UK-India Centre for Advanced Technology for Minimizing Indiscriminate Use of Antibiotics

Workshop III

"Exploring biology of antibiotic resistance and potential targets for early diagnosis and effective management of infectious diseases"

(January 15th – 17th, 2017)

Venue:

Taj Deccan, Hyderabad

Sponsored by

Department of Biotechnology, Govt of India

Medical Research Council, United Kingdom

Organizers:

Dr. Prashant Garg and Dr. V. V. Vamsi Krishna

Meeting Schedule -Day 1, 15.01.2017 (Sunday)

Presentation	Time	Speaker	Topic
Session 1	9.00 – 11.00 am	Antimicrobial Resistance	
Lead talk 1	9.00 – 9.30 am	Prashant Garg/ Nagaveni Shivshetty	Ex-vivo cornea infection model and its utilization in evaluating detection devices
Lead talk 2	9.30 – 10.00 am	Virander Singh Chauhan	Design of conformationally restricted Short peptides; Antimicrobial and self assembling properties
Lead talk 3	10:00 – 10.30 am	Harpal Singh	Early detection of pathogenic bacteria and strategies to overcome drug resistance using MCF7 cell line as a model
Lead talk 4	10.30 – 11.00 am	Hemant Gautam	Antibiotic resistance and future strategies
11.00 – 11.30 am		Tea/ Coffee Break	
Session 2	11.30 – 1.00 pm	Biofilm	
Lead talk 5	11.30 – 12.00am	S Shivaji	Ocular *Escherichia coli*: biofilm formation, antimicrobial resistance and gene expression
Lead talk 6	12.00 – 12.30pm	Joey Shepherd	Novel methods to treat (and grow!) biofilm
Lead talk 7	12.30 – 1.00pm	Dipankar Ghosh/ Pallavi Lahiri	Polymicrobial biofilms and antibiotic resistance: the case of *Pseudomonas aeruginosa* and *Stenotrophomonas maltophilia*.
1.00 – 2.00 pm		Lunch	
Session 3	2.00 – 4.00 pm	Non-antibiotic approaches	
Lead talk 8	2.00– 2.30 pm	Sheila MacNeil	Non-antibiotic approaches to tackling infection
Lead talk 9	2.30 – 3.00 pm	Subhadeep Chatterjee	Role of iron metabolism in bacterial virulence and antimicrobial resistance
Lead talk 10	3.00–3.30 pm	Sanhita Roy	Role of antimicrobial peptides in bacterial keratitis
Lead talk 11	3.30 – 4.00 pm	Maria Katsikogianni	Manufacturing and testing the efficacy of non-fouling/antimicrobial materials
4.00 - 4.30 – pm		Tea/ Coffee Break	
Session 4	4.30–6.00 pm	Miscellaneous	
Lead talk 12	4.30 – 5.00 pm	Sudip Ghosh	Activation and inactivation of metronidazole in *Entamoeba* and *Trichomonas*
Lead talk 13	5.00 – 5.30 pm	Mohitosh Mandal	Targeting chemo-resistant subpopulations in breast cancer: An emerging paradigm
Lead talk 14	5.30 – 6.00 pm	Soumyava Basu	Intraocular T-cell response in ocular TB
7.00 pm onward		Reception Dinner	

Meeting Schedule -Day 2, 16.01.2017 (Monday)

Presentation	Time	Speaker	Topic
Session 5	8.00 – 10.00 am	Non-antibiotic approaches	
Lead talk 1	8:00 – 8.30 am	William Martin	Hyperbranched polymers for the disruption of quorum sensing
Lead talk 2	8.30 – 9.00 am	Nagaraju Konda	Melimine-coated antimicrobial contact lenses
Lead talk 3	9.00 – 9.30 am	Sovan Lal Banerjee	*A new class of smart polymeric material to fight against microbial attack*
Lead talk 4	9.30 – 10.00 am	Anindya Sundar Ghosh	Non-essential PBPs and beta-lactam resistance
10.00 – 10.30 am		Tea/ Coffee Break	
Session 6	10.30 – 1.00 pm	Drug Delivery Systems	
Lead talk 5	10.30 – 11.00 am	Stephen Rimmer	Towards bacteria targeting particles
Lead talk 6	11.00 – 11.30pm	Radha Rangarajan	Novel Antibacterials: The Vitas experience
Lead talk 7	11.30 – 12.00pm	V V Vamsi Krishna	Breaching the membrane barriers for effective drug delivery
Lead talk 8	12.00– 12.30pm	Nikhil Singha	New class of polymeric nano-hybrid material based on POSS and its biomedical applications
Lead talk 9	12.30 – 1.00pm	Pradip Paik	“NO” delivery through crossed-linked polymer capsules
1.00 – 2.00 pm		Lunch	
2.00 – 4 .00 pm		Discussion	
4.00 - 4.30 –pm		Tea/ Coffee Break	
4.30 – 6.00 pm		Tour of LV Prasad Eye Institute, Hyderabad	

Meeting Schedule -Day 3, 17.01.2017 (Tuesday)

Time	Agenda
9.00 – 12.00 pm	Discussion of previous day presentations and compiling report/ Vote of thanks by Dr D Balasubramanian
12.00 – 1.00 pm	Lunch

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Exploring Biology of Antibiotic Resistance and Potential Targets

DBT MRC Workshop

January 15-17, 2017

LV Prasad Eye Institute

Department of Biotechnology
Ministry of Science & Technology,
Government of India

BITS Pilani
Hyderabad Campus

The University Of Sheffield.

MRC Medical Research Council

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Session I
9.00 – 11 AM, 15.01.2017

Antimicrobial Resistance

Moderators

Dipankar Ghosh, Joey Shepherd

Ex vivo cornea infection model and its utilization in evaluating detection devices

Prashant Garg

KallamAnji Reddy Campus, LV Prasad Eye Institute, BanjaraHills,Hyderabad, India.

Infectious diseases of the eye are comon causes of occular damage and blindness in India. Early diagnosis and institution of appropriate therapy are key in reducing both of these nagative outcomes. The microbial cause varies with geographical location and a number of pathogens therefore; identification of the infecting microorganism plays a crucial role in successful treatment. The aim of the present study was to develop a reproducible model of corneal infection using *ex vivo* organ culture of corneas which can be used for drug toxicity studies and evaluating devices.

Poly(N-isopropyl acrylamide) (PNIPAM) is a thermo-responsive polymer used in many biological applications and previous work has shown that antibiotic functionalized PNIPAM-HB-PNIPAM-Van and HB-PNIPAM-Pmx binds Gram positive and Gram negative bacteria respectively . Our preliminary results with series of hydrogels with functionalized polymers had capability to pick up bacteria from infected *ex vivo* corneas. The hydrogel with bound bacteria were subjected to dye which showed a visible colour change indicative of the presence of pathogens. These findings suggest this system aids in the evaluation of microbial detection systems.

Biodata: Dr Prashant Garg has done his specialisation in ophthalmology from RNT Medical College Udaipur, Rajasthan. Prior to joining LVPEI's Cornea and Anterior Segment fellowship in 1996, he served as an Ophthalmologist in private sector hospitals. He later joined as faculty of the Institute in 1997 and since then has progressed steadily in his clinical and research career. Dr Garg has over 60 scientific publications in peer-reviewed journals to his credit and has presented in various forums across the world. He has been a principal investigator for several clinical trials and is a reviewer for ophthalmology journals, such as Cornea, Ophthalmology, Eye, Current Eye Research and British Journal of Ophthalmology. In 2004, he received the American Academy of Ophthalmology's Achievement Award. His specialisation is infectious diseases of the cornea and anterior segment, and eye banking procedures.

Design of conformationally restricted short peptides: Antimicrobial and self-assembling properties

Virander Singh Chauhan

International Centre for Genetic Engineering and Biotechnology, New Delhi, India

We have been working with design, synthesis and characterization of conformationally restricted peptides using alpha beta dehydroamino acids. Using various spectroscopic methods including CD and NMR, in solution, and solid state structures, we have found that presence of alpha-beta dehydrophenyl alanine induces beta turn in short peptides and stabilized helical structures in longer model peptide sequences. Using these design principles we have synthesized peptides with potential as antimicrobial and antifungal agents. Some of the synthesized peptides have shown significant antimicrobial activities. We also found that very short peptides containing dehydrophenylalanine self-assemble into highly stable nanostructures, entrap and release various biomolecules including small drugs like molecules as well as plasmids and small oligonucleotide sequences in slow and sustained manner. Moreover, these short peptide based nanostructures can be easily derivatized at their N-terminal and thus can be used for targeted delivery.

Biodata: Prof. Chauhan obtained his Bachelors, Masters and Doctorate degree in Chemistry from Delhi University. In addition to a brilliant academic record, he has also been an outstanding sportsman and represented Delhi University and Oxford University in athletics and cross country. He won the prestigious Rhodes scholarship (1974) to study at Oxford University. Upon his return to India in 1979, he taught at St. Stephen's College, IIT - Kanpur, and Delhi University. In 1988, he joined the International Centre for Genetic and Biotechnology (ICGEB) and became as Director in 1998, a position he held until 2014.His major scientific contributions are in the fields of malaria vaccine and drug development and in study of peptides of biological importance. An experimental malaria vaccine that was developed entirely in India was taken to clinical trials also in India. His current research is also focused on developing peptide based nanostructures for efficacious delivery of bio molecules different. His scientific interests also include advocacy in infectious diseases like HIV and TB in India. He has published more than 250 research papers and guided more than 50 research students. He is also deeply involved in human resource development through major involvement in selection process of highly prestigious Rhodes scholarships, Inlaks Scholarships and Felix Scholarships for Indian students. Prof. Chauhan has received several of prestigious national and international awards including civil honor Padma Shri in 2012. He is currently a member of UGC and Chairman of the Executive Council of National Assessment and Accreditation Council (NAAC). He is also Chairman of the Pay Review Committee for the 7th Pay Commission for all government funded institutions of Higher Education

Early detection pathogenic bacteria and strategies to overcome drug resistance using MCF7 cell line as a model

Harpal Singh

Centre for Biomedical Engineering, Indian Institute of Technology Delhi,
All India Institute of Medical Sciences, New Delhi, India.

Early detection of pathogenic bacteria is essential for pathogenic disease control, associated health problem and mortality. Functionalized polymeric magnetic nano-constructs (FPMNC) were developed as an effective immunomagnetic separator and sensing platform for selective capturing of *Salmonella typhimurium*. The developed immunoassay was specific and selective with a detection limit of 10 cells/ml much lower than infectious dose of salmonellosis infection. The performance of developed immunoassay was superior to commercially available immunomagnetic microbeads and conventional polystyrene plate based ELISA.

Multidrug resistance is a resistance shown by mammalian cells or microorganisms to single or multiple drugs. Microorganisms employ several mechanism in attaining multidrug resistance such as acquired expression of efflux pumps, decreased cell wall permeability, alter target sites, increased mutation rate. We have developed novel biodegradable poly(lactic acid)-poly(ethylene glycol-propylene glycol-ethylene glycol) (PLA-PEG-PPG-PEG) nanoparticles (NPs) that successfully overcome drug resistance in MCF7 cells over expressing Pgp receptors. PLA-PEG-PPG-PEG NPs were found to be spherical in shape with an average diameter of ~135nm. MCF7 cells were repeatedly challenged with increasing dose of free paclitaxel (PTX) to develop PTX resistant MCF7 (PTX-R-MCF7) cells. The half maximal inhibitory concentration (IC_{50}) of polymer loaded PTX was 50.16nM as compared to 1784.32nM for free PTX in PTX-R-MCF7 cells. PTX loaded polymeric NPs also showed increase cytotoxicity and apoptosis in drug resistant breast cancer cells as compared to PTX based commercially available anticancer drugs Taxol and Abraxane. Paclitaxel loaded PLA-PEG-PPG-PEG nanoparticles had a curative effect on multidrug resistant breast cancer cells by increasing the amount of drug accumulation in the cytoplasm due to cellular uptake of polymer protected PTX through endocytosis, bypassing the P-gp receptors, and thus retaining the anti-proliferative effect of paclitaxel.

Biodata: Dr. Harpal Singh is the Executive Director Stanford-India Biodesign Program, IIT-AIIMS Delhi. He qualified PhD from IIT Delhi and since then he is into biomedical research including biomedical nanotechnology. His active research focuses on the 'Development of polymers to deliver drugs, particularly chemotherapeutic drugs/peptides/DNA, continuously at controlled rate for prolonged period of time'. He has published more than 100 research papers in National and International Journals of repute, presented 60 research papers in National and International Conferences and 10 patents in the area of Polymeric Biomaterials, Nanomedicine, Drug Delivery Systems, Antimicrobial Polymers for Water Disinfection, Medical diagnostics & Synthesis and Modification of Polymers for Biomedical and Industrial Applications.

Antibiotic Resistance and Future Strategies

Hemant Gautam

CSIR- Institute of Genomics and Integrative Biology, Mathura Road, New Delhi, India.

Bacterial infections are increasingly posing a serious threat to modern society as the number of microbial strains resistant to a number of drugs worldwide has increased in the last few years. The result of indiscriminate use of antibiotics, bacteria evolved resistance against many of these agents. In recent year, MRSA strains with a decreased susceptibility to vancomycin have been described in clinical isolates since late 1990s, which were named as vancomycin intermediate resistant *S. aureus* (VISA). MRSA isolates with a high-level of vancomcyin resistance (VRSA) were first recognized in 2002 in USA. Till now few drugs are available which can be used to treat serious MRSA infections such as; vancomycin, daptomycin, linezolid, tigecycline, quinupristitin-dalfopristin and teicoplanin. Recent study on antibiotic resistance pattern of MRSA with special reference to newer antibiotics showed that not only the vancomycin rather resistance against linezolid and daptomycin has also been started to appear. In addition to MRSA, there are several outbreaks due to MRSA has also been reported. Our study also showed that the pathogenic strains with a resistance against all these new generation antibiotics have emerged needs longer dose of drug therapy. Besides these, several other drawbacks of these drugs such as organ toxicity, mode of drug administration, limited uses and increased mortality in patients cannot be neglected. There are many reasons for the drug resistance in developing world as well as developed world. It has necessitated an urgent need of new agents that can effectively act against these strains and restrict their growth and development. To accomplish this requirement as well as non-availability of new generation antibiotics, researchers have diverted attention towards the other sources like natural sources synthetic polymers, natural product derivatives, Vaccine, prebiotic and probiotic, photodynamic therapy combing with new technologies like Bacteriophase biology, CRISPER, Nanoparticles are a new platform for the creation of antimicrobial agents which have also shown some encouraging results against drug resistant bacterial strains.

Biodata: Dr. Hemant Gautam is currently a senior principal investigator and professor at Institute of Genomics and Integrative Biology, New Delhi. His lab works on screening of natural products for skin diseases, evaluation of natural and synthetic molecules against antibiotic drug resistance bacterial strains, purification and characterization of enzymes from isolated microorganisms for diagnostics purpose, etc. He has over 200 publications in peer-reviewed journals of international repute and also authored many books and book chapters. He is a fellow member of various international scientific bodies and has number of prestigious awards.

Session II
11:30 AM – 1:00PM 15/01/2017

Biofilm

Moderators

Prashant Garg, Soumyava Basu

Ocular *Escherichia coli* : biofilm formation, antimicrobial resistance and gene expression

Sisinthy Shivaji

Kallam Anji Reddy Campus, LV Prasad Eye Institute, Banjara Hills, Hyderabad, India

Resistant to antimicrobials is a global phenomenon and is seen in bacteria, fungi and viruses. This emergence is due to indiscriminate use of antibiotics coupled with the ability of the bugs to develop strategies to avoid the killing effect of the drugs. The ability to form a biofilm and become impervious to antimicrobials is a strategy encountered worldwide in a variety of pathogens. Thus studies focused on the molecular basis of biofilm formation would help to devise strategies to hack biofilm and thus overcome antimicrobial resistance. The presentation focuses on ocular *E. coli* with respect to resistance to antibiotics, biofilm forming potential and identification of genes differentially expressed during biofilm formation and drug resistance. The results demonstrate that ocular *E. coli* have the potential to form biofilm and cells in the biofilm are more resistant to antimicrobials. Further several virulent genes like those coding for pili/fimbriae, lipopolysacccharides and exopolysaccharides synthesis, efflux pumps etc. are up regulated.

This is the first study on DNA microarray analysis of an ocular *E. coli* with a potential to form biofilm.

Biodata: Prof. S Shivaji currently serves as the Director of Prof Brien Holden Eye Research Centre at LVPEI. He joined LVPEI, Hyderabad, in August 2013, as a Microbiology Mentor. Prior to this he was associated with Centre for Cellular and Molecular Biology (CCMB), Hyderabad and retired from there as a Director-grade Scientist in 2012 and continued as a consultant at CCMB till June 2013.His research interests include microbial diversity of Antarctica, Arctic, Himalayas, Stratosphere and other cold habitats, molecular basis of cold adaptation, molecular basis of mammalian sperm fertilizing ability, conservation of endangered animals and genetic basis of endometriosis. He is also the co-founder of the Laboratory for the Conservation of Endangered species (LaCONES) a facility dedicated to research on the conservation of Indian endangered animals. He is a fellow of National Academy of Sciences, India, Indian Academy of Sciences, India, Telangana Akademi of Sciences, India, and Fellow of the Association of Microbiologists of India. In recognition of his work in the area of Antarctic Microbiology the government of India awarded him the Antarctic Award for excellence in the field of Biological Sciences in 2002. He is also a recipient of Prof L S Ramaswami Award, Prof T C Anand Kumar Award and Prof N R Moudgal Award by Indian Society for the Study of Reproduction and Fertility for his contributions in area of conservation biology and reproductive biology in the years 2010, 2013 and 2014 respectively. He is a recipient of the first Carl Woese Memorial award, 2014, by the Association of Microbiologists of India. He has published 315 research papers and 2 books and has had several international collaborations.

Novel methods to treat (and grow!) biofilm

Joanna Shepherd

School of Clinical Dentistry, University of Sheffield, Sheffield, United Kingdom

Bacterial biofilm is a global concern, as it can form on almost any surface and is a problem in both the medical field and in industry. Biofilms are less sensitive to antibiotics than planktonic bacteria, and the concurrent rise in antibiotic resistance means we need to seek new solutions to bacterial biofilm infection. We are using low intensity ultrasound as a method of making biofilm more sensitive to antibiotics, and also find that low frequency ultrasound may be effective at killing intracellular bacteria without the use of antibiotics. We are also interested in wound dressings to combat bacterial biofilm in infected chronic wounds and are developing a cerium-containing antibacterial wound dressing amongst others.

Our group at the University of Sheffield is also working with bacteria-binding polymers in collaboration with LV Prasad Eye Institute, with the ultimate aim of being able to detect microbial infection of the cornea and decrease the microbial burden.

Biodata: Joey Shepherd is a non-clinical Lecturer in Microbiology at the University of Sheffield's School of Clinical Dentistry. Her research interests are largely translational in nature and primarily in novel approaches to detecting and treating bacterial infections without traditional use of antibiotics, including the use of polymer-based systems, ultrasound and acoustic vibration, novel wound dressings, and using 3D tissue engineered models to examine effects of infection and treatment on both bacteria and human cells. She currently is a co-supervisor for two PhD students and three postdoctoral researchers with a fourth to be appointed. At present she has collaborations with Sheffield Hallam University, Liverpool John Moore's University, Bradford University, the LVPEI Eye Institute in Hyderabad, India. 11 Institutions across 8 European countries as part of a Horizon 2020 grant, and Smith & Nephew.

Polymicrobial biofilms and antibiotic resistance: the case of *Pseudomonas aeruginosa* and *Stenotrophomonasmaltophilia*

Pallavi Lahiri and Dipankar Ghosh

Special Center for Molecular Medicine & Center for Advanced Research (ICMR-CAR), Jawaharlal Nehru University New Delhi, India.

Polymicrobial infections are increasingly recognized in the aetiology of complex diseases. Unlike mono-microbial infections these diseases present highly complex mechanisms of pathogenesis that are poorly understood and frequently misdiagnosed. A typical case is presented for *Pseudomonas aeruginosa* and *Stenotrophomonas maltophilia*. Both are Gram's –ve superbugs, often associated with nosocomial infections and reported in ocular keratitis. Emerging data indicates this polymicrobial infection presents unique mechanism(s) of exacerbated antibiotic resistance and pathogenesis, which should be factored into treatment regimens to mitigate worse outcomes

Biodata: Dr. Dipankar Ghosh is currently assistant professor at Special Centre for Molecular Medicine, Jawaharlal Nehru University, New Delhi. His research area include early host-microbe interactions, Quorum Signalling in gut microbiome, Probiotics, Mass Spectrometry based metabolomics. He did his PhD from Jadavpur University, Kolkata and postdoctoral training from Cleveland Clinic Foundation, USA.In 2001, Dr. Ghosh received Merlin Bumpus Best Investigator Award. He published number of articles in journals of international repute. He also has a patent for Selective Detection and Analysis of Small Molecules.

Session III
2:00 PM – 4:00 PM 15/01/2017

Non antibiotic approaches

Moderators

Stephen Rimmer, Sudip Ghosh

Non-antibiotic approaches to tackling infection

Sheila MacNeil

Department of Materials Science & Engineering, University of Sheffield, United Kingdom.

For an infection to develop in a wound there are a number of criteria to be met. Usually there is a breach in the epithelial barrier layer, sufficient bacteria need to enter and survive and finally the immune system must be unable for whatever reason to deal with the infection. Finally formation of a biofilm in a wound provides an ideal environment in which cells can withstand the effects of antibiotics.

One challenge in looking at infected wounds is that many in vitro models are too simple and most healthy animal models don't mimic some of the problems that occur in man, such as chronic non-healing ulcers in the elderly. Working with a 3D tissue engineered skin model that is wounded and bacterially infected, colleagues in Sheffield have developed approaches to reduce bacteria binding effectively to host cells in the wound bed (using tetraspanin derived peptides) and have developed polymers which are intrinsically antimicrobial which do not adversely affect the skin cells.

What is currently lacking from our toolkit is an immune competent model of infected skin or cornea in which to study the complexities of bacteria entry into wounds, bacteria biofilm formation, antibiotic resistance and the immune response to bacteria. There is a need to develop immune competent, information rich models of bacterial biofilms for future research.

Biodata: Sheila MacNeil is Professor of Tissue Engineering in the Department of Materials Science and Engineering, joining the department in 2000. She has an undergraduate degree in physiology from the University of Aberdeen and a doctorate on the endocrinology of manic depression from the Medical School of the University of Sheffield. She is academic lead of the Biomaterials and Tissue Engineering Group within the Department. She has previously been Deputy Director of the Kroto Research Institute (from 2005 to 2009) and Director of the University Centre for Biomaterials and Tissue Engineering from 2002 to 2009, promoting interdisciplinary research between engineering, physical sciences and life sciences. Her current projects include developing tissue engineering approaches for reconstruction for burns contractures, for stimulating healing in chronic ulcers and she leads a group of scientists and clinicians developing a tissue engineering approach for repair of the weakened tissues of the female pelvic floor. She also has two Wellcome funded projects with India on corneal tissue engineering and early detection of infection in the cornea (with Professor Stephen Rimmer in Chemistry and Professor Ian Douglas in Dentistry.)

Role of iron metabolism in bacterial virulence and antimicrobial resistance

Subhadeep Chatterjee

Laboratory of Plant-Microbe Interactions, Centre for DNA Fingerprinting and Diagnostics CDFD), Hyderabad, India

Iron is required for virulence of several animal and plant pathogenic bacteria. The availability of iron within the host plays a critical role in the growth and survival of the pathogens. Ability of the pathogens to sequester host iron and respond to host iron status has been proposed to be critical for virulence and survival of plant pathogens. Although iron has been implicated in the virulence of pathogenic bacteria, very little is known about how pathogens acquire complex iron source and maintain iron homeostasis inside host. It has been proposed that pathogens modulate their metabolism and virulence associated functions depending on iron availability, wherein, iron availability act as a signal for coordinated regulation of different cellular functions. Recent work in our laboratory had shown that iron plays a major role in regulating diverse cellular process and production of virulence associated functions. We will discuss about the mechanism of iron dependent regulation of virulence associated function and would like to address how iron and virulence associated functions are co-ordinately regulated in host-pathogen interactions.

Biodata: Subhadeep Chatterjee obtained his M. Sc degree in Biotechnology from Guru Nanak Dev University, Amritsar in 1998. In his post-graduation, He worked on the mechanism of stress response physiology of wheat (Triticumaestivum L). In 1998 he joined CCMB in Dr Ramesh V. Sonti's laboratory to work on Rice-*Xanthomnasoryzaepv. oryzae* (Xoo) interaction. During his Ph. D work he identified and characterized two novel virulence functions of this economically important pathogen of rice

Role of antimicrobial peptides in bacterial keratitis

Sanhita Roy

KallamAnji Reddy Campus, LV Prasad Eye Institute, Banjara Hills, Hyderabad, India.

Microbial keratitis is the most prevalent cause of corneal infection in both developing and industrialized nations. In India and globally, *P.aeruginosa* are major causes of bacterial keratitis, responsible for 8-20% of all bacterial keratitis. It results in severe corneal opacity, ocular pain and visual impairment and predisposing factors include ocular trauma and contact lens wear. During infection, once the corneal integrity is breached, prompt treatment with antibiotics is required to stop the development of infection and its effects such as ulceration, scarring and finally loss of vision. The emergence of bacterial resistance to conventional antibiotics increase the necessities to study alternative therapeutic agents that kill the microbes and also help in modulation of the inflammation. This expedited the research on antimicrobial peptides and their roles in the disease. Corneal scrapings from *Pseudomonas* keratitis patients have been analyzed and differential expression of antimicrobial peptides belonging to different groups has been determined in these patients. We are also looking for agents that might induce the expression of antimicrobial peptides and combat bacterial infection.

Biodata: Dr. Sanhita is currently a scientist at LV Prasad Eye Institute and her lab has been working on host pathogen interactions, innate immune responses in microbial keratitis and endothelial dystrophies. She did her PhD from CSIR-Indian Institute of Chemical Biology, Kolkata and her postdoc from Case Western Reserve University, Cleveland, USA. She has published extensively in highly reputed peer reviewed journals and also has been reviewer for prestigious journals like IOVS, Scientific Reports etc. Her laboratory is also funded by extramural grants obtained from various granting agencies, Govt. of India.

Manufacturing and testing the efficacy of non-fouling/antimicrobial materials

Maria G Katsikogianni

Advanced Material Engineering, Faculty of Engineering and Informatics, University of Bradford, United Kingdom.

Infection is an impediment to the long-term use of medical devices, representing a financial and healthcare burden. Towards the manufacture of small prosthetic joints with antimicrobial properties, 1% and 10% (w/w)of triclosan impregnated polydimethysiloxane (PDMS) samples were compression molded on a flat or sub-micron patterned mould. The samples were assessed in terms of their geometric uniformity and mechanical properties using Atomic Force Microscopy (AFM). Their antimicrobial efficacy was examined against *Escherichia coli*, *Staphylococcus aureus* and *Staphylococcus epidermidis* over 24 h using viable counts and Confocal Laser Scanning Microscopy coupled with live/dead staining. The AFM showed that increasing amounts of triclosan significantly reduced the Young's modulus of the samples and reduced the quality of pattern replication. The antimicrobial studies showed that 1% triclosan killed all tested bacteria on both flat and patterned surfaces within 1 h. In the case of PDMS without triclosan, patterned surfaces reduced bacterial adhesionandviability.Reproducible pattern replication was importantfor ensuring enhancement of the antimicrobial activity of triclosan-impregnated PMDS. This combined physical and chemical strategy provides a novel approach to generating non-fouling properties to medical device biomaterials.

Biodata: Dr. Maria Katsikogianni is a Lecturer in Biomaterials Chemistry at the University of Bradford and an active member of the Biomaterials research community, with a degree in Chemistry and a PhD in Biomedical Engineering. Her research profile lies at the interface of biomaterial science, life sciences and engineering. She has published 19 peer reviewed papers, 3 book chapters and has filed 1 patent.She is particularly interested in the biomimetic design of multifunctional materials for relevant clinical applications, e.g. in the context of engineering and testing non-fouling/antimicrobial materials to prevent bone infections, and in the investigation of bacteria-material interactions. Through patterning at the sub-micron level and the incorporation of antimicrobial agents, a combined physical and chemical strategy is harnessed for the preparation of medical device surfaces that prevent microbial colonization. Enhanced pre-clinical simulation and therefore testing under relevant *in vivo* mimicking conditions informs the design and manufacturing of new materials.

Session IV
4.30-6.00 PM 15/01/2017

Miscellaneous

Moderators

Pradip Paik, Nikhil Kumar Singha

Activation and inactivation of metronidazole in *Entamoeba* and *Trichomonas*

Sudip K. Ghosh

Department of Biotechnology, Indian Institute of Technology, Kharagpur, West Bengal, India,

Entamoeba histolytica (Eh), and *Trichomonas vaginalis (Tv)*, which cause diarrhea, dysentery, and vaginitis, respectively, are each treated with metronidazole. We have identified oxygen-insensitive nitroreductase (ntr) genes in *Eh*, and *Tv*, which are homologous to those that have nonsense mutations in metronidazole-resistant Helicobacter pylori. *Eh* and *Tv* also have nitroimidazole reductase (nim) genes, which are homologous to enzymes expressed in metronidazole-resistant *Bacteroides fragilis*. Recombinant *Entamoeba*, and *Trichomonas* nitroreductases use NADH rather than NADPH of *Helicobacter*. Two recombinant *Entamoeba* nitroreductases increase the metronidazole sensitivity of transformed *Escherichia coli*. Conversely, recombinant NIMs of *Entamoeba* and *Trichmonas* confer very strong metronidazole resistance to transformed bacteria. While *ntr* and *nim* mRNAs are variably expressed by cultured *Eh* and *Tv*, there is no simple relationship to metronidazole resistance in the strains tested. We conclude that microaerophilic protists have bacteria-like enzymes capable of activating metronidazole (nitroreductases) and inactivating metronidazole (NIMs), and these protists display some of the changes (nonsense mutations and gene overexpression) associated with metronidazole resistance in bacteria. An alternative pathway of Metronidazole activation has also been identified in *Entamoeba* through Malik Enzyme pathway

Biodata: Prof. Sudip Kumar Ghosh is currently a professor and head of the department of Biotechnology at Indian Institute of Technology, Kharagpur. His research interests include Molecular and Cellular Parasitology, Nanobiotechnology, Plant Molecular Biology. He is a member of various scientific associations. He has more than 100 publications in Indian and International peer-reviewed journals. He has several projects funded by various government agencies in India.

Targeting Chemo-resistant subpopulations in breast cancer: an emerging paradigm

Mahitosh Mandal

School of Medical Science and Technology, Indian Institute of Technology, Kharagpur, India

Chemotherapy is one of the principal modes of treatment for cancer, but the effectiveness of chemotherapy is limited by drug resistance which is a major challenge in cancer research. Tumour resistance can be either intrinsic (present before treatment), or acquired during treatment by various adaptive responses. At the level of the tumour, various mechanisms can regulate chemo-resistance, such as increased drug efflux, mutations of the drug target, DNA damage repair, activation of alternative signaling pathways and evasion of cell death. Moreover, chemo-resistance can also occur due to positive selection of a drug-resistant tumour subpopulation during assault of chemotherapy. One of the key interest of our group is to understand this unique adaptability of cancer cells during chemotherapy and design targeted therapies for these chemo-resistant clones present in tumour. Our current focus is to answer three big questions 1) what are the changes that occur in molecular level in these chemo-resistant clones which helps them survive the chemotherapy? 2) How these cells adapt to the changing micro-environment and influence other non-cancerous cells in the process? 3) What is the role of cancer stem cell in regulation of chemo-resistance in cancer? We have been able to identify sub-clones responsible for various drug resistance in breast cancer and are currently deciphering their signaling pathways. Survival pathways have always been regarded as one of the major regulators of chemo-resistance. We are investigating the role of MAP kinase pathways in chemo-resistant sub clones of breast cancer. We have also identified significant correlation between chemo-resistance and protective autophagy in breast cancer and unique adaptive changes in metabolic pathways that helps cancer cells to survive chemotherapy. Lastly, we are deciphering how the self-renewal pathways regulate quiescence and chemo-resistance in cancer stem cells.

Biodata: Prof. Mahotosh Mandal is currently serving as an associate professor at IIT Kharagpur. His research group works on cancer biology, angiogenesis, apoptosis, multidrug resistance, drug delivery, signal transduction and biomarkers. Dr. Mandal has about 150 publications in prestigious journals of international repute. He is a Fellow National Academy of Science, Fellow West Bengal Academy of Science and Subha Mukherjee Memorial Award from Physiological Society of India

Intraocular T-cell response in ocular TB

Soumyava Basu

Retina and Vitreous Service, LV Prasad Eye Institute, Patia, Bhubaneswar, India.

Tuberculosis-associated uveitis(TBU) is a common cause of intraocular inflammation in endemic countries. However, absence of definitive diagnosis and unpredictable response to treatment in TBU leads to prolonged visual impairment in significant number of patients. Understanding the immunopathogenesis of TBU is critical to defining the disease as well as customizing its treatment. Our work has demonstrated that the intraocular T-cell response is multifunctional and specific for both mycobacterial and retinal autoantigens, thus revealing a unique milieu in which both microbe-specific and autoreactive T-cells coexist. Additionally the autoreactive T-cells were resistant to activation-induced cell death, which suggests a mechanism for prolongation of intraocular inflammation.

Biodata: Soumyava Basu heads the Retina-Vitreous and Uveitis Services at L V Prasad Eye Institute, Bhubaneswar. He received his medical training from the University of Mumbai, followed by a retina fellowship from L V Prasad Eye Institute, Hyderabad. He has worked on 'Molecular diagnostics for ocular tuberculosis' at Doheny Eye Institute, Los Angeles, USA. In 2013-14, he completed a yearlong sabbatical at the University of Kentucky, USA under the mentorship of Prof Jay Ambati. Dr Basu's research interests lie in molecular diagnostics and immune-pathogenesis of ocular tuberculosis. He has received competitive research grants from Department of Science and Technology and Department of Biotechnology, Government of India. He has published extensively in peer-reviewed international journals and has been a reviewer for nearly all major ophthalmology journals. Dr Basu has been actively involved in framing the Indian Extra-pulmonary TB (INDEX-TB) guidelines. He currently leads the program committee of International Working Group on Ocular Tuberculosis. He has also been the principal investigator for several multi-centric clinical trials.

Session V
8:00 – 10:00 AM 16/01/2017

Non antibiotic approaches

Moderators

Anindya Ghosh, Mahitosh Mandal

Hyperbranched polymers for the disruption of quorum sensing

William Martin

School of Chemistry and Forensic Sciences, Richmond Building, University of Bradford, Bradford, United Kingdom

Bacterial biofilms are complex mixed communities of bacteria which can form on almost any surface. They are a particular problem in the biomedical field as they frequently colonize medical devices such as indwelling catheters and prosthetics, and they are difficult to treat with conventional therapies as they are not sensitive to traditional treatments such as antibiotics, due to their complex architecture. In order to form biofilms, bacteria use Quorum Sensing (QS), which involves the use of molecular signals sent and received by the bacteria forming and maintaining the biofilm. Gram negative organisms, such as *Pseudomonas aeruginosa* which frequently colonizes chronic wounds and is also the main pathogen in the lungs of cystic fibrosis patients, use homoserine lactone (HSL) in the QS process. HSL is released by bacteria and binds to the LasR receptor both internally and in neighboring bacteria, initiating further signaling and cascades of pathogenic factors involved, for example, with bacterial adhesion the surface and release of virulence factors.

Hyperbranched polymers have previously been used for the delivery of bioactive molecules in wound dressings, and the structure of these polymers is ideally suited to functionalization of the multiple end groups with. This poster will describe the synthesis of hyper-branched polymers with HSL homologues covalently attached to them. The ability of these materials to disrupt the QS process will be discussed.

Biodata: Dr. William Martin is a lecturer in chemistry at School of Chemistry and Forensic Sciences, University of Bradford. His research areas include Natural Product Synthesis, Developing Novel Reactions, Mass Spectrometry, Analysis and Synthesis of Archaeologically important bio-markers. He has number of publications in the journals of international repute. He has over 10 years of teaching and research experience.

Melimine-coated antimicrobial contact lenses

NagarajuKonda

KallamAnji Reddy Campus, LV Prasad Eye Institute, Banjara Hills, Hyderabad, India.

Incidence of microbial keratitis has been reported to be 4.1 per 10,000 wearers per year when wearing lenses during the day and 20.9 per 10,000 wearers per year when sleeping in lenses. Several studies have demonstrated that use of silicone hydrogel lenses (the current lens of choice for most practitioners) is actually associated with a doubling of the incidence of non-infectious keratitis. Clearly, there remains an unmet medical need for technology to reduce the incidence of these adverse events. Effective control of adverse responses during contact lens wear is a goal of the contact lens industry, and the development of strategies to reduce significantly the number of ocular adverse events would be of benefit to contact lens wearers worldwide.

Antimicrobial agents are being examined with the aim of developing antimicrobial contact lenses and new forms of antimicrobial lens cases. It is hoped that these developments will result in reduced contact lens-related microbial adverse events. Development of MK requires viable bacteria adherent to contact lenses, and bacterial debris adherent at the lens surface did not cause keratitis. Current talk will assess aspects of various antimicrobial strategies, such as cationic metals and peptides, selenium, quorum sensing inhibitors, and various biocidal and non-cidal agents. In addition, our preliminary work on Melimine-coated contact lenses to reduce the incidence of MK will be presented.

Biodata: Nagaraju Konda is Research Fellow, University of New South Wales, Australia. He is a consultant at Srujana-Center for Innovation, L V Prasad Eye Institute, Hyderabad

Non-essential PBPs and beta-lactam resistance

Dr. Anindya S Ghosh

Department of Biotechnology, Indian Institute of Technology, Kharagpur.India

Penicillin-binding proteins (PBPs) catalyze the final stages of peptidoglycan biosynthesis. As the PBPs are the targets of beta-lactam antibiotics, here we would like to address whether the presence or absence of non-essential PBPs do have any effect in the beta-lactam resistance. To address the issue, we have chosen a DD-carboxypeptidase of *E. coli*, named PBP5, encoded by *dacA* gene and plays a key role in the maintenance of cell shape. Although, PBP5 shares one of the highest copy numbers among the PBPs (~50% of the total PBPs), it is not essential for cell survival. To determine the effect of this redundant PBP on beta-lactam antibiotic susceptibility, *dacA* gene is deleted. As compared to the parent strains, both mutants become susceptible to all the beta-lactam antibiotics tested. Reversion to beta-lactam resistance is observed in the mutants upon complementing with cloned *dacA*, indicating the involvement of PBP5 in maintaining an intrinsic beta-lactam resistance and *dacA* homologues from different Enterobacteriaceae are able to substitute this behaviour of *E. coli* PBP5. Therefore, the involvement of PBP5 in maintaining intrinsic beta-lactam resistance is confirmed, and we speculate that inactivation of PBP5 may be helpful to introduce beta-lactam susceptibility.

In addition, for the survival of *E. coli*, any one of PBP1a or PBP1b is required and the deletion mutants with PBP1a or PBP1b deletion can survive. To check the role of PBP 1a and 1b in beta-lactam resistance first PBP1b (*mrcB*) has been deleted. The PBP1b mutants are 16–32 fold more sensitive to all the representative antibiotics than parent. However, the mutants regain the beta-lactam resistance upon complementation with cloned PBP1b. In search of a specific inhibitor of PBP1b for neutralizing it to mimic a situation resembling PBP1b deletion, we have identified cefsulodin that can inhibit PBP1s without affecting the other PBPs. Accordingly, a combination therapy with cefsulodin is planned with other beta-lactams. Based on the sensitivity assessment, the level of most effective dose of cefsulodin is determined, i.e., $1/4^{th}$ of its MIC value. The combinations of such sub-inhibitory concentration of cefsulodin with other beta-lactam agents are indeed effective against the clinical isolates from various bacterial species with or without beta-lactamase activity. Finally, among the various combinations used, the most effective ones are with the cephalosporin group of beta-lactams that can reduce the resistance up to 32 fold. Therefore, we can conclude that intrinsic beta-lactam resistance can be lowered by proper usage of combination therapy with specific PBP inhibitors.

Biodata: He is currently working as associate professor at department of biotechnology, IIT Kharagpur. His broad research area includes bacterial cell surface macromolecules, emphasizing on penicillin-interactive enzymes (PIEs). Dr. Ghosh has about 32 publications in the journals of national and international repute. He is also a reviewer for number of peer-reviewed journals.

Session VI
10.30 – 1.00 PM 16/01/2017

Drug Delivery Systems

Moderators

William Martin, Sanhita Roy

Towards bacteria targeting particles

Stephen Rimmer

School of Chemistry and Forensic Sciences, Richmond Building, University of Bradford, Bradford, United Kingdom

The presentation will outline our approach to the preparation of particles that can be loaded with antibiotics and which can be used for targeted local delivery to bacteria. Routes to both block copolymers and cross-linked particles will be shown. We will also look in advances in polymer characterization that are key to taking these systems to the clinic. The work will describe our use of DOSY NMR and size exclusion chromatography in methanol and will outline some of the challenges faced during this aspect of our work. Calorimetry is used to determine the solution behavior of these systems and we will describe how we have used this technique to study the response to model peptides (Ala-Ala) that bind to vancomycin functional polymers. The study includes comparison of linear functional polymers to highly branched analogues and will show how placement of the vancomycin ligand at the chain end is required for response to bacteria.

Biodata: Dr. Stephen Rimmer is currently a Professor at School of Chemistry and Forensic Sciences, University of Bradford. He is a Fellow of Royal Society of Chemistry (RSC). His broad research areas include Polymers, Biomaterials, Smart Polymers, Anti-microbial agents, Tissue Engineering, Drug delivery. His lab is focused on the synthesis and analysis of functional polymers and their biological applications. He has number of publications in peer-reviewed journals of international repute. Prof. Rimmer also has 20 years of teaching experience and spent seven years in industrial research.

Novel Antibacterials: The Vitas experience

Radha Rangarajan

Vitas Pharma, Hyderabad, India

Multidrug resistant infections are a major public health problem globally as morbidity and mortality associated with these infections are on the rise. In order to combat drug resistance, new therapies are urgently needed. However, incremental optimizations of existing classes of antibiotics are not the solution as existing mechanisms of resistance will eventually render them obsolete. On the contrary, novel chemical scaffolds are more likely to overcome resistance and provide clear therapeutic benefit. Duringthe Genomics era of the 90s, many new and essential biological targetswere identified and high throughput screening was employed to select chemical scaffolds specific to the target. Unfortunately, these efforts did not translate into new drugs and many large pharmaceutical companies moved away from antibacterial research. What then is the way forward? How does one identify biological targets and chemical scaffolds with a higher probability of success in the clinic? The speaker will draw on her experiences as founder of Vitas Pharmaceuticals, a drug discovery and development company dedicated to Infectious diseases.

Biodata: Dr. Radha Rangarajan is co-founder and CEO of Vitas Pharma, a drug discovery and development company, based in Hyderabad, India. Prior to Vitas, Radha was a scientist in the Drug Discovery division of Dr. Reddy's Laboratories from 2003-2009, where she led research programs in multiple therapeutic areas including, anti-invectives' and metabolic disorders. Radha received her Bachelor's degree in Biology from Stanford University, Master of Science degree from the University of Michigan, Ann Arbor and her Ph.D. in Neurobiology/Genetics from Rockefeller University, New York. She was a postdoctoral fellow at the Harvard School of Public Health where she conducted research on the transmission of the malaria parasite. Radha was a finalist in the ET Start up awards- Woman Ahead category in 2016. She was featured in Biospectrum magazine's 10th anniversary issue as one of India's top women Biotechnology entrepreneurs. Radha is a member of the CII Committee on Biotechnology. She is also member of the American Society of Microbiology. She has published widely, has multiple patents filed and has presented her research at numerous international conferences. She is on the Guest Faculty at the Indian Institute of Technology, Hyderabad.

Breaching the membrane barriers for effective drug delivery

Venkata Vamsi Krishna Venuganti

Department of Pharmacy, BITS Pilani, Hyderabad Campus, Hyderabad, India

Effective topical drug delivery is limited by the formidable barrier properties of epidermal and epithelial membranes. Over the years multiple techniques have been identified to overcome the barrier limitation and enhance the drug transport through the membranes. These broadly include chemical and physical methods of permeation enhancement. Some of the key factors to choose a suitable penetration enhancement method depends on the physico-chemical properties of drug, irritation potential, safety, transient nature of membrane alteration among others. Here, we present the breaching of skin membrane to deliver multiple therapeutics using passive and active methods. Utilization of nanoparticle based formulations further improves the effect of chemical or physical penetration enhancers.

Biodata: Dr. Vamsi Krishna is currently working as Assistant Professor of Dept. of Pharmacy in BITS, Hyderabad. He pursued his Ph. D. (Pharmaceutical Sciences) at South Dakota State University, USA, 2010. His research interests include Nano/micro-carrier mediated Drug Delivery for Transdermal/Topical applications, Non-Viral Carriers for Gene-based Drug Delivery and Development of Biomaterials for Drug Delivery. He has authored many research articles including book chapter. He is reviewer for International Journals of Journal of Biomedical Nanotechnology, Material Science and Engineering C, Drug Development and Industrial Pharmacy, etc. He is the recipient of several grants from DBT, DST, UKICAT-MA by DBT-MRC etc.

New class of polymeric nano-hybrid material based on POSS and its biomedical applications

Nikhil Kumar Singha

Rubber Technology Centre, Indian Institute of Technology, Kharagpur, India

POSS is new classes of 3-dimentional nano-material which consists of alternating Si-O bonds to form a cage like structure where Si atoms are exist as vertices. Depending on the types of functionality present in the vertex positions various types of mono and multifunctional smart materials can be prepared. Here we describethe syntheses of some new class of compounds based on POSS and their potential use in the field of biomedical application especially as a delivery system for drug due to its non-toxicity, biocompatibility, chemical inertness, biodegradability and antithrombogenic properties etc. Methacryloyl-POSS (MA-POSS) was used to polymerize over the surface of grapheme oxide (GO) via surface initiated atom transfer radical polymerization (SI-ATRP) to prepare polymer brush over GO. The hybrid material (GO-PMAPOSS) was synthesized via SI-ATRP of methacryloyl-POSS (MAPOSS) on GO surface and was duly characterized by FTIR, GPC, TEM, FESEM, goniometry and TGA analyses. Later, we introduced this GO-PMAPOSS hybrid material into starch-polyacrylamide based semi IPN hydrogel which was prepared by using free radical polymerization of acrylamide in presence of starch. TEM and FESEM analyses revealed that GO-PMAPOSS hybrid material formed a network like structure inside the hydrogel through self-association of the hydrophobic POSS chains which helped to reduce the platelet adhesion as compared to hydrogel without GO-PMAPOSS hybrid material. The composite hydrogel also showed superior red blood cell compatibility and good cytocompatibility. Moreover, the composite hydrogel was capable of performing controlled release of drug. Functionalize POSS can also be used as an initiator for ring opening polymerization (ROP) reaction. Hydroxyl terminated POSS was used as an initiator to perform a strategic ROP of ε -caprolactone and α -propargyl-ε -caprolactone. After that azide terminated poly(*tert*-butyl acrylate) (P^{t}BA) was grafted onto functional PCL via Cu-catalyzed azide-alkyne 'click' (CuAAC) reaction and later on it was hydrolyzed to get an amphiphilic-POSS tethered PCL-*graft*-PAA polymer. The as prepared polymer was characterized by GPC, NMR, FT-IR analyses and the self-assembly behavior of the amphiphilic graft co-polymer in water at various concentration was analyzed by FESEM and HRTEM analysis. It was observed that depending on the concentration of the graft co-polymer in water it changes its morphology from micelles to worm-like to core-shell structure. Change of the size of the micelle with pH of the solution was measured using DLS analysis and after that the micelle was employed to deliver Rhodamine B, as a model compound.

Biodata: He is currently a Professor at IIT Kharagpur. His current research areas are Tailor-made polymers, Block (AB & ABA) & graft copolymers, Smart self-healing and self-cleaning polymers etc. He has been honored with Prof. M. Santappa award by Society of Polymer Science, India (2014) and Fulbright Senior Fellowship by USIEF, 2013-2014. He has four patents His research is being funded by DST, DBT, CSIR and many companies like Bridgestone Corporation, Tokyo, Japan, etc.

"NO" delivery through crossed-linked polymer capsules

Pradip Paik

School of Engineering Sciences and Technology, University of Hyderabad, Hyderabad, Telangana, India

In the cellular system during chemical reaction, the NO-free radical is an important cellular signaling molecule which has an extensive role in variety biological processes. Appropriate regulation of NO is essential for maintaining the overall health of the body and deficiency, or overproduction is known to be associated with some pathology. NO roles in different physiological events like vasodilation and hypertension in preeclampsia, mucus production, infection and wound care management sleep control and regulation, its role in antimicrobial applications and cancer treatment, and most importantly in proper functioning of the immune system were well documented. A new type of cross-linked polymer nanocapsule has been designed and its efficient delivery to the targeted site will be presented in this talk.

Biodata: Dr. Pradip Paik is currently assistant professor of the School of Engineering Sciences and Technology, University of Hyderabad, India with a 10 member research group. After spending a couple of years in Israel and NUS Singapore Dr. Paik come back to India on 2010. His research area focused on the new bio-materials and nano-capsules design and synthesis for drug and gene delivery and for therapeutic applications. He is co-author of 4 patent (provisional), 80 research articles including proceedings, and a couple of book and book chapters. 2 Ph.D. and 7 M.Tech Scholars have already been completed their dissertation under his supervision. Dr. Paik is recipient of the awards: ISCA 'Young Scientist Award'-2007, SwarnayaJayanty Endowment Fellowship (IIM-2011), Visiting Scientist/Faculty,-Israel 2012 and 2015; Research paper cash awards etc. Many of his scholars awarded for best dissertation and best oral presentation awards. Paik's research group (Advanced Polymers and Biomaterials) is funded by DBT, DST, UGC, BHEL etc.

Workshop discussion:

Like workshops in past, we decided to spend 2 half days on collaborative discussion. To begin the discussion and identify areas of interest among participants they were asked to think and write three areas that they would wish to work if they have funding available to them. The themes that emerged from this discussion were:

- Early detection of pathogenic organisms and drug resistance;
- Biofilm;
- Antimicrobial peptides;
- Targeted drug delivery

Participants were asked to choose groups that match the area their interest and than discuss brainstorm what is the problem and how can we solve it. Subsequent day started with having discussion on low hanging projects and how each project can be executed.

Summary of discussion:

Some of the projects that were considered having potential for collaboration were:

- **Tackling beta lactum resistance using combination therapy with cefsulodin.** The laboratory of **Dr. Anindya S Ghosh (**Department of Biotechnology, Indian Institute of Technology, Kharagpur.India)identified that cefsulodin inhibits PBP1s without affecting the other PBPs a combination therapy ofsub-inhibitory concentration of cefsulodinwith other beta-lactam agents was found to effective against the clinical isolates from various bacterial species with or without beta-lactamase activity. Dr Prashant Garg (L V Prasad Eye Institute expressed interest in testing this combination against beta lectum resistant ocular isolates.

- **Overcome multidrug resistance**: Another approach considered to overcome multidrug resistance was biodegradable poly (lactic acid)-poly(ethylene glycol-propylene glycol-ethylene glycol) (PLA-PEG-PPG-PEG) nanoparticles (NPs) that Prof Harpal Singh (Centre for Biomedical Engineering, Indian Institute of Technology Delhi) has shown to successfully overcome drug resistance in MCF7 cells overexpressing Pgp receptors.
- **Targeted drug therapy using HBPNIPAM:** Prof Rimmer in collaboration with DrVenuganti and Dr Garg is working on using hyper branched PNIPAM polymers for targeted drug delivery.
- **Antimicrobial Peptides as alternative to antibiotics:** Dr V S Chauhan's laboratory (International Centre for Genetic Engineering and Biotechnology, New Delhi) has synthesized peptides with potential as antimicrobial and antifungal agents. The group decided to assess highly branched PNIPAM polymers modified with AMPs and assess their stability and functions. It was decided that group would screen small molecule modulators, molecules from bacteriophages or biosensors that inhibit bacterial cellular metabolism. DrSanhita's laboratory has studied differential expression of antimicrobial peptides belonging to different groups in *Pseudomonas* keratitis patients and felt that looking for agents that might induce the expression of antimicrobial peptides or supplementing from outside for combating bacterial and fungal infections will be worthwhile.
- **Biofilm:** The group realized that organisms within biofilm exhibit much higher levels of drug resistance and exploring the biofilm inhibition using natural or chemical inhibitors or biofilm hackers as an approach for tackling drug resistance will be a good approach for tackling antimicrobial resistance. Dr. SubhadeepChatterjeein a recent work had shown that iron plays a major role in regulating diverse cellular process and production of virulence associated functions including biofilm. Dr. **Joanna Shepherd (**School of Clinical Dentistry, University of Sheffield, Sheffield, United Kingdom) is working on the use of ultrasound for the disruption of biofilm. Dr William Martin has

synthesized hyper-branched polymers with homoserine lactone (HSL) homologues covalently attached to them, which have the ability to disrupt the QS process necessary for biofilm formation.

- **There was a lot of interest tackling problem of drug resistant tuberculosis.** Following activities were decided by the group:
  - To test Vancomycin functionalized polymer for inhibition of M.tuberculosis in culture
  - Work toward animal model – Zebra fish and mice
  - To test different molecules (drugs) that have potential of being effective against drug resistant pathogens
  - Plan in-vitro experiments
  - Meet in Delhi to write grant proposal
- **Rapid detection of infection including drug resistance:** There was interest among the group on exploring different approaches for rapid detection of nature of infection and drug resistance using systems based on bacterial binding polymers, antibodies or aptamers or genome analysis and identifying drug resistance hacking resistance determinants and developing a simple colorimetric or florescent test.
- **Management of parasitic infections**: A section of participants were interested in evaluating surface markers of ameobae for developing a simple to use diagnostic test as well as therapy