

# Bacteriophages: Nature and Exploitation

The BioPark Hertfordshire, Welwyn Garden City, AL7 3AX: 22<sup>nd</sup> Feb 2008

- 9:00 – 9:45 **Registration**
- 9:45 – 10:00 **Introduction by the Chair: “The wonderful world of bacteriophages”**  
*Professor George Salmond, University of Cambridge, UK*
- 10:00 – 10:30 **The impact of bacteriophage on bacterial genome evolution**  
*Dr Nick Thomson, The Wellcome Trust Sanger Institute, UK*  
Since the first bacterial whole genome sequence of *Haemophilus influenzae* was published in 1995 the rate of growth of genome sequencing has surpassed all predictions. The continued reduction in costs and new sequencing technology platforms being developed we can now contemplate not only sequencing a range of organisms which attempt to reflect the full diversity of bacterial genomes but to also go on to sequence multiple strains/pathotypes/geographically defined isolates, from the same species. Consequently, comparative genomics has come of age and has already revealed an increasingly varied number of strategies that have been employed by organisms during their evolution. However, within this diversity there are shared mechanisms of accretion and re-assortment of genetic determinants that have contributed in adaptation to differing lifestyles. Presented will be an overview of the impact that bacteriophage have had on the biology of enteric pathogens, focussing on the salmonellae.
- 10:30 – 11:00 **STX-phages and virulence gene dissemination in pathogens**  
*Dr. Heather E. Allison, School of Biological Sciences, University of Liverpool, UK*  
Since the first outbreak of *E. coli* O157:H7 there has been an explosion in the numbers and types of bacteria that are capable of producing Shiga toxin. The dissemination of Shigatoxigenic potential is mediated by bacteriophages (Stx phages) that are a diverse group of temperate phages defined only by carriage of the *stx* operon. We have characterised many of the factors that play a significant role in Stx phage infections including those that control host recognition and multiple infection events, as well as accessory virulence determinants that may contribute to a lysogen’s ability to survive in a complex microbial environment or colonise the gastrointestinal tract.
- 11:00- 11:10 **Speakers photo**
- 11:10 – 11:30 **Mid-morning break**
- 11:30 – 12:00 **Bacteriophage abortive infection systems**  
*Dr Peter Fineran, University of Cambridge, UK*  
Accumulating evidence demonstrates that viruses are the most abundant biological entities on the planet resulting in an obvious selective pressure for bacteria to acquire resistance to phage attack. Indeed, many mechanisms of phage resistance are known, ranging from bacterial cell surface alterations, through restriction and modification, to abortive infection. I will summarise these systems and describe a phage abortive infection resistance system in the economically important plant pathogen, *Erwinia carotovora* subsp *atroseptica*, the causative agent of the potato blackleg disease. This resistance system seems to work via a novel mechanism.
- 12:00 – 12:30 **Novel anti-phage systems in bacteria**  
*Professor Maggie Smith, Institute of Medical Sciences, University of Aberdeen, Scotland*  
Bacteria are under constant threat from infection by bacteriophages. As a consequence they have evolved a battery of defences against phage infection including restriction/modification systems, abortive infection systems and phage exclusion mechanisms. Recently some completely novel systems have been discovered such as Cas/CRISPR and phage growth limitation. It is obvious that these defence mechanisms have a profound effect on host range and therefore on the use of phage as therapeutic agents.
- 12:30 – 12:50 **Tour of the BioPark**
- 12:50 – 14:00 **Lunch and Poster Viewing**

- 14:00 – 14:30 **Use of phages for detection of bacterial pathogens**  
*Dr Catherine E.D. Rees, University of Nottingham, UK*  
 Phage have a checkered history in terms of pathogen detection tests; many new assays have been heralded as the answer to rapid diagnostics, but few have lived up to these claims. This talk will provide an overview of phage methods for the detection of pathogens but will focus on those tests that have been commercially exploited, and on our own work using phage in combined assays to develop rapid tests for fastidious organisms.
- 14:30 – 15:00 **Biotechnological challenges of phage therapy**  
*Professor Mikael Skurnik, University of Helsinki, Finland*  
 The challenges for successful launching of a profitable phage therapeutic product are discussed. These include intellectual property rights, safety issues, reproducibility, stability and robustness of the product. In optimal case a successful and marketable phage therapeutic product would be a highly purified bacteriophage preparation containing one or several fully characterized phages, accompanied by optimized methods of administration and backed up by properly controlled efficacy and safety studies.
- 15:00 – 15:25 **Afternoon Tea/Coffee and Last Poster Viewing**
- 15:25 – 15:55 **Commercialisation of Phage**  
*Dr Nick Housby, Chief Executive Officer, Novolytics Limited, UK*
- 15:55 – 16:25 **Immune responses following treatment with bacteriophage**  
*Dr John B. March, Pentlands Science Park, Scotland*  
 Our group has performed extensive studies using bacteriophages as DNA vaccine delivery vehicles. Although our interest is primarily in the immune response induced by the expressed vaccine antigen, we have also gathered extensive data covering the immune response to the bacteriophage proteins following exposure to the animal's immune system. Phage have been delivered via a variety of different delivery routes- oral, intradermal, injection etc. The timelines and intensity of anti-phage responses observed, their impact upon bacteriophage titres following re-exposure to phage, together with implications for the treatment of bacterial infections by phage therapy will be discussed.
- 16:25 – 16:55 **Does phage therapy actually work? Results from the first phase 2 clinical trial**  
*Dr. David R. Harper, Biocontrol Limited, UK*  
 Biocontrol has recently completed the first modern, regulated clinical trial of the efficacy of a bacteriophage therapeutic. The phase 1/2 trial targeted *Pseudomonas aeruginosa* ear infections and followed on from the successful veterinary field trial which was reported in 2004. Results from the recently completed trial will be reported, along with plans for future trials against other targets. These results will also be discussed in the wider context, as a proof of concept for the development of bacteriophage-based therapeutic agents for use in Western markets.
- 16:55- 17:00 **Chairman's summing up & close.**

*This meeting was **organised by Euroscicon** ([www.euroscicon.com](http://www.euroscicon.com)), a team of dedicated professionals working for the continuous improvement of technical knowledge transfer to all scientists. Euroscicon believe that they can make a positive difference to the quality of science by providing cutting edge information on new technological advancements to the scientific community. This is provided via our exceptional services to individual scientists, research institutions and industry. The event was hosted by '**BioPark**' ([www.biopark.co.uk](http://www.biopark.co.uk)), a research and development centre in Welwyn Garden City providing specialist facilities and support for bioscience and health technology businesses to grow, and to develop new products and technologies*

#### About the Chair

**Professor George Salmond** has been Professor of Molecular Microbiology in the Biochemistry Department at Cambridge University since 1996. He obtained a PhD in bacterial genetics from Warwick University and an ScD from Cambridge. Before Cambridge, he was Professor of Microbiology at Warwick University. His research group works on multiple aspects of bacterial and bacteriophage molecular biology. In addition to studies on quorum sensing, protein secretion and pathogenesis, he has worked on the mechanisms of bacterial cell division and the regulation and biosynthesis of bioactive secondary metabolites, including antibiotics. His group also works on the isolation, characterisation and exploitation of various bacteriophages of Gram-negative enterobacterial pathogens of animals and plants.

#### About the Speakers

**Professor Mikael Skurnik** – Haartman Institute, Medical Faculty, University of Helsinki, Finland. PhD in biochemistry 1985 at University of Oulu. Postdoctoral fellow 1985-7 with Hans Wolf-Watz at Umeå University, Sweden. 1987-2002 in Turku, Finland, and 2002-present in Helsinki. In Turku several positions including Academy Researcher and Director of Turku Centre for Biotechnology. Appointed professor of

Bacteriology at University of Helsinki in 2002. For the PhD thesis and thereafter has used *Yersinia*-bacteria as model organisms to study molecular biology and genetics of microbial pathogenesis. Has specifically focussed on virulence factors of bacterial surface such as adhesins and lipopolysaccharide, and also on molecular biology of *Yersinia* –specific bacteriophages that utilize those surface structures as receptors. Has supervised 10 PhD-theses. Member of editorial board of Journal of Bacteriology since 1998, and of Molecular Microbiology 2003-4. National editor in APMIS since 2003. Peer reviewer since 1988 for ca. 40 scientific journals. member in several European scientific evaluation committees of grants, research programmes and institutions.

**Dr. Heather E. Allison** obtained her Ph.D. from the University of Florida in 1997. She was a postdoctoral NIH research fellow at the University of Rochester, NY, before working as a research associate at the University of Liverpool on her first bacteriophage project in 1999. She has been a permanent member of academic staff at Liverpool since 2004. Her research interests include examining the processes of Shigatoxigenic conversion by bacteriophages

**Dr Catherine E.D. Rees** - Currently Senior Lecturer in Microbiology in the Food Micro group at Nottingham University. Youth was spent studying Biochemistry at Oxford followed by PhD in Genetics at Leicester University and have since used my training in bacterial genetics to study various aspects of food microbiology. Joined Prof. Gordon Stewart's group in Nottingham working on phage-based methods of detection of *Listeria monocytogenes*. When appointed as a Lecturer continued developing a variety of projects involving phage, from detecting *Mycobacterium* to removing *Campylobacter* from poultry.

**Dr John B. March** - John March was formerly a Principal Research Officer at Moredun Research Institute in Edinburgh. His research has encompassed a range of topics- bovine respiratory disease, diagnostic test and vaccine development, and latterly, the development of bacteriophages as efficient and economic vaccine delivery vehicles. This work has led to the setting up of a new spin out company (Big DNA) which aims to develop this new platform technology, and which Dr March now runs

**Dr Nick Housby** - Nick joined Novolytics in June of 2003 and has over 18 years experience in technology oriented research in both academia and industry and has a broad knowledge base in microbiology, cancer research, immunology, bioinformatics, biochemistry and surface sciences. Following commercial experience at Oxagen Limited (UK) Nick worked in a business development role in the technology transfer office of the University of Warwick. Following this Nick worked as a biotechnology company mentor at the Manchester Incubator Company and has now set up a biotechnology incubator facility at Warwick HRI, a department of the University of Warwick

**Dr Peter Fineran** is a post-doctoral researcher in the Department of Biochemistry at the University of Cambridge where he works with Professor George Salmond and Dr. Kathryn Lilley. He obtained his Ph.D in molecular microbiology with Professor Salmond at the University of Cambridge in 2006 examining networks of gene regulation (including quorum sensing) that control secondary metabolism and virulence in *Serratia*. Prior to his PhD he worked as a research associate in Australia. In 2008 he will begin an academic appointment as Lecturer in the Department of Microbiology and Immunology, University of Otago, New Zealand.

**Dr Nick Thomson** was a Post Doc at the Biochemistry Department at Cambridge University where he focussed on global regulatory systems in an opportunistic human pathogen, *Serratia*, and the phytopathogen, *Erwinia*. He then joined the Pathogen Sequencing Unit (PSU) of the Wellcome Trust Sanger Institute, as a Senior Computer Biologist, and is currently a Project Manager for bacterial whole genome sequence projects of many important microbial pathogens. He currently co-runs the bacterial annotation team where his current work focuses on the genomes of enteric bacteria and the Chlamydia.

**Dr. David R. Harper** is the Chief Scientific Officer and former CEO of Biocontrol Limited, and was a founder of the company. He is the virology editor of the Encyclopedia of Life Sciences (Wiley) and is the author of several textbooks in the field as well as a range of articles and patents. He was Lecturer in Molecular Virology at St. Bartholomew's Medical School in London from 1991 to 1998, and has also worked at the University of Iowa. He has also provided specialist consultancy services to a range of life science companies.

**Professor Maggie Smith**, BSc University of Leeds (Biochemistry and Microbiology), PhD University of Bristol (Bacteriology), Post-Doc Leeds and Glasgow, Lectureships Stirling and Nottingham, Reader and Chair Nottingham, Chair Aberdeen, UK