The tenth day's session started with lecture by V. P. Dimri who talked on 'Nonlinear inversion of resistivity data using Occam's approach'. He mentioned that the resistivity problem is nonlinear in nature and the general practice to linearize this nonlinear problem by neglecting second order derivative terms in the Taylor series of objective function, results in loss of very useful information. The truncation of Taylor series affects the stability of inversion and hence it is recommended to solve a nonlinear problem in a nonlinear manner by using the modified Occam's inversion algorithm. Following this talk, Ramesh Chand (NGRI) talked on 'Recharge estimation using Neutron probe', dealing with direct detection of soil moisture in an unsaturated zone as well as water content in a saturated zone.

The last day's session started with 'Scenario of groundwater pollution in India' by S. N. Rai (NGRI) who discussed the status of groundwater pollution owing to industrial and municipal waste, fertilizers and pesticides, natural sources resulting from water–rock interaction, and seawater intrusions, etc. The last lecture of this contact course was a case study on 'Prediction of groundwater contaminant migration in Patancheru watershed: a post audit' by V. V. S. G. Rao (NGRI) who talked about the assessment of groundwater resources.

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Emerging trends in tuberculosis research*

The Symposium on 'Emerging Trends in Tuberculosis Research' was co-funded by the International Centre for Genetic Engineering and Biotechnology (ICGEB) New Delhi and the Global Alliance for TB Drug Development. The meeting was attended by over 200 international and national participants representing 18 countries and unfolded with an inaugural lecture by Douglas Young (Imperial College School of Medicine, London). He explained the mysteries of *Mycobacterium* infection from the genome perspective.

Following this, Clifton Barry (National Institute of Allergy and Infectious Diseases, Rockville) spoke on understanding the metabolism of mycobacteria. His work highlighted the importance of distinguishing the pathology between disease models in humans and various animal models. His work focused on the patho-physiological conditions that are generated in patients suffering from multi-drug resistant tuberculosis. Work from his lab showed clear differences in the nature of granuloma with highly ordered and tightly organized structures with distinct microenvironments in human samples where bacterial growth in restricted. The saga was carried over by Rajesh Gokhale (National Institute of Immunology, New Delhi), giving an insight into the mechanism and assembly of cell wall lipids of *M. tuberculosis* as well as the complexity of a large repertoire of metabolically diverse proteins coming from a small number of genes of the pathogen.

Valerie Mizrahi (Molecular Microbiology Research Unit, Johannesburg) presented elegant studies demarcating mutations that result in genomic variation. These mutations, she emphasized, are of two types. One is environmental in nature and is so transient that eventually it disappears from the population. The other one gets fixed in the population and is thus heritable. Ultraviolet exposure of various strains resulted in mutations related to drug resistance. This was mapped to the novel damage-inducible C family of DNA polymerases that also induce mutations in other bacteria. She later talked about a reporter system developed by her laboratory to identify such mutations. This system has a potential for effectively screening populations harbouring MDR strains.

Anand Ranganathan (ICGEB) talked about a novel technique of Dicodon shuffling suggesting its applications in various fields of pathogen study, specifically in designing and hunting for novel inhibitor proteins against *M. tuberculosis*. On similar lines, Thomas Dick (NITD, Singapore) gave a lecture on the recent progress in his laboratory in the development of inhibitors against an *Mtb* enzyme called peptide deformylase that has already been shown to be crucial for the growth of the pathogen.

The session on host–pathogen interactions was opened by David Russell who focused on new developments regulating phago-lysosome fusions in *Mtb*-infected macrophages. By employing transposon tagged mutants of *Mtb*, he demonstrated that wild type and mutant mycobacteria segregated phagosomes with altered pH. While wild type bacteria were found in phagosomes with a more acidic pH, mutant bacteria were present in phagosomes with a pH between 5.0 and 5.6. This difference was later mapped to bacterial lipids and other effector molecules thereby identifying bacterial genes directly involved in acidification of phagosomes.

The use of *M. tuberculosis* knockouts in delineating the roles of various genes and operons in *Mtb* was the subject of talk by Anil K. Tyagi (University of Delhi, South Campus). The results of knockout studies in his laboratory indicate that the genes of *mymA* operon that have previously been suggested to have a function in modification of cell wall-associated fatty acids. Also, genes encoding tyrosine phosphatase (*mptp* A and B) play important roles in survival of *Mtb* in the host. Jaya Tyagi (AIIMS, New Delhi) emphasized the regulatory roles played by two component signal transduction systems at the level of protein phosphorylation of eleven putative genes thereby affecting the host–pathogen interactions in lung and leprosy bacilli.

Frank Verreck (Biomedical Primate Research Centre, Netherlands) dealt with the roles played by IL-23 and IL-27 and their subsequent regulation of 'macrophage 1' and 'macrophage 2' populations. While macrophage 1 induces Th1 responses, macrophage 2 subvert Th2 responses. Yossef AvGay presented data on signal transduction pathways in mycobacteria. By combining genetics and biochemical approaches, he demonstrated changes in-

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duced in protein serine/threonine kinases in various mutants generated by his group. In particular, PknG was shown to be involved in the inhibition of phagolysosome fusions and glutamate metabolism.

Dipankar Chatterji (IISc) focused his talk on the DNA-binding protein from starved cells (Dps) from *Mycobacterium smegmatis* and its characterization. In well-designed experiments, he demonstrated the ability of this protein to exist in trimeric and dodecameric forms with altered functions. Crystal structure data further suggested that the C terminal extensions in Dps from *M. smegmatis* and *M. avium* are rich in positively charged amino acid residues. That this region is important was demonstrated by truncated versions that lose DNA-binding ability.

The section on immunology to mycobacteria was opened by David Sherman (University of Washington, Seattle) who highlighted the importance of the RD1 region of *Mtb* and his work showed that secretion of CFP-10 and ESAT-6 from the RD1 region increased the virulence of the bacterium. He emphasized on the use of the transparent zebra fish model of tuberculosis using *M. marinum* as the infecting strain. The beauty of this model lies in the similarity in patho-physiological conditions with human models. This model has the selective advantage in monitoring changes in the activation status of single macrophages and granuloma as a function of time following infection. Using GFP-labelled *M. marinum* in which the RD1 region has been knocked out he demonstrated that RD1 encoded proteins direct infected macrophages to form aggregates that result in granuloma formation.

Work from ICGEB further highlighted the importance of antigens encoded from the RD1 region. Pawan Sharma (ICGEB) discussed the effects of CFP-10 and ESAT-6 in modulating macrophage functions as reflected by downregulation of nitric oxide production by both exogenous addition and endogenous expression of CFP-10. Further, these antigens also dephosphorylate a number of proteins in macrophages and also prevent the ERK/MAP kinases from translocating to the nucleus. Work done by Krishnamurthy Natarajan's group (ICGEB) demonstrated that *Mtb* secretory antigens induce the differentiation and maturation of dendritic cells (DCs). However, this activation of DCs seems to be a strategy employed by mycobacteria to downregulate Th1 responses generated to subsequently released mycobacteria from infected macrophages in an IL-10 and TGF-β dependent mechanism. Continuing in this session, Bernhard Ryffel (Institute de Transgenose, Orleans) spoke about the importance of toll-like receptors in *Mtb* infection. Using knockouts for TLR-2 and TLR-4, he showed that these mice had more severe infection as compared to wild-type.

Gilla Kaplan (Public Health Research Institute, Newark) presented some elegant data demonstrating the importance of polyketide synthase (PKS)-derived phenolic glycolipids in mediating virulence. While infection of monocytes by the lab strain CDC1551 induced IL-12 and a potent Th1 response, infection by HN878 and W4, two members of the W/Beijing strain, induced Th2 responses with high levels of IL-4 and IL-13. The Th2 response was also corroborated with higher bacterial loads in rabbits infected with the Beijing strains.

The session on vaccine development and the choice of appropriate models for vaccine testing invoked a lot of discussion. Peter Andersen (Department of Infections Disease Immunology, Denmark) dwelled on his long-standing interest in employing subunit based vaccines for TB. He proposed a two-pronged strategy of prime boost method of using BCG with subunit vaccines such as ESAT-6 and members of the Antigen 85 complex.

David McMurray (Texas A&M University, Texas) shared some interesting results on the effects of cytokines in the guinea pig model of TB. BCG-vaccinated guinea pigs showed a transient spurt in inflammatory cytokines and chemokines, compared to TGF-β levels that showed a steady increase with time. His recent work on recombinant BCG expressing the pro-inflammatory chemokine RANTES and its effect on modulating cytokine and chemokine expression drew considerable interest among the audience.

S. Vijaya (IISc) shared some of her work on the role played by glycoprotein APA in offering protection in guinea pig model of TB. DNA-based vaccination of APA gave protection against *Mtb* that was comparable to BCG. Interestingly, introduction of APA into BCG completely abrogated this protection against a challenge with virulent *Mtb*.

In order to predict the functions of genes not yet annotated in the genome sequence of *Mtb*, Eric Robin (Harvard School of Public Health, Boston) explained the use of different techniques like transposon site hybridization, mass spectrometry and mimicking *in vivo* environment inside macrophage, *in vitro*. M. Vijayan (IISc) showed analysis of crystal structure of RecA and ribosome recycling factor (RRF) from *Mtb* and *M. smegmatis*. A hypothetical model of storing DNA in grooves of a DNA-binding protein from stationary cells of *M. smegmatis* as per the crystal structure data was also discussed. Based upon the biophysical and structural characterization studies of *cpn10*, a unique chaperonin protein of *Mtb*, Shekhar Mande (CDFD, Hyderabad) proposed its involvement in Ca^{2+} ion chelation leading to modulation of Ca^{2+}-dependent signalling properties *in vivo* in his talk.

Overall, the symposium covered many facets of tuberculosis research. Post-talk discussions focused on the growing menace of tuberculosis in the world with special reference to third world nations. The symposium ended on an appreciative note on the quality of research on TB in India from distinguished speakers from abroad with special reference to the work carried out and presented by students in the form of posters.

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