NEWSLETTER

Indian Institute of Chemical Biology, CSIR, Kolkata-700032

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Indian Institute of Chemical Biology (Council of Scientific and Industrial Research)

MESSAGE FROM THE DIRECTOR

Knowledge, imagination and vision

We see only what we know …….. Goethe

When you look at landmark discoveries in science, they often appear so obvious that sometimes they do not even appear so great. In retrospect, certainty of knowledge makes our vision perfect and clear. However every working scientist knows how difficult it is to arrive at the correct explanation of an unexplained phenomenon, as possibilities are numerous and the most obvious ones are not necessarily the correct ones. In order to arrive at the correct explanation you have to first imagine all the possible ones and then eliminate all but the correct one. Human imagination is almost always limited by personal knowledge and experience. Thus imagination of all the possibilities requires extraordinary breadth of knowledge, not only in the relevant field, but also in related fields. A scientist thus must remain a lifelong student, excited about learning new things. What we call vision, is nothing but imagining possibilities, which are otherwise invisible to the rest. In the words of English writer Jonathan Swift ---"Vision is the art of seeing things invisible".

PROLOGUE

It is my great pleasure to bring out a fresh issue of the Newsletter after a gap of many months. I take the liberty to follow my own inclination to catalogue the world of objects, creating memorable portraits that evoke strong action potential. It is my personal pleasure to do so because I have regarded science as one of the humanities like art, literature and music.

This issue has a pleasant surprise in store - a thought provoking article from Dr. Lalji Singh, Director of the Centre for Cellular and Molecular Biology. Lalji is an extremely busy person, and I consider myself lucky to have enticed him to contribute to our Newsletter. But I also urge all our colleagues and students to write, not a rigorous scientific communication of course (with Impact Factors!) but something with a literary flavour, hovering in the twilight zone of science and literature or fine arts perhaps. It is intellectually satisfying to indulge in some literary exercise after your day to day laboratory activities. The Newsletter is indeed a good forum to express your surrealistic thoughts and also to influence the intellectual climate of the institute. You can make a self-contained, substantive argument, but be careful to keep it short enough to encourage others to read it.

In one of his best write-ups, George Orwell (real name Eric Blair) demonstrated the many uses of language. Incidentally, Orwell was born in Bengal in 1903. He was educated at Eton and earned his leaving by writing novels and essays. He was a socialist and served in the Loyalist forces in the Spanish Civil war. Possibly his best work is Animal Farm. The final phrase "All animals are equal, but some animals are more equal than others" is well known. Orwell's ideas in this essay continue to influence till now both what we think and how we think.

I have had the pleasure of visiting Sir William Dunn School of Pathology, Oxford few months back. In the cafeteria of Dunn School I saw some still pictures of collection of laboratory reagents hung onto the wall. These pictures were taken by one of the associates of Dunn School, Ms. Catherine Yass, in a very ingenious way. I wanted to reproduce her work in our Newsletter and she has kindly consented to this proposal. I have included these pictures not simply because I liked them but because I wish others to come up with novel ideas out of our day to day activities.

In editing the Newsletter I have incurred many obligations and also made new friends as well as some enemies, people belonging to the latter category being statistically insignificant in number. I express my gratitude to Dr. Lalji Singh and Ms. Catherine Yass for their contributions. There may be some slips and errors here and there for which I take full responsibility. Finally I thank our Director Prof. Siddhartha Roy (whom I fondly call as Siddhartha) for giving all the liberty to steer the wheel of this Newsletter in any direction I deem fit. Please make this Newsletter a regular platform of your communications and enrich it with your bright sparks. I look forward to welcoming your write ups as material for the next issue of the Newsletter. Till then, bye.

Syamal Roy, Editor-in-Chief

Licensed out as Product

A patent license agreement has been signed between IICB and M/s. East India Pharmaceutical Works Ltd., Kolkata on 23.05.2006 for utilizing the technology for the treatment and remedy of Prostate problem using a herbal formulation. Using CSIR/IICB technology, the company has marketed this drug in the name of PROSTALYN. Prostalyn inhibits abnormal proliferation within the prostate gland in men and relieves urinary symptoms associated with prostate megaly. This leads to a decrease in its size, improved urinary flow rate, more complete emptying of the bladder, decreased urine retention and relief from the symptoms of prostatic hyperplasia. Dr. B.C. Pal and Prof. Samir Bhattacharya were involved in developing the product.

VIEWPOINT

Neurobiology of language:

The neuroscience of language puts forth a most challenging problem of modern day neurobiology. This remains a unique effort to bridge linguistics with neuroscience. The most fascinating aspect is the ability to create knowledge through language which is unique to humans. Man has always spoken different languages and the major languages were analyzed at length to uncover any common thread to a primeval source. Professor Noam Chomsky of Massachusetts Institute of Technology argues that there is an innate language acquisition device, a neuronal program that prepares them to learn the language. Oddly enough there is an analogy between the human language and the genetic code. Spoken utterances are composed of sequences of a small number of unit sounds or phonemes (represented by the letters of the alphabet). In ancient India, the Sanskrit grammarian Panini (c 520-460 BC) originated the concept of the phoneme in his text on Sanskrit grammar. Like Panini, Chomasky was focused on finding the rules of language. However as Chomsky was from a modern era, he took more scientific, mathematical approach. These phonemes first specify different words, and then, through syntax, the meaning of sentences. The genetic messages are composed of a linear sequence of only four kinds of units, and a sequence of three units specifies a code for 20 kinds of amino acids. These strings of amino acids form a functional protein which is an open ended system. For more than three billion years, evolution of life on earth was restricted to using this generative system. Relatively recently, another generative system has emerged which is the human language. Emma Marris in her recent article in Nature (Nature; 453, 446-448, 2008) states that “The advent of molecular genetics provided a new depth to the analogy. Just as the four nucleosides of DNA can produce a staggering variety of creatures, the alphabet of the world’s language can generate an infinite number of sentences. These alphabets, the words they make, and the sounds and grammar rules that frame them are passed down from parent to child in a process that, at least superficially, resembles the inheritance of DNA.”

It seems to be a very daunting task to understand the neuronal basis of language. There are strong evidences coming from the studies of Dyslexia (a learning disability that manifests primarily as a difficulty with written language particularly with reading and spelling) that analysis of language by our brain has a neuronal basis. Dyslexia reflects a deficit within the language system of the brain, although other systems and processes may also contribute to the difficulty. Some of you must have seen the movie ‘Taare Zameen Par’, the struggle of a child suffering from dyslexia. It reminds me of Francois Truffaut's Film “The 400 Blows”. It is a film that speaks up to some extent for life as in Taare Zameen Par. The underlying sadness of these films is the sadness of the universal estrangement. We need to know how language evokes action potentials in different sets of neurons in our brain. Until we understand the brain and the neuronal basis of language better, the matter is wide open for discussion. The study of language as a biological phenomenon is quite fascinating and we are fortunate to have our own language to communicate with other, among which the release of this newsletter is a case in point.

Syamal Roy

What makes us Human?

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Although our primate relatives split from our common ancestors millions of years ago, their genomes could help solve mysteries about our own evolution and medical problems. They could also give us insights into how evolution works and how new genes and species form. These are some of the good reasons to continue the endeavour to accumulate genome sequence data of various organisms. Recently a draft genome sequence of the common chimpanzee (*pan troglodytes*) has been completed. Genome of the chimpanzees, our closest living relatives, and our genome are 98.8% identical. We shared a common ancestor some six million years ago. The differences between the sequences will reveal the genetic basis for our mental and linguistic capacities and explain why we are susceptible to some diseases that do not affect the great apes. The genome of common chimpanzee differs from human in terms of nucleotide substitutions by only 1.23%. There are about 7,000 Alu elements in human and 2,300 in chimpanzee. There are about 35 million nucleotide differences, 5 million indels and many chromosomal rearrangements. The chimpanzee has 53 human genes with disruptive indels in the coding regions; and genes in this region may be associated with intriguing phenotypes. One such gene encoding myosin heavy chain (MYH16) protein is specifically expressed in jaw muscle of primates and human. The human gene has two missing base pairs in a key region causing a frameshifting mutation and inactivation of the myosin heavy chain (MYH). This resulted in a dramatic reduction in the size of the muscle. This mutation arose 2.4 million years ago, just before the evolution of the modern hominid cranial form. It is hypothesized that a decrease in the jaw-muscle size, produced by inactivation of MYH16, removed a barrier to the remodeling of the hominid cranium which consequently allowed an increase in the size of the brain. Thus a change in a single muscle protein may have been a key step in the evolution of modern humans. It is an important step in defining what makes us human.

The gene coding for the protein Prodynorphin (PDYN) is a precursor molecule for a range of regulatory neuropeptides involved in learning, experience of pain, perception, behavior and memory. In non-human primates, including; chimps, gorillas and orangutans, the promoter of PDYN gene is a single copy consisting of 68 bp, whereas in humans there are up to 4 copies having 5 mutations not seen in other primates. The human promoter introduced into human neural cells induced 20% greater expression of PDYN gene than the chimp promoter. It is reasonable to hypothesis that these changes are the key to what makes us human. FOX P2 gene encodes a homeodomain protein essential for normal human speech. ASPM and Microcephalin genes are essential for normal cerebral cortical size in humans.

Rapidly evolving non-coding regions may harbour the secret of what makes humans different from our nearest primate relatives. The GENE, CALLED HAR1F (Human accelerated regions) does not directly code for a protein. Instead, it lies in a non-coding segment of the genome and produces RNA in the brain cells called Cajal-Retzius, which regulate how the six layers of the cortex are laid down during development. This may interact with a protein called reelin which plays a vital role in this layering of cortex. HAR1 the 118 bp showed most dramatically accelerated change – 18 substitutions in human lineage – since the human-chimpanzee ancestor. Between chimpanzee and chicken only 2 bases changed out of 118 bp indicating that the region was present and functional in our ancestors at least 310 Myr ago.

The human protein-coding genes count at about 20,000-25,000, barely more than C.elegans (19,000 genes), a simple 1000 cell nematode. Yet in human these proteins help build a complex organism of nearly 100 trillion cells precisely arranged into many different organs and structures. Where then are the instructions

for building so complex an organism? Alternative splicing mechanism may generate more than one protein performing different functions. A digital RNA-based regulatory network could spell the difference between human and other animals. Some noncoding RNA (microRNA or miRNA) genes may yield functional RNAs from both introns and exons. These RNAs may then act as signaling or guide molecules to integrate activity at this locus with that of related parts of the network. This may involve secondary or tertiary RNA structures and RNA-mediated catalysis. The differences between chimp and human therefore, might largely be the result of the gene regulatory mechanisms giving different levels of gene expression. Thus, the story of what makes us special is written in our DNA, but not necessarily in our genes.

Are Human still Evolving? – The discovery of ongoing human evolution raises many questions, some of them uncomfortable. What if racial groups turn out not to be biologically equivalent? Is natural selection still driving force in humans, given that our survival is often less dependent on genes than on technology? To what extent might a changing genome lead to changes in attributes we value, such as intelligence? What might our species look live 1000 years from now? Contemporary human evolution may be a minefield that can no longer be ignored.

One obvious example is genes that confer resistance to emerging diseases. Some parts of Africa have seen an increase in the frequency of a gene called CCR5-Δ32, which offers some protection against infection with HIV-1. Caesarean sections, for example, could be selecting for genes that allow babies to grow bigger in the womb. Technology and medicine by enabling almost everyone to have children could be causing reverse evolution, by presenting unfit genes from being purged from the gene pool.

The most important selective pressures continue to be on brain functions. "1000 years from now, people will be much more beautiful, intelligent, symmetrical, healthy and emotionally stable, thanks to 40 generations of genetic screening". Assortative mating is also promoted by contraception. And other reproductive technologies are probably exerting an influence on human evolution too. Willingness to be a sperm or egg donor is being strongly favoured by current selection. It is suspected that next millennium, we will have figured out ways to manipulate our own genome, such that evolution will operate on a whole new set of rules that even Darwin did not envision. Within a few generations, market-based genetic technology will eclipse socio-sexual selection as the driving force in human evolution.

One way in which we could evolve in a truly spectacular fashion is if we colonize other planets. Those colonists and the animals and plants that they take with them will undergo dramatic evolutionary changes in the process of adapting to incredibly different conditions. It is possible that colonists would even become a separate species if there were no interbreeding with people on earth. All in all, it's hard not to conclude that humans are still evolving, probably quite rapidly. "All species are evolving, but at different rates. Trying to predict the direction of evolution is a fruitless exercise. "Evolution is not really a predictive science".

We may not like where we are heading. Perhaps, we will so befoul our planet that only an eccentric and hardy remnant of our species which can survive on earthworms while living in under ground burrows, for instance will remain. "Wherever we end up, it seems clear that the story of human evolution has only just started.

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Publications

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Catherine Yass

Through her work carried out at the Sir William Dunn School of Pathology at Oxford, Catherine Dunn in conjunction with Dr William James strives to amalgamate the seemingly immiscible fields of art which encourages aesthetic ambiguity, and science which demands exact reproducibility of results. Specifically, Catherine Yass has addressed the issue of truth in photography, dispelling the myth that photographs are true to life representations of their subject.

Her method of superimposing a positive onto a negative image, shot within moments of each other with striped filters, while specific, lacks the reproducibility much sought after in scientific pursuits. Her results speak for themselves. Her unique method means that each frame is different, the double capture helping to paint an image in both space and time .The photographs represent a distortion of the truth, they lack scientific reproducibility. They are open to the interpretation of the observer it their personal context.

Double Agent text

I and professor William James were given a research fellowship by the Wellcome trust to collaborate on making a work from science and art that expressed the nature of viruses such as the HIV virus. Together we developed a visual language through using photography and filters. The bottles containing research fluids were photographed as still lives through coloured filters, which made the fluids seem to move through the bottles as if, like a virus they were not easy to contain, and migrated through other substances. The filters were similar to those used in the laboratory to detect viruses in microscopic images.
As well as using filters the photographs are a combination of a positive and negative blue image. This renders the colours even more mysterious and poisonous looking. The title Double Agent refers to the way the virus behaves in order to slip past antibodies. The images are printed up to 2m long so the bottles and objects are enlarged so that they are seen freshly as new and unfamiliar. I was thinking of Alice in Wonderland drinking the potion which made her larger or smaller, and the warnings to young children not to drink unfamiliar substances. The images are shown in light boxes which gives the light in the fluids a translucent feel.
Each image is titled after the labels on the bottles which have the names of the laboratory research teams on them.

Pictures (Double Agent):

Double Agent (Mildred) 2001
Ilfochrome transparency and light box

Double Agent (IM) 2001
Ilfochrome transparency and light box

Double Agent (Tris) 2001
Ilfochrome transparency and light box

Felicitation Ceremony for the Prestigious National Bioscience Award 2007 at NII, New Delhi

National Bioscience Award for Career Development 2007 has been conferred on **Dr. Snehasikta Swarnakar** by the Department of Biotechnology, Govt. of India for her significant contributions on the role of matrix metalloproteinases (MMPs) in gastric ulceration. Her research work has demonstrated that the upregulation of MMP-9 gene is associated with pathogenesis of ethanol-induced, nonsteroidal anti-inflammatory drug (NSAID)-induced, and *Helicobacter pylori* infected gastric ulcers. She has made pivotal contributions on the critical role of melatonin in regulating MMP-9 activity during protection against gastric ulcers as well as endometriosis. Dr. Swarnakar was appointed in Oct 2002 as scientist in the division of Drug Development Diagnostic and Biotechnology in Indian Institute of Chemical Biology. Her field of specialization is Protease Biology, Gastroenterology and Endometriosis. Her professional contributions have won invitation to present papers and chair sessions in several International and National conferences : (a) Indo-French seminar on Structure & Function of Metalloenzymes, Goa, India (b) Global Neem Conference, Coimbatore, India (c) International Drug Discovery Science and Technology, Xi'an, China (d) Gordon Research Conference at Lucca, Italy. Dr. Swarnakar was visiting faculty at The Scripps Research Institute, LaJolla, San Diego and University of Connecticut, Farmington, Connecticut, USA

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