindolylethylene and its derivatives and study of their cytotoxic activity: Our initiative towards synthesizing new biologically active heterocyclic compounds using Lewis acid catalyst has resulted in the observation that $AlCl_3$ could be effectively used for preparing different 3,3'-diindolyl ethylene (DIE) derivatives **43** in one pot from indoles **42** (**Scheme 17**). The structure of 2,2'-diphenyl-3,3'-diindolylethylene (R, R_1, R_2 = H, R_3 = H) was confirmed by X-ray analysis (Figure 9). Some DIE derivatives have shown good to moderate cytotoxic activity against human leukemic cell lines U937 and K562 with IC_{50} 13.0-17.0 M.



Scheme 17. Reagent and conditions: (a) CH_3COCl (1eqv), $AlCl_3$ (1.2 eqv), DCM: $C_2H_5NO_2$ (2: 1), 4-6 h, 50 ^{0}C

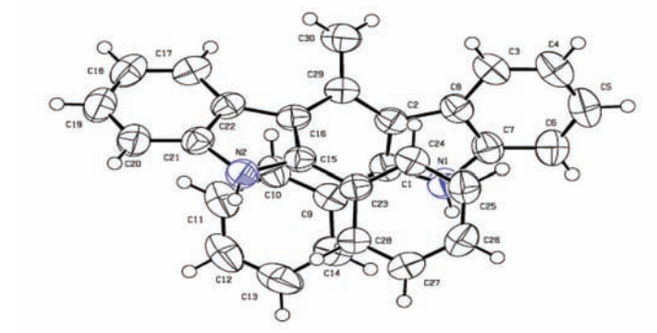
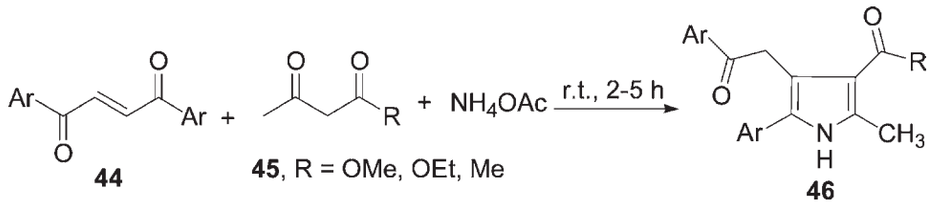


Figure 9. X-ray structure of 2,2'-diphenyl-3,3'-diindolylethylene

Solvent free one-pot synthesis of substituted pyrroles: The pyrrole ring is one of the most common skeletal features present in the heterocyclic compounds. It is found abundantly in natural products and biological important heterocyclic systems such as porphyrins, bile pigments, chlorophylls, coenzymes, corrins and different types of alkaloids. They also play important role for its application in electro luminescent devices as well as supramolecular chemistry. The present trend is to develop environmentally benign synthetic routes for various important organic compounds with attempt to save our environment. Towards a green approach, reaction of *trans*-diaroylethylenes **44** with α-dicarbonyl compounds **45** and ammonium acetate under solvent-free condition at room temperature afforded substituted pyrroles **46** in 81-98% yields (**Scheme 18**). The structure of **46** (R = OMe) was confirmed by X-ray analysis (Figure 10).



Scheme 18. An approach to synthesis of substituted pyrroles

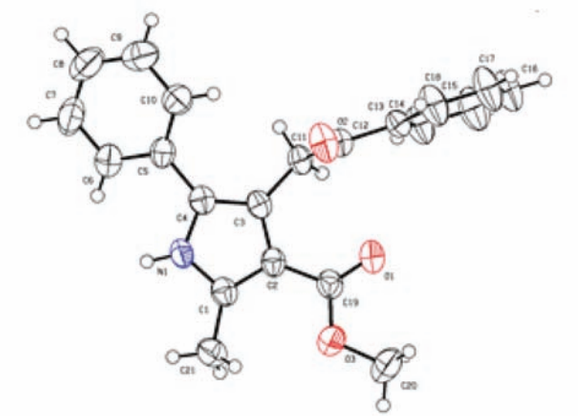
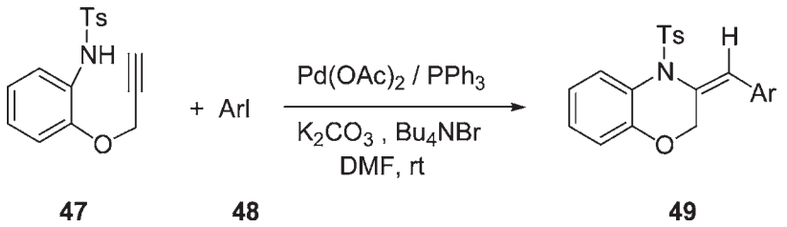


Figure 10. X-ray structure of **46** (R = OMe)

Dr. Chinmay Chowdhury and group

Development of novel methods for the synthesis of heterocycles of biological interests

Heterocyclic compounds, possessing heteroatoms at C-1 and C-4 and fused with an aromatic ring, are important targets because of their wide range of biological and therapeutical properties. Notably, 2*H*-1,4-benzoxazine represents an important heterocyclic core, as several of its derivatives are shown to display a wide range of activities. Particularly, 3-substituted-3,4-dihydro-2*H*-1,4-benzoxazines have been the integral parts of bioactive natural products, potent drugs, and important building blocks. In view of immense importance of 3-substituted-1,4-benzoxazines, synthesis of these compounds through novel methodologies has been targeted. Towards this endeavor, a new, one-pot and general palladium catalyzed procedure has been developed for the synthesis of (*E*)-3-arylidene-3,4-dihydro-2*H*-1,4-benzoxazines (**Scheme 19**). Thus, *N*-tosyl-2-(prop-2′-ynyloxy)aniline **47** reacted with aryl iodide **48** at room temperature in the presence of palladium acetate (5 mol %) and PPh_3 (20 mol %) in DMF to furnish the product **49** with moderate to excellent yields. The method was found to be totally regio- and stereoselective. The evidence in favour of E-stereochemistry came from NOE experiments, $^3J_{CH}$ coupling constant (~7-8 Hz) between the vinylic proton and methylenic carbon (OCH_2) of 1,4-oxazine ring, and single crystal X-ray analysis (Figure 11).



Scheme 19. Palladium catalyzed synthesis of 3-arylidene 1,4-benzoxazines

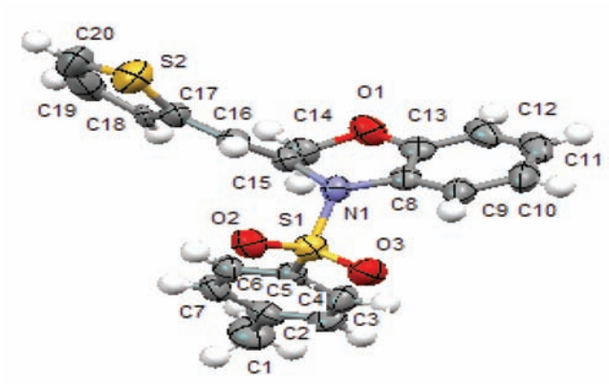


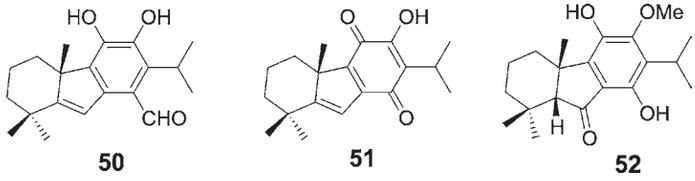
Figure 11. ORTEP diagram of Product **49** (Ar = thienyl)

Based on control experiments and known palladium chemistry, a reasonable reaction mechanism has also been proposed to explain the product formation.

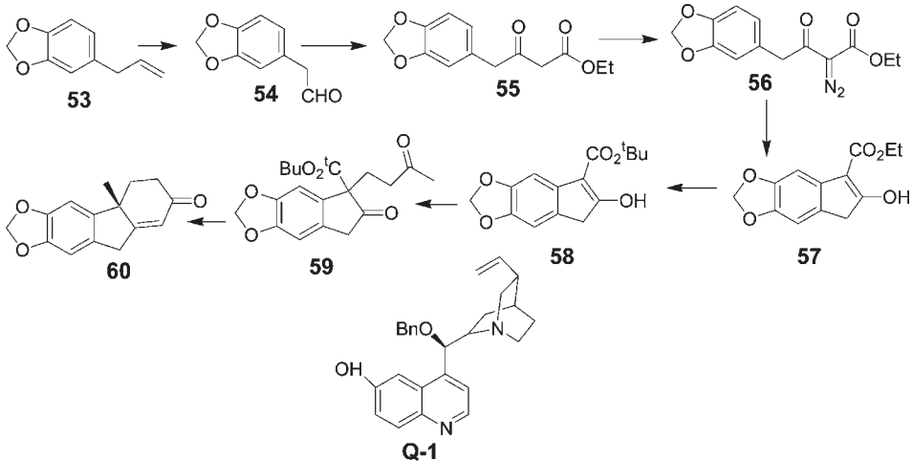
Dr. Asish K Banerjee and group

Novel synthetic routes for natural products: enantioselective approaches and radical cyclization strategies

Abietane diterpenoids, dichronal B (**50**), dichroanone (**51**) and taiwaniaquinol B (**52**) comprising 6-5-6 membered ring systems have been isolated from several tropical medicinal plants some of which exhibit significant biological activities. The racemic syntheses of these natural products have already been established from this laboratory. Therefore our objective is to carry out asymmetric synthesis of these natural products.

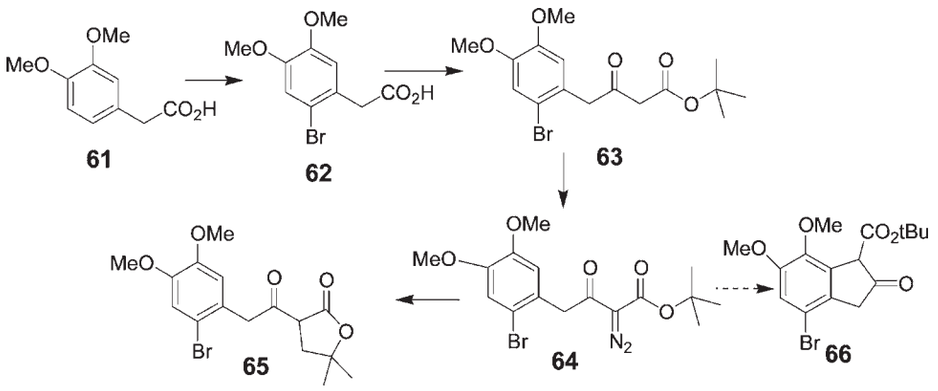


Towards the end, we have made some model studies on the synthesis of dichronal B (**50**) and dichroanone (**52**) as shown in scheme 20.



Scheme 20

In our studies, dihydroxylation of safrole **53** followed by $NaIO_4$ oxidation furnished the desired aldehyde **54**, which was directly reacted with ethyl diazoacetate prepared in situ from ethyl acetoacetate, tosyl azide and NaOH to give the aromatic β-keto ester **55** in 80% yield. The compound **55** was then reacted with tosyl azide to provide the desired diazo compound **56** in 93% yield. Cyclization of **56** with $Rh_2(OAc)_4.2H_2O$ furnished cyclic β-keto ester **57** in 80% yield. Further the β-ketoester **57** was trans-esterified with dibutyltin oxide and *t*-butanol to give *t*-butyl β-ketoester **58**. Asymmetric Michael reaction of **58** with methyl vinyl ketone in presence of quinine derived chiral catalyst **Q-1** afforded the Michael product **59** (88% yield with 96% enantiomeric excess), which could lead to the 6-5-6 ring system **60** present in the natural products.
Encouraged with this result, we subsequently attempted the synthesis of properly aromatic substituted 6-5-6 ring system present in the natural products according to Scheme 21.



Scheme 21

Thus, 3,4-dimethoxyphenyl acetic acid **61** was brominated to give **62**, which was then converted to *t*-butyl β-ketoester **63** in a three-step process. The β-ketoester **63** was converted to α-diazo β-ketoester **64** with *p*-ABSA. Attempted rhodium acetate catalyzed cyclization of **64** afforded γ-lactone **65** instead of the desired indanone **66**. As the desired cyclised β-ketoester was not formed, a new synthetic scheme has been taken up by changing the pattern of aromatic substitutions. Further work is in progress.

Dr. Biswadip Banerji and group

Design, synthesis and biological activities of structurally novel heterocycles as new chemical entities

The group has recently started its research activities on different important aspects of bioorganic chemistry mainly focusing on structure-activity relationship studies of different enzyme inhibitors, function oriented synthesis of small molecules with biological importance, development of cyclic analogues of bioactive peptides etc. We broadly group this entire work under the synthesis of New Chemical Entities (NCEs). This work is based on the design and synthesis of library of small molecules following novel synthetic methodologies.
Design, synthesis and biological activities of new chemical entities (NCE): Our group is engaged in the study of design and synthesis of new chemical entities as different enzyme inhibitors. The design of the molecules is mainly inspired by the natural product derived scaffolds. Primarily we have selected few proteins responsible for different neurological disorders, diabetes, cancer etc. Once synthesized, these molecules will be screened against different enzymes as mentioned earlier. Towards this end, this group is engaged in the design and synthesis of benzimidazolone heterocycles.

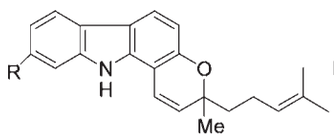
Palladium Catalyzed one pot synthesis of novel heterocycles as enzyme inhibitors: Formation of C-C bonds by palladium catalysed cross-coupling reactions is a common practice to synthesize medicinally important compounds. Among these, one-step simultaneous formation of C-C or C-N bond remains particularly challenging because of its associated problems. Recently in a drug-discovery program, we have undertaken the synthesis of

few therapeutically important heterocyclic scaffolds like bis-isoquinolines by employing palladium catalyzed tandem reaction protocols. These reactions will further be exploited to synthesize small to medium sized library of these scaffolds having suitable pharmacophores.

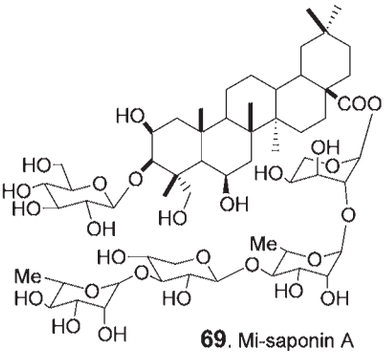
Dr. B. C. Pal and group

Development of herbal medicine

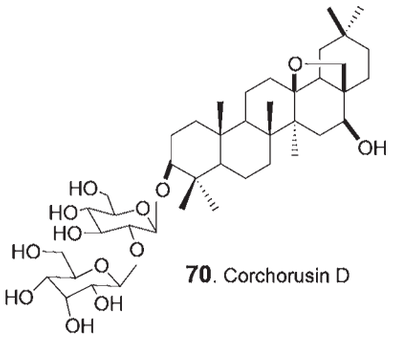
Our group was engaged to identify bioactive lead molecules from Indian medicinal plants. In this regard, we reported biomarkers mahanine (**67**) as anti-leukemic and anti-diabetic Type II molecule, mahanimbine (**68**) as acetyl cholinesterase inhibitory molecule, Mi-saponin A (**69**) as spermicidal molecule and corchorusin D (**70**) as anti-leukemic compound. Bioactivity guided fractionation of plant extract led to the isolation and identification of these marker compounds.



67. R = OH (Mahanine)
68. R = H (Mahanimbine)



69. Mi-saponin A

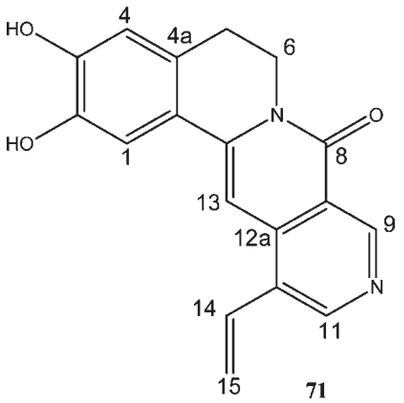


70. Corchorusin D

Dr. Sibabrata Mukhopadhyay and group

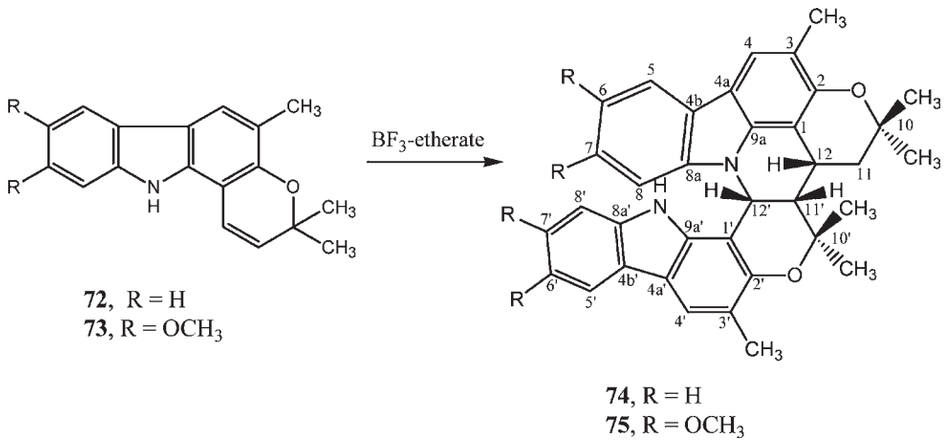
Chemical investigation of medicinal plants for bioactive substances

A new benzopyridoquinolizidine alkaloid, designated as angustinine was isolated from the root bark of *Alangium lamarckii* Thwaites. Investigation on the stem bark of the same plant resulted in the isolation of two known ipecac alkaloids, viz. emetin and cephaline. The structure of the new alkaloid **71** was elucidated on the basis of 2D NMR spectral analysis. It showed anti-asthmatic activity.



71

Murranimbine, a naturally occurring dimeric carbazole alkaloid isolated from the root bark of *Murraya euchrestifolia,* was synthesized in one step by the application of Lewis acid (BF_3-Et_2O) on its monomer girinimbine (**72**, **73**). A new dimer of koenidine was also synthesized following the same procedure (Scheme 22). Structures of these dimeric carbazole alkaloids (**74**, **75**) were determined by detailed spectral analysis. NOESY and COSY relationship in **74** is shown (Figure 12).



Scheme 22. Synthesis of dimeric carbazole alkaloids

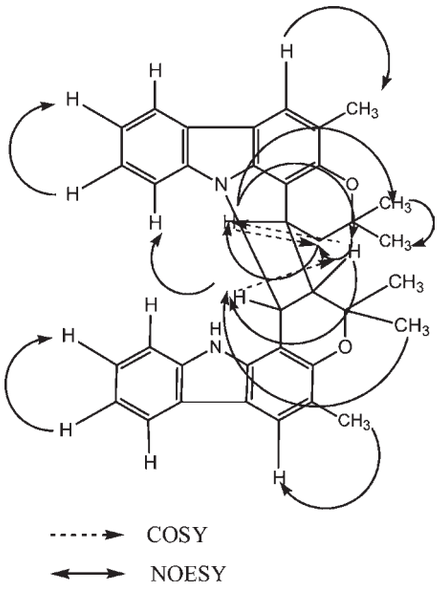


Figure 12. NOESY and COSY relationship in **74**

Dr. Chinmay Chowdhury and group

Bioactive constituents from medicinal plants

In continuation of our investigations for identification of potent anticancer and antiviral agents from Indian medicinal plants, we have chosen to work on the methanol extracts of the leaves of *Semecarpus anacardium*, which was selected through activity guided fractionation. In this pursuit, we have investigated in details its *n*-butanol fraction in order to isolate the pure molecules. We have been able so far to isolate kaempferol-3-*O*-sophoroside as a major constituent along with quercetin-3-*O*-glycoside, kaempferol-3-*O*-glucoside and others as

minor constituents. The definite structures of the aforesaid compounds were established through ID & 2D NMR followed by other analytical evidences. The antiviral screening program of these compounds is currently underway.

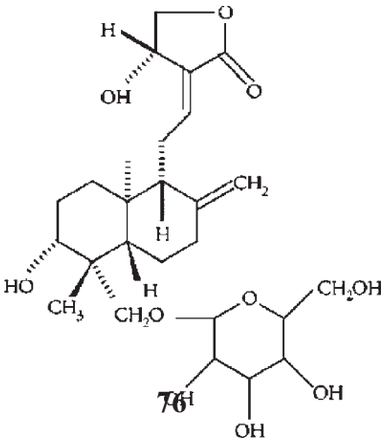
Besides, a series of analogues have been prepared through chemoselective functionalization at C-14 hydroxy of andrographolide and their *in vitro* cytotoxicities were evaluated against human leukaemia cell lines (U-937, THP-1 and K-562). Two of the analogues exhibited significant potency against U-937 and THP-1. Evaluation of the apoptosis caused by these compounds was carried out through flow cytometry as well confocal microscopy. Preliminary studies on structure activity relationship (SAR) revealed that the α-alkylidene-γ-butyrolactone moiety of andrographolide played a major role in the activity profile. The structures of the analogues were established firmly through spectroscopic and analytical data.

Dr. Sukdeb Bandyopadhyay, Dr. Nirup Bikash Mondal and group

Chemical investigation of medicinal plants for bioactive substances

Development of newer bioactive molecules has long been and will continue to be an important area of research. The objective of the project is to identify useful bioactive compounds and development of methodologies for making them readily available. In this endeabom, chemical examination of Indian medicinal plants identified by practitioners of traditional medicine or used as folk remedies in the treatment of various ailments led to the isolation and characterization of active and or novel constituents.

Crystal and molecular structure of a labdane diterpenoid glucoside, andrographiside (**76**), was determined from 2D-NMR and X-ray diffraction data. The 2D-NMR study indicates that the carbohydrate moiety is in α-linkage and the sugar moiety is linked to C-19 of the aglycon. These observations were further confirmed from the X-ray diffraction studies (Figures 13 and 14). Both the six-membered rings are in chair conformation whereas the glucose ring adopts a twist-boat conformation. The molecular geometries and electronic structure of **76** were calculated at the DFT level using the hybrid exchange–correlation functional, BLYP, PW91 and PBE.



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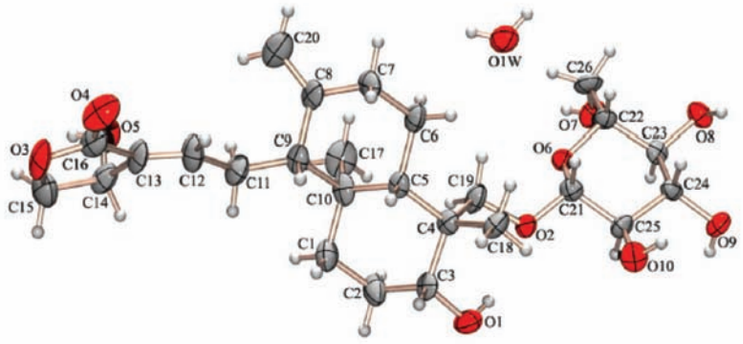


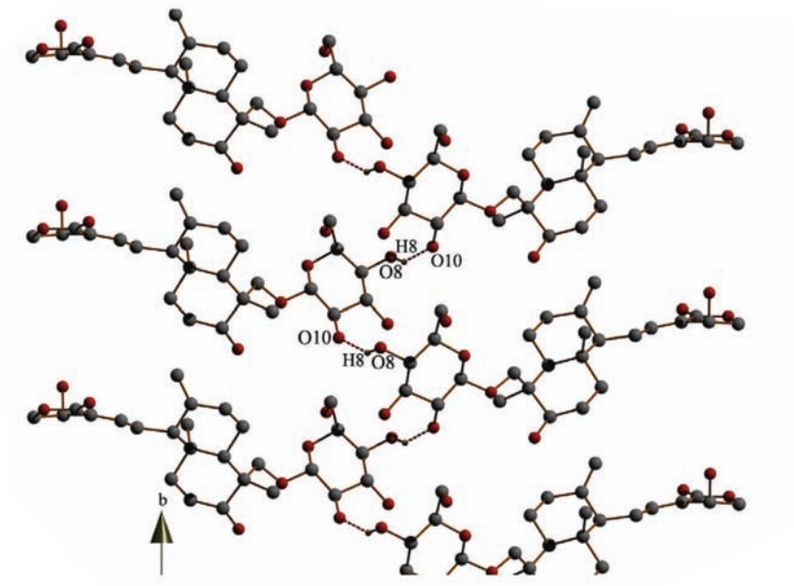


Figure 14. One-dimensional zigzag chain propagating along [0 1 0] direction. Hydrogen atoms not involved in hydrogen bonding have been omitted for the sake of clarity.

Andrographolide, 14-deoxyandrographolide, andrograpanin, andrographiside, deoxyandro-graphiside, and neoandrographolide were isolated from the leaves of *A. paniculata* and evaluated for their sperm immobilizing activity (Figure 15). The mode of spermicidal action was assessed by (a) supravital and double fluoroprobe staining of sperm, (b) hypo-osmotic swelling test, and (c) transmission electron microscopy. Contraceptive efficacy was evaluated by intrauterine application in rat followed by mating, and subsequent assessment of the pregnancy outcome. 14-Deoxyandrographolide with MEC of 200 µg/ml was found to be the most active among the six compounds. It is comparable in activity to nonoxynol (N-9) and exerts its effect in a dose dependent manner. Intra-vaginal administration of 10% 14-deoxyandrographolide did not cause any significant vaginal irritation in rat. The findings strongly suggest that 14-deoxyandrographolide may be used as a nondetergent type spermicidal agent (Figures 16 and 17).

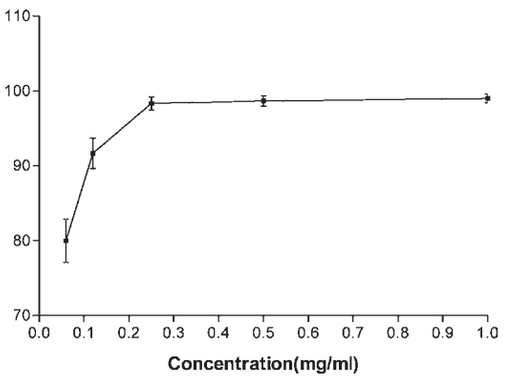


Figure 15. Concentration dependent inhibition of sperm motility

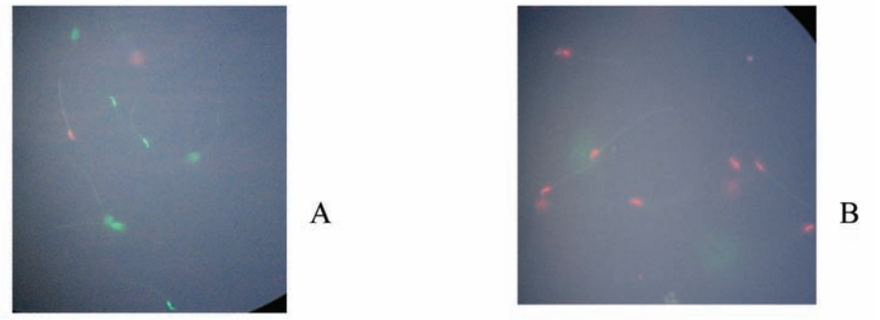


Figure 16. Photomicrograph of SYBR14/PI staining. (A) Control sperm subjected to double fluoroprobe staining; (B) 14-deoxoandrographolide treated sperm. ——► sperm head appeared green due to binding of SYBR14 with the sperm chromatin and ——► treated sperm appeared red due to uptake of PI.

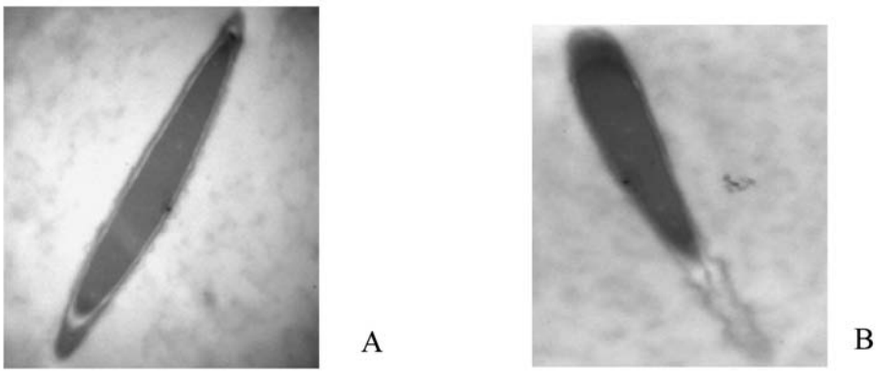
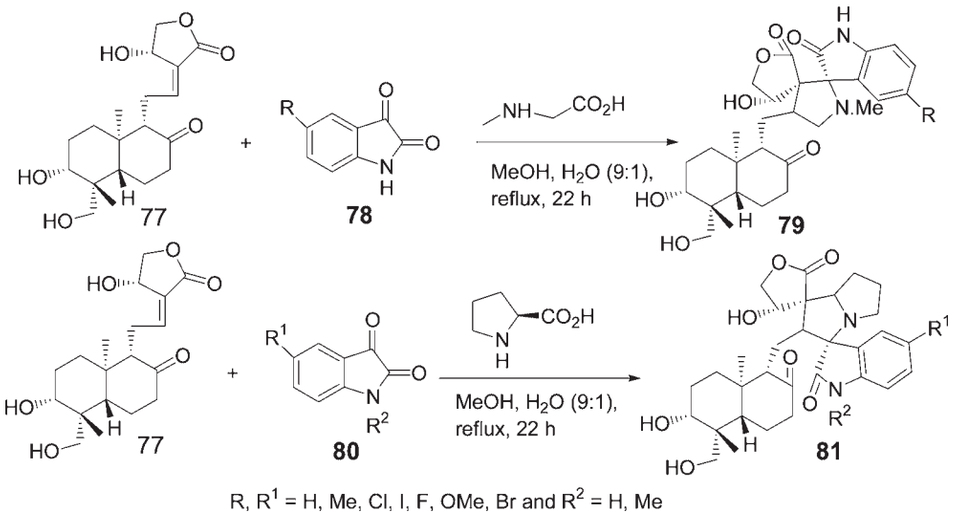


Figure 17. Transmission electron micrograph of sperm sample incubated with or without 14-deoxyandrographolide at MEC. (A) Control spermatozoa showed proper acrosomal membrane while (B) 14-deoxyandrographolide treated sperm exhibit dissolution of the acrosomal cap.

.....► Sperm chromatin with proper acrosomal membrane and .....► treated sperm chromatin with structurally dissolved membrane.

A facile synthesis of novel di-spiro compounds has been achieved via 1,3-dipolar cycloaddition of azomethine ylides generated in situ from isatin derivatives (**78** and **80**) and sarcosine to the conjugated double bond of andrographolide **77** to furnish **79** (Scheme 23). When the amino acid was changed from sarcosine to L-proline, the product formation took a different course as determined by 2D NMR and X-ray crystallographic analysis of the product **81** (R^1 = H, R^2 = Me) (Figure 18).



Scheme 23. Synthesis of dispiro pyrrolidino-oxindolo andrographolide adducts

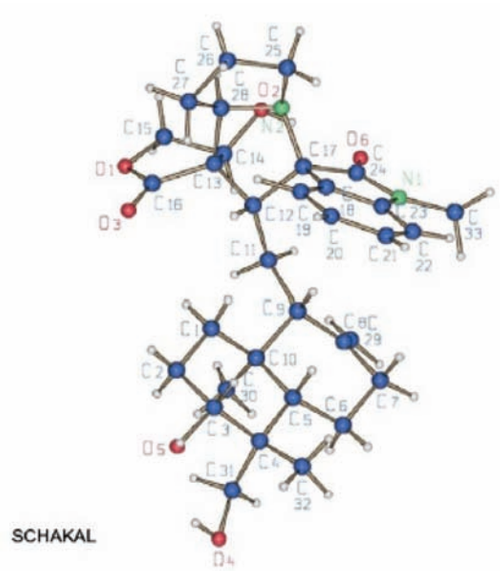


Figure 18. SCHAKAL representations of **81** (R^1= H, R^2 = Me)

Dr. Asish K Sen and group

Structural studies on bacterial cell surface antigen

The objective of this project is to isolate the bacterial cell surface antigenic lipopolysaccharides (LPS) and/or O-antigenic polysaccharides (OPS) and capsular polysaccharides (CPS) from pathogenic strain that is responsible for gastrointestinal disease and elucidate the structures. The lipopolysaccharide from a clinical isolate of *Vibrio parahaemolyticus* O3:K6 has been isolated and purified. The total structure of the OPS is being elucidated. Structural study of the purified CPS from *Vibrio parahaemolyticus* O3:K6 is also under progress.

Synthesis of oligosaccharide:

(i) A new one-pot methodology has been developed for the chemical synthesis of an α-manno pentasaccharide (Figure 19), which binds with a lectin isolated from *Musa paradisiaca* (banana).
(ii) The synthesis of the tetrasaccharide repeating unit of O-antigenic polysaccharide of *Vibrio cholerae* O6 (Figure 20) is in progress.
(iii) Synthesis of a new class of sugar fused azaheterocycles **82** has been initiated (Figure 21).

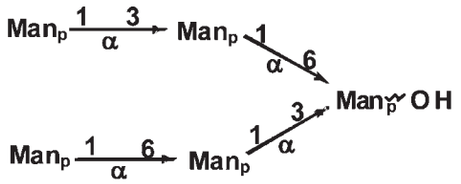


Figure 19: Chemical synthesis of an α-manno pentasaccharide

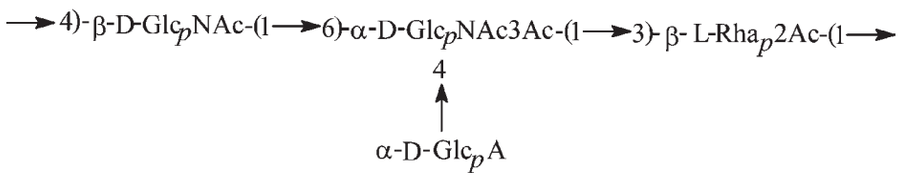


Figure 20: An approach to synthesis of tetrasaccharide repeating unit of O-antigenic polysaccharide of *Vibrio cholerae* O6

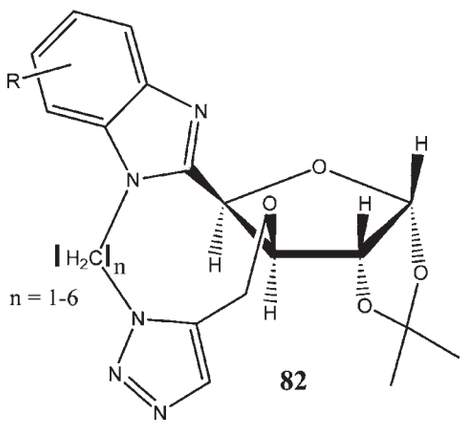


Figure 21. An approach to the synthesis of a new class of sugar fused azaheterocycles

Characterization and structural modification of coir fiber for enhanced longevity:

The project has been sponsored by Coir Board, Kochi from October 2006. The objective of this project is to chemically characterize the constituents of coir fibre from different varieties coir found in southern costal area of India and also to modify the coir fiber by chemical or enzyme procedure to protect them from degradation by light (UV). The work is in progress.

Dr. G. Suresh Kumar and group

Nucleic acid polymorphic structures and their interaction with plant alkaloids

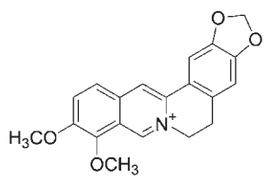
Studies on the binding of alkaloids to RNA triplex: The interaction of the natural protoberberine alkaloids berberine (**83a**) and palmatine (**83b**) and the synthetic derivative coralyne (**83c**) to the RNA triplex poly(U).poly(A)*poly(U) was studied using biophysical and calorimetric techniques. All the alkaloids bind non-cooperatively to the triplex, the affinity of berberine and palmatine being in the order of 10^5 M^{-1} while that of coralyne was one order higher at 10^6 M^{-1} as inferred from spectroscopic studies. The alkaloids stabilized the Hoogsteen base paired (**83d**) third strand of the triplex without significantly affecting the stability of the Watson-Crick base paired (duplex) strands. Fluorescence quenching studies and viscosity experiments gave convincing evidence for a true intercalative binding of coralyne and partial intercalation of berberine and palmatine, to the RNA triplex. This was further supported by the significant polarization of the emission spectra of the complex and the energy transfer from the base triplets to the alkaloids. The conformation of the triplex was perturbed significantly by the binding of the alkaloids, being more by coralyne compared to berberine and palmatine, and also further evidenced by the generation of induced optical activity in the bound coralyne molecules. Calorimetric studies revealed the binding to be favoured by predominantly large negative enthalpy with small favourable entropy contribution in berberine, favoured by negative enthalpy and entropy in palmatine and driven by predominant entropy contributions in coralyne. These results potentiate the use of these alkaloids as specific binders of RNA triplex structures in antigene strategy.

RNA binding of cytotoxic natural alkaloids: binding to protonated RNA and single stranded RNA structures: In continuation of the work on natural alkaloids binding to RNA structures, the binding aspects and energetics of the interaction of berberine, palmatine and coralyne have been studied with double stranded protonated RNAs of cytidine-guanosine (C.G) and inosine-citidine (I.C) sequences using various biophysical techniques. All the three alkaloids bound poly(C^+).poly(G) in a cooperative manner. The binding to both polyribonucleotides was stronger with coralyne than with berberine and palmatine. Evidence for the intercalative binding of coralyne was revealed from fluorescence quenching studies. Isothermal titration calorimetry results suggested that the binding of berberine to both the polymers and of palmatine to poly(I).poly(C^+) was very weak while that of palmatine and coralyne to poly(C^+).poly(G) and poly(I).poly(C^+) was predominantly entropy driven. Circular dichroic (CD) results provided evidence for the perturbation of the RNA conformation with the bound coralyne in a more deeply intercalated position compared to berberine and palmatine, as revealed by induced CD peaks. Taken together, the results suggest that planarity of coralyne appears to be a critical component in the binding to the double stranded RNA conformations that may potentiate its use in RNA targeted drug design.

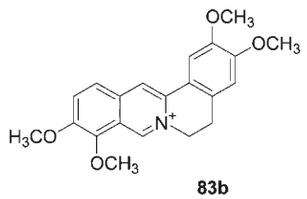
The specificity of coralyne to poly(G), poly(C), poly(I) and poly(U) was also investigated in the light of its ability in inducing self-structure in single stranded poly(A). Multifaceted experiments like competition dialysis, absorption, fluorescence, circular dichroism and calorimetry were employed. Salt dependence and temperature dependence of the binding was also elucidated. Results of competition dialysis, absorption and fluorescence studies revealed that coralyne binds strongly to the polypurines, poly(G) and poly(I) compared to the polypyrimidines, poly(U) and poly(C). Partial intercalative binding due to the stacking of the molecules between the bases was envisaged. The binding was predominantly enthalpy driven with favourable entropy term with a large favourable non-electrostatic contribution as revealed from salt dependent data and the dissection of the free energy. The heat capacity change of -125 and -119 cal. /mol. K respectively for poly(G) and poly(I) and the partial enthalpy-entropy compensation phenomenon observed confirmed the involvement of multiple weak noncovalent interactions. Circular dichroism studies provided evidence for significant perturbation of the conformation of the RNAs, but no self-structure induction was evident in any of the polymers under the condition of the study. This study presents a complete structural and thermodynamic profile of coralyne interaction to four single stranded RNA polynucleotides.

New insights into the DNA binding of old drugs: Comparative binding and thermodynamic profile of intercalation of quinacrine and methylene blue: In this study the binding and thermodynamic aspects of two well known DNA binding molecules methylene blue (**83e**) and quinacrine (**83f**) with four sequence specific polynucleotides, poly(dG-dC).poly(dG-dC), poly(dG).poly(dC), poly(dA-dT).poly(dA-dT) and poly(dA).poly(dT) have been compared. For both the drugs non-cooperative binding phenomena obeying neighbor exclusion principle to these polymers were observed, with an affinity remarkably higher for quinacrine compared to methylene blue. The data of the salt dependence of quinacrine and methylene blue from the plot of log K versus log [Na^+] revealed a slope of around 1.0 consistent with the values predicted by the theories for the binding of monovalent cations and has been analyzed for contributions from polyelectrolytic and non-polyelectrolytic forces. The binding of both the drugs was further characterized by the strong stabilization of the polynucleotides against thermal strand separation in both optical melting as well as differential scanning calorimetry studies. Isothermal titration calorimetry results revealed the binding of both the drugs to poly(dG-dC).poly(dG-dC), poly(dG).poly(dC) and poly(dA-dT).poly(dA-dT) to be exothermic and favoured by both negative enthalpy and large favourable positive entropy changes. The binding of both molecules to poly(dA).poly(dT) was endothermic and entropy driven. The heat capacity changes deduced from temperature dependence of enthalpy gave negative values for the binding of methylene blue and quinacrine to all polymers. New insights on the molecular aspects of interaction of these molecules to DNA have emerged from these studies.

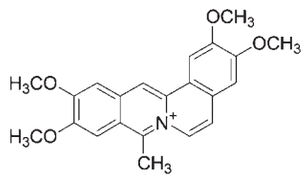
Future programme of this group is to further focus on the study of the various RNA structures and binding of small molecules with particular emphasis on specificity and energetics of interaction of new natural and synthetic alkaloids.



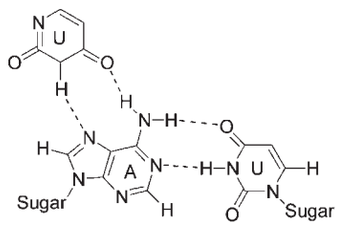
83a



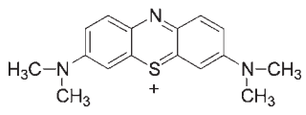
83b



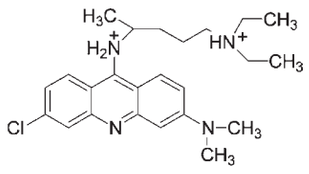
83c



83d



83e



83f

Dr. R. C. Yadav and group

Biophysical studies of the binding of DNA with photoactive dye thionine.

Main findings: (i) A hypochromic and bathochromic shifts, and quenching of fluorescence showed a strong affinity of thionine to DNA. The Scatchard analysis indicates the binding as non-cooperative while thermodynamic parameters suggest it as exothermic and that the hydrophobic contribution in the DNA binding with thionine. For the first time a base specificity of the complexation and energetics of the binding of thionine to DNA has been observed.

(ii) NMR study of single stranded micro RNA (21 mer) does not show peaks in the down field region. Work is in progress for the formation of duplex structure of micro RNA and structure elucidation using NOESY and other correlated NMR spectroscopy.

(iii) Towards the studies on non-linear chaotic system in biological processes, some models have been constructed to know their dynamical behavior. Studies on the synchronization of non-linear oscillators under various constraints are compared with those in biological systems. We have observed multiscroll dynamics for Chua oscillator, a modified Chua oscillator and the Lorenz oscillator. This is being extended to the Van der Poll and Duffing oscillators.

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Administrative Staff

Mr. Sankar Prasad Dutta, Sr. Stenographer

OPERATION AND MAINTENANCE OF SOPHISTICATED INSTRUMENTS

Operation and maintenance of 600 MHz NMR Bruker spectrometer

Dr. Ranjan Mukhopadhyay and Mr. E. Padmanaban

The highly sophisticated 600 MHz Bruker NMR spectrometer has been maintained and analyses of 1242 samples were done during the year for both internal and external research workers. Apart from routine 1D experiments like PMR, PMR (HOD suppression), CMR, DEPT 135, DEPT 90, NOE difference and 2H-NMR, various 2D and 3D experiments are being done regularly.2D experiments include COSY, DQF-COSY, NOESY, NOESY-WG, TOCSY, TOCSY-WG, ROESY, HSQC, HMQC, HMBC, ADEQUATE and HSQCNOESY-15N.The 3D

experiments mostly done were NOESY-HSQC, TOCSY-HSQC, DIPSIHSQC, HNCOCA, HNCACB and HNCA.

Operation and maintenance of 300 MHz NMR Bruker spectrometer

Drs. Ranjan Mukhopadhyay and Tapas Sarkar

The instrument has been extensively used during the year. During the period NMR analyses of 4617 samples (internal and external) were carried out. These covered 1D experiments like routine ^{1}H, ^{13}C (proton decoupled), ^{13}C (proton coupled), DEPT-45, DEPT-90 and DEPT-135. Proton decoupling, 1D-NOE (Nuclear Overhauser Effect) difference experiments and high temperature NMR for many samples were also done. Apart from the 1D experiments as mentioned above, 2D NMR experiments of many samples were also done during the period. These included ^{1}H-^{1}H and ^{1}H-^{13}C COSY (Correlated Spectroscopy), NOESY (Nuclear Overhauser Effect Spectroscopy), HMBC (Heteronuclear Multiple Bond Correlation) and HSQC (Heteronuclear Single Bond Coherence).

Jasco 4200 FT/IR and Jasco 410 FT/IR Spectrophotometer

Dr. P. Jaisankar

The JASCO FT/IR 410 and 4200 Spectrophotometers have been routinely maintained and extensively used to analyze both internal and external samples. About 820 samples have been analyzed during the year. The instruments have given support to the NIPER students also.

LC-MS-MS-Q-TOF Micromass instrument

Dr Asish K. Banerjee and Mr. Diptendu Bhattacharya

One LC-MS-MS (Q-TOF Micor) instrument was installed in the middle of 2003. Since then it has been in use for routine mass spectral analysis of both internal and external samples. Small molecules as well as bio-macromolecules like proteins, carbohydrates etc. are being analyzed. Facilities include determination of their molecular weight, MS-MS experiments etc.

Perkin-Elmer 2400 CHNS/O analyzer Series II System

Dr Asish K. Banerjee and Shri Sandip Chowdhury

The analyzer has been installed and routine analyses of samples have been undertaken.

Jeol MS-700 mass Spectrometer

Dr. S. B. Mandal (with operational support by Shri Sandip Chowdhury)

The Jeol MS-700 instrument has been used for the last one year to analyze molecular weight of various samples of the institute.

Gas Liquid Chromatograph

Dr. Asish K Sen

Two Gas Liquid Chromatography instruments (Agilent 6890 plus and Hewlett-Packard 5890, fitted with FID

detectors) have been maintained and samples were analyzed throughout the year to cater both in-house and external research workers, and industries. During the year, ~150 samples within the institute and ~50 outside samples have been analyzed.

Shimadzu GC-mass spectrometer (GP5050 A)

Dr. Asish K Sen and Mr. Asit Kumar Das

GLC-MS (Shimadzu, Japan) facility was offered to IICB scientists and research fellows, and Scientists, academicians and Industries from elsewhere. During the year, 374 DI & 146 GC-MS samples within the institute and 35 DI & 90 GC-MS outside samples have been analyzed.

DIONEX ICS 3000 Ion Chromatography

Dr. Asish K. Sen and Mr. A. K. Das

This facility has been extended to IICB scientists and scientists from outside.

VP-ITC Model Isothermal Titration Calorimeter and VP-DSC Model Differential Scanning Calorimeter

Dr. G. Suresh Kumar

The VP-ITC model ultra sensitive isothermal titration calorimeter and VP-DSC model differential scanning calorimeter (both from Microcal, LLC USA) for studying the energetics of biomolecular interactions are providing service to researchers from several divisions of our institute.

Jasco J 815 Spectropolarimeter

Dr. G. Suresh Kumar

The circular dichroism unit is providing services to both internal and external workers. Solution conformation of peptides/proteins and nucleic acids are being routinely analyzed.

Single crystal X-ray spectrometer

Dr. Partha Chattopadhyay

Single crystal X-ray spectrometer, Bruker Kappa Apex-2, has been maintained and samples are being analyzed to serve the institute's research workers.

STRUCTURAL BIOLOGY & BIOINFORMATICS DIVISION

Prof. Siddhartha Roy, Drs. M. C. Bagchi, Chitra Dutta, Debasish Bhattacharyya, Nanda Ghoshal, Soumen Datta, Subrata Adak, Krishnananda Chattopadhyay, Jayati Sengupta, Mohammed Islam Khan

Structural characteristics and conformational specificity to a large extent determine the mode of interaction between/or among all the biological macromolecules, leading to expression of their regulated functions. This institute has a long tradition of carrying out research on protein chemistry, molecular modeling of proteins, protein-nucleic acid interactions, nucleic acid-drug interactions, and drug-protein interactions. Clearly, such structure-function studies require multi-pronged approach from different angles involving several areas of biological, chemical and physical sciences. Recently, we have undertaken an effort to bring all these disciplines under a common roof, resulting in the formation of the "Structural Biology & Bio-informatics" division. The charter of this division is to carry out research in areas that focus on structural characterization of potentially prospective biological macromolecules and other small molecules of therapeutic interest against various diseases, e.g. tuberculosis, leishmaniasis, cholera, cancer, diabetes and for other anti-inflamatory, anticonvulsant and immunomodulatory activities. Fundamental studies on protein functions, protein-protein and protein-nucleic acid interactions applying modern sophisticated technologies like nuclear magnetic resonance (NMR), X-ray crystallography, analytical ultracentrifuge, fluorescence correlation spectroscopy, diode array stopped-flow spectrophotometry, mass-spectrometry, quantitative structure activity relationship (QSAR) and 3D-QSAR are also being pursued. Software are being developed for genome / proteome analysis, prediction, modification and analysis of macromolecular structures and for elucidating their interactions with bio-active molecules.

Prof. Siddhartha Roy & group

Asymmetric Recognition of Operator Sites by Phage λ-cI Protein Underpins the Feed-Forward Activation Loop and Prophage Stability

Gene regulatory network of phage λ, involves at least three sequential regulatory loops, creating a sophisticated multi-level switching system. The important central feed forward activation loop is anchored by a stable intermediate state in which four λ-cI dimers cooperatively assemble on O_L1-O_L2 and O_R1-O_R2 with looping of the intervening DNA and concomitant activation of P_{RM}. The stability of this intermediate state is provided by alternate pairwise cooperative binding of λ-cI—structural origin of which is not known. FRET studies demonstrated that λ-cI, an inherently asymmetric dimer, recognizes an asymmetric operator site, preferentially in one orientation. Inversion of operator sites demonstrated that the orientation of O_R2 is crucial for cooperative binding to O_R1-O_R2 and consequent activation of P_{RM}. These orientation preferences prevent the third dimer from cooperatively and simultaneously binding at O_R3, thus creating an intermediate stable state. Phage has evolved an asymmetric repressor to create alternate pairwise cooperativity resulting in a multi-level switching system and a mechanism to meet the requirement of sophisticated developmental program.

Dr. M. C. Bagchi and group

Mathematical Modeling in Drug Design using Structural Descriptors

The major objective of the present project is to study some important topological and other structural parameters of known active compounds as well as many active analogs of the same using various linear statistical methods and non-linear counter propagation neural networks for developing quantitative structure activity relationships of anti-tubercular and anti-cancer compounds.

Design of Potent Fluoroquinolone Derivatives by Structure Based Screening of Virtual Compound Libraries

We are involved in developing reliable and robust QSAR models for a series of fluoroquinolone derivatives against two organisms viz., *M. fortuitum* and *M. smegmatis* with the help of genetic algorithm based partial least squares method. Statistical characteristics associated with the QSAR models are quite acceptable and thus the models have been used for the activity prediction of such fluoroquinolone derivatives. Subsequently, a virtual library of large number of fluoroquinolone derivatives has been generated and virtual screening exercise was performed afterward for antimicrobial activity. Highly active compounds were selected depending on the predicted activity values from the QSAR models. These derivatives were again subjected to molecular docking study to investigate the mechanism of drug binding with the DNA gyrase A protein of *M. tuberculosis* and the compounds showing similar type of binding patterns with that of the existing drug molecules like sparfloxacin were finally considered. It is seen that hydrophobic characteristics of molecular structure together with few hydrogen bond interactions are playing an essential role in antimicrobial activity for the fluoroquinolone derivatives. We are analyzing a few such promising fluoroquinolone derivatives for the prediction of a potent agent against tuberculosis.

3D-QSAR and Molecular Docking Studies of 4-anilinoquinazoline Derivatives

We have made an attempt to formulate the three-dimensional quantitative structure–activity relationship (3D-QSAR) modeling of 4-anilinoquinazoline derivatives having promising anticancer activities inhibiting epidermal growth factor (EGFR) kinase. Molecular field analysis has been applied for the generation of steric and electrostatic descriptors based on aligned structures. Partial least-squares (PLS) method was applied for QSAR model development considering training and test set approaches. The PLS models showed some interesting results in terms of internal and external predictability against EGFR kinase inhibition for such type of anilinoquinazoline derivatives. Steric and electrostatic field effects are considered in the light of contribution plot generated. Finally, molecular docking analysis has been carried out to better understand of the interactions between EGFR target and inhibitors in this series. From the molecular docking studies, it is evident that hydrophobic groups substituted at 6- and 7-positions of the quinazoline ring possessing strong hydrophobic interactions with non polar active residues are likely to enhance EGFR kinase inhibition. On the other hand, presence of hydrophilic residues or polar hydrophobic residues with lower hydropathy indices in this region of interactions may decrease the activity of the 4-anilinoquinazoline compounds.

Dr. Nanda Ghoshal and group

In-silico Studies for Rational Drug Design and Receptor Modelling

Combinatorial Library Enumeration and Lead Hopping using Comparative Interaction Fingerprint Analysis and Classical 2D QSAR Methods for Seeking Novel GABA$_A$ α3 Modulators

Selective modulators of GABA$_A$ α3 (gamma amino butyric acid α3) receptor are known to alleviate the side effects associated with nonspecific modulators. A follow up study was undertaken on a series of functionally selective phthalazines with an ideological credo of identifying more potent isofunctional chemotypes. A bioisosteric database enumerated using the combichem approach endorsed mining in a lead-like chemical space. Primary screening of the massive library was undertaken using the "Miscreen" toolkit, which uses sophisticated bayesian statistics for calculating bioactivity score. The resulting subset, thus obtained, was mined using a novel proteo-chemometric method that integrates molecular docking and QSAR formalism, termed CoIFA (comparative interaction fingerprint analysis). CoIFA encodes protein-ligand interaction terms as propensity values based on a statistical inference to construct categorical QSAR models that assist in decision making during virtual screening. In the absence of an experimentally resolved structure of GABA$_A$ α3 receptor, standard comparative modeling techniques were employed to construct a homology model of GABA$_A$ α3 receptor. A typical docking study was then carried out on the modeled structure, and the interaction fingerprints generated, based on the

docked binding mode, were used to derive propensity values for the interacting atom pairs that served as pseudo-energy variables to generate a CoIFA model. The classification accuracy of the CoIFA model was validated using different metrics derived from a confusion matrix. Further, predictive lead mining was carried out using a consensus two-dimensional QSAR approach, which offers a better predictive protocol compared to the arbitrary choice of a single QSAR model. The predictive ability of the generated model was validated using different statistical metrics, and similarity-based coverage estimation was carried out to define applicability boundaries. Few analogs designed using the concept of bioisosterism were found to be promising and could be considered for synthesis and subsequent screening.

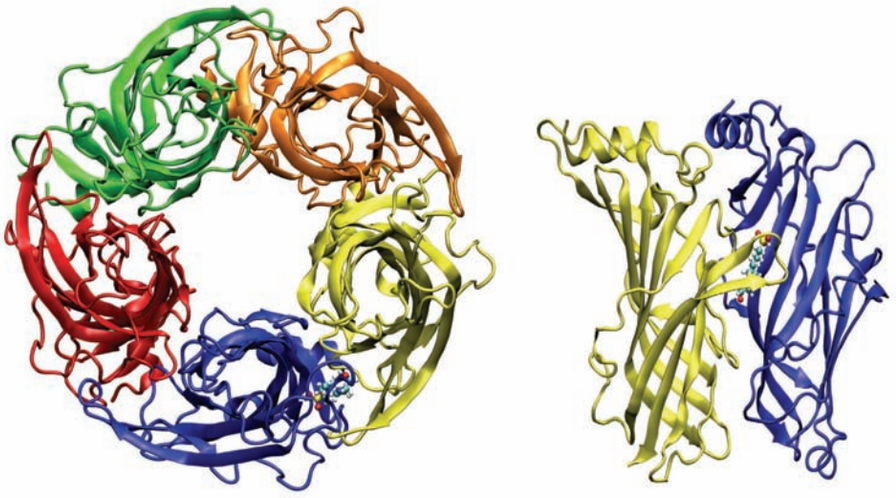


Fig. 1: The pentameric, model of the GABA$_A$ α3 extra cellular domain as viewed form the extracellular side. Chain A (γ2) Blue, Chain B (β2) Red, Chain C (α3) green, Chain D (β2) orange , Chain E (α3)yellow. A close view of the α^3/γ^2 interface that defines the Benzodiazepine binding cavity displaying a HEPES buffer molecule in the binding site rendered in ball-and-stick representation.

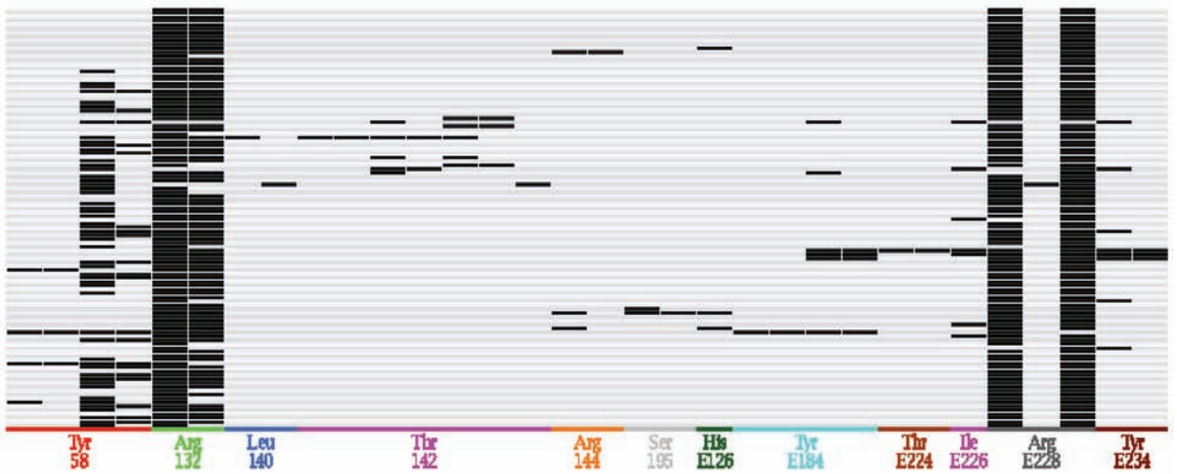


Fig. 2: An Interaction fingerprint generated for the docked complexes with GABA$_A$ α3. The profile shown here represents the interaction features of the ligands with the active site residues.

Investigating the Selectivity Aspect of Pyridine Containing Pyrido[2,3- d]pyrimidin-7-ones by Molecular Dynamics Simulation

Designing selective cyclin-dependent kinase 4 (CDK4) inhibitors is an area of intense research to develop potential anticancer drugs. In continuation of our work on CDK4/6-CyclinD complexes, recently demonstrated

as bonafide cancer targets, the molecular basis governing the selective inhibition of CDK4 by lig17 (6-Bromo-8-cyclopentyl-2-(5-piperazin-1-yl-pyridin-2-ylamino)-8*H*-pyrido[2,3-*d*]pyrimidin-7-one) has been investigated using molecular dynamics simulation. The positive charge on the ligand was determined to be an important contributor for CDK4 selectivity due to the electronegative nature of its active site. Similar studies on CDK2 indicated that Lys89 intrudes into the active site displacing the positive charge on lig17 away from the active center. This propels a drastic conformational change in lig17, weakening its binding interactions with the protein. The pyridine nitrogen (N^{AR}) of lig17 was capable of interacting with His95 (CDK4) through hydrogen bonding. N^{AR} also showed a strong tendency to mediate protein-ligand interactions through a bridged water molecule, only when bound to CDK4. The G-loop of CDK4 was observed to fluctuate extensively when complexed with lig17 and a novel "flipping-out" mechanism exhibited by $Tyr17^{CDK4/CDK4-17}$ is reported in this study. Although these proteins have similar folds, the results from principal component analysis (PCA) indicate that CDK4 and CDK2 follow an anti-correlated behavior towards the accessibility of the active site.

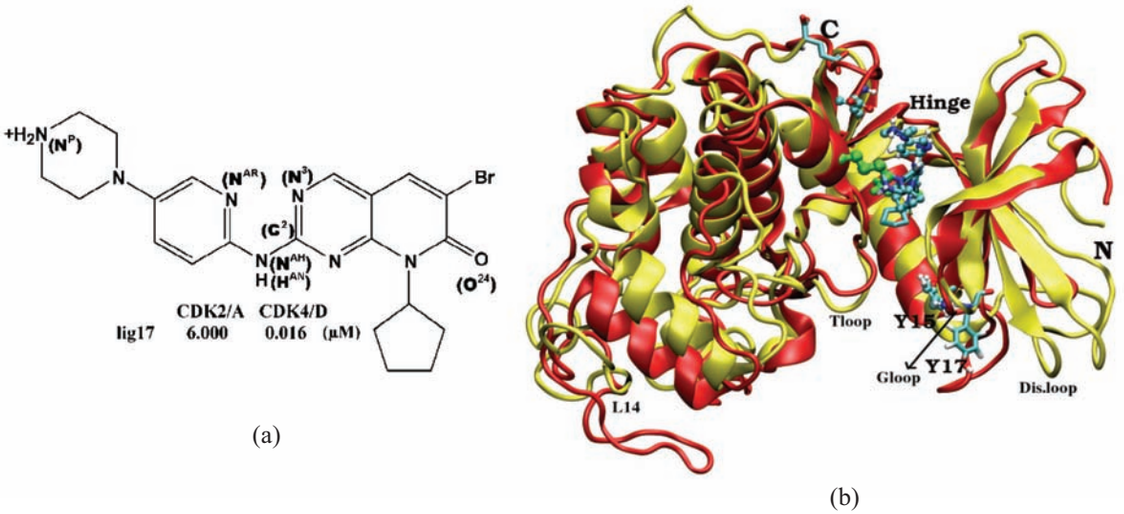


Fig. 3: (a) The ligand selected for study with biological activity, (b) Structural alignment of CDK2-17 (red) and CDK4-17 (yellow) performed on the final structure stored during MD. Tyr15, Leu298 and lig17CDK2 is shown in ball and stick while the corresponding residues in CDK4 Tyr17, Glu303 and lig17CDK4 are shown in cylindrical representation. Also displayed in the figure is the intrusion of Lys89CDK2 (green) into the active site.

Probing the Structure of Leishmania donovani chagasi DHFR-TS: Comparative Protein Modeling and Protein–Ligand Interaction Studies

Dihydrofolate reductase has successfully been used as a drug target in the area of antibacterial, anticancer and antimalarial therapy. It also acts as a drug target for Leishmaniasis. Inhibition of DHFR leads to cell death through lack of thymine (nucleotide metabolism). Although the crystal structures of *L.major* and *T.cruzi* DHFR-TS have been resolved, till now there is no 3D-structural information on DHFR-TS of *Leishmania donovani chagasi* that causes visceral leishmaniasis. Our aim in this study is to model the three-dimensional structure of *L. donovani chagasi* DHFR-TS and investigate the structural requirements for its inhibition. In this paper we describe the highly refined homology model of *L. donovani chagasi* DHFR-TS based on available crystallographic structures by using Homology module of Insight II. Structural refinement and minimization of the generated *L. donovani chagasi* DHFR-TS model has been carried out by Discover 3 module of Insight II and molecular dynamic simulations. The model was further validated through PROCHECK, Verify_3D, PROSA, PSQS and ERRAT programs, which confirm that the model is reliable. Superimposition of the model structure with the templates *L. major* A chain, *L. major* B chain And *T. cruzi* A chain showed RMSD deviations of 0.69 A°, 0.71 A° and 1.11 A°, respectively. Docking analysis of *L. donovani chagasi* DHFR-TS model with methotrexate enabled us to identify specific residues viz. VAL156, VAL30, LYS95, LYS 75 and ARG 97, within the *L.*

donovani chagasi DHFR-TS binding pocket, to play important role in ligand or substrate binding. Docking studies clearly indicated that these five residues are important determinant for binding as they have strong hydrogen bonding interactions with the ligand.

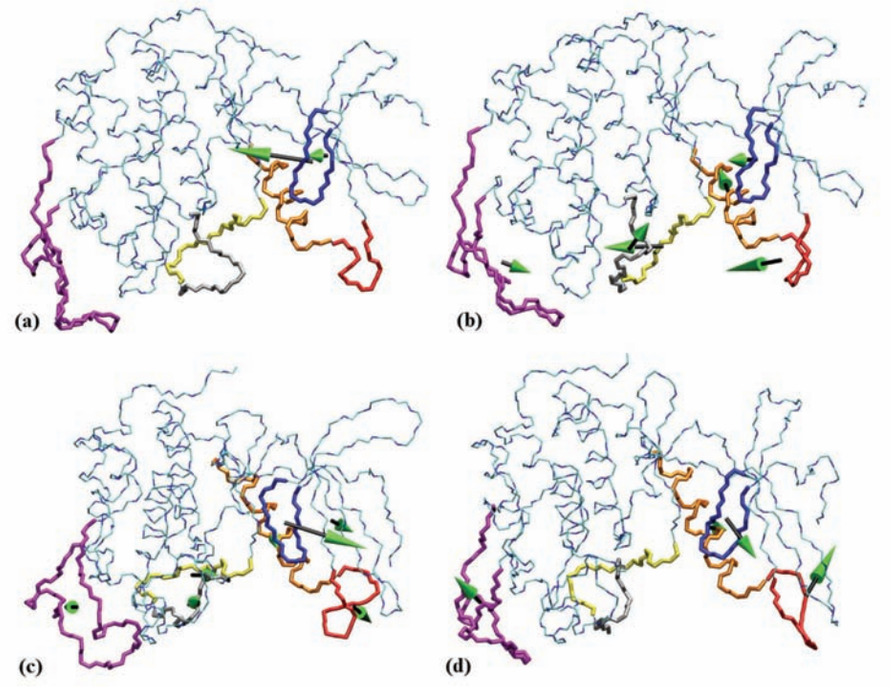


Fig. 4: Visualization of the dominant motions corresponding to first eigenvector in (a)cdk2 (b)cdk217 (c)cdk4 (d)cdk417. The color coded region corresponds to various segments of the protein: Gloop (blue), Disordered loop (red), α1-helix (orange), T1loop (yellow), T2loop (grey) and L14 (magenta). The backbone structure represents the initial conformation of the projection of the eigenvector. The arrow projects the direction of motion of the center of mass of the segments between the two extreme conformations explored by the protein corresponding to the eigenvector.

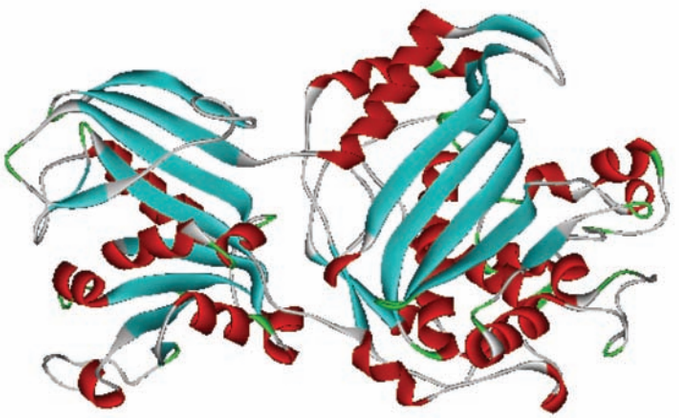


Fig. 5: The final 3D-structure of *L. donovani chagasi* DHFR-TS. The α-helix (red), the β-sheet (cyan) and the β-turns (green)

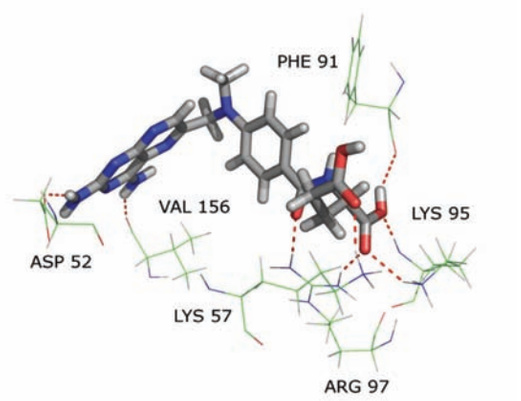


Fig. 6: The hydrogen bonding interactions of the binding site residues of *L. donovani chagasi* DHFR-TS with methotrexate(in pymol)

Deciphering Ligand Dependent Degree of Binding Site Closure and its Implication in Inhibitor Design: A Modeling Study on Human Adenosine Kinase

Protein flexibility plays a significant role in drug research due to its effect on accurate prediction of ligand binding mode and activity. Human Adenosine Kinase (AK), a promising therapeutic drug target against a variety of diseases including hypertension, epilepsy, pain, diabetes, and inflammation, has recently attracted great interest in the search of potent and selective inhibitors. AK represents a highly flexible binding site and is known to exhibit large conformational changes as a result of substrate or inhibitor binding. Here we propose a semi-open conformation for ligand binding in human AK, in addition to the known closed and open forms. The modeling study illustrates the necessity of thorough understanding of the conformational states of protein for docking and binding mode prediction. It has been shown that predicting activity in the context of correct binding mode can improve the insight into conserved interactions and mechanism of action for inhibition of AK. Integrating the knowledge about the binding modes of ligands in different conformational states of the protein, separate pharmacophore models were generated and used for virtual screening to explore potential novel hits. In addition, 2D descriptor based clustering was done to differentiate the ligands, binding to closed, semi-open and open conformations of human AK. The results indicated that binding of all AK inhibitors cannot be described by same rules. Instead, they represent a rule based preference for inhibition. This inference about tubercidins binding to semi-open conformation of human AK may facilitate in finding much extensive space for AK inhibitors.

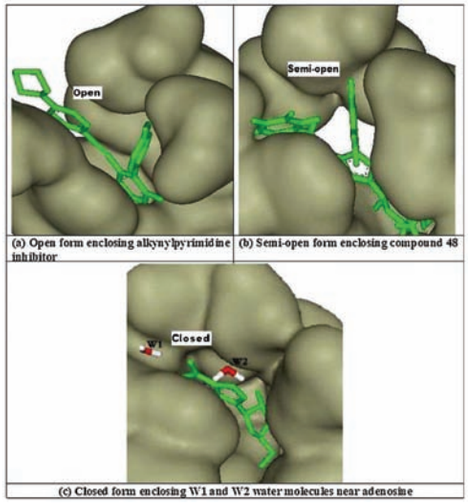
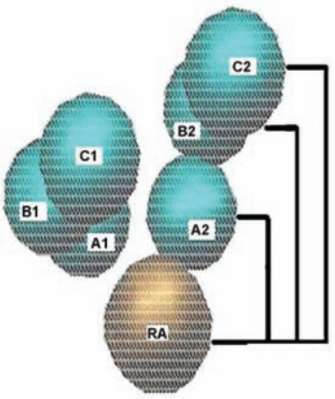


Fig. 7. Degree of closing in human adenosine kinase (a) open form (b) semi-open form (c) closed form.



Scheme	Preferential Groups (1,2)	Fit values with mappings to three schemes		
		Alkynyl-pyrimidine	48	5-Iodo-tubercidin
RA,C1, C2	C1, C2: Hydrophobic aromatic	4.22	3.5	2.7
RA,B1, B2	B1, B2: Hydrophobic aromatic	2.52	2.998	1.74
RA,A1, A2	A1: hydrophobic/ polar,A2: hydrophobic	2.82	2.86	3.10

Fig. 8: Representation of three featured scheme for open, semi-open and close forms; mapping results of alkynylpyrimidine, 48 and 5-iodotubercidin with these pharmacophoric schemes; RA: ring aromatic, A1 and A2: for close, B1 and B2: for semi-open, C1 and C2: for open.

Dr. Chitra Dutta and group

Drug Target Identification in Helicobacter Pylori HPAG1

The Gram-negative bacterium *Helicobacter pylori* HPAG1 is known to be the leading cause of peptic ulcers, chronic atrophic gastritis and gastric cancer worldwide. In the present study, an attempt has been made to identify novel putative targets for therapeutic intervention in the *H. pylori* HPAG1 infections. There are two crucial factors for determination of potential drug targets among the genes identified in a pathogenic genome: essentiality and conservation. The targeted proteins must be essential in the growth, replication, viability or survival of the pathogenic organism, i.e. encoded by genes critical for pathogenic life stages. The target protein should not have any well-conserved homolog in the host in order to address cytotoxicity issues. Using metabolic pathway analysis of the organism and the genome sequence data, potential essential genes of *H. pylori* HPAG1 have been identified. Conservation of different essential genes has been studied by searching any similarity between pathogenic proteins and human proteins through BLAST. 25 proteins were identified as potential targets from 11 unique metabolic pathways that were absent in host human but present in *H. pylori* HPAG1. Lipopolysaccharide being an essential part of gram-negative bacterial outer membrane has an important role in the *H. pylori* HPAG1 virulence, so the targets associated with this metabolic pathway are studied in further detail. Among the list of identified drug targets involved in this pathway, models of three enzymes: 2-dehydro-3-deoxyphosphooctonate aldolase, UDP-3-O-[3-hydroxymyristoyl] acetylglucosamine deacetylase and phosphoheptomerase isomerase were successfully built, using computational methods of structure prediction, especially the homology modeling approach. The enzyme 2-dehydro-3-deoxyphosphooctonate aldolase was studied further in detail. The binding site of the enzyme was predicted and the active site was studied by performing docking study of the enzyme with its biological substrate phosphoenolpyruvate (PEP) (Fig. 9). The residues that might take part in the enzyme-substrate reaction were predicted and most of them were found to remain conserved among other closely related bacteria.

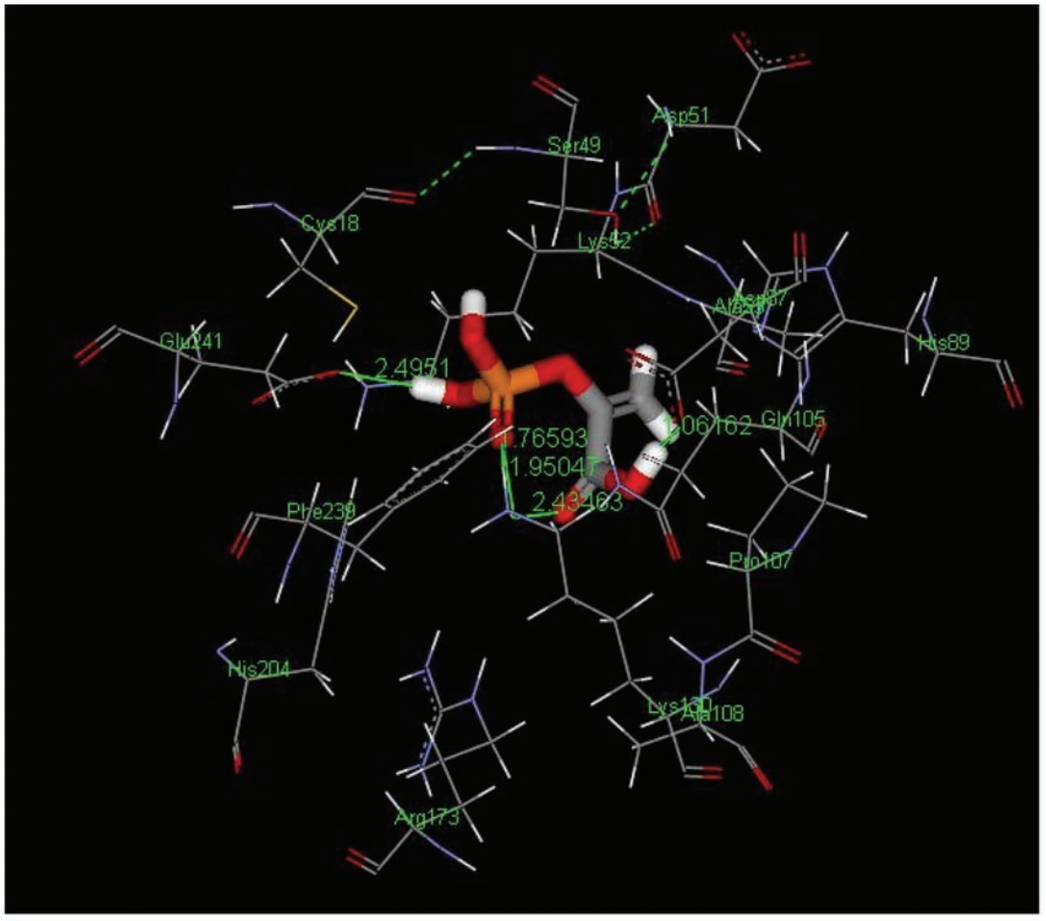


Fig. 9 : **The docking conformation of phosphoenolpyruvate with 2-dehydro-3-deoxyphosphooctonate aldolase of *Helicobacter pylori* HPAG1**

Identification and Characterization of Lineage or Environment-specific Trends in Archaeal Proteomes

Archaea represent an intriguing domain of life, characterized by a unique mosaic-like combination of bacterial and eukaryotic properties and inhabiting some of the most extreme environments on the planet. Recent availability of the complete genome sequence data from more than fifty archaeal species belonging to five different phyla - Crenarchaeota, Euryarchaeota, Thaumarchaeota, Nanoarchaeota, and Korarchaeota - permits comprehensive analyses of their genomic/proteomic features, that may facilitate identification of the cross-phyla divergences, if any, in major molecular traits and thereby, offer an insight into the molecular mechanisms of adaptation of these extremophiles to diverse environmental niches. To this end, the present study offers a comprehensive compositional analysis of a dataset comprised of 23 representative genomes of varying GC-content from diverse extremophilic groups such as thermophiles, halophiles, methanogens and sulphur-reducing archaea, and even some poly-extremophiles from five different phyla of archaea known to date. The analysis revealed that within crenarchaeota and euroarchaeota species, the niche-specific proteome features dominate over the phyla-specific traits. Not only the halophiles and thermophiles, but also the methanogenic or sulphur reducing archaea are characterized by distinct niche-specific trends in amino acid usage. Among the major proteomic properties that differ significantly with the habitat/ life-style of archaeal species are average isoelectric point, hydrophobicity, aromaticity and instability index of proteins. However, in some special cases, the lineage-specific features dominate over ecological adaptation. For instance, *Nanarchaeum equitans*, the only known member of the phyla Nanoarchaeota, is known to possess an extremely basic proteome with atypically higher usage of Lys, while the organism, *Ca. K. cryptofilum* , a member of the phyla *Korarchaeota,* is characterized by very high acidic

proteome, though both these organisms thrive at high temperature. A comparative analysis of gene synteny across different archaeal species have also delineated certain inter- phyla or inter-niche variations in genome architectures of archaea.

Dr Debasish Bhattacharyya and group

Functional Regulation, Assembly and Stability of Proteins/Enzymes, Characterization of Venom Toxins, the Drug 'Placentrex' and Exploring the Biosynthetic Pathway of Podophyllotoxin.

UDP-galactose 4-epimerase that reversibly converts UDP-galactose to UDP-glucose is an important enzyme of galactose metabolism. This enzyme from yeast *Kluyveromysis fragilis* is a homodimer having independent catalytic sites on each subunit. Recently we have conclusively demonstrated that the functioning of its catalytic sites is regulated. This is based on analysis of its kinetic parameters and replacement of bound inhibitor. Later the nature of inhibition of the two catalytic sites by 5'-UMP, has been studied. It has been observed that while the site having high affinity of the substrate follows mixed inhibition inclined to competitive inhibition with 5'-UMP, the low affinity site follows noncompetitive inhibition. Interestingly it appears that in presence of high substrate concentration, deregulation takes place as indicated from Arrhenius plots. Regulation and deregulation of activities of this enzyme seem to protect the pool of activated sugars.

In continuation towards evaluation of medicinal values of 'bromelain' – the pineapple extract, investigations were done to follow its ability to inhibit growth of protein aggregates as well as destabilize protein aggregates once they are formed. Interaction of the fluorophore thioflavin T, chromophore Congo Red, Transmission Electron Microscope, Size Exclusion-HPLC etc were used to follow the course of the reactions. Encouraging results, at least *in vitro*, were obtained that merit its further applications under *ex vivo* conditions. Destabilization of reformed protein aggregates by Russell's viper venom components or its derived peptides are also under investigation. In the biosynthetic pathway of podophyllotoxin, *in vitro* conversion of coniferyl alcohol to higher intermediates towards synthesis of matairesinol is being standardized.

Characterization of the drug 'Placentrex', an aqueous extract of human placenta and a product of M/s Albert David Ltd., has completed its 10 years term (1999-2009). The broad objective of the project is identification of bioactive components and their mechanism of actions. It has been confirmed that the drug contains a peptide that stabilizes trypsin after reversible binding preventing autodigestion. In presence of high concentration of substrate, trypsin is released. This mechanism is important, as regulation of proteolytic activity is essential between different time frames of wound healing. Currently we investigate whether the drug can activate matrix-metalloproteases.

Dr. Saumen Datta & group

Structural Investigations of Macromolecules and their Complexes by X-ray Diffraction Methods.

Type III secretion system (TTSS) is a higly sophisticated protein secretion system evolved in many gram negative pathogenic bacteria, namely, *yersinia* spp., *shigella* spp., *salmonella* spp. *pseudomonas aeruginosa* etc. *Yersinia enterocolitiac*, an enteropathogenic bacteria, transmitted by contaminated food or water, causes gastroenteriris. It uses two TTSS, one plasmid encoded and another genome encoded, to inject virulent proteins into host cytosol. There are many TTSS plasmid encoded proteins, YopH, YopE, YopT, YopN, YopQ, YopP/YopJ and YopO/YpkA – secretory proteins and YscC, J, N, Q, R, S, T, U, V - core proteins forming the injectisom, which are well characterized biochemically. Three dimensional structure are also available for some of the individuals and their complexes. Beside plasmid encoded TTSS, *Y. enterocolitica* also newly detected with a genome encoded TTSS. We have started exploring proteins involed in genome encoded TTSS for three dimensional characterization. Some preliminary results are presente.

Genome encoded TTSS Protein and complexes from *Yersinia enterocolitica*: Yspc, SycB.

This TTSS encodes *Yersinia* secretory apparatus (Ysa) proteins constituting injectisome, *Yersinia* secretory proteins (Ysp) or virulent proteins and their putative chaperone proteins like SycB. We have expressed YspC and SycB recombinantly and were able to form YspC-SycB complex (Figure 10). SycB is a novel chaperone which exists in a dimeric form and makes a 1:1 complex with YspC as confirmed by crosslinking experiments (Figure 11 and 12). The 1:1 complex formation of YspC:SycB is also confirmed by gel filtration chromatography (Figure 13). Interestingly, the soluble complex not only has a monomeric form but also exists in oligomeric form.

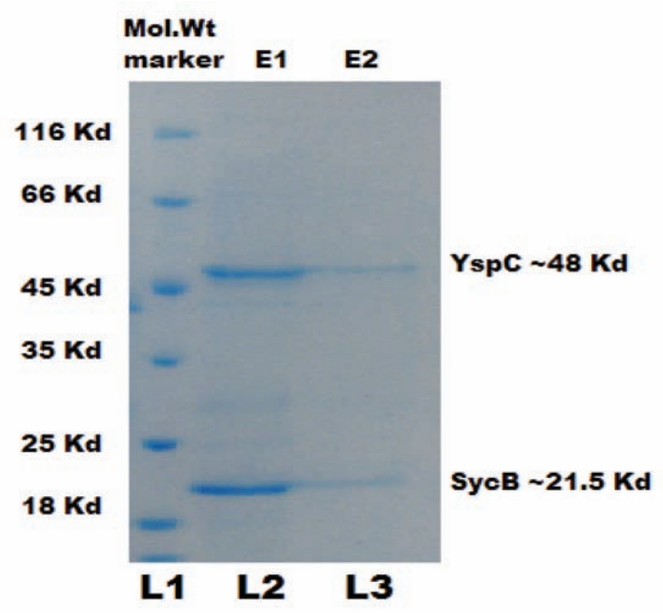


Figure 10: Purified YspC-SycB complex run on a 12% SDS PAGE. Lane 1: protein marker; Lane 2: first elution with 250mM immidazole from a Ni-NTA affinity column; Lane 3: second elution with 250mM immidazole after first elution.

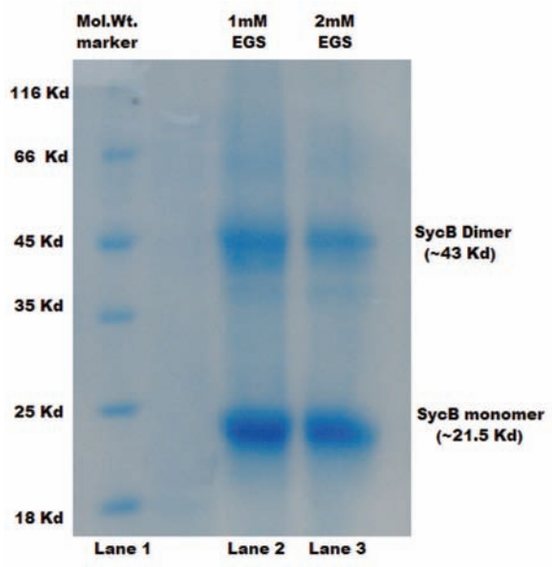


Figure 11: Crosslinking of SycB with EGS run on a 10% SDS PAGE. Lane1 protein marker; Lane 2 SycB crosslinked with 1mM EGS; Lane 3 SycB crosslinked with 2mM EGS. EGS: EthylGlycol bis(SuccinimidylSuccinate)

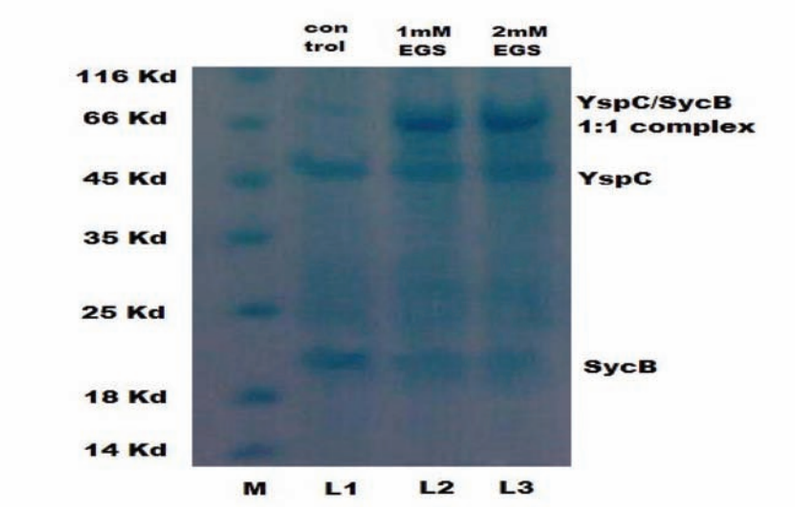


Figure 12: Crosslinking of YspC/SycB complex run on a 10% SDS PAGE. L1 purified YspC/SycB complex, L2 YspC/SycB crosslinked with 1mM EGS, L3 YspC/SycB crosslinked with 2mM EGS, M is the protein marker. YspC/SycB forms a 1:1 complex when crosslinked.

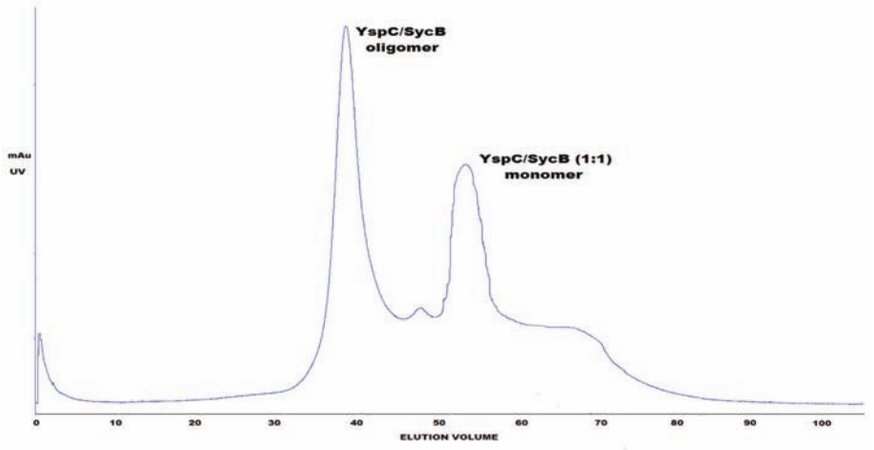


Figure 13: Gel filtration profile of YspC/SycB in 16/60 Sephacryl S-200 HR column showing an elution of oligomeric form in void volume and (1:1) YspC/SycB complex shows an elution corresponding to 67 Kd (YspC/SycB complex is 68.5 Kd).

Genome Encoded TTSS Protein Fragment from *Y. enterocolitica*: SycB-2TPR

In an effort to identify some stable domain of SycB for crystallization purpose, we found a stretch containing successive TPR (Tetra Tricopeptide Repeat) motifs. A region encompassing two TPR motifs were cloned (SycB-2TPR) and expressed. The SycB-2TPR with His-tag was expressed in insoluble form in *E. Coli* but was obtained in soluble form successfully by denaturing/refolding process (Figure 14). The SycB-2TPR with GST-tag was also found a futile attempt to get SycB-2TPR in soluble form (Figure 15).

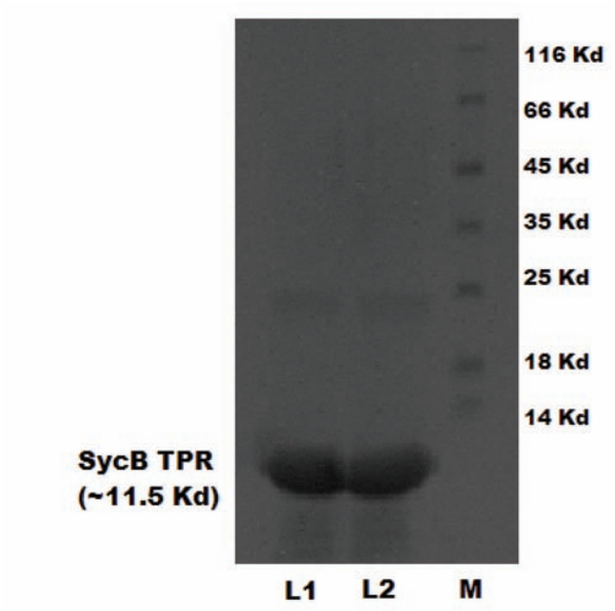


Figure 14: Purification of His-SycB-2TPR, denatured and refolded from inclusion body. L1, shows to first elution from Ni-NTA column, L2 shows second elution from Ni-NTA column. M is the protein marker.

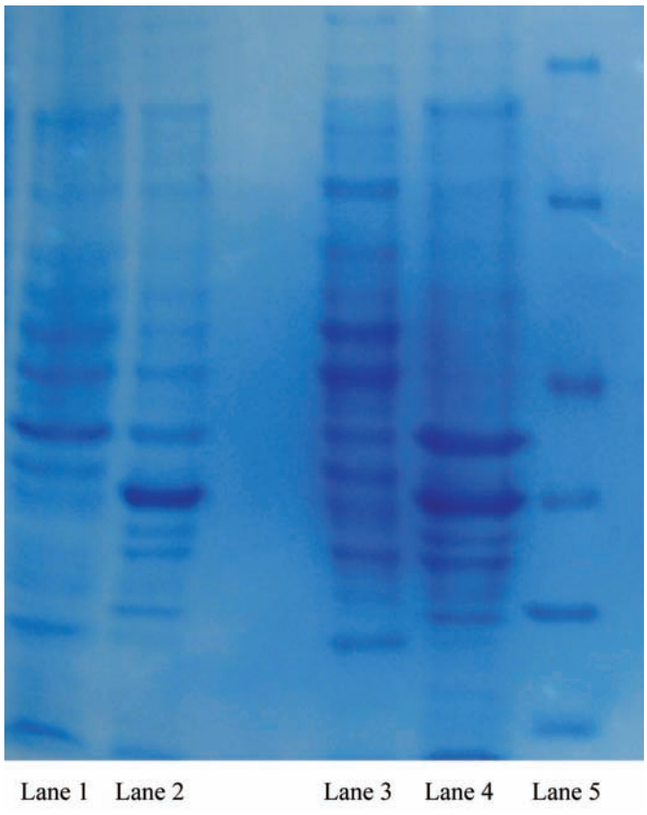


Figure 15: SDS-PAGE of SYCB-2TPR-GST in *E.Coli* BL21(DE3) host induced with 1mM IPTG at 37^{O}C for 4hrs (Lane 1- uninduced, Lane 2 - induced, Lane 3 - supernatant, Lane 4- pellet, Lane 5- protein marker).

Dr Krishnananda Chattopadhyay and group

Effect of Arginine and Other Stabilizers on Protein Aggregation using Fluorescence Correlation Spectroscopy and Other Biophysical Methods.

We have been studying protein conformation, dynamics and aggregation using different biophysical methods including Fluorescence Correlation Spectroscopy (FCS). FCS is an important technique to measure the diffusional and conformational fluctuations of fluorescently labeled molecules at single molecular resolution. These fluctuations could be analyzed by using suitable correlation functions yielding useful information regarding the shape and/or conformational dynamics of a protein. In a recent study, we have shown by a number of orthogonal techniques including analytical ultracentrifugation, dynamic light scattering and native gel electrophoresis that aggregation of bovine serum albumin can be minimized by using high concentration of arginine. Urea induced unfolding transition of cytochrome c has been studied by FCS. Measurements of microsecond dynamics using appropriately labeled cytochrome c indicates formation of an intermediate state, which has been found to be absent in the presence of arginine. The hydrodynamic radii of the protein in its native, unfolded, and intermediate states have been determined using FCS (Fig. 16).

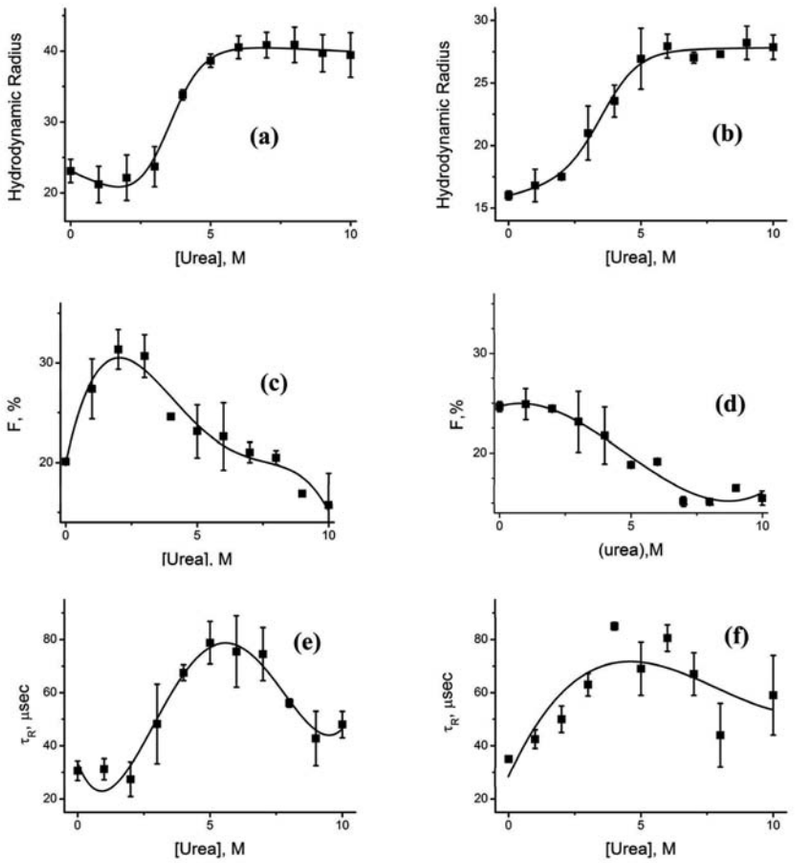


Fig. 16. Urea induced unfolding transitions of tetramethyl rhodamine labelled cytochrome c monitored by different FCS parameters (a) hydrodynamic radius (rH) in the absence of arginine (b) hydrodynamic radius (rH) in the presence of 500mM arginine (c) the amplitude of a fast dynamics component (F) in the absence of arginine (d) F in the presence of 500 mM arginine (e) time scale of a fast component of the correlation function (τR) in the absence of arginine (f) τR in the presence of 500mM arginine. The variations of rH with urea concentrations follow typical two-state behaviors both in the absence (a) and presence of arginine (b). The variation of F in the absence of arginine (c) show formation of a native like intermediate state accompanied by an increase in F. The variation of F in the presence of arginine (d) follows the two-state behavior.

Dr. Subrata Adak and group

Biochemistry of a Novel Plant like Ascorbate Peroxidase from Leishmania major.

Leishmaniasis continues to be a major health problem globally. The situation is becoming alarming due to the lack of an effective vaccine or cost-effective drug. Most available drugs are costly, require long treatment regimes and are becoming more and more ineffective necessitating the discovery of new drugs. Peroxidase represents a heterogeneous group of distinct enzyme family that plays extremely diverse biological functions. Ascorbate peroxidase from *Leishmania major* (LmAPX) has been shown to be central to the redox defense system of *Leishmania*. To investigate further its exact physiological role in *Leishmania*, we attempted to create LmAPX -knockout mutants by gene replacement in *L. major* strains. The null mutant cell culture contains a higher percentage of metacyclic and apoptotic cells compared to both wild type and LmAPX overexpressing cells. Flowcytometric analysis reveals the presence of a higher concentration of intracellular H_2O_2, indicative of increased oxidative stress in parasites lacking LmAPX. IC_{50} value for exogenously added H_2O_2 shows that deletion of LmAPX in *L. major* renders the cell more susceptible to H_2O_2. Real time PCR studies demonstrate an elevated mRNA level of non-selenium glutathione peroxidase in LmAPX null mutant cell line, suggesting that these enzymes were induced to compensate the LmAPX enzyme. The null mutant cells exhibit hypervirulence after infection with macrophages as well as inoculation into BALB/c mice; in contrast, overexpressing cells show avirulence. Collectively, these data provide strong evidence that LmAPX is an important factor for controlling parasite differentiation and survival within macrophages.

Dr. Jayati Sengupta and group

Structural and Functional Analysis of the Machinery of Cellular Protein Factory.

All living organisms utilize ribosome, the protein factory of cell, to translate messenger RNA (mRNA) into proteins. We aim to study 3D structure and dynamics of ribosomes from different pathogenic organisms by employing cryo-electron microscopy technique. We have been purifying ribosomes from some pathogenic organisms. Characterizations of the macromolecules using Electron Microscopy, Atomic Force Microscopy, and other biophysical and biochemical techniques are being carried out.
Simultaneously, intense efforts are going into establishing a state-of-the-art cryo-EM facility at IICB, Kolkata.

Dr. Mohammed Islam Khan & group

Isolation of low molecular weight protease inhibitors & synthesis of nano particles

We have been interested in low molecular weight protease inhibitors. A novel penta – peptide cysteine protease inhibitor has been isolated from an *Actinomycte NCIM 2081*. The peptide has nano – molar inhibitory constant against papin, cathepsin – L and cathepsin – S. It inhabits tumor cell migration in invitro assays at micro – molar concentration. Further studies indicate that the penta peptide inhibits osteoclasts at micro molar level. Presently studies on the potential of this peptide as an anti metastasis and anti osteoporatic molecule are continued.
Our group is also interested in the synthesis of nano particles using enzymes such as reductases and synthetic peptides as caping molecule. Results from our lab suggest that the size of the nano particale synthesized can be controlled by using different size peptides as caping molecule.

Ramalingaswami Fellow

Dr. Saikat Chakrabarti

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Mr. Mohanlal Jana, Jishu Mandal, Mr Samir Roy, Dr. Subhagata Ghosh, Mr. Prosenjit Gangopadhyay,.

Pool Officers, RAs, Research Fellows

Dr. Shampa Mallick, Dr. Rajesh Saha, Neeladri Sekhar Roy, Avishek Majumder, Gitashri Naiya, Prasenjit, Chakraborty, Piya Ghosh, Israr Ahmed, Niharul Alam, Arijit Dutta, Dr. (Mrs.) Dipta Shani Datta, Sisir Nandi, Payel Ghosh, Sandip Paul, Anirban Dutta, Munmun Sarkar, Sanchari Pradhan, Aranyak Goswami, Debashree De, Nupur Banerjee, Debratna Saha, Sangeeta Dutta, Jyotirmoy Mitra, Payel Bhattacharjee, Anwesha Majumder, Savita Bhutoria, Nahren Manuel, R.Vijayan, Prabu. M., Indrani Bera, Lakshmi Maganti, Supratim Dey, Atanu Das, Abhishek Basu, Rakesh Chatterjee, Dr. Rina Shaha, Subhankar Dolai, Rajesh Yadav, Swati Pal, Moumita Bose, Supratim Mukherjee, Sumit Sen santara, Jayasree Roy, Sunny Sharma, Ranendu Ghosh. Shubhasis Haldar, Sujit Basak, Nidhi Joshi, Manidip Shasmal, Bipra Shekhar Chakraborty, Anindya Roychowdhury


67th CSIR FOUNDATION DAY CELEBRATION '09
INDIAN INSTITUTE OF CHEMICAL BIOLOGY
DR. H.K. MAJUMDER
PROF. V. NAGARAJA
PROF. SIDDHARTHA ROY
PROF. P.N. GHOSH
DR. S.R. SARKAR


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PROF. V. NAGARAJA

ELEVENTH FIVE YEAR PLAN (2007-12) PROJECTS

In **11th Five Year Plan**, IICB is involved in 18 projects consisting of 4 Nodal Network Projects and 14 Partner Network Projects. In Partner Network Projects there are two extension Projects of Tenth Plan. One of the projects of X plan, COR-023, is continuing in XIth Plan period as NWP-037 from 2008-09. All the projects are mainly from Biology & Biotechnology sector except one nodal network project which is from Pharmaceuticals, Healthcare & Drugs sector. During this reporting year R&D works of two new projects have been started, one is an Interagency Project entitled, "Synthetic Biology and metabolic engineering of Azadirachtin biosynthesis pathway" and the other is an OSDD Project entitled, "Designing potential lead molecules for inhibition of siderophore biosynthesis in *M. tuberculosis*".

No.	Project Title & Short Name	Project Code	Type of Project	Nodal Lab.	Nodal Scientist of IICB
1.	Evaluation and correction of mitochondrial dysfunction in disease **(Mitochondria)**	**SIP-007**	Supra-institutional	IICB	Dr. Samit Adhya
2.	Engineering peptides and proteins for new generation therapies **(Protein Engineering)**	**NWP-005**	Nodal Network	IICB	Dr. Anil K Ghosh
3.	Development of diagnostics and target-based molecular medicines against allergy, bronchial asthma and chronic obstructive pulmonary disease **(Asthma)**	**NWP-033**	Nodal Network	IICB	Dr. Arun Bandyopadhyay
4.	New insights in cancer biology : Identi-fication of novel targets and development of target based molecular medicine **(Cancer)**	**IAP-001**	Nodal Inter-agency	IICB	Dr. Susanta Roychoudhury
5.	Plasma Proteomics in health, environment and disease (**Plasma Proteomics**)	**NWP-004**	Partner–Network	CCMB	Dr. Rukhsana Chowdhury
6.	Nanomateials and nano-devices for application in health and disease **(Nanomaterials)**	**NWP-035**	Partner – Network	CCMB	Dr. Arindam Banerjee
7.	Pathway engineering and system biology approach towards homologous and heterologous expression of high-value phytoceuticals **(Pathway Engineering)**	**NWP-008**	Partner – Network	CIMAP	Dr. Debasish Bhattacharya
8.	Biological and chemical transformation of plant compounds for production of value added products of therapeutic/aroma value **(Aroma Value)**	**NWP-009**	Partner – Network	CIMAP	Dr. Sibabrata Mukhopadhyay
9.	Identification and validation of drug targets for selected pathogens of national importance (**Drug Target**)	**NWP-038**	Partner – Network	CDRI	Dr. Pijush K Das
10.	*Diabetes mellitus* – New drug discovery R&D, molecular mechanisms and genetic and epidemiological factors **(Diabetes)**	**NWP-032**	Partner – Network	CDRI	Dr. Sibsankar Roy

No.	Project Title & Short Name	Project Code	Type of Project	Nodal Lab.	Nodal Scientist of IICB
11.	Zero Emmision Research Initiative **(Zero Emission)**	**NWP-044**	Partner – Network	CLRI	Dr. Suman Khowala
12.	Exploitation of India's rich microbial diversity **(Metagenomics)**	**NWP-006**	Partner – Network	IMT	Dr. Tushar Chakraborty
13.	Comparative genomics and biology of non-coding RNA in human genome **(Micro-RNA)**	**NWP-036**	Partner – Network	IGIB	Dr. G Suresh Kumar
14.	Drug Target Development using In-silico Biology (**In-silico Biology**)	**CMM-017**	Partner – Network	IGIB	Dr. Chitra Dutta
15.	Discovery, Development and Commercialization of New Bioactives and Traditional Preparations **(Bioactive)**	**NWP-037**	Partner – Network	CSIR-HQ	Dr. Pratap K Das & Dr. HK Majumder
16.	Integrated Analysis for Impact, Mitigation and Sustainability (IAIMS): Regional Climate Modelling at Decadal Scale **(Climate Change)**	**NWP-052**	Partner – Network	CMMACS, Bangalore	Dr. A.K. Giri
17.	Designing potential lead molecules for inhibition of siderophore biosynthesis in *M. tuberculosis*	**HCP-001**	Partner – Network	CSIR-HQ	Dr. N. Ghosal & Dr. P. Jaisankar
18.	Synthetic Biology and metabolic engineering of Azadirachtin biosynthesis pathway	**HCP-002**	Partner – Network	CSIR-HQ	Dr. R. Bhadra

EFYP PROJECT

NODAL PROJECTS

1. **Title:** Evaluation and Correction of Mitochondrial Dysfunction in Disease

Project: Supra-institutional [SIP-007]

Objectives:

[i] To investigate alterations in mitochondrial genes and proteins in primary open angle glaucoma (POAG), using POAG DNA samples and ocular cell models.

[ii] To investigate mutations in the mitochondrial genome and abnormalities of mitochondrial function in relation to the diverse phenotypes among patients with Wilson's disease.

[iii] To investigate mitochondrial gene expression and oxidative stress in hypertrophic heart induced by hyperthyroidism excess of anti-inflammatory drugs.

[iv] To test whether neurodegeneration and mitochondrial decline are correlated in human patients and in animal models of Parkinson's disease.

[v] To investigate mitochondrial dysfunction in diabetes type 2 with special emphasis on the role of PGC1 and uncoupling proteins.

[vi] To investigate mitochondria of eukaryotic pathogens as possible targets for correctional measures.

[vii] To study the role of mitochondrial Reactive Oxygen Species in cancer cell apoptosis and drug resistance.

[viii] To examine mitochondrial functions in ischemic brain (rat model of neurodegenerative diseases) and delivery of correctional complexes and nanoparticles to such brains.

[ix] To develop strategies to correct the effects of disease-causing mitochondrial tRNA mutations (e.g., the tRNALys mutation in Myclonic Epilepsy with Ragged Red Fibers) using a tRNA import complex in patient-derived cybrid models, to develop methods for RNA delivery to mitochondria, and to study the pathways of the intracellular uptake and targeting of such complexes to mitochondria.

[x] To study the role of *Plasmodium falciparum* mitochondria for the parasite growth and liver mitochondrial dysfunction and associated apoptosis during host-parasite (malaria) interaction.

[xi] To study mitochondrial disorder on the development of *Helicobacter pylori* mediated and non-mediated gastropathy.

Significant achievements made during the third year (2009-2010):

⇨ Mitochondrial (mt) dysfunction is associated with numerous disorders including aging. Mutations and deletions in mtDNA have been observed in these situations, but their relative contribution to a particular disorder is unknown, because of the lack of an efficient method for targeting of correctional nucleic acids to the organelle.

During the course of this project, a major advance was made on the development of a novel protocol for mitochondrial gene therapy.

⇨ To examine whether mitochondrial dysfunction is responsible for ventricular dysfunction in hypertrophied heart, several parameters of mitochondrial metabolism were evaluated.

⇨ In studies of redox regulation of cancer cell signaling, it was observed that scavenging ROS enhances efficacy of imatinib, the small molecule inhibitor of Bcr-Abl kinase and a successful drug for chronic myeloid leukemia.

⇨ In cerebral diseases like ischemia- reperfusion massive oxidative damage was noted in neuronal mitochondria. Treatment with Compound-X intercalated in polylactide nanocapsule exerted a neuroprotective effect against cerebral ischemia- reperfusion evoked oxidative damage in aged rat brain mitochondria through restoration of key mitochondrial enzymes such as succinate dehydrogenase and anti-oxidant enzymes such as superoxide dismutase and catalase.

⇨ Established the activation of mitochondrial pathway of apoptosis by oxidative stress has been implicated for hepatocyte dysfunction and apoptosis during malaria. Malarial infection induces mitochondrial pathology by inhibiting mitochondrial respiration, dehydrogenases and transmembrane potential and damaging ultrastructure. Mitochondrial pathology is associated with the development of mitochondrial oxidative stress.

⇨ Investigated the mechanism of antiapoptotic and cell renewal effects of lansoprazole, a proton pump inhibitor, to protect and heal gastric mucosal injury *in vivo* induced by indomethacin, a non-steroidal anti-inflammatory drug (NSAID). This study thus provides the detailed mechanism of antiapoptotic and pro-survival effects of lansoprazole for offering gastroprotection against indomethacin-induced gastropathy.

⇨ Standardization of the membrane viscosity/fluidity quantification of the isolated mitochondria from rat muscle tissue. The clinical evidences suggest that hypothyroid patients have more risk from diabetes than that of normal healthy individuals. Initial study indicates the possibility of mitochondrial dysfunction as a whole is common consequence or cause of these two disorders. The work is in progress to find out other common factors that are linked with these two disorders.

- ⇨ DNA was isolated from 112 POAG patients and 80 controls. The entire mitochondrial genome of patients and controls samples was sequenced. This required 24 PCR and 48 sequencing for each sample. Identification of variants in both patients and controls were done using analyses of the sequences using multiple alignment tools. The variants identified were evaluated for potential alteration of biological activity by in silico analysis (software used SNP score). The software identifies the potential pathogenic variants based on sequence homology, property of amino acid, structural determinants and function. Analysis of the data led to the identification of variants both in patients and control, where the number of variation in patients is almost twice that of controls. Few potential pathogenic changes have been identified in the Complex I, Complex II and Complex III in the patients. However, no such pathogenic changes were identified in Complex V. It is interesting to note that most of the potential changes identified in patients are novel.
- ⇨ Observed an NADH dehydrogenase defect in platelets of Parkinson's disease patients from an Indian population. The finding from the present study of dysfunction at the level of NADH dehydrogenase in PD platelets adds to existing evidence that the specific defect in complex I function found in peripheral tissue may mirror a defect in the brain that plays a role in PD pathogenesis.
- ⇨ Striatal dopamine has been implicated as a major candidate involved in selective striatal neurodegeneration in Huntington's disease. Our study suggested a major role of striatal dopamine in behavioral changes and generation of $^{\cdot}OH$, which may lead to selective striatal neurodegeneration in 3-NP model of Huntington's disease.

EFYP PROJECT

R&D Outputs during the third year (2009-10):

Patents: 1 (one)

Total Number of Publications: 15 (fifteen)

2. **Title:** Engineering Peptides & Proteins for New Generation Therapies.

Project: Nodal Net Work [NWP-005]

Nodal Laboratory: Indian Institute of Chemical Biology (IICB), Kolkata

Participating CSIR Institutes:

Institute of Microbial Technology (IMT), Chandigarh

Institute of Genomics and Integrative Biology (IGIB), Delhi

Centre for Cellular and Molecular Biology (CCMB), Hyderabad

Central Drug Research Institute (CDRI), Lucknow

Objectives:

[a] To engineer defensins of lesser complexity and enhanced anti-microbial properties.

[b] Designing and development of some novel small anti-microbial peptides with reduced toxicity.

[c] Development of peptidomimetics to block protein-protein interaction at the same time membrane penetration capability and increasing bioavailability.

[d] To study protein mis-folding and aggregation through engineering protein that does not mis-fold and aggregate.

[e] To engineer small peptides, which are equivalent to larger transcription factor-with Protein Transduction Domains for cell entry.

[f] Designing and development of recombinant proteins with much more stability and reduced toxicity, which can be used to cure certain life threatening diseases.

[g] New engineering techniques will be developed to produce proteins with new activities: implication in vaccine developments.

[h] To develop process for production of engineering protein.

[i] To engineer streptokinase having weaker immune response towards increasing their utility.

Significant achievements made during the third year (2009 – 2010):

1. **Deamidation mediated inactivation of enzyme proteins:**
Three enzymes, Alcohol Dehydrogenase and Acid Trehalase, from *S. cerevisiae* and Endo-xylanase from mushroom *T. clypeatus* were utilized for this study. Heat and pH induced inactivation (measured in terms of residual activity) of acid trehalase and xylanase showed a higher rate of deamidation and isoaspartyl formation as measured in terms of Protein isoaspartyl methyl transferase (PIMT) activity than in alcohol dehydrogenase. Amino acid analysis showed that percentage of aspartic acids/asparagine residues in acid trehalase and xylanase was much higher than that in alcohol dehydrogenase leading to such an observation.

2. **Dominance of epitope in the environment of another protein: implication in vaccine design**
Dominance of the epitope of a repressor 12-26, was studied in the environment of another protein kinetoplastid membrane protein -11 (KMP-11) and produced 2 different chimeric proteins-1. repressor 12-26 on N-terminal end of KMP-11 and 2. repressor 12-26 on C-terminal end of KMP-11. repressor 12-26 when complexes with MHC classII produces T-cell hybridoma response producing IL-2. Among the two chimeric proteins, only the 1st type shows similar antigen presentation to T-cell hybridoma like free repressor 12-26 peptide. Antigen presentation assay with different MHC class II types, I-Ad, I-Ed and I-Ek all showed similar results. Even the antibody response against repressor 12-26 was detected only in the, repressor 12-26 at N-terminal end of KMP-11 protein primed mice. From this primary data we can say dominant epitope inserted in a protein do not keep their immunodominance always.

3. **Generation of antibody against constrained epitope: implication in vaccine development**
Two different groups of mice which were immunized with the 13-mer peptide and 32-mer peptide respectively and antihapten antibody measured by ELISA. Mice received 32-mer showed high antibody towards the hapten as compare to 13-mer. To determine the nature of the isotype involved it was revealed that IgG2b is high compare to IgG1 and IgG2a signifying that the response is Th1 cell dependent.

4. **Screening of Antileishmanial Activities of Different Peptides *in vitro***
MTT assay of 7 peptides (VRP, VPRP, LRP, VELMEL, ARP, FRP and BNBD-2) were studied for their promastigote killing activity. Among these peptides VRP, VPRP and FRP (10 µg & 15 µg dose) showed more effective proamastigote killing activity & BNBD-2 (25 µg dose) showed the activity almost similar to standard drug Sodium Antimony Gluconate (SAG) at 25 µg dose after 48 and 72 hours incubation. LRP, ARP and VLMEL did not show any promastigote killing activity. VPRP & BNBD-2 did not show any cytotoxicity on mouse peritoneal macrophages but VRP at 15 µg doses showed a little toxicity to macrophages. These three peptides were found to be as effective as SAG against parasite infection in macrophages. Inhibition of parasite infection in macrophages by VRP, VPRP and BNBD-2 on 4 different resistant strains showed no activity.

5. **Aggregation as anti-aggregation compound**
Arginine inhibits aggregation of BSA at pH 7.5 by interacting with the unfolded state of BSA leading to decrease in the surface accessibility of the unfolded chain and increases the co-operativity of the unfolding transition leading to inhibition of the accumulation of the intermediate states.

6. **Synthesis of arginine derivatives:**
Arginine inhibits aggregation of a protein. While the mechanism of its action is not well known, it has been shown to interact with the unfolded states of a protein and destabilize it. We would like to synthesize a number of arginine derivatives to study the effects of structural variation of arginine to protein aggregation. We have synthesized N^{G}-methyl-L-arginine. Synthesis of N^{δ}-methyl-L-arginine is on the way.

7. **Design of p53 peptideomimetic having greater affinity for Mdm2.**
Designed a peptideomimetic based on annulment of electrostatic repulsion between phosphorylated Thr-18 and Asp-21 on p53 transactivation domain. The designed peptides were tested for its effect on one melanoma cell line with wild-type p53 status (SK-Mel-5). It has been observed that the synthesized peptides cause massive apoptosis with about IC50 value of 10-15 μM. Upon attachment of a nuclear localization signal, the IC_{50} value dropped several fold .

R & D Outputs during the third year (2009-10):

Total Number of Publications: 5 (five)

Patents with reference: 1 (one)

Project Asst. engaged : 8 (eight)

EFYP PROJECT

3. **Title:** Development of diagnostics and target-based molecular medicines against allergy, bronchial asthma and chronic obstructive pulmonary disease

Project: Nodal Net Work [NWP-033]

Nodal Laboratory: Indian Institute of Chemical Biology (IICB), Kolkata

Participating CSIR Institutes:

Institute of Genomics and Integrative Biology (IGIB), Delhi

Indian Institute of Chemical Technology (IICT), Hyderabad

Industrial Toxicology Research Centre (ITRC), Lucknow

Indian Institute of Integrative Medicine (IIIM), Jammu

Objectives:

[a] Development of animal model for asthma for evaluation of lead molecules in vivo.

[b] Testing 2-3 lead molecules for anti-asthma activity.

[c] To synthesize NCEs for the biological evaluation as PDE-4 inhibitors.

[d] Toxicological and safety evaluation of lead molecules with anti-asthmatic activity; and evaluation of drug efficacy by plethysmography

[e] Basic research on the role of Stat3 and Socs3 in asthma pathogenesis.

[f] Determination of Pharmacokinetics, Absorption/ Transport, Biotransformation, and Distribution studies.

Significant Achievements made during the second year (2009-2010):

Anticipated Deliverables	Deliverable achieved
In vivo evaluation of lead molecules for antiasthmatic activity	3 molecules tested in vivo.
Development of PDE4 inhibitor	2 molecules are ready.
Toxicological and safety evaluation of lead molecules with anti-asthmatic activity and evaluation of drug efficacy by plethysmography	Toxicity of IICT/TA-67 and ICB/11/D-8 is completed
Synthesis of NCEs based on the lead structures, lead optimization; biological evaluation	ICB/11/D-8 of natural origin has been synthesized and the synthetic molecule is now ready for further testing
Target validation	2 New molecules have been isolated, ICB 38 ICB 39 and their structure has been determined.
Publications	Nil
Patent	One patent is submitted to CSIR.
Social Goods: Human resource development	5 students under Ph.D programme Trainee: 10.

R & D Outputs during the third year (2009-2010):

Total published paper during this tenure: 0 (nil)

Patent Submitted : 1 (one)

Human resource development : 5 students under Ph.D programme

Trainee: 10.

EFYP PROJECT

4. Title: New Insights in Cancer Biology: Identification of Novel Targets and Development of Target Based Molecular Medicine

Project: Inter Agency [IAP-001]

Nodal Laboratory: Indian Institute of Chemical Biology (IICB), Kolkata

Participating CSIR Institutes:

Indian Institute of Chemical Technology (IICT), Hyderabad

Centre for Cellular and Molecular Biology (CCMB), Hyderabad

Central Drug Research Institute (CDRI), Lucknow

Institute of Genomics and Integrative Biology (IGIB), Delhi

Central Glass & Ceramic Research Institute (CGCRI), Kolkata

National Inst. for Interdisciplinary Science & Tech. (NIST), Thiruvananthapuram

Participating Non-CSIR Institute:

National Center for Cell Sciences (NCCS), Pune

Objectives:

[a] Identification of new lead molecules from herbal and synthetic sources against specific cellular targets using high throughput approaches.

[b] Identification of novel anticancer targets based on the knowledge gained from molecular analysis of tumorigenic processes.

[c] Generation of library of small molecules by diversity-oriented chemistry.

[d] Deciphering the regulation of expression of target genes in normal and cancer cells.

[e] Understanding the molecular interactions between target proteins and their partners.

[f] Nano-structered calcium phosphate-based ceramics as drug carrier for the treatment of hepatocellular carcinoma in animal model.

[g] Multi-agent-based simulations of collective cell behaviors with application to cancer.

Significant achievements made during the third year (2009-10):

Objective [a]:

- Library of 20 herbal extracts have been made
- Library of 164 pure compounds have been made
- All above extracts and compounds have been assayed for cell proliferation assay.
- Pharmacokinetic analysis has been initiated for two compounds with anti-proliferation activity
- For one compound mechanistic evaluation has been initiated

Objective [b]:

Tumor suppressor NME23-H2: Detailed analysis of the NM23-H2 (or NME2) chip-chip results indicated that the focal adhesion pathway is perturbed and could be under transcription control of NME2. This was characterized in detail by focusing on a key focal adhesion factor vinculin.

Cell secretome study: Three Glioblastoma (GBM) cell lines HNGC2, U87MG and LN229 were chosen for the study. Proteins and peptides released by these cell lines were investigated using LC-MS based profiling of proteins from the conditioned media collected from these cells. Some of the select proteins will be examined with antibodies in the plasma of glioma patients and compared with plasma from normal subjects, for their utility as biomarker.

Identification of differentially expressed membrane and nuclear proteins in glioma patients using iTRAQ method: Membrane and nuclear proteins have important biological functions such as signaling and cell cycle regulation. The expression level of many of these proteins is altered in cancer cells. Studying membrane and nuclear proteins in detail helps to know cancer biology and to identify drug targets.
Tissue sub cellular fractionation was carried out to extract membrane and nuclear proteins from pooled tissues from normal subjects and from glioblastoma tumor samples. After iTRAQ labeling and SCX fractionation, samples were analyzed by LC-MS/MS approach (nano LC-MADLI and Orbitrap analysis).

Clinical tissue sections and Antibody tissue micro arrays: TMA IHCs have been carried out with nearly 150 retrospective (archival) and prospective tissue sections using close to 20 antibodies. Images are being studied at Nijam's Institute of Medical Sciences (NIMS), Hyderabad and Mumbai site of Human Proteome Research (HPR, Sweden, a collaborative activity).

Possible continuation: Additional proteins identified from the membrane and nuclear differentials can be examined by this approach.

Objective [c] & [d]:

- The spindle assembly checkpoint protein Cdc20 transcriptionally regulates the expression of ubiquitin conjugating enzyme UbcH10
- Our work is exclusively focused on investigating regulation of matrix metalloproteases (MMPs) in inflammatory pathways that eventually lead to cancer. Inflammation is the physiologic response to injury that caused by wounding, chemical irritation and/or infection. MMPs are important key molecule in extracellular matrix (ECM) remodeling and have been implicated in the pathogenesis of cancer metastasis. Our study highlights for the first time an angiogenic action of melatonin via upregulation of VEGF to rescue NSAID-induced gastropathy.

Objective [e]:

(i) Most of the deliverables planned were completed except the NMR structural elucidation for the new formulation and maximum drug loading on the HAp nano particles.

(ii) Two formulation of drug loaded nano HAp have been developed (termed as 'low dose' and 'high dose') after thorough characterization including XRD, FTIR, TGA, UV Vis Spectroscopy, FESEM, TEM, etc.

(iii) Elution kinetics of the drug from the above formulations has been checked at different pH conditions and time interval.

(iv) Thermal stability of the same has also been performed.

(v) Based on the results, one joint patent with IICB is being prepared for national/international applications.

(vi) *In vivo* outcome of the above two formulations were under study. This would be reported as soon as it is available.

R & D Outputs during the third year (2009-2010):

Total Number of Publications: 5 (five)

No. of Project Assistants engaged: 17 (seventeen)

PARTNER NETWORK PROJECTS OF IICB

Partner Network Projects	Objectives
Discovery, development and commercialization of new bioactives and traditional Preperations (**COR-023**)	➢ To revisit Indian biodiversity and Indian Systems of Medicine in the light of current day knowledge in search of therapeutic principle(s) under four disease areas of national importance, namely, Leishmaniasis, Gastric ulcer, Immunomodulation, and Parkinson's disease.
Drug target development using in-silico biology (**CMM-017**)	➢ *In silico* analysis of genome/proteome architectures of various pathogenic bacteria, parasites and fungi for identification of virulence determinants ➢ Studies on mouse and human genome characteristics in an attempt to detect the host factors regulating or regulated by the pathogen invasion.Clustering of some host-parasite interaction pathways with a view to identify some of the networks crucial for the host-parasite interplay. ➢ Development of novel software/algorithms relevant to the study

Partner Network Projects	Objectives
Comparative genomics and biology of non-coding RNA in human genome (**NWP-036**)	➢ To investigate posttranslational control mechanisms involving such RNAs, ➢ To identify co-regulated gene networks using siRNA, ➢ To develop new RNA-based methods for influencing gene expression in subcellular compartments such as mitochondria, andto investigate the structural basis of the interactions between non-coding RNAs and their protein targets
Exploitation of India's rich microbial diversity (**NWP-006**)	➢ To develop state of the art molecular genetics approach to address the relationship between metal microenvironment and microbial communities.
Zero emission research initiative (**NWP-044**)	➢ To identify & scale up of technology and their extension for minimizing environmental risks from leather sector to near zero values.
Diabetes mellitus – New drug discovery R&D, molecular (**NWP-032**)	➢ To understand the basic mechanism of insulin resistance and defect in signaling of type 2 Diabetes. ➢ To identify possible drug targets . ➢ To develop drug against those targets.
Identification and validation of drug targets for selected pathogens of national importance (**NWP-038**)	➢ Identification of pathogen-specific, differentially-expressed proteins of *Leishmania donovani.* ➢ Validation of identified protein as drug targets. ➢ Development of target-specific assays and screening of available synthetic/natural libraries.
Biological and chemical transformation of plant compounds for production of value added products of therapeutic / aroma value (**NWP-0009**)	➢ Up-scaled isolation of parent anti-cancer molecules targeted for chemical and biological transformation ➢ Chemical transformation of selected phyto-molecules for value addition.
Pathway engineering and system biology approach towards homologous and heterologous expression of high -value phytoceuticals (**NWP-008**)	➢ Elucidation of the naturally occurring pathways of podophyllotoxin biosynthesis. ➢ Metabolic engineering of podophyllotoxin pathway in a suitable host ➢ Metabolic engineering of isoflavone biosynthesis pathway ➢ Reprogramming of reprogramming of these metabolic pathways in the selected host perhaps using synthetic transcription factors ➢ Creation of novel genetic switches for use in synthetic biology. ➢ Standardization of purification of the compound from metabolically engineered organism
Nanomaterials and nano-devices for application in health and disease (**NWP-035**)	➢ To synthesize, purify, characterizeand and study suitable linear and denditric peptides for producing and stabilizing metal nanoparticles and cadmium sulfide (CdS) nanoparticles (semiconductor quantum dots). ➢ To examine the cell entry of peptide capped cadmium sulfide (CdS) quantum dots using selective cell lines like normal cell lines (ordinary T-lymphocyte) and diseased cell line (fibroblast T-lymphocyte) and to check the locations of the quantum dots inside the cell , if the nanoconjugate (i.e. peptide capped CdS

Partner Network Projects	Objectives
	quantum dots).To explore self-assembling synthetic peptide based new nanoporous materials and to vary the pore size by varying the peptide based molecular building blocks for achieving the selective gas adsorption properties from a mixture of gases of different molecular dimensions. ➢ To check the biodegradability of these peptide based nanoporous materials. ➢ To fabricate pseudopeptide based nanofibers by peptide capped gold and silver nanoparticles and to study the important electrical and other material properties of these nano-materials. To study the self-assembling synthetic peptide based various nanostructures like nanofibrils, nanorods and nanotubes and to use these peptide nano-structures as templates for the production of gold/silver nanowires and nanocrystals.
Plasma proteomics in health, environment and disease (**NWP-004**)	➢ To identify disease specific biomarkers in easily accessible body fluids, which would constitute safe, effective and non-invasive methods for development of new diagnostic and prognostic approaches. ➢ Plasma proteome profiling in the areas of Arsenicosis, Leismaniasis, Cardiac diseases and ALL will be undertaken.
Integrated Analysis for Impact, Mitigation and Sustainability (IAIMS): Regional Climate Modeling at Decadal Scale (**NWP-052**)	➢ To study the change in arsenic concentration in soil and groundwater trend affected by change of climate - flood or drought and/or land-management practices. ➢ To determine the different rice varieties dependence on bioaccumulation of arsenic under different cultivation methods to combat the crisis of arsenic contamination of rice under severe environmental conditions like flood or draught. ➢ The effect of environmental parameters associated with climate change on the relative activities of the arsenic transforming microbes will be investigated. Specifically, (a) Isolation and identification of bacteria from aquifers (b) Identification of genes associated with arsenic oxidation/ reduction/ detoxification and other processes. (c) Regulation of expression of relevant genes by environmental parameters
Designing Potential Lead Molecules for Inhibition of Siderophore Biosynthesis in Mtb (**HCP 001**)	➢ Development of new safer drugs to treat tuberculosis
Synthetic Biology & Metabolic engineering of Azadirachtin Biosynthesis Pathway **(HCP 002)**	➢ Construction of random BAC library from genomic DNA of *A. indica* ➢ Genome and transcriptome sequencing and computational analysis for assembly of the EST sequences. ➢ Development of assays to measure the toxicity of azadirachtin ➢ Isolation of secondary metabolites from leaves and seed and synthesis of the intermediates. ➢ Cloning of the genes of coding for azadirachtin biosynthesis pathway enzymes in heterologous hosts and developing expression

Partner Network Projects	Objectives

system in *E. coli*/yeast for functional evaluation, like enzyme assays, of targeted genes.

- Reconstruction of biosynthetic pathway of azadirachtin by using information obtained through genetic and biochemical approaches.
- Designing and development of related synthetic biotools like engineering of efflux pumps for transport of metabolites and utilization of these biotools in optimization of the pathways in heterologous hosts.
- Establishing a computational framework (programs and software/ hardware) for simulation of biochemical reaction network dynamics. Building up of computational capabilities and web servers for whole genome annotation.
- Use of deterministic models to understand the effect of changes in regulatory and metabolic pathways.

EFYP PROJECT

PUBLICATION & INFORMATION AND PLANNING, MONITORING & EVALUATION

Drs. Pijush K. Das, K.P. Mohanakumar, Aparesh Bhattacharya, Uday S. Chowdhury, Moonmoon Bhaumik, Tanmoy Mukherjee, Prasanta Chakraborty, Siddhartha Majumder, Mr. Arupesh Majumder, Sekhar Mukherjee, Swadesh K. Sahoo, Binayak Pal, Nikhil K. Das, Pratima Banerjee, Lily Das, Sukhendu Biswas, Gopal C. Sarkar, Pallab Mukherjee, Nishikanta Naskar, Soumalya Sinha, Bideshi Nayak

The scientific management of the different R&D activities of the institute is the primary focus of this division. The diverse activities of this division have been carried out successfully by seven major sections, e.g. [a] Publication & Information; [b] Planning, Monitoring & Evaluation; [c] Art & Photography; [d] ISTAD-IICB; [e] Intellectual Property Management Cell; [f] Business Development Group; and [g] Human Resource Group. The details of the scientific management activities of the individual sections are given below separately for the reporting year.

PUBLICATION & INFORMATION SECTION

Dr. Tanmoy Mukherjee and group

This section is basically catering the diverse informational activities, publication and monitoring of reports. The major contribution of this section lies in assisting scientists in day to day maintenance of the institute activities and innovations, project profiles, publication records and research utilization data. The section is involved in the following wide spectrum of programmes during the report year.

- Preparation of Annual Plan (2010-11) and Budget.
- Preparation of IICB Annual Report (2008-09) and half-yearly reports.
- Preparation of documents released during events.
- Dissemination of information to scientific milieu on relevant subjects.
- Documents on IICB inputs for "CSIR Annual Report 2009-10" and "CSIR Research Output 2009".
- Assistance to scientists, fellows and staff members for participation in seminars, symposia and conferences.
- Maintenance of database for testing and calibration.
- Total management of all technical queries.
- Public relations, advertisement and news and views forum.
- Organization display of exhibition and science news dissemination.
- Advice and comments for management of parliament queries and other related crucial matters of institute.
- Organization of 'OPEN HOUSE' and active help for 'CPYLS-2009' programmes.
- Assist in management of Eleventh Five-Year Plan (2007 – 2012).
- Monthly Report of IICB for PPD,CSIR

Management of Exhibition

Like preceding years, P&I Section has participated in several exhibitions during 2009-10 in and around Kolkata and also outside Kolkata organized by various organizations. IICB has a mandate to carry out basic and applied research in health problems of the country. The main objective of this section is to present recent scientific developments of the institute to the common people. The successful presentation of scientific works and developments of IICB brought in a number of awards through these exhibitions. Mr. Sekhar Mukherjee, a senior member of this section, looks after the exhibition cell. He also arranged two exhibitions at IICB premises on

the occasion of CPYLS-2009 & OPEN HOUSE programme. List of exhibitions are given below.

EXHIBITIONS ARRANGED & PARTICIPATED

Date	Theme	Organised By
September 02-06, 2009	"Advancement and Overall Progress of India" Science Exhibition	Central Calcutta Science& Culture Organisation for Youth, held at Barasat, Kolkata – 700 124
October 28, 2009	IICB Open House Program	IICB Premises. Kolkata.
November 20-30, 2009	Science & Technology Fair, 2009	Institute of Social Science, held at Central Park Fair Ground, Salt Lake, Kolkata
December 12-18, 2009	6th Jatiya Sanhiti Utsav-O -Bharat Mela - 2009	Bangiya Seva Samity & East BhaleyaSmriti Sangha, held at Taldi, South 24-Parganas.
December 14-16, 2009	National Symposium on Science & Technology and the young. (NASI)	University of Calcutta in collaboration with Ram Krishna Mission Institute of Culture, Golpark, Kolkata.
December 20-29, 2009	Sundarban Kristi Mela-O -Loko Sanskriti Utsab - 2009	Milontirtha Society held at Kultali, Narayantala, 24-Parganas South
December 22-31, 2009	25th Sundarban Yuba Mela - 2009	Taldi Bahurupee Sangha, held at Taldi MC High School, South 24-Parganas.
Dec. 31, 2009 - Jan. 01, 2010	CPYLS - 2009	IICB Premises. Kolkata.
March 04-05, 2010	West Bengal State Science & Technology Exhibition.	17th West Bengal State Science & Technology Congress held at West Bengal University of Animal & Fishery Sciences, Belgachia, Kolkata

Management of Laboratory Visit for Students

On the occasion of CSIR Foundation Day (2009) celebration, the members of this section have actively helped for the arrangement of 'OPEN HOUSE' programme where students from various schools/colleges/universities in and around Kolkata visited IICB. A large number of students from different schools and colleges along with their teachers visited various laboratories and interacted with the scientists expressing great interest and enthusiasm. Members of this section also arranged the laboratory visit for students of outside Kolkata colleges and universities. A total of nine (09) numbers of visits were organized throughout the year (2009-10) as listed below.

Sl. No.	Date	No. of Students, Name of the Department & Institute
1.	21.09.2009	28 Students - Post Graduate Dept. of Zoology, Bajali College: Pathsala, Berpeta, Assam
2.	22.09.2009	39 Students - West Bengal University of Technology (WBUT), Salt Lake, Kolkata
3.	23.11.2009	22 Students - Dept. of Zoology, University of North Bengal, Darjeeling
4.	25.11.2009	42 Students – Dept. of Pharmacy, Jadavpur University, Kolkata
5.	08.12.2009	27 Students - Dept. of Biotechnology, Shree M&N Virani Science College, Rajkot, Gujarat
6.	09.12.2009	26 Students - Dept. of Biotechnology, JSS College, Ooty,
7.	21.12.2009	38 Students - Jagdish Bose National Science Talent Search (JBNSTS), Kolkata
8.	05.01.2010	24 Students - Dept. of Zoology, North Eastern Hill University (NEHU), Shilong
9.	17.02.2010	29 Students - Dept. of Biotechnology, Ramkrishna Vidyamandir, Belur, Howrah

Scientist Visit & Events

The P&I Section is also responsible for the announcement and arrangement of seminars for the national and international scientists who often visit the institute and like to share their research activities with IICB faculties. A list of **'Scientist Visitors'** is given in a separate page.

The Institute also organized several significant events with the assistance of this section and **'List of Events'** is also shown separately for the reporting year.

Sectional Members

Dr. Uday S. Chowdhury, Mr. Arupesh Majumdar, Mr. Sekhar Mukherjee, Mr. Nikhil K. Das, Mr. Pallab Mukherjee.

PROJECT MONITORING & EVALUATION SECTION

Dr. K.P. Mohanakumar & group

A Project Monitoring Cell is set up in the institute on August 5, 2009 to aid in the effective management of the institute's intramural, networked, grant-in-aid as well as collaborative R&D projects. Essentially the Division is functioning as a liaison agency between Principal Investigators in the institute-Finance section-Purchase Section and the Grant Giving agency. Proper logistic support for the management, maintenance and monitoring of institute's CSIR and externally funded projects would help in effective, timely and successful implementation and completion of the mission and in turn would reflect the growth of the institute. PME is also entrusted with appropriate dissemination of information regarding ongoing and completed projects and therefore, PME of IICB like other CSIR laboratories is actively involved on the following activities:

- Preparation and timely maintenance of databases for all intramural and extramural research projects in IICB, and tabulation of ECF of the institute.
- Project expenditure monitoring of all projects, including proper procurement of capital goods as sanctioned in the projects.
- Preparation of response to Parliamentary questions in relation to the activities of the institute
- Dissemination of information on all relevant National & International Research Program requests for

applications, including fellowships and maintenance of mandatory registration with such agencies, and liaison with all grant giving agencies.

- Make awareness among scientists regarding terms & conditions of relevant funding agencies.
- Responding to various audit queries in relation to both ongoing and completed projects.
- Participation in institute's annual plan, budget preparation, expenditure status, *etc*.

A list of Extramural projects being implemented in IICB is given in a separate page as **'External Funding'**.

Sectional Members

Dr. Prasanta Chakraborty, Mr. Sukhendu Biswas, Mr. Soumalya Sinha

ART & PHOTOGRAPHY SECTION

Dr. Tanmoy Mukherjee and group

Art Section under the supervision of Mr. S.K. Sahoo has rendered full support to all the staff members during scientific seminars/symposia and all national events by preparing displays, illustrations, posters, exhibits, and slides. Diagrams, charts, graphs for publication in national and international journals are prepared in this section. They are working in collaboration with the photography Section for making each exhibition a great success to highlight the institute achievement. The section also participated in preparing artwork and cover design for Hindi Day and Hindi Report. This section also carried out work for decoration of floor & institute during various scientific and official programmes. Art Section provided following art works to the Institute during this year.

Sl. No.	Jobs Done	Numbers
1.	Numerous illustrations, charts graphs and structures.	161
2.	Various posters for annual functions and official purpose	60
3.	Certificate preparation for Training programme, Ph.D. Course work and staff retirement etc.	117
4.	Name plate preparation for committee meeting, conference and various functions of the Institute	98
5.	Memento and medal design	8
6.	Several slides preparation for presentation, IICB brochure design, News Letter design for IICB website and Index page design for IICB website in both Hindi and Bengali	4
7.	Assistance provided for IICB exhibition stall in and outside Kolkata several times	7

Photography Section under the able guidance of Mr. Binayak Pal has been successful in procuring a digital camera for coverage of most of the events taking place in the institute. The section is continuously supplying all the photos for publications, Annual Reports, Journals and other related documents. Beside they are also assisting the scientists of the institute. Apart from that they also handled photographs of scientific activities and experiments slides for publication in different international journals.

Sectional Members

Mr. Swadesh K. Sahoo, Mr. Binayak Pal, Mr. Nishikanta Naskar

ISTAD SECTION

- Diverse activities of this section were personally supervised by the Head of the Division, Dr. Pijush K. Das with the active help of Dr. Samir K Dutta.

INTELLECTUAL PROPERTY MANAGEMENT CELL

Dr. Tanmoy Mukherjee and group

Intellectual Property Management (IPM) cell in IICB is working in close alliance with Business Development Group (BDG) in IICB and Intellectual Property Management Division (IPMD) of CSIR. With the help of a new Comprehensive Patent Database prepared by this cell, now any information about a patent filed by IICB, since 1990 is just a click away.

This cell has continuously maintained liaison with Scientists of IICB and IPMD, CSIR to protect Intellectual Properties of IICB/CSIR. The IPM Cell, IICB provided all information, clarifications, explanations and reports to IPMD, CSIR regarding new patent applications, granted patents and renewal or lapsing of existing patents in consultation with concerned inventors within corresponding time-limit. During the reporting period, a large number of correspondences were made with IPMD, CSIR, a significant amount of responses were sent for at least 25 patent applications in India and abroad. And a considerable number of communications were made with IICB scientists regarding patent queries to provide necessary information to IPMD, CSIR to obtain productive results. The IPM Cell always extended co-operation to the scientists, IICB in writing and filing patent applications. This cell has prepared, maintained and disseminated all information regarding patent application, status of the application, renewal etc. as, when and where it was required. IPM cell, IICB has provided all necessary information to Business Development Group of IICB for licensed out patents; sent information on patent and technology transfer to IPMD, CSIR regarding Parliamentary Question; prepared necessary document on patents licensed out by IICB; prepared year wise documents on total Patents of IICB filed and granted; prepared Commercial Working Report of IICB Patents for IPMD, CSIR; approved number of Declaration forms for non patentability of publication and sent Renewal / Lapse recommendations of IICB patents for 2008-09 to IPMD, CSIR

Apart from these, some of the significant jobs done are as follows:

1. Maintenance of IICB Patent Database to keep it up-to-date
2. Commercial Working Report for 16 Indian Patents of IICB prepared and sent to IPMD, CSIR.
3. Renewal / Lapse recommendations for 2009-10 of IICB patents prepared for IPMD, CSIR. Reports Prepared for 70 Foreign Patents and 16 Indian Patents.
4. Year wise documents prepared on total Patents of IICB filed and granted.
5. Response to IPMD, CSIR regarding IPER, IPRP, OA, Designated Countries and other queries relating to patent application and filing.
6. Information on patent and technology transfer to IPMD, CSIR regarding Parliamentary Question
7. Approval of Declaration forms for non patentability of publication

During reporting period, the performance at a glance of IPM Cell is as follows:

Patents Filed :

National Patents Filed	...	5 (Complete Filing 4 + Provisional Filing 1)
International Patents Filed	...	10
Total No. of Patents Filed	**...**	**15**

Patents Granted :

National Patents Granted	...	0
International Patents Granted	...	10
Total No. of Patents Granted	**...**	**10**

New Patent Application Submitted	**...**	**1**

FILED ABROAD

S. No.	Title	Inventors	Country	Complete filing date
1	Development of a bifunctional molecule 5-hydroxy-2-phenyl -7-(6-piperidin-1-yl-hexyloxy)-4h-benzpyran-4-one as anti Helicobacter pylori and gastric antisecretory agent	Pratap Kumar Das, Suchandra` Goswami, Annalakshmi Chinniah, Janaswamy Madhusudana Rao, Katragadda Suresh Babu	World	26/02/2010
2	A pharmeceutical composition useful for the treatment of prostate cancer	Sinha Swati, Pal Bikas Chandra, Bhattacharya Samir	Usa	26/02/2010
3	Inhibitors of nuclear factor - kappa B (NF-κB) and inflammatory cytokines	Santu Bandyopadhyay, Bikas Chandra Pal, Parasuraman Jaisankar, Siddhartha Roy, Jayashree Bagchi Chakraborty, Indrani Choudhury Mukherjee, Sanjit Kumar Mahato, Aditya Konar, Srabanti Rakshit, Labanya Mandal, Dipyaman Ganguly, Kausik Paul, Anirban Manna, Jayaraman Vinayagam, Churala Pal	World	12/01/2010
4	Acaciaside-B: a prophylactic contraceptive for human immunodeficiency virus infection/acquired immune deficiency syndrome	Kabir Syed Nazrul, Ray Heramba Nanda, Pal Bikash C, Mitra Debashis	Kenya	01/12/2009
5	Acaciaside-B: a prophylactic contraceptive for human immunodeficiency virus infection/acquired immune deficiency syndrome	Kabir Syed Nazrul, Ray Heramba Nanda, Pal Bikash C, Mitra Debashis	South Africa	30/11/2009

6	Antimonocytic activity of betel leaf extracts	Santu Bandyopathyay, Bikash Pal, Samir Bhattacharya, Mitali Ray, Keshab Chandra Roy	USA	23/11/2009
7	Two novel gnrhs from indian murrel brain: highly potential molecules for induced breeding of fish	Chatterjee Abhijit, Ray Partha, Dasgupta Subrata, Bhattacharya Samir	Japan	11/09/2009
8	Compositions and methods for delivery of protein-coding RNAs to correct mitochondrial dysfunction	Adhya Samit	USA	28/08/2009
9	Compositions and methods for delivery of protein-coding RNAs to correct mitochondrial dysfunction	Adhya Samit	World	28/08/2009
10	Elisa and dipstick based immunoassay for field diagnosis of visceral leishmaniasis (kala-azar) and PKDL	Ali Nahid, Saha Samiran	World	17/04/2009

FILED IN INDIA

S. No.	Title	Inventors	Filing date
1	Synthetic phosphodiesterase 4 (PDE-4) inhibitor with antiasthmatic activity	Vasanta Madhava Sharma Gangavaram, Jhillu Singh Yadav, Radha Krishna Palakodety, Arun Bandyopadhyay, Siddhartha Roy, Santu Bandyopadhyay, Rakesh Kamal Johri, Subhash Chander Sharma, Balaram Ghosh, Mabalirajan Ulaganathan, Sakshi Balwani, Bholanath Paul, Ashok Kumar Saxena	29/01/2010
2	Inhibitors of phosphatidylinositol-3-kinase (PI3) and inducers of nitric oxide (NO)	Santu Bandyopadhyay, Bc Pal, Parasuraman Jaisankar, Prof. Siddhartha Roy, Jayashree Bagchi Chakrabotry, Indrani Choudhury Mukherjee, Sanjit Kumar Mahato, Aditya Konar, Srabanti Rakshit, Labanya Mandal, Dipyaman Ganguly, Kausik Paul, Anirban Manna, Jayaraman Vinayagam, Churala Pa	12/01/2010
3	A novel low molecular weight polypeptide with hydrolysing activity on beta-D-fructofuranosyl-alpha-D-glucopyranoside	Suman Khowala, Sudeshna Chowdhury	10/11/2009
4	Compositions and methods for delivery of protein-coding RNAs to correct mitochondrial dysfunction	Samit Adhya	28/08/2009
5	Flavanoid compounds and process for preparation thereof	Pratap Kumar Das, Suchandra Goswami, Annalakshmi Chinniah, Janaswamy Madhusudana Rao, Katragadda Suresh Babu	18/02/2010

GRANTED ABROAD

S. No.	Title	Country	Inventors	Grant date	Patent No.
1	Use of betel leaf extract to induce IFN-gamma production from human peripheral blood T cells and as a Th1 type immunomodulator	China	Santu Bandyopadhyay, Bikash Pal, Samir Bhattacharya, Mitali Ray, Keshab Chandra Roy	28/05/2008	ZL00820077.7
2	A herbal molecule as potential anti-leukemic drug	China	Santu Bandyopadhyay,Bikas Channdra Pal And Others	22/07/2009	Zl2829404.1
3	Two novel gnrhs from indian murrel brain: highly potential molecules for induced breeding of fish	Japan	Chatterjee Abhijit Ray Partha Dasgupta Subrata, Bhattacharya Samir	23/10/2009	4394954
4	A herbal molecule as potential anti-leukemic drug	USA	Santu Bandyopadhyay, Bikas Chandra Pal, Samir Bhattacharya, Keshab Chandra Roy, Gautam Bandyopadhyay	10/11/2009	7615574
5	Antimonocytic activity of betel leaf extract	Germany	Santu Bandyopathyay, Bikash Pal, Samir Bhattacharya, Mitali Ray, Keshab Chandra Roy	18/11/2009	10085492
6	In vitro method to generate dendritic langerhans type cells	USA	Bandyopadhyay Santu, Roy Keshab, Chandra Gosh, Monidipa Ray, Mitali Pal, Chiranjib, Bhattacharya Samir	29/12/2009	7638329
7	A herbal molecule as potential anti-leukemic drug	Japan	Santu Bandyopadhyay, Bikas Chandra Pal, Samir Bhattacharya, Keshab Chandra Roy, Gautam Bandyopadhyay	15/01/2010	4440767
8	Herbal formulation of a combination of piper betel and murrya koenigii extracts for blocking 5 lipoxygenase activity	Japan	Santu Bandyopadhyay, Keshab Chandra Roy, Mitali Roy, Bikash Chandra Pal, Ranjan Bhadra, Krishna Das, Samir Bhattacharaya	19/02/2010	4460286
9	Anti monocytic activity of betel leaf extracts	USA	Santu Bandyopathyay, Bikash Pal, Samir Bhattacharya, Mitali Ray, Keshab Chandra Roy	09/03/2010	7674487
10	A pharmeceutical composition useful for the treatment of prostate cancer	Europe	Sinha Swati, Pal Bikas Chandra, Bhattacharya Samir	17/03/2010	EP1933945

Sectional Members

Mr. Arupesh Majumdar, Mr. Nikhil K. Das

BUSINESS DEVELOPMENT GROUP

Dr. Asish K. Sen (Jr.) and group

MAJOR ACTIVITIES OF THE GROUP:

1. Liaison with private Industries/ R&D Institutes/ Academic Institutions/ other potential clients.
2. Negotiating Business Plans with Industries and drawing agreements and MoUs.
3. Matters related to Service Tax (registration and filing returns).
4. Conducting meetings (Industry-Institute meet; Introduction of new schemes, Arrangement of visitors and their interactions with scientists, *etc*.).
5. Parliamentary related matters – Responses to Parliamentary questions, *etc*.
6. Distribution of money earned under royalties.
7. Periodic preparation of lists of knowledgebase/products available, dissemination of information on technologies, *etc*.

HUMAN RESOURCE GROUP (HRG)

Dr. Siddhartha Majumdar and group

Human Resource Group (HRG) of IICB has been set up in April 2005 to promote professional Human Resources Management in this institute by evolving and implementing HR development plan.

Activities, Guidance and Initiatives:

- To advance the academic mission of the institute, HRG-IICB provides leadership for continuous improvement in academic programme, student affairs and to define, assess and develop institute's specific training needs.
- Coordinates in-house IICB PhD Course Work programme for IICB pre-doc students as part of the Academic Affairs of the Institute.
- Organises entrance interview for recruiting Research Fellows at IICB.
- Coordinates some selected academic & science-admin affairs concerning Research Fellows/Associates and linkages with other organization/ Agencies/ Institutes.
- Collects and disseminates comprehensive data and information assisting in strategic planning for IICB & CSIR.
- Organises IICB Summer Training Programme for the Post-Graduate students of different Universities, Institutions and Colleges for partial fulfilment of their degrees and involves in different Out-reach Programme

- Organises different innovative / Training / Workshop of consistently high stands for IICB members, Research Fellows & Research Associates.
- Extends training for the external students/faculty through demonstration of methodology/ techniques used in IICB as well as through practical courses, workshops and conferences.
- Recommends name of suitable Scientists/Officers for their nomination in different R&D training programme /workshop organized by CSIR, HRDC and other national level institutes/organizations.

Programs: Guidelines, Information & Initiative

Ph.D. Programme

Objective: IICB offers exciting opportunities to highly motivated and talented students with a keen sense of scientific enquiry for pursuing advanced career for research in the frontier areas of Chemical Biology, Modern Biology or Chemistry leading to PhD on a specific topic.

The major objective of the programme is to generate adequate human resources in the different fields of Biology, Chemistry and related research areas. The duration of this programme is generally five years.

Eligibility Criteria: CSIR-NET qualified candidates / UGC-NET/ ICMR Fellows/ DBT Fellows and subject to clearance of entrance interview.

Junior Research Fellowship for GATE qualified engineering graduates (CSIR-JRF-GATE):
CSIR has introduced a new research fellowship in 2002 for the GATE qualified candidates with B.Tech. / B.Pharm / degree to pursue research leading to PhD. Each CSIR laboratory engaged in biological/biochemical research can have maximum 10 such JRF-GATE Fellows.

Besides the ad-hoc fellowship, IICB advertises for recruiting research fellows to work in grant-in-aid projects and different research schemes.

At a Glance: Research Fellow/ Associates
Number of existing **(Up to March 2010)** Research Fellows/Associates

Funding Agency	JRF & SRF	RA	PDF
CSIR	155	10	0
UGC	26	0	0
DST	01	0	0
DBT	06	0	02
ICMR	05	03	0
TLP	01	0	0

Learning and instructional support: Course Work / Training

Ph.D. Course Work

To educate and train in multidisciplinary areas, IICB offers a mandatory two-semester courses PhD course work for the Research Fellows in their first year, taught by faculty members of in-house as well as from other Institutes/Universities. The main objective of these courses is to make the students acquainted with modern

Biological Sciences, Chemistry and Chemical Biology.

The existing IICB PhD course-work programme constitutes basic and advanced courses. The basic course is for bridging the gap between M Sc and Ph D. The advanced course comprises of frontline areas of research and covers research methodology and review of current literature. Trainings are also provided for development of effective communication and writing skill (scientific) and on bioethics & laboratory bio-safety.

The course comprises of two major disciplines, namely **Basic Course** with [a] Computer Applications; [b] Instrumental Analysis; [c] Statistical Analysis; [d] Basic Biology (for Chemistry students); and [e] Basic Chemistry (for Biological Sciences students); and **Advanced Course** with [a] Advanced Biology (for students engaged in Biological Sciences Laboratory) and [b] Advanced Chemistry (for students engaged in Chemical research). In addition to this, introduction to some interdisciplinary topics viz. System Biology; Synthetic Biology; Cell Tissue Engineering; Chemical Biology etc. are also taught in advanced courses.

Incentives to students: Depending on the academic performance several incentives are offered to meritorious students. These include cash awards to the PhD course work students based on marks, best thesis award etc.

Number of students in IICB Ph.D. Course work -2009-10 : 64

Summer Training / Project Work / Dissertation Work

As per CSIR mandate, IICB provides an excellent environment for training the next generation of researchers towards partial fulfillment of postgraduate degrees. Its mission is to provide students with opportunities to acquire hands on knowledge in biological/chemical sciences and chemical biology research.

IICB has imparted training in the state-of-the-art techniques to several summer students from different Universities & Institutes. The aim is to let young minds feel the thrill and excitement of science by working on a project requiring application and critical appreciation of scientific principles. It also aims at active participation in the learning process through experimentation and putting into practice the knowledge acquired in the classrooms.

The summer program is primarily designed to encourage students from, first-generation college/university students by providing them the opportunity to do basic research in a top-notch research institution, in a supportive learning environment with plenty of interaction with graduate students and faculty. The programme provides a unique opportunity for students who do not have access to top-notch research facilities at their own institution to conduct supervised research in state-of-the-art research facilities. Besides, we also try to accommodate students from disadvantaged backgrounds for pursuing a career in research.

Guidelines: Detailed guidelines can be available in IICB website at HRG site. Under this programme the Institute conducts training of short duration in various disciplines and is absolutely free of any cost. The courses comprise both lectures and practical with emphasis on practical R&D aspects in a particular discipline. The duration of this training programme/Project Work is generally two-three months and maximum six months duration during March and August every year.

Number of Summer Trainee/Project Trainee (2009-10) : 103

Other Activities and initiatives: Nomination in Training & Workshop

- To assist in the process for nominating Scientists and Officers by the Director, IICB in different training programme/workshop [viz. R&D Management, Leadership Development and personal skills up gradation programmes etc. organized by CSIR, HRDC.

Participants in different Training programme:

- ⇨ Dr. Siddhartha Majumdar, Head, HRG has been nominated to participate Workshop on "Dimensions of Nanotechnology: Science, Technology, Business and Society" organized by National Institute of Advanced Studies, Indian Institute of Science, Bangalore during 9-13 February 2009
- ⇨ Organized a seminar on 12th June 2009 at IICB conducted by United States–India Educational Foundation (USIEF) advising different Fellowship opportunities by USIEF.
- ⇨ Multi-Skill Training Programme held for "Group D Staff Members" organized by IICB during 25-26 June 2009.
- ⇨ The following staff members have been nominated for their participation: Ms. China Devi Nayak, Mr. K.C. Nayak, Ms. Gita Ghosh, Ms. Soma Devi, Mr. Asit Mitra, Mr. Gopal Mondal, Mr. Janmenjay Midya, Mr. Pasupati Midya, Mr. S.K.Ghosal, Mr. P.C.Dehury, Mr. M. Adhikary, Mr. Tapan Sarkar, Mr. Dinesh Mahali, Mr. J. Biswas, Mr. Nirapada Haldar and Mr. Mantu Das.
- ⇨ A lecturer on "Effective Scientific writing skill" was organized for IICB Research Fellows & Associates. Speaker: Dr. Samit Adhya, Scientist,IICB.
- ⇨ A two hour lecture on "*Stress Free Living & Positive Thinking* " conducted by the BRAHMA KUMARI, Kolkata Rajayoga Bhawan, 81/1, Bangur Avenue, Block C, (VIP Road side), Kolkata -700 055 was organized on 11th , September, 2009. About thirty IICB employees, faculty & and students participated.
- ⇨ Thought-provoking Motivational Training Programmmme "LIVING IN EXCELLENCE-1" was organized for IICB Technical Staff members on 25-03-2010 where 28 members participated.
- ⇨ Motivational Training Programmmme "LIVING IN EXCELLENCE-2" was organized for IICB Administrative, Purchase, Finance & General Staff members on 19-05-2010 where 39 members participated.

Members:

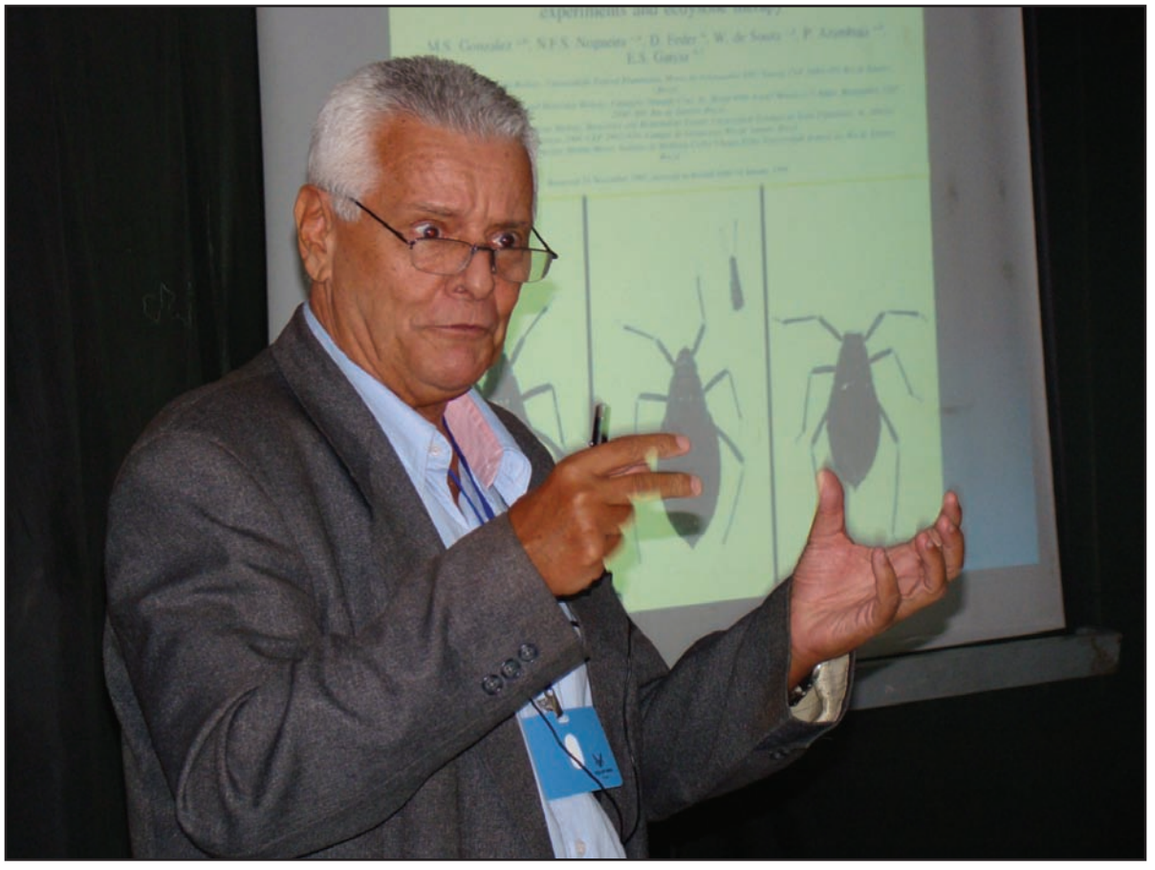
Ms. Lily Das, Ms. Pratima Banerjee, Md. Ayub Shah, Sri. B. Nayak

SCIENTIST VISITORS

No.	Date	Speaker	Title of Lecture
1.	28.05.2009	Dr. Debu Chakravarti Northwestern University, USA.	"Regulatory Mechanisms in Transcriptional Signaling by Nuclear Receptors"
2.	12.06.2009	Dr. Anindito Sen Genetics, University of Virginia	Structural studies on Type IV pili and bacteriophage of Pseudomonas syringae
3.	14.07.2009	Dr. Kamal Uddin Saikh (USAMRIID), U.S.	Adaptor protein in Inflammation: targeting MyD88 for treating Septic shock.
4.	17.07.2009	Dr. Suvojit Bose Stanford University, USA.	Chemo-genetic analysis of Ribozyme function "Growth of hen Iysozyme aggregates at
5.	23.07.2009	Dr. R. Swaminathan IIT, Guwahati, ASSAM	"Growth of hen Iysozyme aggregates at alkaline pH : Meehanism and Inhibition"
6.	27.07.2009	Dr. Prolay Das Brookhaven Laboratory, USA	A brief study on Charge transfer, Damage Response and Self Assembly of DNA
7.	05.08.2009	Dr. Samajit Bhattacharyy, Stanford University. USA.	"The role of post-synapticdensity proteins in AMPA receptor traffickings"
8.	07.08.2009	Dr. Aparajita Dey Anna University, Chennai, India	Cytochrome P450 2E1 and liver injury
9.	10.08.2009	Kingshuk Roy Choudhury, University College Cork.	Analysis of spatial distribution of cellular markers using radial plotting
10.	12.08.2009	Dr. Sulagna Banerjee Anna University, Chennai	Genomics to Functional Glycomics: The Sory of protists
11.	20.08.2009	Dr. Indrajit Das Chembiotek Int. Pvt. Ltd. Kolkata	Carbohydrates: A versatile Chiral Building Blocks for Aminosugars and Branched-Chain Sugars.
12.	26.08.2009	Prof. S. E. Hasnain, Vice-Chancellor University of Hydrabad. (A. P.)	Molecular mimicry and hijack of host machinery by Mybobacterium tuberculosis for its own survival and dissemination.
13.	27.08.2009	Dr. Nandkumar Khaire University of Oxford, UK.	Regulation of Tumor Suppressor Activity of Retinoblastoma Protein by Lysine Methylation.
14.	14.10.2009	Dr. Rupsi Mitra Stanford University, USA.	Combating stress : Gene therapy and environmental enrichment.
15.	15.10.2009	Dr. Kaustubh Datta Mayo Clinic Cancer Centre, USA	Survival promoting function of vascular endothelial growth factor-C in prostate cancer cells during oxidative stress.
16.	23.10.2009	Dr. Manas Santra University of Massachusetts, USA	Identification of FBXO31 as a novel G1/S checkpoint regulator in DNA damage pathway.
17.	26.10.2009	Dr. Dipak Datta Children Hospital, USA	Pro-tumorigenic Signals of Calcineurin Inhibitors: Beyond Immunosuppression
18.	04.11.2009	Dr. Pranab Halder Dr. Reddy's Labratories, Hyderabad	Studies on Aza-heterocycles : The journey from Medicinal Chemistry to Process Chemistry.

No.	Date	Speaker	Title of Lecture
19.	20.11.2009	Prof. S K Datta Northwestern University, Chicago	Restoring Immune Regulation in Human Autoimmune Disease. Autoimmune Disease.
20.	23.11.2009	Dr. Amitabha Mukhopadhyay National Inst. of Immunology, N. Delhi	Hemoglobin Endocytosis : A Novel Way to Acquire Heme by Leishmania.
21.	24.11.2009	Dr. Raja M C Genotypic Technology, Bangalore	Next Generation Sequencing (NGS) Technologies and Application.
22.	27.11.2009	Dr. Manish Kumar McGill University, Canada	A Quest to Predict Function
23.	30.11.2008	Dr. Andreas Klamt Leverkusen, Germani	Thermo physical Data of Liquid Systems from ab initio Quantum Chemistry
24.	04.12.2009	Dr. Surajit Ghosh Euro. Mole. Bio. Lab. Heidelberg	Biomimetic assembly with minimum components.
25.	14.12.2009	Dr. Raja Biswas AIMSRC, Cochin	"Bacterial Cell Wall: Structure, Function and Infection Interface".
26.	16.12.2009	Dr. Srinivas V. KAVERI Dir. of Res. at INSERM, Paris	"Function and dysfunction of our Immune system: Novel concepts Challenges and hopes for tomorrow"
27.	16.12.2009	Prof. Haruki Nakamura Osaka University	New and powerful method for insilico drug screening and its applications.
28.	17.12.2009	Dr. Sujou Mukherjee Ohio State University, USA	"Application of solid state nmr spectroscopy as a tool structure and drug design"
29.	21.12.2009	Dr. Max Gottesman Columbia University, USA	Cell Cycle regulation of CAMP levels.
30.	11.01.2010	Dr. Ravi Kumar Kadeppagari LSU Health Science Centre, USA	Modulation or Subversion of Cellular Processes by Viral Proteins.
31.	18.01.2010	Dr. Saurabh Chatterjee NIEHS, NIH, USA.	"Calcineurin induced protein radicals modulate follicular dendritic cell death and B cell differentiation".
32.	29.01.2010	Dr. Partha Chakraborty Boston School of Medicine, USA	"Molecular Energy Sensors in Lipid Metabolism".
33.	15.02.2010	Dr. Sandip Bhattacharyya Vanderbilt University, USA	"Glucocorticoid Effects on Toll-like Receptor Signaling:Identification of New Targets for Glucocorticoid"
34.	18.02.2010	Dr. Susanne Liebe Leica Microsystem, GmbH, Germany	LatestInnovations in Confocal Imaging; White light Laser and STED
35.	19.02.2010	Dr. Amit Srivastava Boston, USA.	"Smart Global Health: Medical Technologies for the Developing World"
36.	22.02.2010	Dr. Supratim Datta California, USA	"Towards understanding the large conformational changes of cobalamin-dependent methionine synthesis"

No.	Date	Speaker	Title of Lecture
37.	10.03.2010	Dr. Sabyasachi Das Emory University, Atlanta	Cross-talk between microRNA and immunoglobulin lambda variable region genes.
38.	10.03.2010	Dr. Subhra Chakraborty NIPGR, New Delhi	Insights into species immune and stress response by comparative transcriptome & proteome analysisin crop plants
39.	15.03.2010	Prof. Ruiz I Altaba Univ. of Geneve Switzerland	Role of Hedgehog–GLI signalling in stem cells, cancer and cancer stem cells
40.	22.03.2010	Dr. Subrata Kundu Texas A & M University	Size and shape Selective Synthesis of Metal & Semiconductor Nanomaterials for Environmental Biological Catalysis and Device Application.
41.	26.03.2010	Dr. Surya Mani Tripathi IIT, Kharagpur	Importance of Intellectual Property Management in Public R & D Institutions.



EVENTS 2009 - 2010

Date	Salient Details
April 02, 2009	IICB, Kolkata, celebrated its 53rd Foundation Day at IICB premises. Dr. Gopinath Balakrish Nair, Director, National Institute of Cholera and Enteric Diseases, Kolkata was present in the occasion as Guest-in chief.
June 25-26, 2009	The Human Resource Group of IICB, Kolkata has organized a two-day programme on "Multi-Skill Training Programme for Non-Tech Gr. D Staff-Members of IICB".
June 29, 2009	Foundation Stone Laying Ceremony for its second campus at Salt Lake, Kolkata. The auspicious ceremony was attended by Prof. Samir Brahmachari, DG, CSIR, Prof. Suranjan Das, Vice Chancellor, Calcutta University, Mr. Anil K. Agarwal, Principal Secretary, Department of Science & Technology, Govt. of West Bengal and all the Staff members and students of IICB along with a large number of distinguished guests and scientists from the city.
August 26, 2009	Visit of Prof. S.E. Hasnain, Vice-Chancellor, University of Hyderabad (A. P.) for Scientific Lecture on "Molecular mimicry and hijack of host machinery by Mycobacterium tuberculosis for its own survival and dissemination".
September 8, 2009	A one-day Career Development Workshop for Young Scientists of India was held. This workshop was aimed to update young scientists from different research institutes in and around Kolkata about the present and upcoming opportunities for doing collaborative research and available schemes for foreign research collaborations and support, particularly in the field of biomedical research.
September 14, 2009	The Institute observed Hindi Day Celebration. Prof. Ratna Mukherjee of St. Xavier's College Kolkata graced the occasion as the Chief Guest.
September 18, 2009	Visit of Dr. K. Kasturirangan, Member, Planning Commission, Dr. A.K.Verma, Adviser (S&T), Planning Commission and Dr. Indrani Chandrasekharan, Adviser (E&F), Planning Commission.
October 8, 2009	The Institute observed the 67th Foundation Day of CSIR. Prof. Siddhartha Roy, Director, IICB presided over the function in which Prof. Pradip Narayan Ghosh, Vice-Chancellor, Jadavpur University, Kolkata was present as Guest-in chief. Prof. V. Nagaraja, Chairman, Department of Microbiology and Cell Biology, Indian Institute of Science, Bangalore delivered the Foundation Day invitation lecture.
December 1–2, 2009	Indo-Russian Workshop was held. The focus of the workshop was on "Complex Networks: Dynamics and Synchronization". Nine Russian delegates attended and presented their works. Two scientists from Germany, one from Spain and one from United States also joined the workshop.

Date	Salient Details
December 1–4, 2009	The 14th All India Congress of Cytology and Genetics (AICCG) was hosted by IICB. This year, Fogarty Training workshop, a program in collaboration with the University of California, Berkeley, USA, funded by NIH, USA was organized along with the 14th AICCG meeting. The main topic of the workshop was "Molecular Epidemiology, Environmental Health and Arsenic Exposure Assessment".
December 10–11, 2009	Indo-Brazil Symposium on Infectious Diseases-2009, jointly organized by IICB & JNCASR, Bangalore. A group of renowned scientists from Brazil under the leadership of Prof. Eloy S. Garcia and several distinguished scientists of India participated.
December 16, 2009	Visit of Dr. Srinivas V. Kaveri, Director of Research, INSERM, Paris and Lecture on "Function and dysfunction of our Immune system: Novel concepts Challenges and hopes for tomorrow" and visit of Prof. Haruki Nakamura, Osaka University for scientific discussion and technical lecture on "New and powerful method for insilico drug screening and its applications".
December 21, 2009	Lecture on "Cell Cycle regulation of cAMP levels" by Dr. Max Gottesman, Columbia University, USA.
February 23-25, 2010	Probabilistic Risk Assessment Modeling for groundwater Arsenic mitigation (PRAMA) meeting was held. The meeting was attended by investigators from both the participating institutions, IICB, Kolkata, and University of Manchester, Manchester, UK, and also experts on arsenic studies as well as policy makers on behalf of Government of West Bengal.
March 15, 2010	Visit of Prof. Ruiz I. Altaba, University of Geneva, Switzerland for Scientific Lecture on "Role of Hedgehog – GLI signaling in stem cells, cancer and cancer stem cells".

Construction Work at IICB Salt Lake Campus in progress

Computer Division

Dr. Asoke Kr. Dasgupta & Group

Scientific Activities:

The SPERMA, sperm motility analyzer, a unique computer based instrumental system has been developed for the first time to determine sperm motility (velocity), using a spectrophotometer for clinical and biological applications.

The objective of the new project with DST is to calibrate and standardize this unique instrumental system, SPERMA, and correlate the vertical motility parameters experimentally with fertilizing ability of the spermatozoa. The unique software has been developed for acquisition of analog data.

Technical Support:

[i] Maintain the Local and Wide Area Network.

[ii] Maintenance of server applications and hardware.

[iii] Maintain Computational facilities.

IICB has IT Division which hosts all servers on the LAN and WAN. The backbone of the LAN has been upgraded to 1 GB with FO connectivity through CISCO Layer 3 and Layer 2 switches. The LAN is connected to dedicated leased line of 6 MB and 12 MB bandwidth from Reliance & Tata Communications. Facility management of this system is outsourced. Computational facilities are mostly desktop & workstation based.

In House Maintenance:

The Division looks after about 500 Nodes with various problems, like Hardware, Software and Network problems. IICB Website has been modified from time to time on regular basis. Internet website has been introduced for internal use, which includes various types of official work, *viz.* Administrative matters, Office Memos, News *etc*. The Intra Website is updated from time to time on regular basis.

Academic Activities:

[i] Dr Asoke Kr. Das Gupta has been nominated as a Member of the NIPER, Kolkata Advisory Committee.

[ii] Dr Asoke Kr. Das Gupta has been nominated as a faculty member of NIPER, Kolkata & IICB Ph.D. Course Work for the year 2009-2010.

Library & Documentation Division

Mr. N. C. Ghosh, Mrs. P. Chatterjee, Mr. S. Bhakta, Mr. S.K. Naskar, Mrs. S. Ganguly, Mr. P.K. Das, Mr. M. Halder, Mr. S. Nath, Mr. Asoke Ram,

The Knowledge Resource Centre (Library & Documentation Division) provides critical library information support to the S&T personnel, research scholars and outsiders constantly using both the archival print documents and contemporary digital and print resources available in its rich collection. In address to the increasing demands for information it has been developing steadily its holdings containing books (texts & reference), journals (print & online), serials, monographs, technical reports etc. It has also developing a very good collection in Hindi. It provides ADONIS service, (CD-ROM databases) containing about 743 scholarly journals in full text almost from 1991 to 2002 in the biomedical, chemical and pharmaceutical disciplines. Apart from these the division has been trying to fulfill the users demand from other CSIR-DST KRCs also through a web-enabled resource sharing platform "JCCC".

CSIR E-Journal Consortium is a CSIR Network Project under 10th Five Year Plan being implemented by NISCAIR providing access to full text for thousand of world class STM Journals and online databases like Web of Science, DII, DELPHION to the CSIR & DST Institutions including the Knowledge Resource Centre, IICB

The collection includes major publishers like Thomson Reuters, RSC, ACS, Wiley Blackwell, Springer, OUP, CUP, Emerald, Sage, NPG, Taylor & Francis and others. Access to NKRC (CSIR-DST E-journals Consortium) is available at http://124.124.221.7/

Collections	Upto 31.03.2010
Books (including Hindi)	13671
Journals (print + online)	185
Bound volumes	32000
ADONIS (CD-Rom Database)	743 journals covered full text (1991-2002)
Annual Reports	3856
Thesis (CDs)	23

Services:

The **Reading Room** of the division is fully air-conditioned. During this period a good number of readers visited the reading room for consulting daily newspapers and printed journals and other technical reports.

The division undertook **Literature Search** for the Scientists, Research Fellows and external library users on the subjects of their interest and delivered a good amount of output of that nature.

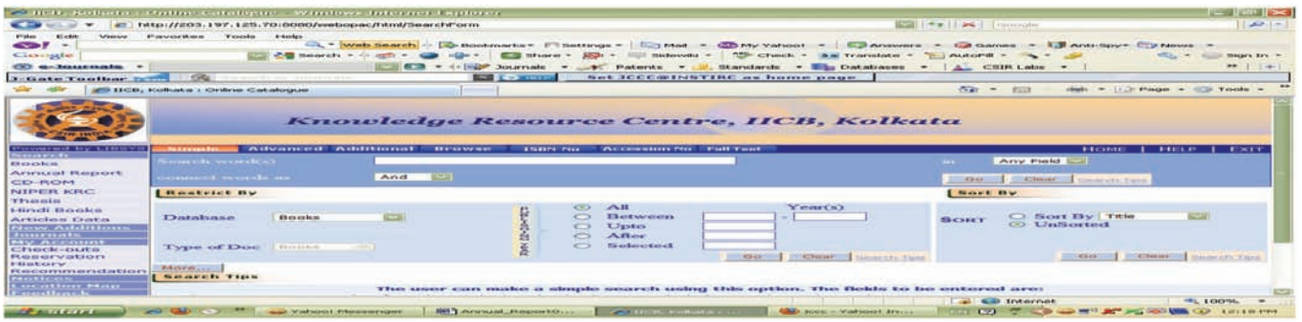
From ADONIS database a good number of article searched and print outs delivered to the scientists, research scholars and other users according to their requirement submitted to the division during the period under review.

The internal users are only eligible to get books/loose issues of journals/ bound volumes of other printed documents issued in their names for the specified period of time as loan. During the period under review a good number of documents issued/returned by the internal users through the **Circulation** desk of the division.

"JCCC" is a web-enabled resource sharing platform among the CSIR-DST Institutions and the division worked very efficiently in sharing scholarly literature among sister institutions to mitigate the users need optimally.

Photocopying of the required documents, for the consumption of the researchers (fair use) is a very important service, has been rendering by the division constantly and during the period it served the users in great way by this service also.

The functions and services of the Knowledge Resource Centre are managed in fully computerized environment by using the library management software **LIBSYS (version 4 release 5)** with unlimited access to web OPAC (Online Public Access Catalogue). The OPAC is available at: http://115.248.74.252:8080/webopac/html/SearchForm

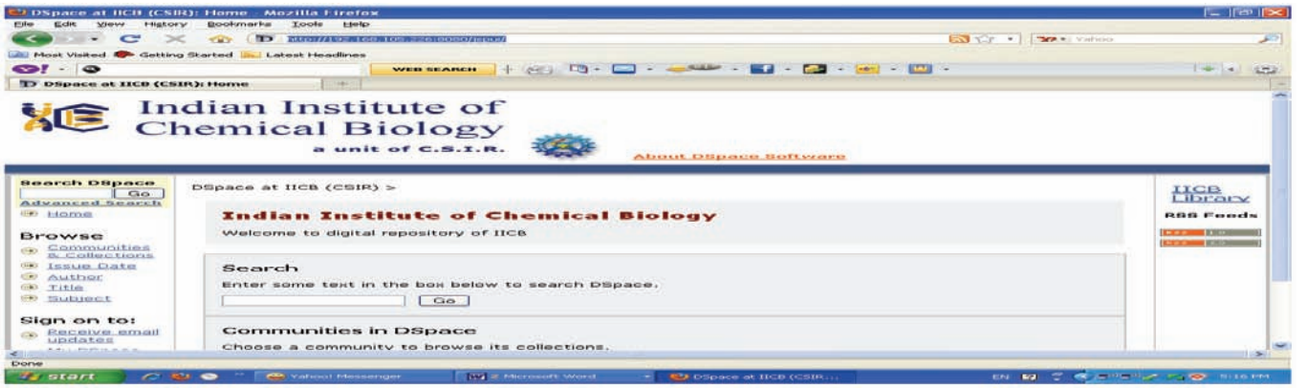


Users' Awareness cum Training Programmes (2 nos.) arranged on various information resources available in the Division and NKRC for maximizing the utilization of knowledge resources in the best possible way among the researchers.

During the period under review a good number of users, both internal and external availed **Reference and Referral** services rendered by the division.

The **News Papers Section** of the Division maintaining nine daily newspapers in Bengali, English & Hindi for its users.

Institutional Repository (IR) has been established using D-Space – an open source software with an aim to provide online access to mostly pre-print of IICB research publications, Thesis in full text, Annual Reports, News Letters etc. Under this period only a few thesis are uploaded in the system and can be viewed in intranet at:http//192.168.105.226:8080/jspui/



IICB is the mentor of NIPER, Kolkata. **NIPER-Knowledge Resource Centre** has been also functioning in the library premises. During this period a good number of books (text & references) on Medicinal Chemistry, Pharmaco-informatics and Natural Products have been added to its collection. Online access to **SciFinder** (single user) also subscribed by the centre during the period under review.

CENTRAL INSTRUMENTATION

Dr. S.K. Dana, Tapan K. Mukherjee, Surojit M. Roy, Ajoy K. Pramanik, Tarak P. Nandi

The Central Instrumentation Division takes care of the repair and maintenance of all scientific instruments of the institute. The division is actively involved in developing the infrastructure and basic amenities for major equipments of the institute. It supports central facility of Centrifuge, Ultracentrifuge, UV/VS spectrophotometers and Lypholyzer. Maintenance is provided on small and essential instruments which are of high demand like fraction collector, electrophoresis apparatus, high voltage power supplies, voltage stabilizer and high vacuum systems. The division operates the audio-visual systems, video conferencing system of the institute. In addition, the division initiated R&D efforts on developing new biomedical equipments. This division also carried out investigations on experimental chaos synchronization in electronic circuits under external funding from DST and DAE. Training on experimental nonlinear dynamics is provided to young students and researchers from India.

A group of scientists, technical officers and skilled technicians assist in the operation, repair and maintenance of scientific instruments. A few research scholars and project assistants are working towards Ph.D. degrees on nonlinear dynamics using theoretical as well as experimental methods.

Research and Development

Research and development have been initiated in the instrument division with the purpose of developing new apparatus for biological research. An important R&D initiative is related to develop new understanding of dynamical behaviors in biological and physical systems and to search for their applications. Nonlinear dynamical approach is mainly adopted for understanding living systems' behaviors like cardiac arrhythmia, neuronal interaction in the brain under pathological condition. Trends of research are set around the world in recent years to understand these aspects using concept of synchronization in nonlinear oscillators and complex networks. The focus of our current research is to investigate some of these aspects using mainly experiment on chaotic electronic circuits and with appropriate numerical studies of paradigm models. The basic idea is to set a trend of interdisciplinary research bringing together the knowledge of physics, electronic and biology to explore complex dynamics of natural systems. A few fundamental aspects of chaos synchronization, namely, anomalous phase synchronization and phase flip bifurcation, robust antisynchronization and amplification of chaos, phase synchronization has been explored and their experimental evidences in electronic circuits are also reported.

A new initiative is undertaken using radio-telemetric EEG/ECG measurement and data analysis to understand rat's brain function under drug-induced condition in collaboration with the neurobiology group of the institute.

Collaboration with many national and international institutions has been established. Some of the premier institutions in the country like Presidency College, Kolkata, School of Physical Sciences, JNU, New Delhi, Department of Physics and Astronomy, Delhi University, Institute for Plasma Research, Gandhinagar and Physical Research Laboratory, Ahmedabad, Centre for nonlinear dynamics, Bharathidadsan Unviersity, Trichy and LNMIIT, Jaipur are participating in the joint research. Institutions from abroad such as the Institute of Physics, University of Postdam, Germany; Department of Mathematics and Computer Sciences, Elizabeth State University, North Carolina, USA, Institute of Physics, Academia Sinica, Taiwan and Faculty of Bioengineering, University of Pharmacy and Medicine, Iasi, Romania and Moscow State University, Russia, Oldenburg University, Germnay have started collaboration.

Research Fellows

Mr. Ranjib Banerjee, Senior Research Fellow
Mr. Sourav K. Bhowmick, Seniro Research Fellow
Mr. Chittaranjan Hens, Project Assistant

Extramural Research Activities

An international collaboration between IICB and University of Medicine and Pharmacy, Iasi, Romania is continued on control and synchronization of chaos supported by the Department of Science and Technology (DST), India and Ministry of Education and Research, Romania.

Invited Lectures

(1) Invited as a faculty to lead a session on nonlinear electronics in the *Winter School on Hands-on-Research on Complex systems 2009*, University FABC, Sao Paulo, Brazil sponsored by the Abdus Salam ICTP, Trieste, Italy.

(2) A series of lectures on e*xperimental nonlinear dynamics* in the DST-SERC school on nonlinear dynamics, Department of Physics and Astronomy, Delhi University.

(3) Invited Theoretical Physics Lecture Series on nonlinear electronics chaotic oscillators in the Centre for Nonlinear Dynamics, Bharatidasan Unviersity, Trichy.

(4) Invited talk in the University of Rouen, France.

(5) Invited lecture on "Instrumentation in Biochemical Research", Department of Zoology, North Bengal University.

EXTERNAL FUNDING

Project Title	:	Synchronization nonlinear systems: Theory and Experiment
Funding Agency	:	Department of Science and Technology, New Delhi
Total Fund	:	16.56 lakh (Duration: 2006-2009)
Principal Investigator	:	Dr. Syamal Kumar Dana
Co-Investigators	:	Dr. Prodyot K. Roy, Department of Physics, Presidency College, Kolkata
		Prof. Abhijit Sen, Institute for Plasma Research, Gandhinagar, Gujarat
		Dr. Gautam C. Sethia, Institute for Plasma Research, Gandhinagar, Gujarat

Project Title	:	Chaos Synchronization: Exploring technology prospects
Funding Agency	:	Department of Atomic eneegy, Board of Research in Nuclear Sciences, Mumbai.
Fund	:	15.47 lakh (Duration: 2009-2012)
Principal Investigator	:	Dr. Syamal Kumar Dana
Co-Investigators	:	E. Padmanaban, IICB, KOlkata
		Dr. Prodyot K. Roy, Department of Physics, Presidency College, Kolkata
		Prof. Abhijit Sen, Institute for Plasma Research, Gandhinagar, Gujarat
		Dr. Gautam C. Sethia, Institute for Plasma Research, Gandhinagar, Gujarat

Honours and Awards

Reviewer of International Journals: CHAOS, Physics Letters A, European Journal of Physics.

Conference

Attended one-week workshop on "Exploring Complex Dynamics in High-Dimensional Chaotic Systems: From Weather Forecasting to Oceanic Flows" in the Max Planck Institute for Physics of Complex Systems, Dresden, Germany and presented a poster.

Publications: Journal

S.Chakraborty, S.K.Dana, Experimental evidence of Shil'nikov chaos and mixed-mode oscillation in Chua circuit, *CHAOS* 20, 023107 (2010).

Grosu, R.Banerjee, P.K.Roy, S.K.Dana, Designing coupling for synchronization of chaotic oscillators, *Phy.Rev.E* 80,016212 (2009).

A.Nandi, S.K.Bhowmick, S. K. Dana, R.Ramaswamy, Design strategies for the creation of aperiodic nonchaotic attractors, *CHAOS* **19**, 033116 (2009).

ANIMAL HOUSE

Dr. A. Konar, Dr. H.N. Ray, Dr. R. Ghosh, Mr. S. S. Verma, Mr. A. Das Mr. R. Sarkar, Mr. A.Sardar. Mr. J. Middya, Mr. P. Middya, Mr. T. Sarkar, Mr. Lalu Sardar, Mr.G.Sardar , Mr. S. Midya

The animal facility in IICB is a cpcsea registered (Registration No 147/1999/CPCSEA) key-source for supply of authentic animals used in biomedical research programs of the Institute. All (animals) but a few special strain of mouse, are bred and supplied from the in-house breeding colony. Moreover, some other research institutes who have their CPCSEA registration also collect animals from the surplus stock of the facility for their IAEC approved research projects.

The animals are produced and kept in a scientifically maintained environment (Room Temp.24,2°C; relative humidity 55–60%; light and dark schedule 12:12hrs; illumination 400 lux at 1 mt above the floor). They are raised under strict health and genetic monitoring. The house keeping of the facility acclaimed high appreciation not only from the associated scientists but also the representatives of CPCSEA, representative of different NGOs and private entrepreneurs, visiting guests and scientists.

Animals (specially mouse) were purchased from other registered breeders only when the required strain was not available in the colony or when animals of same specification was required in a bulk. However, proper utilization of animals was strictly monitored and animals were produced in such a number, that the number of unutilized animals be minimum but the scientists get their animals as and when they require.

The species and strains of animals, routinely maintained in the facility are as follows:

Mice-Balb/C, C57BL/6J, Rat-Sprague Dwalley, Hamster-Golden, Guinea Pig-English, Rabbit-New Zealand White.

A brief account of animal produced/supplied from the animal house in during this period is given in the following table :

Species	Stock on 1st April 2009	No. of animals		Total (A)	No. of animals issued		No. of animals		Total (B)	Stock on 31.3.2010
		Produced	Purchased		Produced	Purchased	died in-stock	Supplied to other R&D organization		
Mouse	2115	4140	80	6335	4703	80	-	4783	1552	
Rat	1097	5054	0	61511	4168	0	0	40	4208	1943
Hamster	497	320	0	817	475	0	0	0	475	342
Rabbit	80	64	0	158	26	0	0	32	58	86
Guinea pig	35	50	0	85	09	0	0	0	09	76

ENGINEERING SERVICES UNIT

Dr. A. K. Sen, Mr. U. K. Barua, Mr. S. Saha, Mr. B. Jayakumar, Mr. S. Ray, Mrs. N. Bage, Mr. D. Banik, Mr. M. B. Malakar, Mr. P. K. Chanda, Mr. G. Malik, Mr. S. Basak, Mr. S. N. Mondal, Mr. S. Pradhan, Mr. S. Biswas, Mr. S. R. Tudu, Mr. S. Nath, Mr. S. Mazumder, Mr. Ujjal Roy, Mr. A. Karmakar, Mr. A. Pal, Mr. S. K. Ghosal, Mr. B. Das.

The Engineering Services Unit (ESU) is comprised of the civil engineering, electrical engineering and air-conditioning & refrigeration sections.

Electrical Engineering Section

The electrical engineering section renders essential services and infrastructure support to R&D activities and other public utilities of the Institute. The section maintains and supplies steady power supply through 6.6 MVA power sub-station of the institute and monitors for uninterrupted power supply system from CESC source. The section also supplies emergency power through available DG Sets and conducts its operation & maintenance.

List of major works completed during the year:

- Renovation of LT power distribution system of sub-station under IRR.
- Renovation of Electrical installations of Room Nos. 17, 239, 235, 206, library *etc*.
- AMC for internal & external electrification works of Electrical installations.
- Installation of 2x500 KVA new DG-sets for Emergency power at IICB.
- Installation of capacitor bank.
- Feeder connections of LT cubicle panels and other allied works of power substation.
- Renovation of electrical lines and power distribution system of several laboratories.
- Documentation of existing electrical distribution system of IICB including layout and schematic diagrams.

The works that are under progress:

- Renovation of electrical lines and power distribution system of selected laboratories.
- AMC for internal & external electrification works of Electrical installations.
- Maintenance & service overhauling of 6.6 KV HT power supply system.
- Maintenance of 2x500 KVA DG Set.
- Installation testing and commissioning of existing 1x62.5 KVA silent type DG Set at Scientist apartment cum NIPER hostel campus.

Air-conditioning and Refrigeration Section

This section looks after the AC facility in all the laboratories, library, auditorium, administrative wings and most importantly the animal house. It also takes care of the refrigerators and deep freezers in the laboratories, maintains the cold rooms and constant temperature rooms and is also responsible for the maintenance of the lifts.

***List of major works in the past one year*:**

- Annual maintenance of window and split AC units.
- Annual maintenance of 2x80 TR AC plant for animal house.
- Installation of two modular cold rooms and two constant temperature rooms.

***The following works are in progress*:**

- Renovation and refurbishing of the central AC plant is in progress to cater for the library and auditorium.
- Construction of a class 10000 Clean Room for Protein Micro Array facility.
- Maintenance of cold and constant rooms.
- Annual maintenance of AC's, Lifts, AC power plant etc.

Civil Engineering Section

The Civil Engineering Section renders services in broad areas of infrastructure development, renovation of laboratories and common facilities, maintenance of campus, sewerage and drainage systems, cleaning and house-keeping work.

List of major works carried out during this period:

- Repair, renovation and up-gradation of different laboratories and offices.
- Construction of Central AC Plant Room.
- Repair and renovation of buildings and services (AMC).
- Repair and renovation of tissue culture rooms and laboratories.
- Repair, renovation and up-gradation of CSIR hostels at Prince Anwar Shah Road.
- Tendering process for development of new campus at Salt Lake and appointment of HSCC as PMC.

The following works are in progress:

- Renovation of auditorium and several laboratories.
- Overall beautification of the campus and interior.
- Construction of a new meeting room.
- Planning of extension of IICB laboratory building and construction of new Animal House through PMC.
- Repair and renovation of buildings and services through AMC.
- Repair and maintenance of CSIR Scientists' Apartment Complex at Prince Anwar Shah Road.
- General cleaning and house-keeping of CSIR Scientists' Apartment Complex at Prince Anwar Shah Road.
- Construction of new IICB campus at Salt Lake, Kolkata.

Administration

GENERAL ADMINISTRATION

A wide range of functions are carried out by General Administration which cater to the life cycle of an Officer of the Scientific, Administrative and Technical Cadre encompassing manpower planning, cadre management, recruitment, role definition / allocation, skill assessment, workplace learning, career advancement, transfer, employee benefits, retirement, performance assessment etc. In addition Administration is also responsible for arrangement of all logistics and managing the day to day affairs of the Institute.

Officers in General Administration

- Dr. S.R. Sarkar, Controller of Administration
- Mr. S.K. Chaudhuri, Administrative Officer
- Mr. K. Bhattacharjee, Section Officer
- Mr. Siddhartha Dey, Section Officer
- Ms. Shampoo Sengupta, Section Officer
- Mr. P.K. Saha, Section Officer
- Mr. Ashok Putatunda, Section Officer

COA & AO's Secretariat

- Mr. Sudip Ghosh, Jr. Stenographer
- Mr. Sankar Kr. Santra, Jr. Stenographer

Sections in General Administration & Associated Staff

[i] ***Recruitment, Committee & CR***

- Mr. Siddhartha Dey, Section Officer
- Ms. Indira Kundu, Asstt.(G) Gr.I
- Mr. Tapan Das, Tech. Gr.II(2)
- Mr. Raju Pal, Asstt.(G) Gr.II
- Mr. Ranjit Debnath, Asstt.(G) Gr.II
- Mr. Saugata Das, Asstt.(G) Gr.II

[ii] ***Establishment***

- Ms. Shampoo Sengupta, Section Officer
- Mr. Kanu Mondal, Asstt.(G) Gr.I
- Ms. Anjana Mandi, Asstt.(G) Gr.I
- Ms. Ratnabali Adhikari, Asstt.(G) Gr.I
- Ms. Sanhita Ganguli, Asstt.(G) Gr.I
- Mr. R. N. Hansda, Asstt.(G) Gr.I
- Mr. T.K. Sinha Roy, Asstt.(G) Gr.II

[iii] ***Bill & Cash***

- Mr. K. Bhattacharjee, Section Officer
- Mr. Phelaram Dhank, Tech., Gr.II(4)
- Mr. D.K. Kisku, Asstt.(G)Gr.II
- Mr. Prem Singh, Asstt.(G) Gr.I
- Mr. Tarun Dutta, Asstt Manager-cum-Store Keeper
- Mr. Alok Ray, Asstt.(G) Gr.II
- Mr. Atanu Moitra. Gr.II(2)
- Mr. Paresh Sarkar, Gr.II(2)
- Mr. Ratan Bage, Asstt.(G)Gr.I
- Mr. Jayanta Pal, Asstt.(G)Gr.II
- Mr. Suresh Balmiki
- Mr. Kailash Nayek, Gr.C(N/T)

[iv] ***General***

- Mr. P.K. Saha, Section Officer
- Mr. D.R. Chakrabarty, Asstt.(G) Gr.I
- Mr. Nandalal Routh

[v] ***Receipt & Issue***

- Mr. A. Putatunda, Section Officer
- Mr. Saibal Giri, Sr. Stenographer
- Mr. Brihashpati Das

FINANCE & ACCOUNTS

This wing of administration is mainly concerned with keeping record of budgetary requirements, controlling & monitoring the expenditure and preparing budget for the Institute regarding plan & non-plan expenditure, which is about Rs.67-72 crores per annum. Keeping track of progressive expenditure of budget for every month, keeping financial records for 17 Networked Projects, externally funded projects, disbursement of pension to pensioners, accounting and auditing files routed through Establishment, Purchase and other scientific decisions. TO Seek grant from outside bodies, *i.e.* UGC, ICMR, DBT *etc*., monthly remittance of P. Tax, I. Tax, Service Tax, etc. and incorporating entire vouchers of the Institute in IMPACT software. Through IMPACT entry, our Annual Accounts and Balance Sheet is generated for onward transmission to CSIR,HQ.

Functional hierarchy of Finance & Accounts wing is follows:

- Shri S.K. Das, F&A Officer
- Shri A.K. Jha, S.O. (F&A)
- Shri A.K. Tiwary, S.O. (F&A)
- Shri Sanjoy Mukhopadhyay, Asstt. (F&A) Gr.I

- Shri Anil K. Chanda, Asstt. (F&A) Gr.I
- Smt. Banani Dutta, Asstt. (F&A) Gr.I
- Smt. P.L. Saha, Asstt. (F&A) Gr.I
- Shri Asit Kr. Roy, Asstt. (F&A) Gr.II
- Shri Mihir Kr. Dutta, Asstt. (F&A) Gr.II
- Shri Vishal Agarwal, Asstt. (F&A) Gr.III

STORES & PURCHASE

The Stores & Purchase Division caters to the research and other requirement of IICB. The annual procurement budget of IICB is about Rs 500 million annually comprising of research consumables like chemicals, glass wares, plastic wares etc and various capital items. After successful implementation of online procurement and stores systems since 2007, the division had introduced web based ordering system from last year and continued successfully in the reporting year for Sigma products, Vendor Managed Inventory program, stock of consumable of companies like Fisher, SRL, Spectrochem, Merck, RFCL, JT Baker, Tarson, Axygen, BD falcon, Invitrogen, Takara-clontech, MN, Gilson & Eppendorf Pipettes, Computer cartridges of HP, Corning and so on. The division assists scientists and other users to utilize their budget grant within the project deadlines. The division also undertakes the issue of total logistic chain of items from anywhere in the world to IICB that are either purchased by IICB or being sent as free gifts. It also undertakes customs clearance with concessional customs duty within demurrage free clearing time from Kolkata Airport and Sea port. Adjustment of OB, replies to audit and other statutory authorities, assistance to accounts for bank re-conciliation are other activities performed by the division.

The division is manned by the following personnel

- Shri US Das, COSP
- Shri NK Saha, SPO
- Shri R Ghosh, SO(S&P) Gr. I
- Shri TK Mitra, Assistant (S&P) Gr. I
- Shri P Naskar, Assistant (S&P), Gr. I
- Shri ABS Roy, Assistant (S&P), Gr. I
- Shri R Roy, Assistant (S&P), Gr. I
- Shri B Das, Assistant (S&P), Gr. II
- Smt B Pal, Assistant (S&P), Gr. II
- Shri A Sen, Assistant (S&P), Gr. III
- Shri P Sarkar, Assistant (S&P), Gr. III
- Shri RP Gorh, Technician

Official Language Activities of the Institute

The requirement of the Official Language has been successfully implemented in compliance with the Official Language Act. Bilingual letters have been written to various legions as per rules. The rule 3(3) of the Official Language Act is also being complied by the institute as memorandum, tenders, notices, general orders etc issued in bilingual form.

The Institute observed Hindi week from 10-14 September 2009.

On the 10th of September 2009 competitions like Hindi noting, drafting and essay competitions were held in the Institute.

On 11 September 2009 a workshop was conducted by Mr. Satish Pandey, Training Officer of Central Translation Bureau Kolkata. The topic on which the workshop was conducted was "Problems coming on the way of use of technical vocabulary". He explained the correct use of various Hindi words and its different practical uses and dealt with problems coming on the way of using them.

On the 14th September the Institute observed Hindi Day Celebration. Prof. Ratna Mukherjee of St. Xavier's College, Kolkata graced the occasion as the Chief Guest. The Director of the Institute, Prof. Siddhartha Roy congratulated and encouraged the participants of various competitions. The Chief Guest applauded the keen interest of the employees of the Institute in participating in the competitions at large scale and expressed her wish to keep up the spirit.

Smt. Manju Shirin, Asst. Director of Hindi Implementation, Home Ministry was invited as the judge of the competitions and encouraged everybody to join the competitions arranged by the Hindi cell of the Institute. Three other Hindi workshops were held during this year. The whole programme was conducted by Smt. Ambalika Nag, Sr. Hindi Translator. Lastly the Controller of Administration, Dr. S. R. Sarkar moved the vote of thanks.

This year many Hindi reference books were also bought in the library.

New Hindi software from CDAC was installed in the computers of the Institute. The Institute attained a remarkable achievement with the launch of Hindi website this year.


THIS FOUNDATION STONE
WAS LAID BY
PROF. SAMIR KUMAR BRAHMACHARI,
DIRECTOR GENERAL, CSIR AND SECRETARY,
DSIR, GOVERNMENT OF INDIA, NEW DELHI.
इस आधारशिला की स्थापना प्रो. समीर कुमार ब्रह्मचारी, महानिदेशक,
वै. औ. अ. प. एवं सचिव, डी. एस. आई. आर., भारत सरकार, द्वारा की गयी।
এই ভিত্তি-প্রস্তর অধ্যাপক সমীর কুমার ব্রহ্মচারী, মহা-অধিকর্তা, সি. এস্. আই. আর.
এবং সচিব, ডি. এস্. আই. আর., ভারত সরকার,কর্তৃক স্থাপিত।
PROF. SIDDHARTHA ROY
DIRECTOR, IICB, KOLKATA
THE 29TH OF JUNE, 2009

Extramural Activities

INFECTIOUS DISEASES & IMMUNOLOGY

Invited Lectures

Dr. H. K. Majumder

Topic : A tyrosyl DNA phosphodieterase I from kinetoplastid parasites Leishmania donovani capable of removing topo I-DNA covalent linkages during during repair process
Venue : SBC (India), Pune.
Date : Novmber 1, 2009

Topic : Keynote address on 'Recent advances in biotechnology research in India
Venue : JU, Kolkata organized by Science Association of Bengal, Kolkata.
Date : February 27, 2010

Topic : Lecture delivered on 'Development of antileishmanial drugs targeted to DNA topoisomerase I'
Venue : Burdwan University, Department of Biotechnology.
Date : March 11-12, 2010

Topic : DNA topoisomearses, the wonder enzymes: A study in Leishmania parasites
Venue : Department of Botany, Visva Bharati sponsored by Study Circle, VB in the seminar on 'Series of Lectures in Modern areas of Life Sciences'.
Date : March 13, 2010

Dr. Pijush K. Das

Topic : Immunomodulator of natural origin for macrophage-associated diseases
Venue : Acharya Prafulla Chandra Roy Memorial Symposium on Chemistry Today (2009) by Indian Chemical Society, Rajabazar Science College, Calcutta University.
Date : August 1-2, 2009

Topic : Immunomodulator of natural origin for macrophage-associated diseases using leishmaniasis as the model macrophage disease.
Venue : X International Symposium on Vectors and Vector Borne Diseases, Goa University, Goa.
Date : November 4-6, 2009

Topic : Possible mechanism of neutralizing macrophage oxidative damage by *Leishmania* parasites
Venue : 14th All India Congress of Cytology & Genetics by IICB and Dept. of Genetics, Calcutta University at Central Glass & Ceramic Research Institute, 196, Raja S.C. Mullick Road, Kolkata 700 032.
Date : December 1-4, 2009

Topic : Cyclic nucleotide signaling in the establishment of *Leishmania* infection In macrophages
Venue : Indo-Brazil Symposium on Infectious Diseases, IICB and Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), Bangalore.
Date : December 10-11, 2009.

Topic : Therapy by herbal immunomodulators for macrophage-associated diseases using leishmaniasis as the model macrophage disease
Venue : Workshop on modern Techniques in Biology, Pune University, Pune.
Date : February 17, 2010

Topic : Mechanism by which *Leishmania* parasites establish infection within macrophages of human host
Venue : Workshop on modern Techniques in Biology, Pune University, Pune.
Date : February 18, 2010

Topic : Mechanism by which *Leishmania* parasites establish infection within macrophages of human host: cyclic nucleotide signaling
Venue : Series of Lectures by Eminent Scientists in Modern Areas of Life Sciences, Vishabharati University, Santiniketan.
Date : March 13, 2010

Dr. Chitra Mandal

Topic : Flow-cytometric monitoring of disease-associated expression of 9-*O*-acetylated sialoglycoproteins in combination with known CD antigens, as an index for MRD in children with acute lymphoblastic leukaemia
Venue : New frontier of hematology and oncology, Kolkata.
Date : April 9-10, 2009

Topic : Mysteries of 'third language of life' unveiled in leukemia : Key note address
Venue : SBC, Kolkata Chapter, Digha, West Bengal.
Date : September 4-6, 2009

Topic : Carbohydrates play mysteries role in leukemic patients
Venue : JB Center of Excellence, 1300, Rajdanga Main Road, Kasba, Kolkata 700 107 for Jagadis Bose National Science Talent Search (JBNSTS) students.
Date : September 6, 2009

Topic : Promising role of sugar molecules in leukemia research
Venue : Institute of PG Medical Edn & Research, IPGMER, Kolkata.
Date : October 27, 2009

Topic : 9-*O*-acetyl sialic acids: A promise in future therapy and management of childhood acute lymphoblastic leukemia
Venue : World Congress on Cellular & Molecular Biology (WCCMB), Indore.
Date : November 2-6, 2009

Topic : Sialylation affects the immune status of the host: a tale of unraveling the disease biology of visceral leishmaniasis

Venue : 16th Annual symposium of Ranbaxy Science Foundation on "Emerging Frontiers in Immuno-genomics of Infectious Diseases", National Institute of Immunology, New Delhi.

Date : November 4, 2009

Topic : Power of carbohydrates in diagnosis and therapy of leukemia

Venue : UGC sponsored conference on 'playing God: expanding Frontiers of Biotechnology at Gurudas College.

Date : November 6-7, 2009

Topic : 9-*O*-acetylated sialoglycoproteins in visceral leishmaniasis: The multifaceted trigger modulating the erythrocyte biology

Venue : 20th International Symposium on Glycoconjugates (Glyco XX), San Juan, Puerto Rico, U.S.A

Date : November 29 - December 6, 2009

Topic : Sialic acids acquired by *Pseudomonas aeruginosa* are involved in reduced complement deposition and siglec mediated host-cell recognition

Venue : Guha Research Conference (GRC), Ullal, Mangalore, Karnataka.

Date : December 19-23, 2009

Topic : Proteomic alteration in host cells and plasma: A story of unraveling the disease biology of visceral leishmaniasis

Venue : 5th AOHUPO Proteomics Conference 2010, at CCMB, Hyderabad.

Date : February 23-25, 2010

Topic : Sialic acids in Haematopoietic stem cells of childhood acute lymphoblastic leukaemia

Venue : 29th Annual Convention of the Indian Association of Cancer Research at Amrita Institute Of Medical Sciences & Research Centre, Cochin, India.

Date : February 20-23, 2010

Topic : Exploration of Indian potential herbal sources for future new drugs: A promise for treatment of a variety of cancers

Venue : Refresher course on Application of Bioinformatics on Modern Biology for College and University Teachers.

Date : March 8-31, 2010

Dr. Syamal Roy

Topic : Treatment of Kala azar: A new approach" WHO Expert Committee meeting on Leishmaniasis

Venue : Dacca, Bangladesh.

Date : June 13-16, 2009

Topic : Immunotherapy of experimental visceral leishmaniasis

Venue : de Duve Institute, Brussels.

Date : October 6, 2009

Topic : Poor stability of peptide-MHC complex formation may specify defective cellular immunity in leishmaniasis
Venue : Indo-Brazil Symposium on Infectious Diseases, Calcutta.
Date : December 10-11, 2009

Topic : Prophylactic versus Therapeutic vaccines in leishmaniasis
Venue : Institute Pasteur, Tunis, Tunisia.
Date : February 3, 2010

Dr. Nahid Ali

Topic : Control strategies for kala-azar
Venue : Research Council meeting, IICB, Kolkata.
Date : August 24, 2009

Topic : Single dose combination therapy with stearylamine-bearing cationic liposome associated paromomycin cures *Leishmania donovani* infection in BALB/c mice.
Venue : 2nd Indo-Brazil Symposium on Infectious Diseases, Kolkata.
Date : December 10-11, 2009

Topic : Phenotypic characterization and functional role of $CD4^{+}CD25^{+}FoxP3^{+}$ regulatory T cells in Indian kala-azar
Venue : Molecular Immunology Forum, Raichawk, West Bengal.
Date : January 15-17, 2010

Dr. Rupak K. Bhadra

Topic : Molecular evidences favoring step-wise genesis of Mozambique *Vibrio cholerae* O1 El Tor hybrid strain
Venue : The 13th International Conference on Emerging Infectious Diseases of the Pacific Rim: Focus on Enteric Diseases held in Kolkata.
Date : April 6-9, 2009

Topic : Molecular basis of stringent response in *Vibrio cholerae*
Venue : Indo-Brazil symposium on 'Infectious Diseases' held in Kolkata.
Date : December 10-12, 2009

Topic : CTX phage driven evolution of *Vibrio cholerae* as a cholera pathogen
Venue : Indian Science Congress Association, program held at the National Institute of Cholera & Enteric Diseases, Beliaghata, Kolkata.
Date : March 31, 2010

Dr. Uday Bandyopadhyay

Topic : Neem bark extract prevents nonsteroidal anti-inflammatory drug—induced gastropathy by inhibiting gastric mucosal apoptosis and favoring mucosal cell renewal

Venue : International Symposium on Aromatic and Medicinal Plants (AROMED), Central Institute of Medicinal and Aromatic Plants. Lucknow.

Date : February 21-24, 2010

Topic : Non-steroidal anti-inflammatory drug (NSAID)-induced gastropathy: critical role of mitochondrial pathology and apoptosis in gastric mucosal cell

Venue : International symposium on Frontier of Protein Sciences and Institute for Protein Research Retreat (IPR retreat) Osaka University, Senrichuo and Awaji Island, Japan.

Date : November 14-17, 2009

Dr. Malini Sen

Topic : Evaluating Wnt and WISP: A molecular approach

Venue : SBC Symposium.

Date : June 11, 2010

Chairing a session

Dr. H. K. Majumder

Chief Guest : National Symposium on 'Inborn Diseases of Metabolism' organized by Calcutta Society for Advancement of Human Development & Research at Central Glass & Ceramic Research Institute, Kolkata on July 27, 2009.

Chief Guest : National Science Day Celebration at the Heritage Institute of Technology, Kolkata on February 25, 2010.

Chaired a session on 'Biodiversity conservation strategy'at Bose Institute, Kolkata in the seminar on 'Biochemistry and Ford Security 'organized by Indian Science News Association, Platinum Jubilee celebration on February 26, 2010.

Chaired a session in the International symposium on 'Fifty years of discovery of cholera toxin: a tribute to Dr. S. N. De on October 25-27, 2009.

Dr. Pijush K. Das

Chaired a session on Parasite/Virus/Rickettsiae at the Xth International Symposium on Vectors and Vector Borne Diseases, Goa University on November 4-6, 2009.

Chaired a session on Host-Pathogen Interactions at Indo-Brazil Symposium on Infectious Diseases, IICB and Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), Bangalore on December 10-11, 2009.

Dr. Chitra Mandal

Chaired a session in the conference World Congress on Cellular & Molecular Biology (WCCMB), held at Indore during November 2-6, 2009.

Chaired a session in the 20th International Symposium on Glycoconjugates (Glyco XX), held at San Juan, Puerto Rico, U.S.A during November 29 - December 6, 2009.

Chaired a session in the 29th Annual Convention of the Indian Association of Cancer Research held at Amrita Institute Of Medical Sciences & Research Centre, Cochin, during February 20-23, 2010.

Invited as an Expert for project presentations by talented Jagadis Bose National Science Talent Search (JBNSTS) science students from various States of Eastern India at JB Center of Excellence, Kolkata on February 7, 2010.

Delivered Keynote address, SBC, Kolkata Chapter held at Digha, West Bengal during September 4-6, 2009.

Chaired a session in the 2nd Indo-Brazil Symposium on Infectious Diseases, Kolkata, December 10-11, 2009.

Dr. Rupak K. Bhadra

Chaired a session in the 14th All India Congress of Cytology & Genetics & Fogaty International Workshop on Molecular Epidemiology, Environmental Health & Arsenic Exposure Assessment, organized by IICB (CSIR), Kolkata and held at CGCRI (CSIR), Kolkata during December 1-4, 2009.

Dr. Mridula Misra

Chaired an oral paper session of Radiopharmacy/ Radiochemistry on December 5, 2009 at 41st Annual Conference of Society of Nuclear Medicine (India), 2009 at Jaipur, India

Academic performance: Teaching, examining and training

Dr. H. K. Majumder

Guest Professor, Department of Biophysics, Molecular Biology and Genetics, Calcutta University.

Guest Professor, NIPER, Kolkata.

Dr. Pijush K. Das

Guest Professor, M.Sc. (Biophys & Mol. Biol), M.Sc. (Biotechnology), M.Sc. (Microbiology), M.Sc. (Genetics) of Calcutta University, M.Tech (Biotech) of Jadavpur University and M.Tech (Biotech) of West Bengal University of Technical Education for teaching Biochemistry and Cell Biology.

Examiner in the M.Sc. (Biochemistry), M.Sc. (Biophysics & Molecular Biology), M.Sc.(Biotechnology), M.Sc. (Microbiology), M.Sc. (Genetics) at Calcutta University and M.Tech. (Biotech) at Jadavpur University.

Dr. Chitra Mandal

Teaching at NIPER, Kolkata, as a Guest faculty member.

Teaching Immunology (Stem cells) in the course work offered to PhD student of IICB, Kolkata.

Training Summer students selected by Indian Academy of Science, Bangalore.

Appointed as the external examiner to conduct viva voce examination of a few Ph.D thesis submitted to (i) Jadavpur University, Kolkata; (ii) J.N.U, New Delhi; (iii) National Institute of Immunology (NII), New Delhi and (iv) PGIMER, Chandigarh.

Member of Project review committee of ICMR.

Reviewer of MERIEUX research grant proposal.

Reviewer of many project proposals submitted for funding to CSIR, DST, DBT, ICMR.

Reviewer of many manuscripts submitted to several International and National journals.

Dr. Syamal Roy

Teaching Post graduate students in Bioengineering at Jadavpur University, Kolkata 700032.

Dr. Nahid Ali

Teaching immunology in the course work offered to Ph.D. students of IICB.

Reviewer of project proposals submitted to CSIR and ICMR.

Supervised the project work of six students, five M.Sc. and one M.Tech., working as summer trainees.

Reviewer for Expert Opinion for Drug Delivery, Journal of Parasitology, BMC Immunology, Nanomedicine, New Technology, Biology and Medicine, Scholarly Research Exchange, International Journal of Integrative Biology, etc.

Dr. Rukhsana Chowdhury

Examiner, Shyama Prasad Mukherjee Fellowship interview, CSIR

Examiner, M.Sc. (Biotechnology) Calcutta University.

Examiner, Ph.D, Indian Institute of Science, Bangalore.

Member of Ph.D committee, West Bengal University of Health Sciences.

Dr. Rupak K. Bhadra

Acted as an external examiner of Ph.D. viva voce examination of Jadavpur University, Kolkata.

Served as an M.Sc examiner of Department of Microbiology, Bijoygarh College.

Served as an external reviewer for research proposals submitted to DST, DBT, CSIR etc.

Acted as a reviewer for Elsevier, SGM, BMC Series, Wiley-Blackwell etc.

Teaching of M.Pharm students of NIPER, Kolkata.

Taking course work classes of the students enrolled in Ph.D. at IICB.

Teaching of M.Sc. Physiology students of Presidency College, Kolkata.

Dr. Uday Bandyopadhyay

Guest Professor, Department of Biochemistry, CU

Examiner, NIPER, Kolkata

Deputation Abroad

Dr. Chitra Mandal

Attended 20th International Symposium on Glycoconjugates (Glyco XX), during November 29 - December 6, 2009 at San Juan, Puerto Rico, U.S.A and deliver an Invited talk and chaired a session.

Dr. Syamal Roy

WHO Expert Committee meeting on Leishmaniasis. June 13-16, 2009, Dacca, Bangladesh.

Coordinators' meeting, European Commission Funded Project "New tools for monitoring drug resistance and treatment response in Visceral Leishmaniasis in the Indian subcontinent", October 8-9, 2009 Antwerp, Belgium.

Steering Committee Meeting European Commission Funded Project "Development of a DNA vaccine for Visceral Leishmaniasis" February 3-5, 2010, Tunis, Tunisia.

Dr. Rupak K. Bhadra

Visited Sandia National Laboratories, Albuquerque, New Mexico, USA for a training program on 'Controlling Laboratory Biorisks' from April 27 to May 2, 2009.

Visited San Diego and Scripps Institute, La Jolla, California, USA for a presentation in the 44th Joint Meeting and Conference of the US-Japan Panel on Cholera and Other Bacterial Enteric Infections held in San Diego, California, USA from October 12-14, 2009.

Visited Institute For Protein Research (IPR), Osaka University, Japan to present our work on *V. cholerae*'s secretome at IPR Retreat 2009 held in Osaka, Japan from November 14-17, 2009.

Papers/abstract presented in the conference

Dr. Chitra Mandal

Kaushik Bhattacharya, Mahanine mediate apoptosis through crosstalk between Apo-1/Fas signaling and the Bid protein and via mitochondrial pathways in human leukemic cells, Venue: SBC, Kolkata Chapter, Digha, West Bengal, Date: September 4-6, 2009 (Oral presentation).

Chandan Mandal, S. Mondal, S. Chandra, CN Mandal and Chitra Mandal, Down regulation of membrane-bound Neu3 constitutes a new potential marker for leukemia and induces apoptosis suppression of neoplastic cells Venue: SBC, Kolkata Chapter, Digha, West Bengal, September 4-6, 2009 (Oral presentation).

Arup Kumar Bag, 5th AOHUPO Proteomics Conference 2010, at CCMB, Hyderabad, February 23-25, 2010 (Attended).

Anjon Talukder, 5th AOHUPO Proteomics Conference 2010, at CCMB, Hyderabad, February 23-25, 2010 (Attended).

Dr. Rupak K. Bhadra

Bhadra, R. K., Halder, K., Das, B. Molecular evidences favoring step-wise genesis of Mozambique *Vibrio cholerae* O1 El Tor hybrid strain. The 13th International Conference on Emerging Infectious Diseases of the Pacific Rim: Focus on Enteric Diseases held in Kolkata, India, April 6-9, 2009.

Pal, R. R., Kharlyngdoh, J. B., Das, B., Bhadra, R. K. Mutational analysis of stringent response related *dksA* gene of *Vibrio cholerae*. Presented at the 44th Joint Meeting and Conference of the US-Japan Panel on Cholera and Other Bacterial Enteric Infections held in San Diego, California, USA, October 12-14, 2009.

Pal, R. R., Das, B., Kharlyngdoh, J. B., Bhadra, R. K. Functional characterization of stringent response related *dksA* gene of *Vibrio cholerae*. Presented at the International conference on 'Fifty years of discovery of cholera toxin: A tribute to SN De' held in Kolkata, India during October 25-27, 2009.

Kharlyngdoh J. B., Das, B., Bhadra, R. K. Proteomic analysis of secreted proteins of *Vibrio cholerae*. Presented at the International Symposium on Frontier of Protein Sciences and Institute for Protein Research Retreat held in Osaka, Japan during November 16-17, 2009.

Das, B., Bhadra, R. K. Molecular basis of stringent response in *Vibrio cholerae*. Presented at the Indo-Brazil symposium on 'Infectious Diseases' held in Kolkata, India during December 10-12, 2009.

Conference/Symposia/workshops organized

Dr. Hemanta K. Majumder

Organised the Indo-Brazil Sympoium on Infectious Diseases at Kolkata during December 11-12, 2009.

Dr. Chitra Mandal

Convenor of 17th Annual meeting of Molecular Immunology Forum (MIF), Kolkata during January 15-17, 2010.

Dr. Syamal Roy

Organized Leish DNAVax Flow Cytometry Workshop under the aegis of the European Commission (EC), November 4-8, 2009.

Dr. Rupak K. Bhadra

Served as one of the Organizing Secretaries and organized the International Symposium on 'Fifty Years of Discovery of Cholera Toxin: A Tribute to SN De' held In Kolkata, India during October 25-27, 2009.

Served as a Treasurer and organized the 14th All India Congress of Cytology & Genetics & Fogaty International Workshop on Molecular Epidemiology, Environmental Health & Arsenic Exposure Assessment, organized by IICB (CSIR), Kolkata and held at CGCRI (CSIR), Kolkata during December 1-4, 2009

Served as a Treasurer and organized the Indo-Brazil symposium on 'Infectious Diseases' held in Kolkata, India during December 10-12, 2009.

Dr. Mridula Misra

Organised a "Training Programme and Workshop on Laboratory Safety" on September 7, 2009 for the students and staff of IICB, Kolkata.

Major Infrastructural facilities

Dr. Chitra Mandal

Helped in developing Proteomic center.

Dr. Syamal Roy

Setting up the protein-microarray facility.

Dr. Rupak K. Bhadra

Setting up BSL-3 laboratory facility.
Maintenance of Scanning Electron Microscope (Tescan, Model VEGA II LSU) facility.

CELL BIOLOGY AND PHYSIOLOGY

Invited Lectures

Dr. K. P. Mohanakumar

Topic : Characterization of dopaminergic neurons derived from mouse ES cells using serum free medium and functional assessment of the transplants in a hemiparkinsonian model

Venue : Medical Faculty Conference Hall, Dongguk University, South Korea

Date : August 21, 2009

Topic : Lecture – I: Mitochondrial basis of Parkinson's and Huntington's diseases

Venue : Department of Neuroscience, Mahidol University, Salaya, Tahiland

Date : August 20 (Forenoon), 2009

Topic : Lecture – II: Stem cell differentiation and transplantation in Parkinson's disease

Venue : Department of Neuroscience, Mahidol University, Salaya, Thailand

Date : August 20, 2009

Topic : Cybrid neurons mimic protein aggregation pathologies and nuclear and mitochondrial transcriptomes of Parkinsonian brain

Venue : 22nd Biennial Meeting of the International Society for Neurochemistry, Busan, S. Korea

Date : August 21-29, 2009

Topic : Mitochondria and Neurodegenerative Diseases

Venue : Indo-German Workshop on Neuroscience, Institute of Neuroscience and Medicine INM4, Research Centre Jülich, GERMANY

Date : October 8-9, 2009

Topic : *Ayurvedic* medication for Parkinson's disease, two sides of the coin: Search for the good and bad molecules in the traditional medicine

Venue : Indo-US Bilateral Conference on Translational Neuroscience: New Trends in Mental and Neurodegenerative Disorders Research at the Department of Pharmacology, University of Illinois at Chicago, Chicago, USA

Date : October 15-16, 2009

Topic : Dopamine feeds to mitochondrial instability in Huntington's disease

Venue : International conference on Neuroscience Updates & Society for Neurochemistry (India) Annual Meeting, Department of Biotechnology, Cochin University of Science & Technology, Kochi

Date : December 13, 2009

Topic : Experimental models of Parkinson's disease

Venue : APSN School of Neurochemistry, Department of Biotechnology, Cochin University of Science & Technology, Kochi

Date : December 7-12, 2009

Topic : Mitochondrial dysfunction in Huntington's disease

Venue : Guha Research Conference, Ullal, Mangalore

Date : December 21, 2009

Topic : Production of cybrids for studying neurodegenerative disease: the basis, problems and advantages

Venue : One-Day Symposium on Bioanalytical Techniques. Department of Biochemistry, NEHU, Shillong

Date : March 26, 2010

Dr. Arun Bandyopadhyay

Topic : Redistribution of Annexin A6 in cardiomyocytes in association with increased oscillations/contractile activity

Venue : Fifth International Conference on Annexins, Beurdox, France

Date : September 20 - 24, 2009

Topic : Mechanism of Cardiac Malfunction due to Excess of glucocorticoid.

Venue : International Conference on Integrative Phsyiology: Modern Perspective & Golden Jubilee Celebration of the Physiological Society of India Organized by Physiological Society of India, Kolkata

Date : November 12-14, 2009

Topic : Molecular Mechanism of Glucocorticoid-induced Cardiac Malfunction.

Venue : 97th Indian Science Congress, Thiruvananthapuram

Date : January 3 -7, 2010

Dr. S. N. Kabir

Topic : A close look into the molecular mechanisms underlying ovarian dysfunction in galactosaemia

Venue : Prof. A. K. Mukherjee Memorial Oration, International Conference on Integrative Physiology: Modern Perspective, and Platinum Jubilee Celebration of Physiological Society of India, Science City Convention Centre, Kolkata

Date : November 12-14, 2009.

Topic : Galactose-mediated ovarian toxicity is independent of its repressive effects on growth differentiation factor-9

Venue : International Conference on Reproductive Health and the 20th Annual Meeting of the Indian Society for the Study of Reproduction and Fertility, University of Rajasthan, Jaipur

Date : February 8-10, 2010

Topic : The size of ovarian follicular reserve modulates the expression of GDF-9 and NOBOX, and dictates the rate of follicular atresia

Venue : The 97th Indian Science Congress, Thiruvananthapuram

Date : January 3-7, 2010

Topic : Galactose can mediate ovarian follicular atresia independent of its repressive effects on growth differentiation factor-9.

Venue : Golden Jubilee International Seminar, The University of Burdwan

Date : March 17–19, 2010.

Mrinal K. Ghosh

Topic : EGFR Signaling and Wnt Signaling in GBM and Stem Cells

Venue : Barrackpore Rastraguru Surendra Nath College, Kolkata at UGC sponsored Symposium

Date : Febrary 13, 2010

Dr. Sib Sankar Roy

Topic : The role of Pitx2 homeodomain transcription factor and its associated co-factors in maintaining ovarian functions

Venue : Platinum Jubiee symposium of Physiological Society of India (PSI), held at Kolkata

Date : November 12-14, 2009.

Title : The interactive role of Pitx2 homeodomain transcription factor in gonadal function and disorders

Venue : 14th All India Congress of Cytology and Genetics,

Date : December 01-04, 2009

Topic : Pitx2-mediated transcriptional regulation in ovary: its implications in ovarian disorders

Venue : 21st IUBMB and 12th International Congress of Biochemistry and Molecular Biology, held at Shanghai, China

Date : August 02-07, 2009

Topic : Transcriptional regulation of ovarian genes by the homeodomain transcription factor Pitx2: its implications in ovarian disorders

Venue : New Biology Section, Indian Science Congress Association, Tirubanantapuram,

Date : January 3-7, 2010.

Topic : Genetic Regulations in Metabolic Disorders

Venue : Refreshers course in Life Sc, at Ballygunge Science College

Date : February 12, 2010.

Dr. Tuli Biswas

Topic : Mechanism of apoptotic death in erythrocytes leading to the development of anemia during chronic exposure to arsenic

Venue : International Conference on Integrative Physiology: Modern Perspective & Platinum Jubilee Celebration of the Physiological Society of India, Kolkata

Date : November 12–14, 2009

Charing session

Dr. K. P. Mohanakumar

Chaired the Session "Relevance of Mitochondrial DNA Mutations and Gene Products in Neurodegenerative Disease Pathophysiology", at the 22nd Biennial meeting of the International Society for Neurochemistry, Busan, South Korea, Tuesday, August 25, 2009

“Neuroprotection in Neurodegenerative Diseases”. At the International conference on Neuroscience Updates, Department of Biotechnology, Cochin University of Science & Technology, Kochi, on Dec 13, 2009

Chaired the Session on “Young Scientists’ Colloquium” at the NeuroUpdate-2010 meeting held at Meghnad Saha Auditorium, CGCRI, Kolkata on February 14, 2010.

Dr. Arun Bandyopadhyay

Chaired a session in 14th All India Congress of Cytology and Genetics and Fogarty International Workshop on Molecular Epidemiology, Environmental Health and Arsenic Exposure Assessment held in IICB Kolkata, December 02, 2009.

Dr. S. N. Kabir

Chaired a session in Current Trends in Biological Sciences, Organized by Society of Biological Chemists (India), Kolkata Chapter, September 04-05, 2009, Digha.

Chaired the session: Dr. T.C. Anandkumar Memorial Gold Medal Award Lecture by Prof. A. J. Rao, 20th Annual Meeting of the Indian Society for the Study of Reproduction and Fertility, February 08-10, 2010, University of Rajasthan, Jaipur, India.

Inaugurated and chaired a session in the UGC-sponsored National Seminar on Imerging Issues in Physiology and Allied Sciences, March 26, 2010, Vidyasagar University, Medinipur.

Dr. Tuli Biswas

Chaired a session in the, International Conference on Integrative Physiology: Modern Perspective & Platinum Jubilee Celebration of the Physiological Society of India, held at Kolkata on November 12–14, 2009

Chaired a session in the, All India Congress of Cytology and Genetics & Fogarty International Workshop, held at Kolkata on December 02-04, 2009

Dr. Tushar Chakraborty

Conducted a session On Darwin & Darwininsm , Organized by Darwin Bicentinery Committee , at Bagbazar Reading Library Hall, Kolkata

Academic Performance : Teaching, examining and training

Dr. K. P. Mohanakumar

Reviewed 21 manuscripts for J. Neurochem., Cell. Mol. Neurobiol., Neurosci. Res., Neurotoxicology, Neurosci. Lett., Hippocampus, J. Chem Neuroanat., Behav. Brain. Res., and Nitric Oxide.

Taught for one month (April – 28, 2009) at IISER Thiruvananthapuram.

Evaluated and prepared reports on 8 CSIR-EMR, 3 DST and 2 DBT projects submitted by various institutions.

Trained 3 summer students, and 2 graduate students from outside organization.

Trained 16 young scientists and graduate students from the Asia Pacific Region on stereotaxic applications, dissection of brain regions, and micropuch technique for isolating discrete brain nuclei and HPLC.

Dr. S. N. Kabir

Guest lecturer and member of the Board of Examiners in Physiology, M. Sc., Presidency College, Kolkata.

Guest lecturer, moderator and examiner, M.Sc., Physiology, Rammohan College, Kolkata.

Guest lecturer and Examiner, M.Sc, Physiology, Calcutta University.

Guest lecturer and Examiner, M.Sc, Physiology, Vidyasagar University.

Guest lecturer, M.Sc, Physiology, Krishnath College, Murshidabad.

Dr. Mrinal K. Ghosh

Teaching on “Cell Signaling” in the course work offered to Ph. D. students of IICB, Kolkata.

Lecturer and Examiner of NIPER, Kolkata [Topic: Drug metabolism, Toxicity and Metabolic disorders].

Dr. Padma Das

Supervised two students in project work as part fulfillment of their various degrees like M.Tech and M.Sc

Dr. Sib Sankar Roy

Appointed as UGC Visiting Teacher at Tripura University, Agartala, to teach a course to MSc Life Science students.

Acted as Examiner of MSc (Biochemistry), MSc (Microbiology) at Calcutta University and external examiner MSC of Tripura University, Agartala.
External examiner, MSC (Tech BI) Bioinformatics examination, DOEACC, Kolkata, Jadavpur University Campus, held on September 02, 2009.

External examiner, Dissertation and viva voce examination, M.Phil (Glycobiology), 2nd semester, of West Bengal University of Technology, held at WBUT, October 22, 2009.

Moderator of MSc (Human Physiology) Examination at Tripura University, Agartala.

Teaching MSc (Endocrinology Special paper), Physiology of University of Calcutta.

Trained three Summer trainees, two of them came from Amity University, Noida (April-July, 2009) and one from North Bengal University (June-July, 2009), as a part of CSIR-NBU Scientific collaboration (MOU).

MSc Physiology students of Vidyasagar University were trained in my laboratory with different Molecular Biology and Biochemical techniques (May 04-06, 2009).

Dr. Sumantra Das

Delivered a course of lectures on Neurobiology as part of curriculum (Special paper) for second year M. Sc. students of the Department of Biochemistry as well as first year M. Sc. students of the Department of Neuroscience, Calcutta University.

Lecturer and Examiner of NIPER, Kolkata

External examiner & Question setter for M. Sc. / Ph.D in Neuroscience at the National Brain Research Centre, Manesar, Haryana.

Supervised the project work of two M. Sc. students working as Summer Trainee.

Dr. Tuli Biswas

External examiner of PhD thesis and viva-voce of Calcutta University and Jadavpur University Examiner of 'Seminar Presentation' as a part of 'IICB Advanced PhDCourse work Examination Research guide of four predoctoral students and one project fellow

Supervised the project work of Ms. Riti Roy for the submission of dissertation in connection to B.Tech degree in Biotechnology, National Institute of Technology, Durgapur, West Bengal.

Evaluated scientific and technical of research proposals submitted for funding to CSIR and DST, Govt.of India.

Dr. Tushar Chakraborty

Lecturer & Examiner of NIPER, Kolkata

Resource Person & Lecturer on M Sc Course in Science Communication Conducted by the National Council of Science Museum

Delivered Nishikanta Mandal Memorial Oration at Medinipur Gope College, on Gene & Culture

Trained Two Students as Summer Trainee

Served as a reviewer for the Science Communication Journal, Propagation, published by NCSM
Published a book in Bengali to promote public understanding of genetics. Title : Gene : Bhabana, Durbhabana, (ISBN978-83-908117-3-4)

Deputation abroad

Dr. K. P. Mohanakumar

Deputed to Busan, S. Korea to deliver a talk and Chair a Symposium at the 22nd Biennial Meeting of the International Society for Neurochemistry, during August 19-30, 2009.

Visited Germany to talk at the "Indo-German Workshop on Neuroscience" at the Institute of Neuroscience and Medicine INM4, Research Centre Jülich, Germany, October 08-09, 2009.

Deputed to USA to talk at the "Indo-US Bilateral Conference on Translational Neuroscience: New Trends in Mental and Neurodegenerative Disorders Research" at the University of Illinois at Chicago, Chicago, during October 15-16, 2009

Dr. Arun Bandyopadhyay

Visited France for delivering invited talk in Fifth International Conference on Annexins, Beurdox, France, September 20- 24, 2009.

Dr. Sib Sankar Roy

21st IUBMB and 12th International Congress of Biochemistry and Molecular Biology, held at Shanghai, China, during August 02-07, 2009 and presented data as Invited Speaker.

Conference/Symposium/Workshop organized

Dr. K. P. Mohanakumar

NeuroUpdate-2010. A national Symposium of the neurobiologists and neurologists to understand the basis of neurological and psychiatric disorders. Joint Organizing Secretary with Prof. P. K. Gangopadhyay, National Medical College, Kolkata. Held at Meghnad Saha Auditorium, CGCRI on the February 14. 2010.

APSN School of Neurochemistry joint organizer along with Prof. C.S, Paulose, Head Department of Biotechnology. Held on December 7-12, 2009 at the Department of Biotechnology, Cochin University of Science & Technology, Kochi.

Dr. S. R. Dungdung

Das A., Saha S., Bhoumik A., Das S., Ghosh P., Majumder G.C. & Dungdung S.R.: Effect of different Biochemical regulators of sperm flagellar motility on sperm vertical velocity. In International Conference on Integrative Physiology : Modern Perspective and Platinum Jubilee Celebration of Physiological Society of India. Science City Convention Centre, Kolkata, November 12-14, 2009.

Papers/Abstract presented in the conference

Dr. K. P. Mohanakumar

Appukuttan TA, Navneet AK, Banerjee R and Mohanakumar KP. Low but not high doses of vitamin D3 protects against MPP^+-induced oxidative stress and dopaminergic neurodegeneration in rats. NIMS University, Jaipur, Annula meeting of the Indian Academy of Neurosciences, December 18–20, 2009.

Chakraborty J, Pandey M, Navneet AK, Appukuttan TA, Varghese M, Usha R and Mohanakumar KP Alteration of profilin-2 and its implication in 3-nitropropionic acid neurotoxicity NIMS University, Jaipur, Annula meeting of the Indian Academy of Neurosciences, December 18–20, 2009.

Tripathy D and Mohanakumar KP Characterization of mouse embryonic stem cell derived neurons: Effects of transplantation in rotenone model of Parkinson's disease in rats NIMS University, Jaipur, Annula meeting of the Indian Academy of Neurosciences, December 18–20, 2009.

Tripathy D and Mohanakumar KP. Characterization of mouse embryonic stem cell derived neurons: Effects of transplantation in rotenone model of Parkinson's disease in rats. Neuro-Update-2010 held at Meghnad Saha Auditorium, CGCRI on February 14, 2010

Dr. Arun Bandyopadhyay

Mishra S., Ghosh G., Banerjee P., Bandyopadhyay A. Redistribution of Annexin A6 in cardiomyocytes in association with increased oscillations/contratile activity. Fifth International Conference on Annexins, Beurdox, France, September 20 -24, 2009.

Ghose Roy S., De P., Mukherjee D., Chander V., Konar A., Bandyopadhyay D., Bandyopadhyay A. Mechanism of Cardiac Malfunction due to Excess of glucocorticoid. International Conference on Integrative Physiology: Modern Perspective & Golden Jubilee Celebration of the Physiological Society of India Kolkata, November 12-14, 2009.

Bandyopadhyay A., Ghose Roy S., De P., Mukherjee D., Chander V., Konar A., Bandyopadhyay D. Molecular Mechanism of Glucocorticoid-induced Cardiac Malfunction. 97th Indian Science Congress held in Thiruvananthapuram, January 03-07, 2010.

De K., Mukherjee S., Bandyopadhyay A. Proteomic approach to study the differential protein expression in hypertrophied rat heart. 5th AOHUPO Congress and 14th ADNAT Convention & 1st PSI Conference on New Perspective in Proteome Research organized by CCMB, Hyderabad, February 21-25, 2010.

Dr. S. N. Kabir

Syed N. Kabir, Sayani Banerjee. The size of ovarian follicular reserve impacts the expression of GDF-9 and NOBOX, and modulates the rate of follicular atresia. 14th World Congress of Gynecologic Endocrinology, Florence, Italy, March 04-07, 2010.

Syed N. Kabir, Sayani Banerjee. Female reproductive aging is master-planned at the level of ovary. 12th FAOBMB International Congress of Biochemistry and Molecular Biology (IUBMB-2009-Congress) Shanghai, China, August 02-07, 2009.

Durba Pal, Sudeep Sabde, Herambananda Ray, Bikas C. Pal, Debashis Mitra, Syed N. Kabir. Acaciaside-B-

enriched fraction of *Acacia auriculiformis* possesses spermicidal as well as anti-HIV activity with wide margin of safety. 14th World Congress of Gynecologic Endocrinology, Florence, Italy, March 4-7, 2010.

Piyali Saha, Bikas C. Pal, Syed N. Kabir. Puerarin, a selective estrogen receptor modulator, disrupts embryo-uterine communication and inhibits implantation. 14th World Congress of Gynecologic Endocrinology, Florence, Italy, March 04-07, 2010.
Soma Aditya (Bandyopadgyay), Sayani Banerjee, Syed N. Kabir. The size of ovarian follicular reserve impacts the rate of follicular atresia by modulating the expression of GDF-9 and NOBOX. Golden Jubilee International Seminar, The University of Burdwan, March 17-19, 2010.

Dr. Mrinal K. Ghosh

Kiran Kumar Naidu G. "Regulation of ?-catenin in Cancer through P68, Stat3 and AKT Activation Pathways" at the 11th Annual Conference of the Society for Biological Chemists (Kolkata Chapter) on "Current Trends in Biological Sciences" held at Digha from September 4-6, 2009.

Ms. Tapashi Mandal. "Cross regulation of Stat3 and Wnt/â-catenin Signaling: Implications in cancer" at the 29th Annual Convention of Indian Association for Cancer Research on "Biology of Cancer Stem Cells" held at AIMS, Kochi from February 20-23, 2010.

Dr. Padma Das

Deepak Kumar, Rupashree Sen, Rajneeta Roy, Mitali Chatterjee, Padma Das. Evaluation of Anti-proliferative activity of the methanolic extract of *Sesbania grandiflora* flower. 2 days symposium on current trends in Biological science. September 04-06, 2009

Dr. Sib Sankar Roy

Sib Sankar Roy, Shyam Sundar Nandi, Pamela Ghosh, Moitri Basu. The interactive role of Pitx2 homeodomain transcription factor in gonadal function and disorders. Platinum Jubiee symposium of Physiological Society of India (PSI), held at Kolkata during November 12-14, 2009.

Moitri Basu, Shyam Sundar Nandi, Pamela Ghosh, Kunal Kumar Basu and Sib Sankar Roy. Pitx2-mediated transcriptional regulation: its implications in gonadal development and disorders. SBC symposium on Biology, Digha, August 2009.

Sonali Ghosh and Sib Sankar Roy. Regulation of VEGF-induced cell invasion and MMP gene expression in ovarian cancer cell lines SKOV3 and PA-1: role of different transcription factors. Annual Meeting of SBC (I), Univ. of Puna, Pune, December, 2009.

Debanjali Mitra and Sib Sankar Roy. Hypothyroidism induced differential gene expression of MMPs,PLODs and cytokines in ovary. Annual Meeting of SBC (I), Univ. of Puna, Pune, December, 2009.

Shyam Sundar Nandi, Moitri Basu, Kunal Kumar Basu and Sib Sankar Roy. The interactive role of the Pitx2 homeodomain transcription factor with Lhx3 and GCMa, in gonadal development. Annual Meeting of SBC (I), Univ. of Puna, Pune, December, 2009.

Sib Sankar Roy, Shyam Sundar Nandi, Moitri Basu and Pamela Ghosh. Transcriptional regulation of ovarian genes by the homeodomain transcription factor Pitx2: its implications in ovarian disorders. Indian Science Congress, Thiruvanantapuram, January 3-7, 2010.

Debanjali Mitra, Samir Kumar Saha and Sib Sankar Roy**.** Hypothyroidism associated ovarian dysfunction in connection with differential gene expression of MMPs, PLODs and cytokines in ovary. Platinum Jubiee symposium of Physiological Society of India (PSI), held at Kolkata during November 12-14, 2009.

Kunal Kumar Basu and Sib Sankar Roy. The signaling of the homeodomain transcription factor Pitx2 in ovary: special emphasis to Wnt/b-catenin pathway. Platinum Jubiee symposium of Physiological Society of India (PSI), held at Kolkata during November 12-14, 2009.

Moitri Basu, Pamela Ghosh, Samir Kumar Saha_and Sib Sankar Roy. The homeodomain transcription factor Pitx2 tranactivates Plod2 gene in ovary: its possible association with ovarian disorders. Platinum Jubiee symposium of Physiological Society of India (PSI), held at Kolkata during November 12-14, 2009.

Shyam Sundar Nandi and Sib Sankar Roy**.** The interactive role of the homeodomain transcription factor Pitx2 with another transcriptional regulator GCMa, in gonadal development. Platinum Jubiee symposium of Physiological Society of India (PSI), held at Kolkata during November 12-14, 2009.

Sonali Ghosh and Sib Sankar Roy. Regulation of VEGF induced MMP expression and invasion in ovarian cancer cell line SK-OV3: involvement of different MAP kinases and transcription factors in it. Platinum Jubiee symposium of Physiological Society of India (PSI), held at Kolkata during November 12-14, 2009.

Sudarshan Bhattacharya, Saptarshi Dutta and Sib Sankar Roy**.** Effects of Thyroid Disorders and Insulin resistance on Mitochondrial Biogenesis and Function. Platinum Jubilee symposium of Physiological Society of India (PSI), held at Kolkata during November 12-14, 2009.

Dr. Tuli Biswas

Sen, G.and Biswas, T.: “Quercetin enhances apoptosis of the infected host cells, facilitating elimination of parasites during visceral leishmaniasis”. International Conference on Integrative Physiology. Modern Perspective & Platinum Jubilee Celebration of the Physiological Society of India, Kolkata, November 12–14, 2009.

Mandal, S., Sen, G., Biswas, T.: “Redox imbalance contributes to progressive liver damage during chronic exposure to alcohol in rats”. International Conference on Integrative Physiology. Modern Perspective & Platinum Jubilee Celebration of the Physiological Society of India, Kolkata, November 12–14, 2009.

Biswas, D., Sen, G., Biswas, T.: “Development of anemia in human population exposed to arsenic through drinking water in West Bengal”. Fogarty International Workshop & Final Meeting of Probabilistic Risk Assessment Modeling for Groundwater Arsenic Mitigation, Kolkata, February 23-25, 2010.

Recognitions/Awards/Prizes

Dr. K. P. Mohanakumar

Elected for the Lalitha Kameswaran Oration of the South Regional Indian Pharmacological Society and delivered the talk at PSG Institute of Medical Sciences and Research on the November 12, 2009.

Elected member of the Committee on Aid and Education in Neurochemistry (CAEN) of the International Society for Neurochemistry, UK.

Elected President of SNC, India at its last General Body meeting held on December 14, 2009 at CUSAT, Cochin.

Dr. S. N. Kabir

Prof. A. K. Mukherjee Memorial Oration at International Conference on integrative Physiology : Modern Perspective, and Platinum Jubilee Celebration of Physiological Society of India, Science City Convention Centre, Kolkata, November 12-14, 2009. Topic: A close look into the molecular mechanisms underlying ovarian dysfunction in galactosaemia.

Dr. Sib Sankar Roy

Appointed as a UGC visiting teacher by Tripura University, Agartala

MOLECULAR & HUMAN GENETICS

Invited lectures

Dr Samit Adhya

Topic : Transport and targeting of exogenous RNA to intracellular mitochondria
Venue : Leopoldina Symposium on Molecular Genetics of chloroplasts and mitochondria, Berlin, Germany
Date : 20-23 September, 2009

Dr. Kunal Ray

Topic : Quest of Genetic Root in Community,
Venue : LVPEI, Bhubaneshwar,
Date : May 1, 2009

Topic : Molecular Pathogenesis of Wilson's Disease: what we know and what ought to be done
Venue : CGCRI, Kolkata,
Date : July 21, 2009

Topic : Human Genome Project and Beyond……on State level seminar on Playing God: Expanding Frontiers of Biotechnology
Venue : Gurudas College, Narkeldanga, Kolkata,
Date : November 6, 2009

Topic : Genetic Studies of Eye Diseases in India
Venue : International Symposium on Genetics and Epigenetic Basis of Complex Diseases, CCMB, Hyderabad
Date : December 6, 2009

Topic : Molecular pathogenesis of POAG: A study on eastern Indian patient cohort.
Venue : Symposium on Recent Advances in Ophthalmic Genetics and Gene Therapy, Narayana Nethralaya, Bangalore
Date : February 2, 2010

Topic : Pharmacogenomics Medicine & The New Face of Genetics.
Venue : Refresher Course in Life Science, Dept of Botany, Calcutta University.
Date : February 15, 2010

Topic : Molecular genetics and functional studies on Oculocutaneous albinism
Venue : Annual meeting of Indian Society of Human Genetics, Sanjay Gandhi Medical Institute, Lucknow,
Date : March 7, 2010

Dr. A.K. Giri

Topic : Arsenic in drinking water: genetic and genomic approaches for identify arsenic susceptibility and health effects
Venue : 10th International Conference on Environmental Mutagens, Firenze (Florence), Italy
Date : August 20-25, 2009.

Topic : Health effects, genetic damage and genomic approaches to identify arsenic susceptibility
Venue : 4th PRAMA International Workshop, University of Manchester, U.K.,
Date : September 1-4, 2009.

Topic : Arsenic contamination in ground water: Health effects, cytogenetic and molecular approaches to identify arsenic susceptibility
Venue : International Conference on Environmental Occupational & Lifestyle Conerns Transdisciplinary Approach, Nirmal Bhavan, Bangalore
Date : September 16-19, 2009

Topic : Genetic and Genomic Approaches to Decipher Arsenic Toxicity and Susceptibility
Venue : International Conference on Molecular Tools in Environmental Toxicology, National Environmental Engineering Research Institute (NEERI), Nagpur,
Date : September 23-24, 2009.

Dr. Susanta Roychoudhury

Topic : Genomic instabilities in human cancer
Venue : Guha Research Conference 2009, Ullal, Mangalore
Date : December 19-23, 2009

Topic : Transcriptional regulation of spindle assembly checkpoint gene *CDC20* in response to DNA damage
Venue : Transcription Assembly meeting, Jawaharlal Nehru University, New Delhi
Date : February 26-27, 2010

Topic : Chromosomal Instability in Human Cancer: regulation by tumor suppressor gene p53
Venue : Symposium on DNA repair, genomic instability, and cancer, Department of Zoology, Banaras Hindu University, Varanasi
Date : March 4-5, 2010

Topic : Differential regulation of the spindle assembly checkpoint gene, UBE2C by wild type and mutant p53
Venue : International symposium on role of genomics in clinical practice and 35th Annual conference of Indian Society of Human Genetics, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow
Date : March 6-8, 2010

Session Chairman

Dr. Kunal Ray

Chaired a session in the Annual Meeting of Indian Association of Special Libraries & Information Centres, IACS, Kolkata (November 5, 2009).

Chaired a session on Molecular Medicine : Lens, Retina and Glaucoma Genetics on February 3, 2010 in Symposium on Recent Advances in Opthalmic Genetics and Gene Therapy at the Narayana Nethralaya, Bangalore (February 3-4, 2010)

Dr. A. K. Giri

Chaired a session at the 4th PRAMA International Workshop at the University of Manchester, U.K. from September 1-4, 2009.

Academic Performance / Teaching

Dr. A. K. Giri

Trained one International Student Mr. James K. Kearns, of the Department of Chemistry, University of Massachusetts, USA has been selected as a Research Intern under the Indo-US Science and Technology Forum (IUSSTF) and Oak Ridge Associated Universities (ORAU) Research Internship in Science & Engineering (RISE) Program in Science. He has worked in my laboratory for a period of four months from September 2009 to December 2009.

Working as a Teacher and also as an Examiner at the Genetic Department, Centre of Advanced Study, Department of Botany, University of Calcutta.

Teaching NIPER Students at IICB.

Trained 12 Fogarty trainee at the Fogarty Monthly meeting at IICB in the session 2009 to 2010.

Dr. Keya Chaudhuri

Supervised students (Samik Bhattacharya, WBUT, Neha Todi WBUT, Soujanya Ganguly, CU; Snigdha Ray, CU; Somashree Sengupta AMITY University; Sarani Sen, VIT; B Prakash, Madras University; Deepsikha Biswas, VIT; Upasana Saha RBU; Sayantani Roy, MIT; Atul Katarkar, NIPER; Saheli Dhar, NIT Durgapur) in dissertation work for the partial fulfillment of their M.Sc, MTech degrees Lecturer and Examiner of NIPER, Kolkata

Dr. Kunal Ray

An honorary lecturer and examiner of the M. Sc. (Biotechnology), M. Sc. (Genetics), and M. Sc. (Neuroscienes), Calcutta University.

An honorary lecturer and examiner of the M. Sc. (Biotechnology), Jadavpur University.

An honorary lecturer and examiner of NIPER at IICB.

Delivered lectures in the UGC sponsored courses in Calcutta University.

Member (External Expert) of a committee to perform function of Postgraduate Board for M.Sc. course in Genetics.

Member of Monitoring Committee for National Fund for Basic & Strategic Research (NFBSRA)
Evaluate research proposals submitted to DST, DBT, CSIR etc. for funding.

Supervised ten students in the mandatory project work as part fulfillment of their various degrees like BTech, MSc and MTech.

Supervised six graduate students working towards PhD.

Associate Editor, Journal of Genetics (published by Springer).

Reviewed papers for (i) Investigative Ophthalmology & Visual Sciences, (ii) Molecular Vision, (iii) BMC Genetics, (iv) BMC Molecular Biology, (v) Archives of Ophthalmology, (vi) Journal of Biosciences, (vii) Journal of Investigative Dermatology, (viii) Journal of Genetics

Dr. Susanta Roychoudhury

Delivered Lectures in Cell Biology course in M. Sc. (Biophysics, Molecular Biology & Genetics), Calcutta University

Delivered Lectures in Cancer Genetics course in M.Sc. (Biotechnology), Calcutta University.

Delivered Lectures in Cancer Genetics course in integrated Ph.D, West Bengal University of Technology, Kolkata.

Delivered Lectures on Genomics in graduate program for Ph.D. students of Indian Institute of Chemical Biology, Kolkata.

Delivered Lectures on Recombinant DNA technology, mutation and DNA-protein interaction in M.S. (Pharma), NIPER, Kolkata

Dr. Suvendra Nath Bhattacharya

Served as a guest lecturer at the Dept. of Biophysics and Molecular Biology, University of Calcutta.

Deputation abroad

Dr.A. K. Giri

Visited University of California, Berkeley, USA from April 1-7, 2009 as a Faculty visitor of the Fogarty International Training Program at IICB in collaboration with University of California, Berkeley, USA.

Dr. S. N. Bhattacharya

Short Term Fellowship from International Human frontier science program Organization (HFSPO) to Friedrich Miescher Institute, Basel, Switzerland during the month of June 2009.

Papers/Abstracts presented in the Conference

Bornita Das, Rajdeep Chowdhury, Sibabrata Mukhopadhyay and Keya Chaudhuri, Identification of garlic components responsible for reduction of sodium arsenite induced toxicity in a symposium organized by the Society of Biological Chemists (India)-Kolkata Chapter at Digha, West Bengal, held on Sepember 4-6, 2009

Avirup Chakraborty, Sanjit Mukherjee, Richa, Sweta Pattanayak, Jaygopal Roy and Keya Chaudhuri, Collagen types in OSF: an electron microscopic and immunohistochemical studies. in a symposium organized by the Society of Biological Chemists (India)-Kolkata Chapter at Digha, West Bengal, held on September 4-6, 2009

Avirup Dutta, Raghunath Chatterjee and Keya Chaudhuri. Comparative genomic study of pathogenic strains of *Vibrio cholerae* using Design-Island. In an International symposium on "SN De: a tribute to 50 years of discovery of cholera toxin" organized by NICED, Bose Institute and IICB, Kolkata, at Hayatt Regency, Kolkata, October 25-27, 2009

Swati Bhowmick, Debashree Chatterjee and Keya Chaudhuri. Monocyte derived dendritic cells are activated by *Vibrio cholerae* stimulated epithelial cells. In an International symposium on "SN De: a tribute to 50 years of discovery of cholera toxin" organized by NICED, Bose Institute and IICB, Kolkata, at Hayatt Regency, Kolkata, October 25-27, 2009

Tapasi Das, Sanjit Mukherjee, Pallashree Saha and Keya Chaudhuri. Inhibition of *Vibrio cholerae* induced Nuclear Factor-κB activation and interleukin-8 (IL-8) expression by quercetin in intestinal epithelial cells. In an International symposium on "SN De: a tribute to 50 years of discovery of cholera toxin" organized by NICED, Bose Institute and IICB, Kolkata, at Hayatt Regency, Kolkata, October 25-27, 2009

Samir Mandal, Murugan, G Suresh Kumar and Keya Chaudhuri. Interaction of Taq DNA polymerase with bullet shaped gold NANOPARTICLES: Change of folding structure and reactivity. In a symposium on "Recent Trends in Biophysics" organized by the Indian Biophysical Society at Banaras Hindu University, Varanasi, February 13-15, 2010.

Avirup Dutta, Raghunath Chatterjee and Keya Chaudhuri. In silico comparative genomic study of four pathogenic strains of *Vibrio cholerae.* In a symposium organized by Science Association of Bengal on the occasion of National Science Day celebration, at K P Basu Memorial Hall, Jadavpur University, Kolkata.

Sanjit Mukherjee, Jay Gopal Ray, Aniruddha Dam, Sudipto Mukhopadhyay and Keya Chaudhuri Digital Infrared Thermographic Imaging (DITI): A future early diagnostic tool for Head & Neck pathology. In a symposium organized by Science Association of Bengal on the occasion of National science day celebration, at K P Basu Memorial Hall, Jadavpur University, Kolkata.

Subhadip Chakraborty, Suddhasil Mookherjee, Deblina Banerjee, Mansi Vishal, Abhijit Sen, Indian Genome Variation Consortium and Kunal Ray; Association of WDR36 SNPs with Primary Open Angle Glaucoma, Annual meeting of Indian Society of Human Genetics at Sanjay Gandhi Medical Institute, Lucknow (March 6-8, 2010) [Poster presentation].

Sanchari Pradhan, Chitra Dutta & Kunal Ray; IGDD (Indian Genetic Disease Database): A New Mutation Database on Genetic Diseases common in Indian Population, Annual meeting of Indian Society of Human Genetics at Sanjay Gandhi Medical Institute, Lucknow (March 6-8, 2010) [Poster presentation].

Tufan Naiya, Shyamal K. Das, Kunal Ray and Jharna Ray; Role of *GCH1* Gene in Indian Dystonia Patients, Annual meeting of Indian Society of Human Genetics at Sanjay Gandhi Medical Institute, Lucknow (March 6-8, 2010).

Bhattacharyya, S. N. miRNA mediated translation repression and P-bodies: the complex world of post-transcriptional gene regulation an invited talk in the meeting held at TIFR, Mumbai 14-16th September 2009. "Young Explorer in Indian Biology, Dept. of Biochemistry, Tata Institute of Fundamental Research, Homi Bhabha birth centenary commemorations 2008-2010.

Bhattacharyya, S. N. miRNA mediated translation repression and P-bodies. an invited talk at 14th All India Congress of Cytology and Genetics. the December 1-4, 2009

Bhattacharyya, S.N. miRNA mediated post-transcriptioal gene regulation in mammalian cells. an invited talk on Indo-US Bilaterral workshop on Epigenetic Regulation and Genome Control held at Center for Cellular and Molecular Biology, Hyderabad, India. December 16-18, 2009.

Banerjee Nilanjana and Giri Ashok K. Chronic arsenic exposure impairs immune functions of exposed individuals. Poster presented in 14 th All India Congress of Cytology and Genetics & Fogarty International Workshop on Molecular Epidemiology, Environmental Health and Arsenic Exposure Assessment at Indian Institute of Chemical Biology from December 1-4, 2009

Bhattacharya Udayan and Giri Ashok K. Apoptosis induction by black tea polyphenols: do caspases play the central role? Poster presented in 14 th All India Congress of Cytology and Genetics & Fogarty International Workshop on Molecular Epidemiology, Environmental Health and Arsenic Exposure Assessment at Indian Institute of Chemical Biology from December 1-4, 2009

Giri Ashok K. A decade of research on Arsenic exposed population in West Bengal at IICB: A cusory glance. Oral presentation at 5th and Final PRAMA (Probabilistic Risk Assessment Modelling for Groundwater Arsenic Mitigation) meeting at Indian institute of Chemical Biology Kolkata from February 23-25, 2010

Banerjee Nilanjana, Samanta Maityera, Mondal Debapriya, Banerjee Mayukh, Kundu Manjari, Bhattacharya Udayan, Ganguly Bhaswati, Polya D.A. and Giri A.K. Relative contributions of drinking water and rice towards arsenic toxicity in West Bengal, India. Oral presentation at 5th and Final PRAMA (Probabilistic Risk Assessment Modelling for Groundwater Arsenic Mitigation) meeting at Indian institute of Chemical Biology Kolkata from February 23-25, 2010

Banerjee Mayukh, Polya D.A. and Giri A K. Consumption of Arsenic accumulating rice contributes significantly to arsenic-induced genetic damage. Oral presentation at 5th and Final PRAMA (Probabilistic Risk Assessment Modelling for Groundwater Arsenic Mitigation) meeting at Indian institute of Chemical Biology Kolkata from February 23-25, 2010

DRUG DEVELOPMENT, DIAGNOSTICS & BIOTECHNOLOGY

Invited Lectures:

Dr. Aparna Gomes

Topic : Anticancer activity of snake venom.
Venue : BITS-Pilani, Goa.
Date : October 7, 2009.

Topic : Cytotoxic activity of Indian Snake venom
Venue : Recent Advances in snake venom Research and snake bite therapy: National and International Perspectives Tezpur University, Assam.
Date : December 18-19, 2009

Dr. Snehasikta Swarnakar

Topic : Gastric cancer in eastern Indian population and association with functional polymorphism of MMPs.
Venue : New frontier in hematology and oncology, Kolkata,
Date : April 9-10, 2009.

Topic : Matrix metalloproteinases in gastric cancer: Gene polymorphism and the risk.
Venue : Thakurpukur Cancer Hospital, Kolkata,
Date : July 18, 2009.

Topic : Increased matrix metallproteinase-9 activity in non-steroidal anti-inflammatory drug induced gastric ulcer: Regulation by Vitamin E.
Venue : Vitamin E Satellite Symposium, Rome, Italy
Date : August 25-26, 2009

Topic : MMP: New challenges in gastric inflammation: Matrix metalloproteinases as key player.
Venue : Annual meeting of SBC, Pune.
Date : October 29-31, 2009

Topic : Gastric inflammation: A new perspective.
Venue : SaBIC, TIFR, Bombay.
Date : November 1-3, 2009

Topic : Acute arsenic toxicity during embryo implantation and regulation of MMP activity.
Venue : All India Congress of Cytology and Genetics at Kolkata,
Date : December 1-4, 2009

Topic : Gastric inflammation in diabetes mellitus: Oxidative stress and matrix metalloproteinases regulation
Venue : SFRR-India, Hyderabad.
Date : January 11-13, 2010

Topic : Gastric cancer in eastern Indian population and association with functional polymorphism of MMPs.
Venue : Cancercon, IIT Madras,
Date : February 18-20, 2010

Topic : Regulation of MMP-3 by oxidative stress during progression of endometriosis: Protection by melatonin.
Venue : RCOG Annual Meeting
Date : February 23-25, 2010

Dr. Suman Khowala

Topic : *Jalam Amritam*
Venue : Hindi Day workshop at Central Glass and Ceramic Research Institute, Kolkata
Date : September 14, 2009

Topic : Role of differential aggregation in regulating the stability and kinetic efficiency of extracellular and intracellular cellobiase in *Termitomyces clypeatus*
Venue : Benaras Hindu University
Date : December 4-6, 2009

Dr. Sharmila Chattopadhyay

Topic : Neutraceutical & Medicinal potential of the genetically modified pudina.
Venue : 2nd International Symposium on Medicinal and Neutraceutical Plants, AIIMS, New Delhi,
Date : November 25-27, 2009

Topic : Mentha arvensis- with enhanced antioxidant potential to combat ROS mediated disease conditions
Venue : Gordon Research Conference on Plant Metabolic Engineering New Hampshire, USA**.**
Date: July 12-17, 2009.

Chairing session

Dr. Aparna Gomes

Chaired a session in International Conference on Integrative & Personalized Medicine and 42nd Annual Conference of Indian Pharmacological Society held at Swabhumi, Kolkata, December 10-12, 2009.

Dr. Snehasikta Swarnakar

Chaired a session in **New Frontier in Hematology and Oncology**, Kolkata, April 9-10, 2009.
Chaired a session in **PULMOCON 2009**, Kolkata, September 5-6, 2009.

Dr. Sharmila Chattopadhyay

Chaired a session in **2nd International Symposium on Medicinal and Neutraceutical Plants**, AIIMS, New Delhi, India November 25-27, 2009.

Academic Performance/Teaching

Dr. Tarun Kumar Dhar

Reviewer of several papers to be published in Analytica Chimica Acta, Analytical Chemistry, J. Chromatography, J. Sci. Food & Agric., Mycotoxin Research.

Dr. Aparna Gomes

Member, Human Ethical Committee in Presidency College, Kolkata.

Reviewer of Indian Journal of Pharmacology, Indian Journal of Biotechnology,

Toxicology, Phytotherapy Research, Journal of Ethnopharmacology, Protein and peptide letter, Chinese Journal of Physiology. Evaluated Research Proposals submitted to ICMR, DST.

Dr. Snehasikta Swarnakar

Acted as examiner of M.Sc Biochemistry, Environmental Science and Microbiology, Calcutta University and, Biochemistry and Biophysics, Kalyani University.

Editorial board member of International Journal of Biomedical Science, 2008.

Reviewer of paper published in Indian Journal of Biochemistry and Biophysics, Evidence Based Complementary and Alternative Medicine, UK, Journal of Cellular Physiology, USA and Free Radical Biology and Medicine, USA, Current drug delivery, USA, World Journal of Surgical Oncology, China

Reviewer of external projects under CSIR and DST

Board member of SFRR-ASIA, 2008

Examiner of Ph. D viva at Jadavpur University

Taught UGC refresher course at Calcutta University, Topic: 'Gastric inflammation: A new perspective'

Dr. Nirmalendu Das

Guest Professor, Dept. of Biochemistry& Biophysics, University of Kalyani, Kalyani, Nadia, WB acted as an external examiner at Department of Biochemistry & Biophysics, University of Kalyani, Kalyani, Nadia, WB.

Acted as an external examiner at Department of pharmaceutical Technology, JU, WB.

Member, Academic council, Dept of Microbiology, St Xaviers College Kolkata

Dr. Suman Khowala

Ph. D. examiner of Agharkar Research Institute, Pune; Biochemistry Department, Acharya Nagarjuna University, Guntur; Dept of Biochemistry, Anna Malai University, Chidamabaram; Department of Genetics, Madurai Kamraj University. Bidhan Nagar College, Salt Lake, Kolkata.

Papers/Abstracts presented in the Conference

Saha (Biswas), A., and Gomes, A. 'A small fibrinolytic protein toxin purified from Indian Naja kaouthia venom' presented at 2-Day National Symposium on Recent Advances in Snake Venom Research and Snake-bite Therapy: National and International Perspectives (Snak-Symp 09), Tezpur University, Tezpur, 2009.

Saha, A. and Gomes, A. 'A novel protein Najakase purified from Indian Naja kaouthia venom possesses fibrinolyitic potential' presented at International Conference on Integrative and Personalized Medicine and 42nd Annual Conference of Indian Pharmacological Society, Kolkata, 2009.

Halder, B. and Gomes,A. 'Anticancer effects of black tea polyphenols on human malignant melanoma cells' presented in the International Conference on Integrative & Personalized Medicine and 42nd Annual Conference of Indian Pharmacological Society held at Swabhumi, Kolkata, December 10-12, 2009.

Bhattacharya, S. and Gomes, A. 'Antitumor activity of Bungarus caereleus venom on Ehrlich Ascites Carcinoma bearing mice'. presented in the International Conference on Integrative & Personalized Medicine and 42nd Annual Conference of Indian Pharmacological Society held at Swabhumi, Kolkata, December 10-12, 2009.

Das Gupta, S. and Gomes, A. 'Anticancer potentials of a protein toxin (Hbf1) from the Indian black scorpion (Heterometrus bengalensis) venom'. presented in the International Conference on Integrative & Personalized Medicine and 42nd Annual Conference of Indian Pharmacological Society held at Swabhumi, Kolkata, December 10-12, 2009.

Das, T. and Gomes, A. 'Anticancer activity of Naja naja venom fraction on leukemic cell lines' presented in the International Conference on Integrative & Personalized Medicine and 42nd Annual Conference of Indian Pharmacological Society held at Swabhumi, Kolkata, December 10-12, 2009

Das, T. and Gomes, A. 'Antitumor activity and antioxidant role of Naja naja venom fraction on Ehrlich Ascities Carcinoma (EAC) in animal model' presented at 2-Day National Symposium on Recent Advances in Snake Venom Research and Snake-bite Therapy: National and International Perspectives (Snak-Symp 09), Tezpur University, Tezpur, 2009.

Besra, S. E., Roy, S. and Besra, S. 'Anti-Cancer activity of haemolymph of fresh water edible crab Sartoriana spinigera'. The 4th Asian Congress on Autoimmunity, Suntec Singapore, International Convention & Exhibition Centre,1 Raffles Boulevard, Suntec City, Singapore, September 11-13, 2009.

Besra, S. E., Roy, S., Hembram, P., Paul, S. and Besra, S. 'Anti-leukemic with Immunomodulatory activity of Haemolymph of fresh water edible crab Sartoriana spinigera' 33rd Annual Conference of the Australasian and South East Asian Tissue Typing Association (ASEATTA), New Delhi, November 12-15, 2009.

Karmoker, P., Swarnakar, S., Mishra, A and Paul, S. 'Role of matrix metalloproteinase-9 and -2 in tumorogenesis' presented at New frontier in hematology and oncology, Kolkata, April 9-10, 2009.

Mishra, A., Paul, S. and Swarnakar, S. 'Upregulation of MMP-9 in alcohol induced acute liver damage' presented at SBC annual meeting, Kolkata chapter, Digha, West Bengal, September 4-6, 2009.

Dey, S., Gupta, A and Swarnakar, S. 'Association of functional polymorphisms in MMP-9 and -7 with susceptibility of gastric cancer presented in eastern Indian population.' Presented at All India Congress of Cytology and Genetics & Fogarty International Workshop, Kolkata, December 1-4, 2009.

Ghosh, A. K., Ghosh, S. and Basistha, B. 'Regulation of Trehalose metabolism by methylation in *Saccharomyces cerevisiae*.' Presented at International Conference, Separation Science, Singapore, Biopolis Park, Singapore, August 26, 2009.

Lahiri, S. and Ghosh, A. K. 'Purification and Characterization of neutral trelalase-invertase compex from *Candida utilis*.' presented at 33rd.All India Cell Biology Conference 2009 & International Workshop on Cell Cycle Regulation, held at School of Life Sciences, Univ. of Hyderabad, December 10-13, 2009.
Khowala, S. and Banik, S. P. 'Role of differential aggregation in regulating the stability and kinetic efficiency of extracellular and intracellular cellobiase in *Termitomyces clypeatus,*' presented at International Conference on Emerging Trends in Biotechnology at Benaras Hindu University, Varanasi, December 4-6, 2009.

Ghanta, Srijani, Bhattacharyya, D. and Chattopadhyay, S. 'Accumulation of Anticancer Compound-Podophyllotoxin in Methyl Jasmonate Induced Cell Suspension Culture of *Podophyllum hexandrum*' presented at 17th West Bengal State Science & Technology Congress, West Bengal University of Animal & Fishery Sciences, Kolkata, March 4-5, 2010.

Ghanta, S., Sinha, R. and Chattopadhyay, S. 'Over- expression of glutathione synthetase confers metal tolerance in transgenic mint' presented at 14th All India Congress of Cytology and Genetics & Fogarty International

Workshop on Molecular Epidemiology, Environmental Health And Arsenic Exposure Assessment, Central Glass And Ceramic Research Institute, Kolkata, December 1-4, 2009.

Bhattacharyya, D., Ghanta, S. and Chattopadhyay, S. 'Subtracted cDNA library construction from methyl jasmonate induced cell suspension culture of *Podophyllum hexandrum*' presented at National Symposium on Plant Cell Tissue & Organ Culture: The Present Scenario, Ramakrishna Mission Institute of Culture, Kolkata, March 3-5, 2010.

Sinha, R., Darukhshan, M. and Chattopadhyay, S. 'Evaluation of transgenic *Mentha arvensis* by proteomic approach' presented at National Symposium on Plant Cell Tissue & Organ Culture: The Present Scenario, Ramakrishna Mission Institute of Culture, Kolkata, March 3-5, 2010.

Banerjee, A., Bhattacharyya, D. and Chattopadhyay, S. 'ESTs analysis from cDNA library of *Phyllanthus Amarus*' presented at National Symposium on Plant Cell Tissue & Organ Culture: The Present Scenario, Ramakrishna Mission Institute of Culture, Kolkata, March 3-5, 2010.

Banerjee, A., Bhattacharyya, D., Darukhshan, M. and Chattopadhyay, S. 'Cloning of Pinoresinol- Lariciresinol Reductase gene from *Phyllanthus amarus*' presented at 14th All India Congress of Cytology and Genetics & Fogarty International Workshop on Molecular Epidemiology, Environmental Health And Arsenic Exposure Assessment, Central Glass And Ceramic Research Institute, Kolkata, December 1-4, 2009.

Mukherjee, S., Sen, S., Dutta, S. K. and Dastidar, S 'Effective elimination of drug resistance in pathogenic Pseodomonas aeruginosa by antipsychotic agent thioridazine' presented at 33rd All India Medical Microbiologist Conference, Mysore, November 5-8, 2009.

CHEMISTRY

Invited Lectures:

Dr. Chinmay Chowdhury

Topic : Synthesis of heterocyclic compounds of biological interests
Venue : Chemistry Department, Visva-Bharati University, UGC sponsored current trends in chemistry
Date : March 7, 2010.

Dr. G. Suresh Kumar

Topic : Isoquinoline alkaloids as potential RNA binding natural products
Venue : Banaras Hindu University, Varanasi
Date : February 13-16, 2010.

Dr. Asish K Sen

Topic : Bioactive polysaccharides and oligosaccharides; structure and synthesis
Venue : Indian Association for the Cultivation of Science in an International Symposium on Organic Chemistry: Trends in 21st Century
Date : December 10-12, 2009.

Academic Performance / Teaching

Dr. B. C. Pal

Guest faculty member, NIPER, Kolkata.

Taught IICB Ph. D. Course work and Master Program in Instrumentation, Jadavpur University.

Served as Ph.D. examiner of Jadavpur University

Dr. A. K. Banerjee

Reviewer of *Organic Letters* and *Journal of Organic Chemistry* (ACS)

Guest faculty member, NIPER, Kolkata

Dr. P. Jaisankar

Guest faculty member, NIPER, Kolkata

Ph. D. Course work of IICB, Kolkata

Reviewer of *Organic Letters* (ACS)

Ph. D. thesis Examiner of Madras, Osmania and Jadavpur Universities

Dr. S. Mukhopadhyay

Honorary Lecturer in Postgraduate Teaching in Chemistry Department, Calcutta University

Guest faculty member, NIPER, Kolkata

Dr. G. Suresh Kumar

Guest faculty member, NIPER- Kolkata and PhD Course work of IICB

An external viva voce examiner for MTech Biotechnology & Integrated PhD Molecular Biology course of West Bengal University of Science and Technology, Kolkata

PhD thesis examiner of Osmania University, Hyderabad and Jadavpur University

Reviewer of Chemical Research in Toxicology, J. Physical Chemistry B (ACS), Molecular BioSystems (RSC), Biophysical Chemistry, Biochimica et Biophysica Acta, Journal of Chemical Thermodynamics, Journal of Pharmaceutical and Biomedical Analysis (Elsevier), DNA and Cell Biology, Future Oncology

Dr. Partha Chattopadhyay

Honorary guest faculty member for Post Graduate Teaching, Department of Chemistry, Scottish Church College, Kolkata

Honorary guest faculty member, NIPER- Kolkata

Reviewer of *Journal of Organic Chemistry* (ACS), *Tetrahedron* and *Tetrahedron Letter* (Elsevier Science Ltd.)

Dr. Asish K Sen

Ph.D. thesis examiner of Burdwan University, Jadavpur University and CFTRI, Mysore

Ten lectures given to M.Tech. students at Raja Bazar Science College, Calcutta University, January-February, 2009

Honorary guest faculty member, NIPER- Kolkata

Dr. R. C. Yadav

Acted as a member in the selection committees for Scientists and Technical Officers in the Indian Association for the Cultivation of Science (IACS) and in Central Mechanical Engineering Research Institute (CMERI), Durgapur

Training Received

Dr. P. Jaisankar

DST-sponsored "Advanced Techno Management Programme for Middle Level Scientists" conducted by Administrative Staff College of India (ASCI), Hyderabad from 4th January to 5th February 2010

Conferences/Symposia/Workshops

Dr. G. Suresh Kumar

Co-chaired one session at the symposium on recent trends in biophysics at Banaras Hindu University, Varanasi, February 13-16, 2010

Dr. Asish K. Sen

Acted as a convener, CPYLS-2008 Programme of CSIR

Chaired a Technical Session at the XXIV Carbohydrate Conference, Dept of Pharmacy, Lachoo Memorial College of Science & Technology, Jodhpur, Rajasthan, December 7-9, 2009

Dr. R. C. Yadav

Acted as treasurer and organizing committee member in the Indo Russian Workshop, held at IICB during December 1-2, 2009.

Acted as treasurer and organizing committee member in the International Symposium on Complex Dynamical Systems and Applications held at Digha Science Center, Digha, West Bengal during December 4-6, 2009

Papers/Abstracts presented in the conference

Dr. P. Jaisankar

A First One-pot Synthetic Route to Chiral 3,3'-Bipyrroles: Mandal M & Jaisankar P. 46th Annual Convention

of Chemists and International Conference on Recent Research Trends in Chemical Sciences organized by the Indian Chemical Society, December 2-6, 2009, VIT-Vellore, Tamil Nadu

A facile one-pot synthesis of substituted pyrrole - a green approach: Mahato S K, Vinayagam J, Dey S, Ajay K T & Jaisankar P. International Sympoisum on Organic Chemistry - Trends in 21st Century, , January 10-12, 2010, Indian Association for the Cultivation of Science

Dr. G. Suresh Kumar

Islam M. M. & Suresh Kumar G. Isoquinoline alkaloids; highly specific RNA binders. 21st IUBMB and 12th FAOBMB International Congress of Biochemistry and Molecular Biology, July 30-August 7, 2009, Shangai, China.

Sinha R. & Suresh Kumar G. Isoquinoline alkaloids targeted to RNA triplex: Binding studies of berberine, palmatine and coralyne to poly(U).poly(A)*poly(U). Organic Chemistry: Trends in 21st Century, December 10-12, 2009, Kolkata.

Bhadra K. & Suresh Kumar G. Energetics of isoquinoline alkaloids-DNA binding by high sensitive calorimetry. International Conference on Physics Biology Interface, December 13-16, 2009, Kolkata.

Saha B., Islam M. M., Paul S., Samanta S., Ray S., Santra C., Ray Choudhury S., Dey B., Das A., Ghosh S., Mukhopadhyay S., Suresh Kumar G. & Karmakar P. DNA binding and hydrogen peroxide induced DNA cleavage activity of a unique Cu(II) complex, [Cu(mal)2](picH)2.5H2O. International Conference on Physics Biology Interface, December 13-16, 2009, Kolkata.

Paul P., Yadav R.C. & Suresh Kumar G. Biophysical studies on the DNA binding of thionine. Symposium on Recent Trends in Biophysics, February 13-16, 2010, Varanasi.

Saha I., Hossain M. & Suresh Kumar G. Interaction of cationic phenazinium dyes with DNA: a comparative study. Biophysical studies on the DNA binding of thionine. Symposium on Recent Trends in Biophysics, February 13-16, 2010, Varanasi.

Basu, A. & Suresh Kumar, G. DNA binding studies of synthetic 9-substitute berberine derivatives, Biophysical studies on the DNA binding of thionine. Symposium on Recent Trends in Biophysics, February 13-16, 2010, Varanasi.

Roy Chowdhury S., Islam, M. M. & Suresh Kumar G. Binding of the benzophenanthridine alkaloid sanguinarine to double stranded polynucleotides; insights into the structural and energetics aspects of the interaction. Symposium on Recent Trends in Biophysics, February 13-16, 2010, Varanasi.

Hossain, M. & Suresh Kumar G. New insights into thebase and sequence specificity of DNA binding by methylene blue and quinacrine. Symposium on Recent Trends in Biophysics, February 13-16, 2010, Varanasi.

Bhadra K. & Suresh Kumar G. Isoquinoline alkaloids as strong G-quadruplex stabilizing ligands of human telomeric DNA. Symposium on Recent Trends in Biophysics, February 13-16, 2010, Varanasi.

Pandya P., Islam M.M., Suresh Kumar G. & Kumar S. Small molecule nucleic acids binding; molecular approaches. Symposium on Recent Trends in Biophysics, February 13-16, 2010, Varanasi.

Giri P. & Suresh Kumar G. Comparative studies on the interaction of cytotoxic alkaloid coralyne with adenine rich RNA structures. Symposium on Recent Trends in Biophysics, February 13-16, 2010, Varanasi.

Mandal S., Murugan., Suresh Kumar G. & Chaudhuri K. Interaction of TAQ polymerase with bullet shaped gold nanoparticles; change of folding structure and reactivity, Symposium on Recent Trends in Biophysics, February 13-16, 2010, Varanasi.

Suresh Kumar G. Isoquinoline alkaloids as potential RNA binding natural products. Symposium on Recent Trends in Biophysics, February 13-16, 2010, Varanasi.

Dr. Asish K Sen

Sen A K, Choudhury B P, Mazumder K & Sarkar S. Bioactive polysaccharides and oligosaccharides: structure and synthesis. International Symposium on Organic Chemistry: Trends in 21st Century, December 10-12, 2009, Dept. of Organic Chemistry, Indian Association for the Cultivation of Science, Kolkata.

Sarkar S, Dutta S, Vijayan M & Sen A K. Synthesis of a unique mannopentose having specificity toward a lectin isolated from Musa paradisiaca, XXIV Carbohydrate Conference, December 7-9, 2009, Dept of Pharmacy, Lachoo Memorial College of Science & Technology, Jodhpur, Rajasthan.

STRUCTURAL BIOLOGY & BIOINFORMATICS DIVISION

Invited Lectures

Dr. M. C. Bagchi

Topic : Mathematical modeling & statistical methods in drug design : QSAR of anti tuberculosis drugs
Venue : Advances and Applications in Mathematical Modeling, NAL, Bangalore.
Date : May 23–25, 2009

Topic : Usefulness of calculated molecular descriptors in QSAR modeling
Venue : Sixth Indo-US Workshop on Mathematical Chemistry, Heritage Institute of Technology, Kolkata.
Date : January 8–10, 2010

Dr. Chitra Dutta

Topic : Selction-Mutation Balance in Genome Evolution
Venue : Department of Biochemistry & Biophysics, Kalyani University.
Date : February 25, 2010

Topic : Genome projects & Beyond
Venue : Gurudas College, Kolkata.
Date : September, 2009

Dr. Debasish Bhattacharyya

Topic : Role of bromelain in the disintegration of amyloid aggregates
Venue : Institute of Technology and Marine Engineering, PO. Amira, WB.
Date : March 24, 2010

Topic : Destabilization of protein aggregates by Bromelain
Venue : Department of Botany, Calcutta University Refreshers course.
Date : January 16, 2009

Topic : Toxins from Russell's viper venom of Eastern India origin
Venue : Department of Biotechnology, Tezpur University, Assam. At a National Seminer on venom toxins.
Date : December 18-19, 2009

Dr. Subrata Adak.

Topic : Ascorbate peroxidase from *Leishmania major* controls the differentiation of promastigotes by regulating oxidative stress
Venue : Indo-US Bilateral Workshop at Heriatage Village, Gurgaon.
Date : December 20, 2009.

Chairing a session

Prof. Siddhartha Roy

Chaird a session on International Symposium on "Frontiers of Protein Sciences" held at Osaka University, Japan during November 12-17, 2009.

Delivered a lecture at Hokkaido University, Sapporo, Japan.

Academic Performance/Teaching

Dr. M. C. Bagchi

Acted as a Guest Faculty Member, Paper setter and Examiner in Biostatistics for the M.S.(Pharm) course of National Institute of Pharmaceutical Education and Research (NIPER), Kolkata.

Served as a reviewer for Molecular Diversity, Current Computer Aided Drug Design journals.

Acted as an external member of AICTE project & member of project staff recruitment committee, Department of Pharmaceutical Technology, Jadavpur University.

Acted as a coordinator of Statistics course for Ph.D. students of IICB.

Acted as the Organizing Secretary of the Sixth Indo-US Workshop on Mathematical Chemistry held at the Heritage Institute of Technology, Kolkata during January 8-10, 2010.

Dr. Chitra Dutta

Guest Lecturer and Examiner: M. Sc. (Genetics), M.Sc (Microbiology), M. Sc. (Neuroscience), M. Sc. (Biotechnology) in Calcutta University; NIPER, Kolkata
Examiner: BIT – Kolkata, DOEACC – Kolkata

Dr. Debasish Bhattacharyya

Served as a guest lecturer at the Department of Bio-technology, Jadavpur University, Calcutta (M.Sc. Biotechnology, Semester I).

Served as a guest lecturer at the Department of Zoology, Bethune College, University of Calcutta (M.Sc. Part I, Proteins and Enzymology, Semester I).

Served as a guest lecturer at the Department of Life Sciences, University of Tripura, Agartala for one week in November 2009.

Dr. Nanda Ghoshal

Acted as Examiner for M.Pharm. final (thesis and corresponding oral) examination, J.U., held in June, 2009 at Pharmaceutical Technology Div., J.U.

Teaching at NIPER, Kolkata, as a Guest Faculty Member (for the Academic Year 2009-10).

Taken classes as a faculty in the training programme "Computer Course for Biologists" for Research Scholars, organized by IICB on the following topics during July-September, 2009: Introduction to Molecular Modelling. Molecular Modelling in relation to Drug Designing.

Evaluated a Research Project Proposal entitled, "Interaction of different Drug molecules (natural compounds) with human serum albumin: mass spectrometry, spectroscopic and molecular modeling studies", submitted to CSIR for funding.

Dr. Subrata Adak

Examiner in M.Sc. (Microbiology) and M. Sc. (Biochemistry) of Calcutta University.

Dr. Jayati Sengupta

Acted as external examiner for project thesis of MS (Pharm) students, NIPER, Kolkata.

Acted as external expert for assessment of JRF (up-gradation to SRF (CSIR)), IACS, Kolkata.

Took Basic and Advance Electron Microscopy classes under the Ph.D. course work program conducted by IICB, Kolkata.

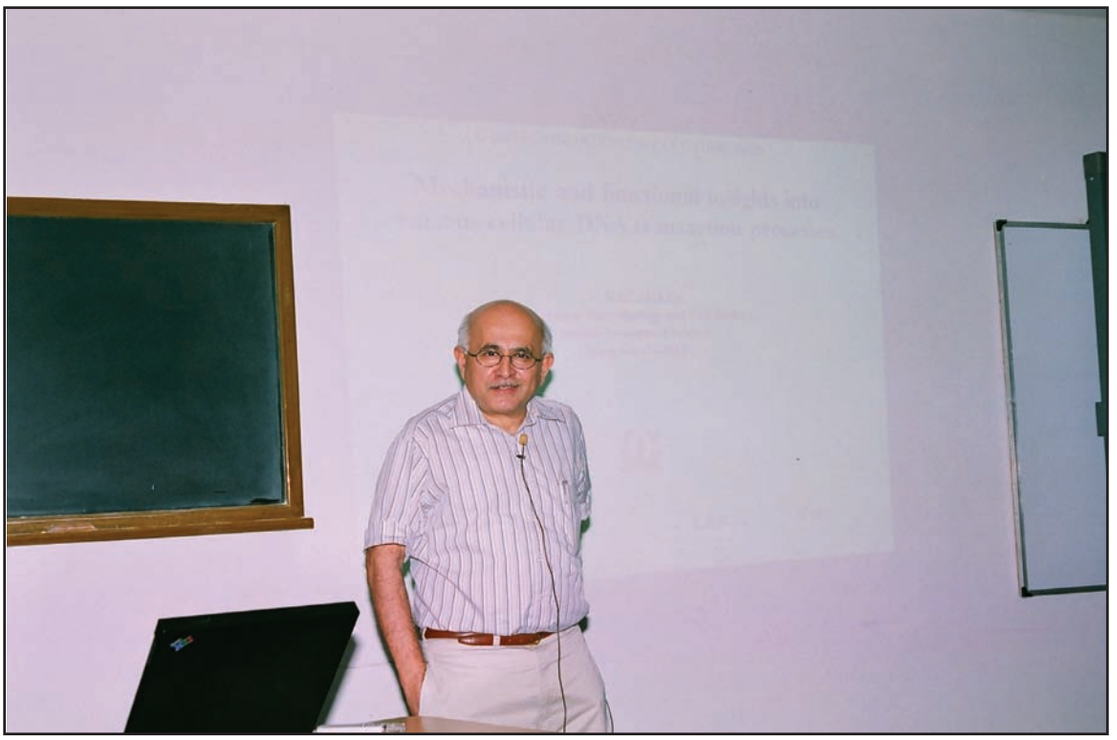
Deputation Abroad:

Dr Debasish Bhattacharyya

Participation at the International Conference of 'Separation Science' held at Singapore between August 26-28, 2009

Papers/Abstract Presented in the Conference:

Quantification of protein bound SDS by Rhodamine B: a method for identification of kinetically stable proteins' Reema Bhattacharya, Debratna Mukherjee and Debasish Bhattacharyya, International conference at Singapore, August 26-28, 2009.



External Funding

INFECTIOUS DISEASES & IMMUNOLOGY

Principal Investigator : **Dr. H. K. Majumder**
Project Title : Leishmania Donovani unusual bi-subunit topoisomerseI: solving the new twist in topoisomerase research related to evolution, functional conservation and preferential sensitivities to the specific inhibitors of Type IB family
Funding Agency : DBT, Govt. of India
Total Fund : Rs. 25 Lakhs
Duration : June 2006-June 2009

Principal Investigator : **Dr. Pijush K. Das**
Project title : Cyclic nucleotide signaling in the infectivity of an eukaryotic intracellular pathogen like Leishmania
Funding Agency : DST, Govt. of India
Total Fund : Rs. 22.00 Lakhs
Duration : November 2006 to November 2009

Principal investigator : **Dr. Chitra Mandal**
Project Title : The influence of 9-O-Acetylated cell surface expressed sialoglycan on angiogenesis of bone marrow-associated leukaemias
Funding Agency : ICMR-German
Funds (1st year) : Rs. 13,28,623
Duration : May 2009- April 2012

Principal investigator : Dr. Susanta Roychoudhury
Co-Investigator : **Dr. Chitra Mandal**
Project Title : Identification of new molecular targets for the development of anti-cancer agents"
Funding Agency : DBT, Govt. of India
Total Funds : Rs. 162.65 Lakhs
Duration : 2007-2012

Principal investigator : **Dr. Syamal Roy**
Project Title : New tools for monitoring drug resistance and treatment response in visceral leishmaniasis in the Indian subcontinent
Funding Agency : European Commission
Total Fund : 288,000.00 Euro
Duration : 2009-2013

Principal investigator : **Dr. Syamal Roy**
Project Title : Development of a DNA vaccine for Visceral Leishmaniasis
Funding Agency : European Commission
Total Funds : 130,000.00 Euro
Duration : 2009-2012

Principal Investigator : **Dr. Nahid Ali**
Project Title : A comparative evaluation of the potency and durability of Leishmania donovani gp63 DNA and Protein-based vaccines against experimental visceral leishmaniasis
Funding Agency : DST, Govt. of India
Total Fund : Rs. 23.23 Lakhs
Duration : 2008-2011

Principal Investigator : **Dr. Tripti De**
Project Title : Protective efficacy of purified constituents of Centella asiatica leaf extract in an experimental model of visceral leishmaniasis.
Funding Agency : DBT, Govt. of India
Total Fund : Rs. 20 Lakhs
Duration : March 2008-February 2011

Principal Investigator : **Dr. Malini Sen**
Project Title : Role of Wnt5a Signaling in Inflammation in Rheumatoid Arthritis
Funding Agency : DBT, Govt. of India
Total Fund : Rs. 54 Lakhs
Duration : April 2008-March 2011

Principal Investigator : **Dr. Malini Sen**
Project Title : Role of WISP3 in Maintenance of Cartilage Integrity.
Funding Agency : DST, Govt. of India
Total Funds : Rs. 35 Lakhs
Duration : March 2008 to Feb.2011

Principal Investigator : **Dr. (Mrs.) Mridula Misra**
Project Title : Tyr3-Octreotide derivatives : Synthesis, Radiolabeling and Application as Tumor Targeted Radiopharmaceuticals
Funding Agency : DAE, BRNS, Govt. of India
Total Fund : Rs. 19 Lakhs
Duration : 2009-2012

Principal Investigator : **Dr Mita Chatterjee Debnath**
Project title : Physico chemical and biological Evaluation of transition metal chelates of some sulfur containing amino acids
Funding Agency : ICMR Govt. of India
Total Fund : Rs. 3.1 Lakhs (for first year)
Duration : 2009-2012

Principal investigator : **Dr Mita Chatterjee Debnath**
Project title : Evaluation of some 99mTc chelates of fluoroquinolones and nitrofuryl Thiosemicarbazones for detecting sites of infection.
Funding Agency : Dept of Atomic Energy (BRNS). Govt.of India
Total fund : Rs 16.045 lakhs
Duration : 2010-2013

CELL BIOLOGY & PHYSIOLOGY

Principal Investigator : **Dr. S. N. Kabir**
Project title : Characterization of anti-HIV properties of Acaciaside-B and pre-clinical studies towards its development as a potential microbicide-spermicide formulation
Funding agency : DBT, Government of India
Total fund : Rs 36.87 lakh
Duration : July 2009 to June 2012

Principal Investigator : **Dr. Mrinal Kanti Ghosh**
Project Title : Regulation of Stat: Understanding Mechanisms to counteract Prostate Cancer
Funding Agency : DST-SERC
Total Fund : Rs. 5.43 lakhs
Duration : 2009-2010

Principal Investigator : Dr Chinmoy Chowdhury
Co-Investigator : **Dr Padma Das**
Project title : Chemical & Biological Evaluation of Selected Indian Medicinal Plants for Anti-cancer Activities
Funding agency : DST, Govt. of India, New Delhi
Total Fund : Rs 16, 22,000/-
Duration : 2010-2013

Principal Investigator : **Dr. Sandhya Rekha Dungdung**
Project Title : Purification and characterization of sperm motility inhibiting protein factor from goat epididymal plasma and fertility management.
Funding Agency : ICMR, Govt. of India
Total Fund : Rs. 8.41 lakhs.
Duration : 2007 – 2010

Principal Investigator : **Dr. Sandhya Rekha Dungdung**
Co-Investigator : Dr. Asoke Dasgupta
Project Title : Further studies on upgrading the recently developed computerized spectrophotometer sperm motility analyzer and its application for assessing sperm fertility potential.
Funding Agency : DST, Govt. of India
Total fund : Rs. 20.94 Lakhs
Duration : 2008 –2010

Principal Investigator : **Dr. Sib Sankar Roy**
Project Title : The role of Pitx2 homeodomain transcription factor to regulate ovarian function
Funding agency : DST
Total fund : Rs. 23.53 lakhs
Duration : 28.09.2007 to 27.09.2010

Principal Investigator : **Dr. Sib Sankar Roy**
Project Title : Isolation, molecular characterization and biological evaluation of anti-diabetic principles from a few Indian medicinal plants
Funding agency : DST-Industry-Institute
Total fund : Rs. 20.26 lakhs
Duratiion : 25.06.2007 - 24.06.2010

MOLECULAR & HUMAN GENETICS

Principal Investigator : **Dr. Susanta Roychoudhury**
Co-Investigator : Dr. Chitra Mondal
Project Title : Identification of new molecular targets for the development of anti-cancer agents.
Funding Agency : DBT, Govt. of India
Total Fund : Rs. 162.65
Duration : 2006 - 2011

Principal Investigator : **Dr. Susanta Roychoudhury**
Project Title : Identification of susceptibility alleles for the development of head and neck cancer in Indian population
Funding Agency : DBT, Govt. of India
Total Fund : Rs. 44.51
Duration : 2006 - 2010

Principal Investigator : **Dr. A. K. Giri**
Project Title : Molecular Epidemiology and Environmental Health
Funding Agency : Fogarty International Training Fund from the University of California, Berkeley, USA
Total Fund : $16,500.00
Duration : 2009 - 2010.

Principal Investigator : **Dr. A. K. Giri**
Project Title : PRAMA Project under UKIERI
Funding Agency : University of Manchester
Total Fund : 4072.00 GBP
Duration : 2009 - 2010

Principal Investigator : **Dr. Suvendra Nath Bhattacharyya**
Co-Investigator : Prof. Siddhartha Roy
Project Title : Role of the ELAV Protein HuR in microRNA-mediated Gene Regulation in Normal and Transformed Human Cells
Funding Agency : Indo-Swiss Joint Research Projects, DST
Total Fund : Rs. 27.5 lakh
Duration : February 2009-January 2012

Principal Investigator : **Dr. Suvendra Nath Bhattacharyya**
Project Title : Mechanism of mRNA compartmentalization in the cytoplasm of mammalian cells
Funding Agency : The Wellcome Trust London
Total Fund : 472,118 GBP
Duration : October 2009 - September 2014

Principal Investigator : **Dr. Suvendra Nath Bhattacharyya**
Project Title : Co-regulation of gene expression by miRNA and AU-rich element binding protein HuR in mammalian cancer cells
Funding Agency : The Lady Tata Memorial Trust
Total Fund : Rs. 31 lakh
Duration : April 2009 - March 2014

DRUG DEVELOPMENT, DIAGNOSTICS & BIOTECHNOLOGY

Principal Investigator : **Dr.(Mrs.) Aparna Gomes**
Co-investigator : **Dr. J. R. Vedasiromoni**
Project Title : Pharmacological and molecular actions of Snake venom anticancer protein fraction (s) on experimental animals and on leukemic cell lines
Funding Agency : ICMR, Govt. of India
Total Fund : Rs.23.8 lakhs
Duration : 2007 – 2010

Principal Investigator : **Dr. Snehasikta Swarnakar**
Project Title : Targeting metalloproteinase(s) for new therapeutic in gastric cancer
Funding Agency : DBT, Govt. of India
Total Fund : Rs.9.0 lakhs.
Duration : 2008 – 2011

Principal Investigator : **Dr. Snehasikta Swarnakar**
Co-investigator : **Dr.(Mrs.) Aparna Gomes**
Project Title : Prevention of gastric ulceration by black tea: An insight intoextracellular matrix remodeling of gastric tissues
Funding Agency : NTRF
Total Fund : Rs.8 lakhs.
Duration : 2009 – 2012

Principal Investigator : **Dr. Sharmila Chattopadhyay**
Project Title : Role of Glutathione as a signaling molecule
Funding agency : DST., Govt. of India.
Total Cost : Rs. 23 lakhs
Duration : 2007-2010

Principal Investigator : **Dr. Sharmila Chattopadhyay**
Project Title : Indian Medicinal Plants to combat kala-azar"
Funding agency : ICMR, Govt. of India.
Total Cost : Rs. 28.5 lakhs
Duration : 2007-2010

CHEMISTRY

Principal investigator : **Dr. B. C. Pal** and Prof. S. Bhattacharya (Visva Bharati)
Title of Project : Isolation, molecular characterization and biological evaluation of anti-diabetic principle(s) from Indian medicinal plants
Funding agency : DST
Total Fund : Rs. 20.26 lakhs (IICB component)
Duration : 2007 –2010

Project Coordinator and Coinvestigator : **Dr. Nirup Bikash Mondal**
Principal Investigators : **Dr. Smritinath Chakraborty** and Dr. Sanchita Lala
Title of Project : Active targeting of nanoparticles grafted with ligands to the cells of the reticulo-endothelial system by receptor mediated endocytosis and their application against macrophage-associated diseases
Funding Agency : DBT
Total Fund : Rs. 51.72 lakhs
Duration : 2008-2011

Principal investigator : **Dr Partha Chattopadhyay**
Title of project : Synthesis of benzannulated medium ring heterocycles by using intramolecular Buchwald–Hartwig reaction and their binding studies to nucleic acids and proteins
Funding Agency : DST
Total Funds : Rs.18 Lakhs
Duration : 2008-2011

Principal Investigator	:	**Dr. Asish K Sen**
Title of project	:	Chemical characterization and modification of coir fiber for enhanced longevity, and their physico-chemical studies
Funding Agency	:	COIR BOARD, Govt. of India
Total Fund	:	Rs. 29.48 Lakhs
Duration	:	October 2006- September 2011

Principal Investigator	:	**Dr. Chinmay Chowdhury**
Co-Investigator	:	Dr. Padma Das
Title of project	:	Chemical & biological evaluation of selected Indian medicinal plants for anti-cancer Activities
Funding Agency	:	DST
Total Fund	:	Rs. 16.22 lakhs
Duration	:	2010 - 2013

STRUCTURAL BIOLOGY & BIOINFORMATICS DIVISION

EXTERNAL FUNDING

Principal Investigator	:	**Dr. M. C. Bagchi**
Project Title	:	Anti-tubercular Drug Design by Calculated Molecular Descriptors A QSAR Approach
Funding Agency	:	Department of Biotechnology (Govt. of India).
Total Funds	:	Rs. 12.07 lakhs
Duration	:	September 2006 – September 2010

Principal Investigator	:	**Dr. Chitra Dutta**
Project Title	:	Establishment of Sub-DIC at IICB
Funding Agency	:	Department of Biotechnology, (Govt. of India).
Total Funds	:	Rs. 53 lakhs
Duration	:	2002-2007 (extended up to 2012)

Principal investigator	:	**Dr Debasish Bhattacharyya**
Project title	:	Regulation of activity and assembly of multineric proteins
Funding agency	:	DST
Total funds	:	Rs. 20.00 Lacs
Duration	:	2006 December – 2009 November(under consideration of extension)

Principal Investigator	:	**Dr. Nanda Ghoshal**
Project Title	:	Designing Potential Lead Molecules for Inhibition of Siderophore Biosynthesis in Mtb.
Funding Agency	:	CSIR, (OSDD) Govt. of India
Total Fund	:	Rs. 14.244 lakhs
Duration	:	December 2009 – December 2011

Principal investigator	:	**Dr. Saumen Datta**
Project title	:	Structural Insights into the Type III Secretion System (TTSS) of Pathogenic Bacteria
Funding agency	:	DST
Total funds	:	Rs. 22.51 Lacs
Duration	:	2007-2010

Publications

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Kar S, Ukil A, Sharma G & Das PK. 2010. MAPK-directed phosphatases preferentially regulate pro- and anti-inflammatory cytokines in experimental visceral leishmaniasis: involvement of distinct protein kinase C isoforms. *J. Leukocyte Biol.* **88:** 9-20.

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CELL BIOLOGY & PHYSIOLOGY

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DRUG DEVELOPMENT, DIAGNOSTICS & BIOTECHNOLOGY

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Books/Reviews/Popular Articles

INFECTIOUS DISEASES & IMMUNOLOGY

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MOLECULAR & HUMAN GENETICS

Polya DA, Polizzotto ML, Fendorf S, Rodriguez-Lado L, Hegan A, Lawson M, Rowland HAL, Giri AK, Mondal D, Sovann C, Al Lawati WMM, van Dongen BE, Gilbert P and Shantz A. 2010. Arsenic in ground waters of cambodia. *In*: Water resources and development in South-East Asia" (Eds. K Irvine, T Murphy, V Vanchan & S Vermette), SE Asia Centre, New York, pp. 31-56.

DRUG DEVELOPMENT, DIAGNOSTICS & BIOTECHNOLOGY

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Chattopadhyay S. Novel neutraceutical properties of *Stevia rebaudiana* (Bertoni) Bertoni. *In*: Bioactive natural products (Eds. VK Gupta & AK Verma), Studium Press LLC, USA, 2009.

Banerjee A and Chattopadhyay S. *Phyllanthus amarus*: A versatile plant for therapeutic importance. *In* "Prospective in Cytology & Genetics" (Eds. AK Giri, A Mukherjee & M Mukherjee), Vol. 14, pp. 251-260, 2009.

Paul S and Swarnakar S. Arsenic toxicity in embryo implantation: matrix metalloproteinases as key regulator. *In:* Prospective in cytology & genetics" (Eds. AK Giri, A Mukherjee & M Mukherjee), Vol. 14, pp. 45-54, 2009.

CHEMISTRY

Maiti M and Suresh Kumar G. 2009**.** Biophysical aspects and biological implications of the interaction of benzophenanthridine alkaloids with DNA. *Biophys. Rev*. **1:** 119-129.

Doctorates from the Institute

INFECTIOUS DISEASES & IMMUNOLOGY

No.	*Name of Ph.D candidate*	*Title of the thesis*	*Name of Supervisor*	*Year*
1.	Dr. Abha Bhagat	Gene induction in host-pathogen interaction	Dr. Rukhsana Chowdhury	2009
2.	Dr. Amit Roy	Inhibition of Eukaryotic DNA topoisomerase I: Understanding the mechanisms of cell death and Drug Resistance	Dr. Hemanta K. Majumder	2009
3.	Dr. Angana Ghoshal	Exploring the role of sialic acids in Leishmaniasis	Dr. Chitra Mandal	2009
4.	Dr. Chandan Mandal	Enzymatic modulation of Sialic acid in childhood acute lymphoblastic leukemia (ALL)	Dr. Chitra Mandal	2009
5.	Dr. Kausik Paul	Studies on anti-leishmanial compounds of synthetic and herbal origin	Dr. Santu Bandyopadhyay	2009
6.	Dr. Siddhartha Kumar Bhaumik	Complete soluble antigen from a UDP -galactose N-Acetylglucosamine-1-4-galactosyl transferase expressing *Leishmania donovani* induces complete protection in an experimental model of visceral leishmaniasis	Dr. Tripti De	2009
7.	Dr. Subha Banerjee	Studies on the role of membrane fluidity of antigen presenting cells in experimental visceral leishmaniasis : Therapeutic role of cholesterol	Dr. Syamal Roy	2009
8.	Dr. Waliza Answar	Human C-reactive protein: Its potential role in different pathological conditions	Dr. Chitra Mandal	2009
9.	Dr. Arun Kumar Haldar	Studies on the cellular and molecular basis of immunoregulation by selective compounds in experimental visceral leishmaniasis	Dr. Syamal Roy	2010
10.	Dr. Partha Palit	Pharmacological study and liposomal formulation evaluation of novel 4-amino quinaldine derivatives and generic drugs as anti-leishmanial, anti-cancer and anti-microbial agents	Dr. Nahid Ali	2010
11.	Dr. Smriti Mondal	Immune regulation in visceral leishmaniasis	Dr. Nahid Ali	2010

No.	Name of Ph.D candidate	Title of the thesis	Name of Supervisor	Year
12.	Dr. Suchandra Chowdhury	The study of 9-*O*-acetylated sialoglycoconjugates on haematopoietic precursor cells	Dr. Chitra Mandal	2010
13.	Dr. Susanta Kar	Signaling events involved in manipulating macrophage defense machinery by natural immunomodulators using visceral leishmaniasis as model macrophage disease	Dr. Pijush K. Das	2010

CELL BIOLOGY & PHYSIOLOGY

No.	Name of Ph.D candidate	Title of the thesis	Name of Supervisor	Year
14.	Dr. Shrabanti Kumar	Evaluation of spermicidal potential and assessment of safety margins of some plant-based terpenoids in animal models	Drs. S. N. Kabir & N. B. Mondal	2009
15.	Dr. Sudipa Saha Roy	Elucidation of reduced survival of erythrocytes during anemia in visceral leishmaniasis	Dr. Tuli Biswas	2009
16.	Dr. Reena Haobam	Neural transplantation in experimental model of Parkinson's disease	Dr. K.P. Mohanakumar	2010

MOLECULAR AND HUMAN GENETICS

No.	Name of Ph.D candidate	Title of the thesis	Name of Supervisor	Year
17.	Dr. Ashima Bhattacharjee	Studies on glaucoma genes : Molecular defects in primary open angle glaucoma patients	Dr. Kunal Ray	2009
18.	Dr. Chaitali Mishra	Analysis of Polymorphic variant of wild type and Mutant p53 Gene in Head and Neck Cancer	Dr. Susanta Roychoudhury	2009
19.	Dr. Nilanjana Bhattacharjee	Studies on the biochemical characterization of proteinaceous protease inhibitor of plant origin	Dr. Samir Dutta	2009
20.	Dr. Sanhita Roy	Studies on the characterization of plant protease inhibitor for understanding their structure function relationship	Dr. Samir Dutta	2009
21.	Dr. Sujata De Chaudhuri	Assessment of health effects, cytogenetic damages and genetic variants in the population exposed to arsenic through drinking water	Dr. Asoke K. Giri	2010

DRUG DEVELOPMENT/ DIAGNOSTIC& BIOTECHNOLOGY

No.	*Name of Ph.D candidate*	*Title of the thesis*	*Name of Supervisor*	*Year*
22.	Dr. Amrita Chakraborty	Stimulation of menthol production in cell culture of *Mentha piperita*	Dr. Sarmila Chattopadhyay	2009
23.	Dr. Avijit Poddar	Potential Herbal Antileishmanial Agent to Combat Visceral Leishmaniasis	Dr. Sarmila Chattopadhyay	2009
24.	Dr. Krishnendu Ganguly	Studies on extra-cellular matrix remodeling and angiogenesis in non-steroidal anti-inflammatory drug-induced gastric ulcer : Effect of melatonin	Dr. S. Swarnakar	2009
25.	Dr. Samudra Prosad Banik	Regulation of secretion of sucrase and cellobiase in the secretory pathway of *Termitomyces clypeatus*	Dr. Suman Khowala	2009
26.	Dr. Subho Dasgupta	Experimental evaluation of scorpion venom as an anti-cancer agent	Dr. Aparna Gomes	2009
27.	Dr. Sudeshna Chowdhury	Co-aggregation of sucrase with cellobiase in the regulated secretory pathway of filamentous fungus *Termitomyces clypeatus*	Dr Suman Khowala	2009
28.	Dr.Krishnendu Ganguly	Studies on extra cellular matrix remodeling and angiogenesis in nonsteroidal anti-inflammatory drug-induced gastric ulcer: Effect of melatonin	Dr S Swarnakar	2009
29.	Dr. Annalakshmi Chinniah	Newer Anti Peptic Ulcer Principles(s) from Indian Biodiversity : Target Based Search in Preclinical Experimental Models	Dr. Pratap K. Das	2010

CHEMISTRY

No.	*Name of Ph.D candidate*	*Title of the thesis*	*Name of Supervisor*	*Year*
30.	Dr. (Mrs.) Churala Pal	Synthetic studies and pharmacological evaluation of bis- and tris-indolyl alkane/arane derivatives	Dr. Parasuraman Jaisankar	2009
31.	Dr. Debkumar Nandi	Search for safe antineoplastic and anti inflammatory bioactive compounds from traditional indian medicinal plants	Drs. P. Jaisankar & J.R. Vedasiromoni	2009
32.	Dr. Md. Maidul Islam	Interaction of isoquinoline alkaloids with ribonucleic acids	Dr. G. Suresh Kumar	2009

STRUCTURAL BIOLOGY & BIOINFORMATICS

No.	*Name of Ph.D candidate*	*Title of the thesis*	*Name of Supervisor*	*Year*
33.	Dr. Soumi Guha Polley	Structural basis of protein-protein and protein-nucleic acid interaction	Prof. Siddhartha Roy	2009
34.	Dr. Reema Bhattacharya	Fruit and stem bromelain from pineapple (*Ananus comosus*) : Stabilization and biochemical characterization of the enzymes	Dr. Debasish Bhattacharya	2009

Honours and Awards

INFECTIOUS DISEASES & IMMUNOLOGY

Dr. H. K. Majumder

- Member of the Institutional Ethical Committee, Institute of Post Graduate Medical Education & Research (IPGMER), Kolkata. 2007-till date.
- Member of the Research Advisory Committee of the Central Sericulture Research & Training Institute, Berhampur, Murshidabad, West Bengal.
- Member of the Selection Committee for SRF/RA of CSIR.
- Member of the Section Committee (VII) of Indian National Science Academy (FNA)
- Member of the Fellowship Scrutiny Committee of National Academy of Sciences, India (FNASc).
- Sir J.C. Bose National Fellowship by the Department of Science and Technology, Government of India in 2009.
- Chairman of the NASI, Allahabad Kolkata Local Chapter (NASI), w.e.f. 31.12.2007.
- Chairman**,** Expert Committee for State Innovation Award, Govt. of West Bengal.
- Chairman, State Level Climatic Change Committee**,** Govt. of West Bengal.
- Working Chairman of the West Bengal State Council of Science & Technology-2004 onwards.

Dr. Pijush K. Das

- Member of the American Association of Immunologists.
- Departmental Core Committee Member of the Recruitment and Assessment Board (RAB) of CSIR.
- Member of CSIR-NET Life Sciences
- Member of Board of Studies of Calcutta University
- Reviewer of National & International journals.

Dr. Chitra Mandal

- Elected Fellow of The Indian National Science Academy (F.N.A.), India in the year of 2009
- Elected member of West Bengal Academy of Science and Technology (WAST) in the year 2009
- Reviewer of National and International journals
- Reviewer of National and International projects for National and International fundings

Dr. Syamal Roy

- Member, Scientific Advisory Committee (SAC), Institute of Pathology, Indian Council of Medical Research (ICMR), Safdarjung Hospital Campus, New Delhi - 110029
- Member, Scientific Advisory Committee (SAC), Rajendra Memorial Research Institute of Medical Sciences (RMRI), Indian Council of Medical Research (ICMR), Agam Kuan, Patna-800007

Dr. Uday Bandopadhay

- Editorial board member of the Journal "World J Gastrointestinal Pathophysiology.

CELL BIOLOGY & PHYSIOLOGY

K. P. Mohanakukar

- Elected for the Lalitha Kameswaran Oration of the South Regional Indian Pharmacological Society and delivered the talk at PSG Institute of Medical Sciences and Research on the 12th November 2009.
- Elected member of the Committee on Aid and Education in Neurochemistry (CAEN) of the International Society for Neurochemistry, UK.
- Elected President of SNC, India at its last General Body meeting held on 14th December 2009 at CUSAT, Cochin.

Dr. Sib Sankar Roy

- Appointed as a UGC visiting teacher by Tripura University, Agartala.

MOLECULAR & HUMAN GENETICS

Dr. S. Adhya

- Member, Board of Examiners and Ph.D Committee, Calcutta University
- Member, Research Advisory Committee, Monovikas Kendra, Calcutta
- Member, Project Advisory Committee, Center for DNA Fingerprinting and Diagnostics, Hyderabad
- Member, Board of Studies, St. Xavier's College.

Dr. Keya Chowdhury

- Member, Departmental Core Committee of the Recruitment and Assessment Board (RAB) of CSIR for CFTRI, Mysore.
- Reviewer of papers for (i) Journal of Bacteriology, ASM Press, USA; (ii) Infection & Immunity, ASM press, USA (iii) Journal of Clinical Microbiology, ASM press, USA (iv) Antimicrobial Agents & Chemotherapy, ASM Press, USA (v) Applied & Environmental Microbiology, ASM Press, USA (vi) Clinical and Vaccine Immunology, ASM Press USA; (vii) PLoS One, Public Library of Science; (viii) BMC Immunology, Biomed Central, London, UK; (ix) BMC Bioinformatics, Biomed Central, London, UK (x) Journal of Cellular Biochemistry, Wiley-Interscience, USA; (xi) Microbial Pathogenesis, Elsevier, The Netherlands; (xii) Apoptosis, Springer, Germany; (xiii) Journal of Medical Microbiology, SGM,UK (xiv) Food and Chemical Toxicology, Elsevier, The Netherlands (xv) Journal of Public health & Epidemiology, Academic journals, Africa.

Dr. A. K. Giri

- Elected as a Member of the Executive Council (2009-2013) of the International Association of Environmental Mutagen Societies (IAEMS).

Dr. Susanta Roychowdhury

- Elected as the Fellow, National Academy of Science, India Fellow, West Bengal Academy of Science and Technology

Dr. Suvendra Nath Bhattacharya

- International Senior Research Fellow of the Wellcome trust London, UK start date 01 October 2009.
- Short-term postdoctoral fellowship from International HFSPO (Human Frontier Science Program Organization).
- Young Researcher award from the Lady Tata Memorial Trust in April 2009

DRUG DEVELOPMENT, DIAGNOSTICS & BIOTECHNOLOGY

Dr. Snehasikta Swarnakar

- Prof AN Bhaduri Memorial lecture award 2009 by Society of Biological chemist, India, 2009
- Advisory Board member of Africa Bound Corporation, Senegal, Africa and BIRDS, WB, India
- Biographical record in Who's Who in the World 2010, by Marquis publication, USA
- Advisory Board member of Africa Bound Corporation, Senegal, Africa and BIRDS, WB, India

Dr. Suman Khowala

- Nominated as Member of management council of The Biotech Research Society, India (2009-11).
- Nominated as General Secretary of Kolkata Chapter of IICB-Jadavpur University, The Biotech Research Society, India (2009-11).

Dr. Sharmila Chattopadhyay

- Received US$ 500 as cash prize as a best presenter from GORDON RESEARCH CONFERENCE on "PLANT METABOLIC ENGINEERING", Newhampshire, USA. July 12-17th 2009.

Dr. Samir Kr. Dutta

- Panel judge, 14th AICCG and Fogarty International Workshop, CGCRI, Kolkata, December, 1-4, 2009.

CHEMISTRY

Dr. G. Suresh Kumar

- Editor, *International Journal of Physical Sciences* (Academic Journal)
- Member, Editorial Advisory Board, *African Journal of Biochemistry* Research (Academic Journal)
- Member, Editorial Advisory Board: *The Open Natural Product Journal* (Bentham Sciences)
- Elected to the National Executive Council of Indian Biophysical Society (2009-2011)
- Elected as Secretary, DNA Society of India (2009-2014)

Dr. Partha Chattopadhyay

- Member of the Editorial Board of Referees, ARKIVOC, USA from 2008-onwards

Dr. Asish K Sen

- Elected as Hon. Vice President of the Association of Carbohydrate Chemists & Technologists (India) 2008-2010
- Member, Advisory Committee, Niper-Kolkata

Dr. A. K. Banerjee

- Acting as Project Director of NIPER, Kolkata.
- Member of the Steering Committee, Dept. of Pharmaceuticals, Ministry of Chemicals & Fertilizers, Govt. of India
- Member of Joint Counseling Committee for the Master program in NIPER Mohali-Punjab

STRUCTURAL BIOLOGY & BIOINFORMATICS DIVISION

Prof. Siddhartha Roy

- G.P. Chatterjee memorial award (2009-10) from Indian Science Congress Association.

Dr. Chitra Dutta

- Member, Editorial Board, International Journal of Soft Computing & Bioinformatics
- Member, Advisory Board, NIPER-Kolkata
- Reviewer, Nucleic Acids Research, DNA Research, Bioinformatics, BMC Genomics, BMC Evolutionary Biology, Microbiology etc.

Dr. Debasish Bhattacharyya

- Selected as a member of the editorial board of the 'Journal of Chromatography B' for 3 years term (2008-2011).

Dr. Nanda Ghoshal

- Received Dr. Gopal Chandra Bhattacharyya Memorial Science Award, 2010, from Science Association of Bengal.
- Reviewer, J. Medicinal Chemistry, J. Bioorganic & Medicinal Chemistry, *J Mol Graph Model*., Chemical Biology & Drug Design, Eur. J. Med. Chem.
- Reviewer, Projects submitted for financial assistance to CSIR.

Dr. Subrata Adak

- Awarded Raman Research Fellowship

Dr. Krishnananda Chattopadhyay

- Awarded the Indo US Science and Technology Fellowship

Staff List of IICB as on APRIL 01, 2010

Staff Strength at a Glance

Director	...	...	1
Scientist – Gr. IV	...	...	71
Engineer	...	...	4
Technical – Gr. III	...	...	50
Technician – Gr. II	...	...	38
Helper – Gr. I	...	...	18
Ministerial Officer	...	...	18
Ministerial Staff	...	...	48
Gr. D (Non-Technical)	...	...	15
Canteen Staff	...	...	10
TOTAL	**...**	**...**	**273**

Detailed Staff List

Scientific and Technical

Sl. No.	Employee's Name	Emp. ID	Deisgnation
1.	Prof. Siddhartha Ray	489	*Director*
2.	Dr. H.K. Majumdar	23	*Scientist Gr. IV(6)*
3.	Dr. Samit Adhya	37	*Do*
4.	Dr. Pijush K. Das	40	*Do*
5.	Dr. S.B. Mondal	76	*Do*
6.	Dr. K.P. Mohanakumar	77	*Do*
7.	Dr. Tarun K. Dhar	63	*Do*
8.	Dr. A.K. Sen (Jr)	65	*Do*
9.	Dr. (Mrs.) Chitra Mandal	60	*Do*
10.	Dr. Anil K. Ghosh	68	*Do*

Sl. No.	Employee's Name	Emp. ID	Deisgnation
11.	Dr. Syamal Roy	93	*Do*
12.	Dr. (Mrs.) Keya Chaudhuri	83	*Do*
13.	Dr. Sumantra Das	87	*Do*
14.	Dr. S.B. Mukhopadhyay	80	*Scientist Gr. IV(5)*
15.	Dr. Santu Bandyopadhyay	97	*Do*
16.	Dr. Partha Chattopadhyay	81	*Do*
17.	Dr. Manish Ch. Bagchi	78	*Do*
18.	Dr. S.N. Kabir	90	*Do*
19.	Dr. (Mrs.) Chitra Dutta	95	*Do*
20.	Dr. Ashok Kumar Giri	402	*Do*
21.	Dr. Debashish Bhattacharya	96	*Do*
22.	Dr. Shyamal Kumar Dana	86	*Do*
23.	Dr. (Mrs.) Aparna Gomes	91	*Do*
24.	Dr. Nirmalendu Das	100	*Do*
25.	Dr. (Mrs.) Nahid Ali	103	*Do*
26.	Dr. Susanta Roychowdhury	98	*Do*
27.	Dr. U.S. Chowdhury	84	*Do*
28.	Dr. Kunal Ray	415	*Do*
29.	Dr. M.I. Khan	548	*Do*
30.	Dr. Ashish Kr. Sen (Sr)	55	*Scientist Gr. IV(4)*
31.	Dr. Aparesh Bhattacharya	59	*Do*
32.	Dr. G. Suresh Kumar	105	*Do*
33.	Dr. (Miss) Moonmoon Bhowmik	110	*Do*
34.	Dr. Samir Kr. Dutta	111	*Do*
35.	Dr. Sukdeb Bandopadhyay	102	*Do*
36.	Dr. Nirup Bikash Mondal	107	*Do*
37.	Dr. (Mrs.) Tuli Biswas	109	*Do*
38.	Dr. Arun Bandyopadhyay	445	*Do*
39.	Dr. P. Jaisankar	112	*Do*

Sl. No.	Employee's Name	Emp. ID	Deisgnation
40.	Dr. S.N. Chakraborty	94	*Do*
41.	Dr. Rupak Kr. Bhadra	124	*Do*
42.	Dr. (Mrs.) Rukhshana Chowdhury	115	*Do*
43.	Dr. (Mrs.) Nanda Ghoshal	119	*Do*
44.	Dr. Ram Chandra Yadav	154	*Do*
45.	Dr. Ranjan Mukhopadhyay	114	*Do*
46.	Dr. Asish Kr. Banerjee	116	*Do*
47.	Dr. (Mrs.) Suman Khowala	118	*Do*
48.	Dr. Tushar Kanti Chakraborty	99	*Do*
49.	Dr. (Mrs.) S.R. Dungdung	120	*Do*
50.	Dr. Tanmoy Mukherjee	125	*Do*
51.	Dr. Sibsankar Ray	443	*Do*
52.	Dr. Pratap Kr. Das	62	*Scientist Gr. IV(3)*
53.	Sri U.K. Barua	464	*Do*
54.	Dr. (Mrs.) Padma Das	117	*Do*
55.	Dr. (Mrs.) Debjani Mondal	123	*Do*
56.	Dr. Aditya Konar	441	*Do*
57.	Mrs. N.V.M. Khalko	122	*Do*
58.	Dr. (Mrs.) Tripti De	433	*Do*
59.	Dr. Soumen Datta	503	*Do*
60.	Dr. Chinmay Chowdhury	520	*Do*
61.	Dr. Uday Bandopadhyay	521	*Do*
62.	Dr. K.N. Chattopadhyay	523	*Do*
63.	Dr. Mrinal Kanti Ghosh	524	*Do*
64.	Dr. (Mrs.) Malini Sen	527	*Do*
65.	Dr. (Mrs.) Jayati Sengupta	532	*Do*
66.	Dr. S.N. Bhattacharya	530	*Do*
67.	Dr. (Mrs) Sarmila Chattopadhyay	447	*Do*
68.	Dr. Subrata Adak	472	*Do*

Sl. No.	Employee's Name	Emp. ID	Deisgnation
69.	Dr. (Miss) Snehasikta Swarnakar	473	*Do*
70.	Dr. Biswadip Banerji	540	*Do*
71.	Dr. Subhas Ch. Biswas	547	*Do*
72.	Dr. Saraswati Garai	528	*Scientist Gr. IV(1)*
73.	Dr. (Mrs.) Mridula Misra	142	*Technical Officer Gr. III(7)*
74.	Dr. (Mrs.) Krishna Das Saha	143	*Do*
75.	Sri H.N. Roy	152	*Do*
76.	Dr. (Mrs.) S.E. Besra	145	*Do*
77.	Sri Tapan Kumar Mukherjee	140	*Do*
78.	Sri Tapan Kr. Chakraborty	159	*Do*
79.	Sri A.K. Das	151	*Do*
80.	Dr. (Mrs) Mita Chatterjee Debnath	432	*Technical Officer Gr. III(6)*
81.	Sri S.K. Sahoo	163	*Do*
82.	Dr. S. Majumdar	164	*Do*
83.	Sri Chirantan Debdas	535	*Do*
84.	Sri Mohan Lal Jana	167	*Do*
85.	Dr. Prashanta Kr. Chakraborty	169	*Do*
86.	Dr. Kalidas Paul	168	*Do*
87.	Sri Shekhar Ghosh	467	*Do*
88.	Sri A.K. Bairagi	165	*Do*
89.	Sri Sandip Saha	494	*Ex. Engineer Gr. III(6)*
90.	Sri Susanta Ray	514	*Asst. Exec. Engineer Gr. III(4)*
91.	Sri B. Jayakumar	517	*Do*
92.	Mrs. Nirali Bage	466	*Junior Engineer, Gr. I*
93.	Sri Samir Kr. Roy	171	*Technical Officer Gr. III(5)*
94.	Dr. Ashok Kumar Dasgupta	172	*Do*
95.	Sri Narayan Ch. Ghosh	499	*Do*
96.	Sri Surajit Mohan Roy	166	*Do*
97.	Sri Gautam Gupta	170	*Do*

Sl. No.	Employee's Name	Emp. ID	Deisgnation
98.	Sri Binayak Pal	448	*Do*
99.	Mrs. Aparna Laskar	449	*Do*
100.	Dr. Sankar Kumar Maitra	174	*Do*
101.	Dr. (Mrs) Gayatri Tripathi	462	*Do*
102.	Dr. Ardhendu Kr. Mandal	175	*Do*
103.	Dr. Tapas Sarkar	177	*Do*
104.	Dr. Subhagata Ghosh Miss	179	*Do*
105.	Sri Arupesh Majumdar	180	*Do*
106.	Sri Sekhar Mukherjee	477	*Do*
107.	Sri R.N. Mandi	185	*Do*
108.	Dr. Ramdhan Majhi	184	*Do*
109.	Sri P. Gangopadhyay	186	*Do*
110.	Sri Asish Mullick	187	*Do*
111.	Mrs. Dipika Roy	188	*Do*
112.	Sri Kshudiram Naskar	162	*Technical Officer Gr. III(4)*
113.	Sri Rajat Bandopadhyay	181	*Do*
114.	Mrs. Purnima Chatterjee	173	*Do*
115.	Mrs. Banasri Das	176	*Do*
116.	Sri Diptendu Bhattacharya	178	*Do*
117.	Sri E. Padmanaban	496	*Do*
118.	Sri Pratap Ch. Kayal	182	*Do*
119.	Sri Sandip Chowdhury	411	*Technical Assistant Gr. III(2)*
120.	Mrs. Arti Khetrapaul	463	*Do*
121.	Sri Swapan Kr. Mondal	465	*Do*
122.	Sri Jishu Mandal	495	*Technical Assistant Gr. III(1)*
123.	Sri Debashis Banik	513	*Do*
124.	Sri Sandip Chakraborty	516	*Do*
125.	Sri T. Muruganandan	539	*Do*
126.	Sri Chinthapalli Balaji	545	*Do*

Sl. No.	Employee's Name	Emp. ID	Deisgnation
127.	Sri Ajoy Kr. Pramanik	195	*Technician Gr. II(4)*
128.	Sri M.B. Malakar	219	*Do*
129.	Sri S.K. Basak	220	*Do*
130.	Sri Phelaram Dhank	309	*Do*
131.	Sri Goutam Malik	224	*Do*
132.	Sri Gopal Ch. Sarkar	234	*Do*
133.	Sri P.K. Chanda	236	*Do*
134.	Sri S.N. Mondal	237	*Do*
135.	Sri S.K. Prodhan	239	*Do*
136.	Sri S.C. Das	241	*Technician Gr. II(3)*
137.	Sri S.R. Tudu	251	*Do*
138.	Sri Swapan Kumar Naskar	244	*Do*
139.	Md. Ayub Shah	344	*Do*
140.	Sri Sheo Shankar Verma	242	*Do*
141.	Sri Tapas Chowdhury	246	*Do*
142.	Sri Pradip Mondal	383	*Do*
143.	Sri A.K. Sen	478	*Do*
144.	Sri Tarak Prasad Nandi	247	*Do*
145.	Mrs. Sutapa Ganguly	248	*Do*
146.	Sri Sanjib Biswas	249	*Do*
147.	Sri R.P. Gorh	250	*Do*
148.	Sri Sarit K. Sarkhel	245	*Do*
149.	Sri Nishikanta Naskar	252	*Do*
150.	Sri Pallab Mukherjee	253	*Do*
151.	Sri Ranjit Das	345	*Do*
152.	Sri Abhijit Paul	450	*Technician Gr. II(2)*
153.	Sri Anirban Manna	410	*Do*
154.	Sri Samir Majumder	426	*Do*
155.	Md. M. Ahmed	360	*Do*

Sl. No.	Employee's Name	Emp. ID	Deisgnation
156.	Sri Paresh Sarkar	409	*Do*
157.	Sri Sujit Kr. Majumdar	416	*Do*
158.	Mrs. Mahua Bhattacharjee	419	*Do*
159.	Sri Prabir Kr. Das	418	*Do*
160.	Sri Atanu Maitra	417	*Do*
161.	Sri Tapan Das	460	*Do*
162.	Sri Ujjal Roy	529	*Technician Gr. II(1)*
163.	Sri Arup Karmakar	534	*Do*
164.	Sri Soumalya Sinha	546	*Do*
165.	Sri R. Mahato	258	*Helper Gr. I(4)*
166.	Sri Sunil Nath	272	*Do*
167.	Sri R.N. Jana	274	*Do*
168.	Sri Prahlad Das	275	*Do*
169.	Sri Bhaskar Basu	440	*Do*
170.	Sri Shyamal Das	279	*Helper Gr. I(3)*
171.	Sri Sasthi C. Sil	356	*Do*
172.	Sri Madan Halder	479	*Do*
173.	Sri Amerika Das	280	*Do*
174.	Sri Nimai Charan Prodhan	282	*Do*
175.	Sri Sambhu Raul	351	*Do*
176.	Sri Suresh Balmiki	353	*Do*
177.	Sri U.N. Mandi	358	*Do*
178.	Sri Nandalal Routh	352	*Do*
179.	Sri S.K. Banik	361	*Do*
180.	Sri Ashoke Sardar	501	*Helper Gr. I(1)*
181.	Sri Ram Kumar Sarkar	502	*Do*
182.	Sri Shyamal Nath	519	*Do*

Administration

Sl. No.	Employee's Name	Emp. ID	Deisgnation
1.	Dr. S.R. Sarkar	544	*Controller of Administration*
2.	Sri U.S. Das	515	*Controller, Stores & Purchase*
3.	Sri S.K. Chaudhuri	497	*Administrative Officer*
4.	Sri S.K. Das	498	*F&A Officer*
5.	Sri N.K. Saha	549	*Stores & Purchase Officer*
6.	Sri Subhas Ch. Dutta	290	*Sr. Security Officer*
7.	Sri Kausik Bhattacharjee	492	*Section Officer (General)*
8.	Sri Siddhartha Dey	485	*Do*
9.	Mrs. Shampoo Sengupta	525	*Do*
10.	Sri P.K. Saha	468	*Do*
11.	Sri Asok Putatunda	542	*Do*
12.	Sri Asim Kr. Jha	518	*Section Officer (F&A)*
13.	Sri Abhimanyu Kr. Tiwary	533	*Do*
14.	Sri Tapan Kumar Mitra	320	*Section Officer (Stores & Purchase)*
15.	Sri Ranjan Ghosh	543	*Section Officer (Stores & Purchase)*
16.	Sri S.K. Chhatui	312	*Private Secretary*
17.	Sri Nilratan Biswas	538	*Do*
18.	Sri Debdas Guhathakurta	313	*Do*
19.	Sri Kanu Mondal	392	*Assistant (General) Gr. I (ACP)*
20.	Sri Ratan Bage	397	*Do*
21.	Sri K.C. Das	302	*Assistant (General) Gr. I*
22.	Mrs. Ratnabali Adhikari	304	*Do*
23.	Sri D.R. Chakraborty	306	*Do*
24.	Mrs. Anjana Mandi	308	*Do*
25.	Mrs. Sanhita Ganguly	427	*Do*
26.	Mrs. Monalisa Mukhopadhyay	428	*Do*
27.	Miss Lily Das	330	*Do*
28.	Mrs. Indira Kundu	331	*Do*

Sl. No.	Employee's Name	Emp. ID	Deisgnation
29.	Sri R.N. Hansda	334	*Do*
30.	Sri Prem Singh	335	*Do*
31.	Sri D.K. Kisku	340	*Assistant (General) Gr. II*
32.	Sri Alok Ray	396	*Do*
33.	Sri Jayanta Pal	510	*Do*
34.	Sri Tarun Kr. Sinha Roy	508	*Do*
35.	Sri Raju Pal	507	*Do*
36.	Sri Ranjit Debnath	509	*Do*
37.	Sri Saugata Das	511	*Do*
38.	Sri Sukhendu Biswas	512	*Do*
39.	Sri A.K. Chanda	327	*Assistant (F&A) Gr. I*
40.	Mrs. Banani Dutta	476	*Do*
41.	Sri Sanjoy Mukhopadhyay	343	*Do*
42.	Mrs. P.L. Saha	332	*Do*
43.	Sri Asit K. Roy	336	*Assistant (F&A) Gr. II*
44.	Sri M.K. Dutta	338	*Do*
45.	Sri Vishal Agarwal	506	*Do*
46.	Sri Panchanan Naskar	322	*Assistant (S&P) Gr. I*
47.	Sri A.B.S. Roy	328	*Do*
48.	Sri Rajib Ray	536	*Do*
49.	Sri Bisweswar Das	342	*Do*
50.	Mrs. Bula Pal	363	*Assistant (S&P) Gr. II*
51.	Sri Pradipta Sarkar	505	*Do*
52.	Sri Arnab Sen	504	*Do*
53.	Mrs. Ambalika Nag	321	*Sr. Hindi Translator*
54.	Sri M.P. Banerjee	469	*Sr. Stenographer (ACP)*
55.	Sri Nikhil Kumar Das	315	
56.	Sri Sankar Prasad Dutta	316	*Do*
57.	Sri Dipak Kr. Guin	318	*Do*

Sl. No.	Employee's Name	Emp. ID	Deisgnation
58.	Sri Asim Roy	323	*Do*
59.	Mrs. Pratima Banerjee	324	*Sr. Stenographer*
60.	Sri Shankar Bhakta	325	*Do*
61.	Sri Rabindranath Das	393	*Do*
62.	Sri Saibal Giri	405	*Do*
63.	Sri Sankar Santra	490	*Do*
64.	Sri Gautam Saha	453	*Jr. Stenographer*
65.	Sri Sudip Ghosh	454	*Do*
66.	Smt Moumita Majumdar	491	*Do*
67.	Sri Ashok Ram	348	*Gr-D (NT) (Upgraded / ACP)*
68.	Sri Bideshi Nayak	349	*Do*
69.	Mrs. Chaina Devi Nayak	366	*Gr-D (NT) (Upgraded)*
70.	Sri Kailash Chandra Nayak	365	*DO*
71.	Mrs. Gita Ghosh	364	*Do*
72.	Mrs Soma Devi Sharma	401	*Do*
73.	Sri Gopal Ch. Mandal	412	*Do*
74.	Sri Asit Mitra	413	*Do*
75.	Sri Janmanjoy Midya	431	*Do*
76.	Sri Pasupati Midya	430	*Do*
77.	Sri Shyamal Kr. Ghosal	423	*Do*
78.	Sri P.C. Dehury	414	*Do*
79.	Sri Manoranjan Adhikary	425	*Do*
80.	Sri Tapan Sarkar	424	*Do*
81.	Sri Dinesh Mehali	451	*Group-D (NT)*
82.	Sri Tarun Dutta	367	*Asstt. Manager-cum-Store Keeper*
83.	Sri Amal Dutta	369	*Coupon Clerk*
84.	Sri Balaram Panda	368	*Halwai-cum-Cook*
85.	Sri Sudhangshu Halder	373	*Tea Maker*
86.	Sri Bimal Das	372	*Bearer*

Sl. No.	Employee's Name	Emp. ID	Deisgnation
87.	Sri Ashok Sadhukhan	371	*Bearer*
88.	Sri Badal Haldar	370	*Bearer*
89.	Sri Jagabandhu Biswas	374	*Wash Boy*
90.	Sri Mantu Das	376	*Sweeper*
91.	Sri Nirapada Halder	375	*Sweeper*

Retirement List from April 01, 2009 to March 31, 2010

Sl. No.	Name of the Staff	Designation	Date of Retirement
1.	Sri Utpal Haldar	Technical Officer	01-04-2009 (VR)
2.	Dr. V.S. Giri	Scientist	31-05-2009
3.	Sri M.K. Ghosh	Assistant, Gr.I	31-05-2009
4.	Dr. Anindya Dasgupta	Scientist	18-06-2009 (Resigned)
5.	Mrs. Rita Sikdar	Assistant, Gr.I	01-6-09 (Expired)
6.	Sri R.L. Bhattacharjee	Assistant, Gr.I	31-08-2009
7.	Sri Brihaspati Das	Lab. Assistant	30-09-2009
8.	Sri S.N. Dey	Technical Officer	31-10-2009
9.	Dr. B.C. Pal	Scientist	31-01-2010
10.	Sri K.M. Dutta	Technical Officer	31-01-2010
11.	Sri B. Bhattacharjee	Private Secretary	28-02-2010
12.	Sri M.P. Banerjee	Sr. Stenographer	31-03-2010

New Appointment from April 01, 2009 to March 31, 2010

Sl. No.	Name of the Staff	Designation	Date of Appointment
1.	Dr. Biswadip Banerjee	Scientist Gr.IV(3)	01-07-2009
2.	Sri Soumalya Sinha	Technician Gr. II(1)	23-07-2009
3.	Sri Ch. Balaji	Technical Assistant	24-07-2009
4.	Dr. S.C. Biswas	Scientisst Gr.IV(3)	27-07-2009

Name of Emeritus Scientists / Prestigious Fellowship Holder

Sl. No.	Name of Emeritus Scientists	Position
1.	Dr. P.K. Dutta	Emeritus Scientist
2.	Dr. Basudev Achari	Emeritus Scientist
3.	Dr. Alok Kr. Dutta	Emeritus Scientist
4.	Dr. Anup Bhattacharjee	Emeritus Scientist
5.	Dr. Saikat Chakraborty	Ramalingswami Fellow

Name of Staff Joined on Transfer

Sl. No.	Name	Designation	Date of joining
1.	Sri Asok Putatunda	Section Officer (G)	17-04-2009
2.	Sri Ranjan Ghosh	Section Officer (SP)	04-05-2009
3.	Dr. S.R. Sarkar	Controller of Administration	27-07-2009
4.	Dr. M.I. Khan	Scientist 'F'	05-10-2009
5.	Sri N.K. Saha	Stores & Purchase Officer	11-01-2010

Research Council 2009-2010, IICB

Dr. Seyed E. Hasnain, Chairman
Vice-Chancellor
University of Hyderabad
Hyderabad - 500 046

Dr. A. N. Bhisey
Former Director
Cancer Research Institute
7, Yug Prabhat Society
Naryan Pathara Marg, Mahim
Mumbai - 400 016

Dr. K. N. Ganesh
Director
Indian Institute of Science Education and Research (IISER)
900, NCL Innovation Park
Dr. Homi Bhabha Road
Pune - 411 008

Prof. R. V. Hosur
National Facility for High Field NMR
Tata Institute of Fundamental Research
Homi Bhabha Road, Navy Nagar
Mumbai – 400 005

Prof. K. Muniyappa
Head, Department of Biochemistry
Indian Institute of Science
Bangalore – 560 012

Dr. P. Bhatnagar
Senior Vice President
New Drug Discovery Research
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प्रबंध परिषद्
(1 जुलाई, 2007 से 31 दिसम्बर, 2009 तक)
Management Council
(For the period from 01.07.2007 to 31.12.2009)

01. प्रो. सिद्धार्थ राय, निदेशक, आईआईसीबी 01. Prof. Siddhartha Roy, Director, IICB	अध्यक्ष Chairman
02. डॉ. अमलेन्दु सिन्हा, निदेशक, सीआईएमएफ़आर, धनबाद 02. Dr. Amalendu Sinha, Director, CIMFR, Dhanbad	सदस्य Member
03. डॉ. पीयुष कुमार दास, वैज्ञानिक, ग्रुप-IV(6), आईआईसीबी 03. Dr. Pijush Kr. Das, Scientist, Gr. IV(6), IICB	सदस्य Member
04. डॉ. के. पी. मोहानाकुमार, वैज्ञानिक, ग्रुप--IV(6), आईआईसीबी 04. Dr. K. P. Mohanakumar, Scientist, Gr. IV(6), IICB	सदस्य Member
05. डॉ. सुशान्त रायचौधुरी, वैज्ञानिक, ग्रुप--IV(5), आईआईसीबी 05. Dr. Susanta Roychowdhury, Scientist, Gr. IV(5), IICB	सदस्य Member
06. डॉ. (श्रीमती) तृप्ति दे, वैज्ञानिक, ग्रुप--IV(3), आईआईसीबी 06. Dr. (Mrs.) Tripti De, Scientist, Gr. IV(3), IICB	सदस्य Member
07. डॉ. एस. चट्टोपाध्याय, वैज्ञानिक, ग्रुप--IV(3), आईआईसीबी 07. Dr. S. Chattopadhyay, Scientist, Gr. IV(3), IICB	सदस्य Member
08. श्री एस. एन. दे, तकनीकी अधिकारी, ग्रुप--III(7), आईआईसीबी 08. Shri S. N. Dey, Technical Officer, Gr. III(7), IICB	सदस्य Member
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10. प्रशासनिक अधिकारी, आईआईसीबी 10. Administrative Officer, IICB	सदस्य सचिव Member-Secretary

(1 जनवरी, 2010 से 31 दिसम्बर, 2011 तक)
(For the period from 01.01.2010 to 31.12.2011)

01. प्रो. सिद्धार्थ राय, निदेशक, आईआईसीबी 01. Prof. Siddhartha Roy, Director, IICB	अध्यक्ष Chairman
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03. डॉ. समित आध्या, वैज्ञानिक, ग्रुप-IV(6), आईआईसीबी 03. Dr. Samit Adhya, Scientist, Gr. IV(6)	सदस्य Member
04. डॉ. के. पी. मोहानाकुमार, वैज्ञानिक, ग्रुप--IV(6), आईआईसीबी 04. Dr. K. P. Mohanakumar, Scientist, Gr. IV(6), IICB	सदस्य Member

05.	डॉ. (श्रीमती) चित्रा दत्ता, वैज्ञानिक, ग्रुप--IV(5), आईआईसीबी	सदस्य
05.	Dr. (Mrs.) Chitra Dutta, Scientist, Gr. IV(5), IICB	Member
06.	डॉ. शिव शंकर राय, वैज्ञानिक, ग्रुप--IV(3), आईआईसीबी	सदस्य
06.	Dr. Sib Sankar Roy, Scientist, Gr. IV(3), IICB	Member
07.	डॉ. उदय. बन्दोपाध्याय, वैज्ञानिक, ग्रुप--IV(3), आईआईसीबी	सदस्य
07.	Dr. Uday Bandopadhyay, Scientist, Gr. IV(3), IICB	Member
08.	डॉ. (श्रीमती) मृदुला मिश्र, ग्रुप--III(7), आईआईसीबी	सदस्य
08.	Dr. (Mrs.) Mridula Mishra, To Gr. III(7), IICB	Member
09.	वित्त तथा लेखा अधिकारी, आईआईसीबी	सदस्य
09.	Finance & Accounts Officer, IICB	Member
10.	वरिष्ठ सीओए/सीओए/प्रशासनिक अधिकारी, आईआईसीबी	सदस्य सचिव
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Our goal is to achieve perfection

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