on the complexity of mutational effects on bacterial phenotypes

LI08Th1300

Offered paper – Evolution and Pathoadaptation of *Pseudomonas aeruginosa* in Cystic Fibrosis Patients

Rasmus L. Marvig[1,2], Helle K. Johansen[1], and Søren Molin[2]

[1] Department of Clinical Microbiology, Rigshospitalet, Copenhagen, Denmark [2] Department of Systems Biology, Technical University of Denmark, Lyngby, Denmark

Advances in genome sequencing have made it feasible to sequence multiple genomes of the same lineage of bacterial pathogens as they evolve in their human hosts. Here, we analyzed the genomes of >500 longitudinally collected clinical isolates of *Pseudomonas aeruginosa* sampled from Danish cystic fibrosis (CF) patients. Our phylogenetic analysis reveals the patients to be infected by 53 different clone types of *P. aeruginosa*. Identification of the same clone type over time revealed that 36 of the clone types were causing persistent infections, enabling us to decipher the recent within-host evolutionary history of each of these lineages. We found the 36 lineages to exhibit mutational convergence in 56 pathoadaptive genes in which the host environment imposed a selection for mutations. Furthermore, our results showed that mutation of downstream transcriptional regulators in regulatory networks involved in adaptation was contingent upon the mutation of upstream regulators in the same regulatory network. In conclusion, we identified adaptive trajectories generic to *P. aeruginosa* in the CF environment, and elucidated how mutation of regulatory networks shows historical contingency. Knowledge of pathoadaptive mutations and evolutionary contingency may help the development of therapeutic strategies against *P. aeruginosa* infections.

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Offered paper – Genetic Variation is Localised to Hypermutable Sequences During Persistent Meningococcal Carriage

Mohamed Alamro[1], Neil Oldfield[2], Odile Harrison[3], David Turner[2], Dlawer Ala'Aldeen[2], Martin Maiden[3], Christopher Bayliss[1]

[1] University of Leicester, Leicester, UK, [2] University of Nottingham, Nottingham, UK, [3] University of Oxford, Oxford, UK

Many bacterial pathogens and commensals exhibit phase variation or antigenic variation of surface antigens due to mutations in hypermutable sequences. Alterations in these surface structures mediate adaptation to fluctuations in the selective pressures encountered during colonisation and persistence in their hosts. *Neisseria meningitidis* is a major agent of meningitis and septicaemia but is usually found as an asymptomatic coloniser of the human nasopharynx. Several genes in this species are subject to phase variation due to alterations in simple sequence repeat (SSR) tracts. Multiple isolates of *Neisseria meningitidis* were collected from 21 individuals subject to persistence colonisation for up to six months. SSRs of nine outer membrane proteins were analysed for alterations in repeat number by fragment analysis. Two genes exhibited trends towards lower expression levels. Reductions in expression were also detected for combinations of these phase variable genes. The levels of phase variation were compared to recombination-mediated antigenic variation of pilE, encoding the major pilin sub-unit, and to allelic variation as detected from whole genome sequences of these isolates. We conclude that localised hypermutation in contingency loci is the major mechanism mediating adaptation of meningococci during persistent carriage in the upper respiratory tract of humans.

LI08Th1345

Offered paper – Multiple independent emergence and rapid expansion of pertactin-deficient *Bordetella pertussis* in Australia

Connie Lam[1], Sophie Octavia[1], Lawrence Ricafort[1], Vitali Sintchenko[2,3], Lyn Gilbert2, Nicholas Wood[3], Peter Mcintyre[3], Helen Marshall[4], Nicole Guiso[5], Anthony D Keil[6], Andrew Lawrence[4], Jenny Robson[7], Geoff Hogg[8], and Ruiting Lan[1]

[1] University of New South Wales, Sydney, Australia; [2] The University of Sydney, Sydney, Australia; [3] Westmead Hospital, NSW, Australia; [4] University of Adelaide, Adelaide, Australia; [5] Institut Pasteur, Paris, France; [6] Princess Margaret Hospital for Children, Perth, Australia; [7] Sullivan Nicolaides Pathology, Brisbane, Australia; [8] The University of Melbourne, Melbourne, Australia

The circulation of *Bordetella pertussis* isolates which do not express the vaccine antigen pertactin has recently emerged or has been increasing in highly vaccinated populations including France, Finland, Japan and the United States. To determine whether such isolates are present in the Australian *B. pertussis* population, isolates collected between 1997 and 2012 were tested for the expression of the 3 main vaccine antigens; pertussis toxin (PT), pertactin (PRN) and filamentous haemagglutinin (FHA). All isolates expressed PT and FHA. All isolates collected prior to 2007 also expressed PRN, however 30% (96/320) of *B. pertussis* isolates did not express the vaccine antigen, Prn. Multiple mechanisms of prn inactivation were documented, including IS481 and IS*1002* disruptions, a variation within a homopolymeric tract and deletion of the entire *prn* region. The mechanism of Prn non-expression in 16 (17%) isolates could not be determined at the sequence level. These findings suggest that Prn non-expressing *B. pertussis* arose independently multiple times since 2008 rather than by expansion of a single Prn-negative clone. All but one isolate had ptxA1/ prn2/ *ptxP3*, the alleles representative of the currently circulating strains in Australia, a pattern consistent with continuing evolution of *B. pertussis* in response to vaccine selection pressure.

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Genomic evolution of *Helicobacter pylori* within its human host

Xavier Didelot

Department of Infectious Disease Epidemiology Imperial College, London, UK

Helicobacter pylori is a bacterial pathogen that infects the stomach of about half of the human worldwide population. It can be carried asymptomatically for many years, but can also lead to severe disease, including gastric cancer. To understand the evolutionary dynamics of *H. pylori* within its human host, we compare whole genome sequences of multiple isolates from the same carriers. Such