

The International Conference on Bacteriophage Research and Antimicrobial Resistance - a Report

Theme: Paradigm shift in Antimicrobial therapy – Antibiotics to Bacteriophages.

Convener: Dr. N. Ramesh, Assistant Professor, SBST, VIT Vellore

A two day-long International conference on Bacteriophage Research and Antimicrobial Resistance (ICBRAMR '19) was recently held at the Vellore Institute of Technology, Vellore, Tamilnadu.

The Conference was organized jointly by the School of Bio Sciences and Technology (SBST), VIT in association with Society for Bacteriophage Research and Therapy (SBRT), India.

Highlighting the recent trends in Antimicrobial resistance and the search for alternative treatment options, the Chief guest Dr. Srikanth Prasad Tripathy, Director-in-charge, ICMR-National Institute of Research in Tuberculosis, Chennai and the Special guest Prof. Elizabeth Kutter, the First lady of Phage Research and Professor Emeritus, Evergreen State College, Olympia, USA, urged the scientific community to work tirelessly to discover a new weapon to combat the challenging antimicrobial resistance.

Dr. V Pragasam, Dean of the School of Bio Sciences and Technology, VIT welcomed the gathering and Prof. Sanjay Chhibber, President, Society for Bacteriophage Research and Therapy introduced the Society and its function to the participants and other dignitaries. Dr. S. Narayanan, Pro Vice Chancellor, VIT introduced VIT and talked about the achievements and accolades of the institute. The conference souvenir was released and the guests planted a tree to end the inaugural session of the event.



Inaugural session of ICBRAMR '19. The Chief Guest Dr. Srikanth Prasad Tripathy, Director-in-charge, ICMR-National Institute of Research in Tuberculosis, Chennai addressing the gathering.

The conference had keynote lectures by 20 renowned speakers who spoke on the latest developments in the field of Bacteriophage research and Antimicrobial resistance and around 300 participants across the globe had the opportunity to interact and share their experiences with the speakers.



ICBRAMR '19 participants

Conference at a glance

Prof. Kutter delivered the first lecture on “Bacteriophages: Biology and Applications”. She started with a brief introduction on T4 phage and about usage of bacteriophages in treating patients infected with multidrug resistant bacteria and pan drug resistant bacteria at the Eliava Institute, Tbilisi, Georgia.

Phage therapy is not approved for human use in most countries, including India, and conclusive evidences through clinical studies is urgently needed to convince the scientific community and Clinicians in India to practice phages. **Prof. Chhibber**, President, SBRT and Professor at Panjab University presented his findings on “From Concept to Product: Challenges at various stages in creating a successful and commercially viable phage preparation for therapeutic applications” and **Prof. Gopal Nath**, Secretary, SBRT and Professor at Banaras Hindu University gave his lecture on “Preclinical and Clinical Bacteriophage Therapy” where he shared few case studies of patients with diabetic ulcers and bacteremia.

Prof. Vinod Kumar, Vice President, SBRT also delivered a keynote lecture on “Building a future with bacteriophage; an alternative protagonist”. While finishing his lecture, he said that the regulatory authorities and the end users should encourage building the future with phage as an antibacterial agent in therapies since the impact of antibiotics is fading.

Dr. Mark Toleman from the School of Medicine, Cardiff University, UK, who has an extensive knowledge on antimicrobial resistance and particularly on the Asian region delivered an effective lecture on “Controlling resistance in *E. coli*” outlining the genetic diversity of *E.coli* in UK and India

and the natural role of phages controlling MLST *E. coli* and its prevalence. Considering the widespread existence of improper usage of antibiotics, the next keynote lecture was delivered by **Dr. Ashok J Tamhankar** from Karolinska Institutet, Sweden on “Global scenario of antimicrobial resistance”.

Dr. Balaji V, Dr Joy Sarojini Michael and Dr. Biju George from Christian Medical College, Vellore talked about the surveillance systems, antibiotic resistance profiling in both Gram positive and Gram negative bacteria among Indian population, TB prevalence and diagnosis and the problems associated with MDR bacteria in the process of transplantation, respectively. **Dr C P Girish Kumar** from National Institute of Epidemiology, Chennai also discussed the prevalence of antibiotic resistance in Gram negative bacteria in India.

Dr Sebastian Leptihn, Zhejiang University, ZJU-UoE INSTITUTE, China shared his data on Filamentous Phage Biology and their Impact on Human Health and **Dr. Urmil Bajpai** from Acharya Narendra Dev College, New Delhi gave a lecture on “A Multipronged Quest for Anti-Mycobacterial Solution: Bacteriophages, Endolysins and small molecules”.

Mr. Pranav Johri who was the first person to receive phage therapy from India shared his success story with the participants and **Dr. Jeremy Barr** from Monash University, Australia through Video conference shared the well-known phage therapy of Tom Patterson who battled the MDR *Acinetobacter baumannii* infection.

The conference also had talks from industry experts like **Dr. Aradhna Vipra** from Gangagen Biotech, Bengaluru talked about the phage product development for non-clinical applications - From Laboratory to Field and Dr Manavi Dang and Dr Devjani De from **Dang's Lab** Gurgaon, Haryana discussed on “Turning the Tables on MDROs” highlighting the importance of Film Array for the early detection of antibiotic escalation in ICU patients.

We also had an enlightening lecture from a different perspective by **Dr. Taruna Anand** who discussed about the isolation and characterization of bacteriophages for bovine infection.

Prof. Graham Hatfull from the University of Pittsburgh presented how his SEA-PHAGES program helped in treating a 15-year-old girl suffering from drug-resistant mycobacterial infection.

Finally we had **Dr. Prasanth Manohar** who obtained his PhD under the guidance of me and now a postdoc at ZJU-UoE INSTITUTE, China talked on the topic “Antimicrobial Resistance and Phage Therapy: Our Research Lab at VIT” giving an overview on the extensive work carried out during his Ph.D. at VIT.

Poster presenters were awarded during the valedictory ceremony.

About the conference

Speaking about the conference Dr. N. Ramesh, Assistant Professor and Convener, ICBRAMR '19 said that this conference aimed at bringing together Indian and international communities working in the field of Bacteriophage and AMR to discuss new and exciting advances in the field. This conference was enlightened by the words and experience shared by the 7 international keynote speakers from USA, UK, Sweden, Australia and China and 14 national keynote speakers from 8 states. A total of 60 institutes, 10 states and 2



union Territories from India and 2 international participants from Vietnam and UK has registered for this conference.

Dr. N. Ramesh, Assistant Professor and Convener, ICBRAMR

'19

We were really blessed and fortunate to have Prof. Elizabeth Kutter, the First lady of Phage Research at our conference and her knowledge, wisdom and experience is a real bonus for the participants who had the chance to meet and interact with her. She is definitely a role model for the young researchers who at the age of 80 is still active and enthusiastic in leading phage research and therapy in the world. She has been involved in phage therapy at the Eliava Institute, Tbilisi, Georgia where patients with chronic bacterial infections gets treated with bacteriophages.

A country with huge population and high demand, antibiotics are often prescribed at an incorrect dose, frequency, or duration in India. The irrational use of antibiotics has led to several Gram positive and Gram negative bacteria which causes serious infections, are now developing resistance to antibiotics being prescribed by the doctors. As the world enters into a post-antibiotic era, millions are expected to die each year from infections once easily treated. There is an urgent need to identify alternative options to overcome this menace of antibiotic resistance and Phage therapy may be an alternative and potential weapon against infectious diseases.

Phage therapy has been an age old practice followed in Western Europe and Soviet Union but the advent of antibiotics in the 1940s led most Western practitioners to prescribe antibiotics over phages. Meanwhile, drug-resistant bacteria started cropping up and now the world is turning its head towards phage therapy.

Bacteriophages are naturally occurring viruses that can be found in the environment – on land, in water, and even in sewage. Our Antibiotic resistance and Phage Therapy laboratory at VIT has been working on the isolation of bacteriophages from soil, water and sewage samples against clinical pathogens since 2013 and we had encouraging results which was published in several reputed journals of high impact factor.

Talking about his research, his research is currently focusing on identification of antibiotic resistant bacteria in the clinical samples. The antibiotics that are mainly in focus are gentamicin, carbapenems, colistin and tigecycline. Clinical samples were collected from hospitals and infectious bacteria are isolated and identified. Gram negative bacteria such as *E. coli*, *K. pneumoniae*, *E. cloacae*, *P. aeruginosa*, *A. baumannii* and Gram positive bacteria like Methicillin resistant *Staphylococcus aureus* (MRSA) are being studied for their resistance mechanism. Carbapenem resistance genes such as NDM, OXA, IMP, VIM, KPC, GIM, DIM, BIC, AIM, SHM and GES are amplified through PCR. At present 1100 Gram-negative bacteria are under study and 70 different carbapenem resistant genes were screened.

His research is also focused on identifying new bacteriophages against Gram negative bacteria and Gram positive bacteria. Four bacteriophages infecting *E. coli*, *K. pneumoniae* and *E. cloacae* have been shown efficacious *in vivo* through experiments using *Galleria mellonella* as model organism. His lab is the first in India to use *Galleria mellonella* as model for pre-clinical studies for phage therapy says Dr. N. Ramesh. He also published an efficient procedure to lyophilize phages which otherwise being produced as suspensions.

“Phages can undergo physical stresses in aqueous solution (suspensions) such as pH/temperature changes, agitation and exposure to denaturants, which can lead to aggregation and phage loss. To

maintain stability during long-term storage of phages, preparation of lyophilization powders is one of the effective mechanisms that need more exploration” explains Dr. N. Ramesh.

Highlights of the conference

Talking about success, the conference has set a platform for the people working on phages from India and the level and diversity of discussion were just outstanding, says Dr. N. Ramesh. He shared some of the key moments of the conference.

- Concerns were raised about the problem of potentially low phage retention at the site of infection when administered. Prof. Chhibber explained through his findings how phages can be retained at the site of infection by a suitable lipid based delivery system.
- The release of endotoxin due to bacterial lysis places another limitation on the phage treatment and questions were raised on the purity of the phages being administered to the patients.
- Dr. Jeremy Barr talk had an answer and through his publication in *PeerJ Journal*, an optimized protocol to clean phage preparation for the administration of phages clinically. He also shared how this preparation saved a Tom Patterson who recovered from the MDR *Acinetobacter baumannii* infection.
- The conference also had Mr. Pranav Johri, who presented how he is helping patients from India getting access to Phage therapy and also shared that more than 60 patients received phage therapy in India through his Vitalis Phage therapy initiative.
- Issues raised repeatedly on how to design clinical trials that adequately assess both phage therapy's safety and efficacy and what type of regulations were followed in India regarding phage therapy for the timely approval to deliver phages to patients who need it?
- Prof. Vinod Kumar emphasized that although there is no dedicated regulatory mechanisms exist for phage therapy in India, still consent from two doctors who is treating multidrug resistant infections along with some forms from DCGI, India is required.
- Nearly all of the panelists emphasized that along with phages there must be appropriate use of current medications. They also stressed the use of phages as an adjuvant for antibiotics.
- The conference participants also had the opportunity to learn how complex pathogens like mycobacteria can be targeted by mycobacteriophages through video lecture by Prof. Hatfull. He also explained how phages can be engineered to be more efficacious in the treatment.

Several participants asserted that new drugs were also needed to treat infections caused by Gram negative and Gram positive pathogens and they all agreed in unison that Phage therapy is a possible solution

Concluding his interaction with us he says “I think even though we have a lot of phages, or we appear to have a fairly large group of phage scientists right now, let's not be so complacent about that. Bacteria is too smart”

The ICBRAMR '19 Conference was held at the Dr. M. Channa Reddy Auditorium, VIT, Vellore with the aim to illuminate and disseminate the knowledge about antimicrobial resistance and Bacteriophage Research and its applications among the students, clinicians, academia, industry and researchers.

Inaugural Session

The Inaugural Session has Dr. Srikanth Prasad Tripathy, Director-in-charge, ICMR-National Institute of Research in Tuberculosis, Chennai, invited as the Chief Guest and Prof. Elizabeth Kutter, the First lady of Phage Research and Professor Emeritus, Evergreen State College, Olympia, USA was the Special Guest for the event. Dr. V Pragasam, Dean of the School of Bio Sciences and Technology, VIT welcomed the gathering and Prof. Sanjay Chhibber, President, Society for Bacteriophage Research and Therapy introduced the Society and its function to the participants and other dignitaries. Dr.N. Ramesh, Convener of the conference talked about the conference. Dr. S. Narayanan, Pro Vice Chancellor, VIT introduced VIT and talked about the achievements and accolades of the institute. The conference souvenir was released and the guests planted a tree to end the inaugural session of the event.

The conference attracted a total number of 270 participants, 102 abstracts, 7 international speakers and 12 national speakers.

Session I: Chair - Dr. A J Tamhankar and Co-chair - Prof. Gopal Nath.

Dr. Kutter delivered the first lecture on “Bacteriophages: Biology and Applications”. She started with a brief introduction on T4 phage and phage usage in infections with multidrug resistant bacteria. The next talk was delivered by Dr. Chhibber on “From Concept to Product: Challenges at various stages in creating a successful and commercially viable phage preparation for therapeutic applications”. The first session was chaired by

Session II: Chair – Prof. Sanjay Chhibber and Co-chair - Dr. Urmi Bajpai.

Dr. Gopal Nath, Secretary, Society for Bacteriophage Research and Therapy (SBRT), Banaras Hindu University, Varanasi, gave a keynote lecture on “Preclinical and Clinical Bacteriophage Therapy; Our Recent Experiences”. During his lecture, he also briefed about the society and its contribution in bacteriophage research following which he shared few case studies of patients with diabetic ulcers and bacteremia. Dr. Vinoth Kumar, Vice President, SBRT also delivered a keynote lecture on “Building a future with bacteriophage; an alternative protagonist”. While finishing his lecture, he said that the regulatory authorities and the end users should encourage the building the future with phage as an antibacterial agent in therapies since the impact of antibiotics is fading. Dr. Mark Toleman from the School of Medicine, Cardiff University, UK, who has an extensive knowledge on antimicrobial resistance and particularly on the asian region delivered an effective 5h keynote lecture on “Controlling resistance in *E. coli*” outlining the genetic diversity of *E.coli* in UK and India and the natural role of phages controlling MLST *E.coli* and its prevalence. Considering the widespread existence of improper usage of antibiotics,

the next keynote lecture was delivered by Dr. Ashok J Tamhankar on “Global scenario of antimicrobial resistance”.

Session III: Chair – Dr. Aradhna Vipra and Co-chair - Dr. Mark Toleman.

Dr. Balaji V from Christian Medical College, Vellore talked about the Antimicrobial Resistance Trend in GLASS pathogens and also about the surveillance systems, antibiotic resistance profiling in both Gram positive and negative bacteria among Indian population. Dr Joy Sarojini Michael, Christian Medical College, Vellore, gave a lecture on different types of technology platforms that are currently used in tuberculosis diagnosis pipeline. Dr. Biju George, CMC, Vellore, discussed the problems associated with MDR bacteria in the process of transplantation. Poster sessions were held in C5 hall beside Anna auditorium between 4:00 pm and 5:00 pm.

Session IV: Chair – Prof. Vinod Kumar and Co-chair – Dr. Taruna Anand

Dr Sebastian Leptihn, Zhejiang University, ZJU-UoE INSTITUTE, China on Filamentous Phage Biology and their Impact on Human Health. His talk was focused more on studying spontaneous mutation in AMR and discovery and characterization of phages against *E.coli* for the treatment of Urinary Tract Infections. The next keynote lecture addressed the approaches, strategies used in phage therapy on a topic “A Multipronged Quest for Anti-Mycobacterial Solution: Bacteriophages, Endolysins and small molecules” and delivered by Dr Urmi Bajpai from Acharya Narendra Dev College, New Delhi. Day 2 also had impactful invited lectures and poster sessions. The 4th invited lecture was delivered by Dr C P Girish Kumar, National Institute of Epidemiology, Chennai where he discussed the prevalence of prevalence of antibiotic resistance in gram negative bacteria and its genes using PCR.

Poster sessions were held in C5 hall beside Anna auditorium between 11:00 am and 12:00 pm.

Mr. Pranav Johri and Mrs. Apruva Johri from Vitalis Phage Therapy delivered lectures on the practical applications and its challenges. Mr. Pranav is the founder of the company and he shared his own personal experience on receiving phage treatment for his ailment. He said that the successful recovery due to phage therapy led him to establish a phage therapy company in India.

A video lecture by Dr Jeremy Barr, Monash University, Australia, on the topic “When antibiotics fail...Phage therapy of a multidrug resistant infection”. The lecture covered the topics such as causes of infections, antibiotics resistance crisis and search for alternative therapies like bacteriophages.

Another video lecture by Prof. Graham Hatfull, University of Pittsburgh on the topic “Mycobacteriophages: Diversity, dynamics and Therapy” was also screened during the session.

Session V: Chair - Dr. Sebastian Leptihn and Co-chair - Dr. Sangeeta Ahiwale

Dr. Aradhna Vipra talked about the phage product development for non-clinical applications - From Laboratory to Field and after the inspiring lecture, we also had an enlightening lecture from a different perspective by Dr. Taruna Anand who delivered on the topic “Careful Cocktail designing after assessment

of diversity, host specificity and biological characterization of bacteriophages against mastitis causing Staphylococci in bovines”. She discussed about the isolation and characterization of bacteriophages for bovine infection. Dr Manavi Dang and Dr Devjani De discussed on “Turning the Tables on MDROs” highlighting the importance of FilmArray for the early detection of antibiotic escalation in ICU patients and ending the session, Dr. Prasanth Manohar talked on the topic “Antimicrobial Resistance and Phage Therapy: Our Research Lab at VIT” giving an overview on the extensive work carried out at the fully equipped bacteriophage facility, “Antibiotic Resistance and Phage Therapy Lab” at VIT as he obtained his PhD under the guidance of Dr. Ramesh Nachimuthu, who was the convener of this conference.

A general body meeting of the Society, SBRT also held during the conference and the official bearers are going to continue their designation and they selected Dr.N. Ramesh as an editor for society’s newsletter.

Valedictory Session

The best poster awards were given under three different categories; Under Bacteriophage Research category the first, second and third prizes were awarded to Dr. Gokul Nair from IISER, Bhopal. Dr Ajith Madhavan from AMIRTA School of Biotechnology, Kerala and Dr. Deepak Kumar, Institute of Medical Sciences respectively. Under the Antimicrobial Research category, the first, second and third prizes were awarded to Dr. Sarath R, SRM Institute of Science and Technology, Chennai, Dr. Shanthini Thamaraisevan, VIT, Vellore, Dr. Pradeep A N, S S Institute of Medical Sciences & Research Centre, Karnataka respectively. Under Antimicrobial Compounds category, the first prize was awarded to Dr. P Chandrasekar, VIT Vellore. The second prize was awarded to Dr. Ritam Das, Acharya Narendra Dev College, New Delhi and the third prize was awarded to Dr. R Parthasarathy, Indian Institute of Science, Bangalore.

Finally, the conference ended with a Valedictory which was preceded by Dr V Pragasam - Dean, SBST, VIT, Vellore, Dr Sanjay Chhibber, President-SBRT, Dr C S Vinoth Kumar, Vice- President-SBRT, Dr Gopal Nath, Secretary -SBRT and Dr N Ramesh - Convenor-ICBRAMR'19 delivered the vote of thanks.