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**Trendys Meeting 2003**

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TRendys in Biochemistry, started as a small scientific discussion group in IISc Bangalore a decade ago by Prof. T Ramasarma, has now grown to the stature of an important national forum primarily through the nurturing efforts of Prof. K Subba Rao (University of Hyderabad) and other like-minded scientists. TRendys held its 10th meeting at the Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad on 24th and 25th November, 2003. Students and scientists from various universities and institutes in Hyderabad attended the meeting. A series of lectures by eminent scientists, experienced and budding, covering new facets of Biochemistry, Molecular Bio-logy and some recent advances in the Clinical Sciences were indeed impressive. Prof. S E Hasnain (Director, CDFD) presented the welcome address, followed by a brief introduction by Prof. K Subba Rao.

Prof. Ramasarma (CDFD, Hyderabad) spoke on the fascinating aspect of nucleic acid catalysis. The discovery of RNA-catalysts (ribozymes) demolished the central dogma that proteins are exclusive cellular catalysts. He revealed the mechanistic aspect of how polynucleotides can gain catalysis and proposed a hypothesis about catalysis involving intramolecular electron transfer over H-bond interlinked by -electron clouds of nucleotide structures. By elaborating on the extensive secondary structures occurring in ribozymal RNA with canonical and unusual H-bonds, Prof. Ramasarma explained the possible existence of -H pathways in ribozymes.

The next lecture, “Channels - facts and fears… Nobel prizes notwithstanding” by Prof. V Sitaramam (University of Pune, Pune) highlighted the prize winning work of Roderick MacKinnon (Nobel Prize for Chemistry in 2003) on channels in cell membranes. He described how potassium channel with extraordinary selectivity for potassium still maintained diffusion rates nearly matching self-diffusion in water. He also touched up on aquaporins, the membrane water channels, which play critical role in controlling water contents of the cells. Aquaporins, in fact, form tetramers in the cell membrane and facilitate the transport of water. However, water pores are completely impermeable to charged species, such as protons, a remarkable property that is critical for conservation of membrane's electrochemical potential, but paradoxical at the same time, since protons can be transported readily through water molecules.

Dr. Shashidhara, Centre for Cellular and Molecular Biology (CCMB), Hyderabad described how membrane trafficking paves the way to morphogen gradient and the mechanisms on how concentration gradient of the morphogen is established to confer different identities to the cells in a multicellular (specific Ex. *Drosophila*). He covered many aspects on the endocytic pathway in the secretion of signal molecules from the source cells, their movement through the target tissues and transduction of signal from endocytic compartments/vesicles.

Dr. Gopal Kundu (NCCS, Pune) chose the signal transducer *Nuclear factor-κB (NF-κB)* which plays a crucial role in many of the signaling events to unravel the emerging mind-boggling complexities of various signal transduction pathways. *NF*-κ*B* is a family of transcription factors that has been shown to be involved in regulation of several diseases. The speaker elaborated on how in the nucleus *NF*-κ*B* modulates the expression of a variety of genes including those encoding cytokines, growth factors, cell adhesion molecules and urokinase type plasminogen activator, thereby modulating events such as apoptosis, proliferation, cellular motility, etc.

Application of gene chips/microarrays in cancer diagnostics was touched by Prof. P Kondaiah (IISc, Bangalore) in his talk, “Molecular signatures of cancer: Do they improve patient management?”. He discussed how by labeling cancerous cell and its normal counterpart using two different fluorescent dyes and hybridizing them together on a oligo/cDNA gene chip can help identify upregulated or downregulated genes in cancerous cells. By nailing down on few such target genes one can explore these key molecules for cancer therapeutics. He described how difficult it is to predict clinical outcome of such a disease on the basis of histology, but gene expression profiles using microarray can help define a set of genes thus providing quite a strong indicator of long-term survival.

The possibility of development of male contraceptives including the use of synthetic androgen like 7-α-methyl-19-nortestosterone which is more potent than testosterone and is more efficacious in controlling fertility was discussed by Prof. A J Rao (IISc, Bangalore). Hormonal approaches to male contraception based on the suppression of luteinizing hormone secretion require androgen replacement treatment to maintain sexual behaviour and secondary sexual characteristics. Androgen supplementation not only involves large and frequent doses of testosterone esters, but also results in undesirable effects on the prostate gland.

In a thought-provoking seminar on kinetics and energetics of protein folding, “Say no to what they say how proteins fold” Dr. Abani Bhuyan (University of Hyderabad) discussed newer concepts on protein folding and put forth his views on (i) the folding time correlation with the energy of native state, (ii) the folding transition-state region that appears rather late at a time when a substantial fraction of native contacts are already formed, and (iii) the rate-limiting barrier which is early and low in energy and has shortcomings.

Though protein folding is essential for stability and activity of the proteins, its degradation is equally important for basal protein turnover. The major regulatory mechanism controlling protein degradation is by unbiquitin-proteosome mediated pathway. Dr. S Jonnalagadda (Osmania University) discussed in detail, the two main steps in the ubiquitination pathway: (i) covalent attachment of a polyubiquitin chain to the substrate, and (ii) specific recognition of this signal, and degradation of the tagged protein by the proteosome.

Dr. Shekhar Mande (CDFD, Hyderabad) highlighted the X-ray crystallography as a major tool in understanding biological phenomena. Rapid advancements in these techniques in recent years have facilitated study of complex problems. He explained the structure and functioning of some of the important protein complexes, such as ATPase, now recognized as tiny molecular motors.

Stem cell research in recent years has seen a lot of ‘hype and hope’ among the scientific community. While the hype is on bioethical issues, the hope is the use of stem cells as elixirs of life, supposedly a wonder cure of everything. The 10th TRendys meeting figured two such talks. Prof. D Balasubramanian of L V Prasad Eye Institute (LVPEI), Hyderabad revealed how limbal stem cells in India are cultured for corneal transplants. The discovery that the limbus has a supply of (adult) stem cells led to the possibility of harvesting and cultivating them in order to produce the corneal epithelium. He described how the amniotic membrane and the limbal stem cells taken from the healthy eye are co-cultured together *in vitro* and few days of culturing results in desired epithelium which is then grafted to the diseased eye. There was a lot of excitement in the audience as the video clippings showed successful transplantation and total recovery of the damaged eyes in the patients. Dr. Shyamala Mani, National Brain Research Centre (NBRC), Gurgaon, elaborated on the neuronal stem cells, their diffrentiation and utility in curing a number of neuronal diseases like Alzheimers, Parkinsons, etc.

Dr. Sanjeev Khosla (CDFD, Hyderabad) gave an interesting talk on epigenetic circuitry focusing the phenomenon of imprinting which can be loosely defined as the gamete-of-origin dependent modification of phenotype, that is, the phenotype elicited from a locus is differentially modified by the sex of the parent contributing that particular allele. He described various examples of maternally and paternally imprinted genes. One of the major highlights of this talk was on chromatin remodeling and how methylation of the CpG islands regulates gene expression. He also discussed recent advances in cancer epigentics where it has been shown that tumor suppressors are turned off by hypermethylation.

The series of interesting lectures at the TRendys 10th meeting came to an end with the exciting presentation of Dr. Raj Gopal (Tata Consultancy Service, Hyderabad) on the power of *in silico* approach, a recent trend in “Designing novel protein folds”. He highlighted construction of a novel functional, but unnatural protein using sophisticated computer algorithms. He discussed the paper by Baker and colleagues later published in *Science*, November 21, 2003 issue (Kuhlman *et al*, *Science*, 2003, 302, 1364) on successful understanding of the language proteins, wherein through an integrated approach of protein design algorithms with protein structure-prediction algorithms, researchers predicted a 93-amino acid protein structure called ‘Top7’. They synthesized ‘Top7’ to determine its 3D-structure by NMR spectroscopy and X-ray crystallography and found that the solved crystal structure was almost identical to the predicted structure. The speaker while admitting that designing a specified protein fold is a big achievement, he was keen on encouraging researchers to explore larger questions about how proteins evolved and why nature “chose” certain protein folds over others and a bigger challenge lies ahead in future for designing of proteins with specified functions.

The new concepts, hypotheses and views of the speakers lead to active discussions and contemplations on the varied topics. The meeting concluded with views from the speakers and the students regarding outcome of the two-day symposia. It was noted that meetings like TRendys are informative, especially on emerging areas in Biochemistry and Molecular Biology and provide a forum for scientific discussion on thought-provoking ideas nurturing and inculcating the scientific temper.

It was also decided by the ‘Standing Committee’ of TRendys that from next year onwards the first lecture (one hour duration) of the meeting would be given by a person specially invited for the purpose and the lecture will be known as “TRendys Oration”.