

**A9 Deep sequencing analysis to investigate the importance of within host genetic diversity and evolution of influenza A viruses for the development of resistance against neuraminidase inhibitors**

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Currently approved neuraminidase inhibitors (NAI) for the treatment of influenza A virus infections are prone to induce viral drug resistance development due to the rapid evolutionary dynamics of the neuraminidase (NA) and hemagglutinin (HA) proteins. Both HA and NA proteins are subject to antigenic drift and the epistatic interactions within and between these proteins can lead to genetic diversity that enables the virus to easily develop resistant mutations under selective pressure in a host. To study NAI resistance and clinical outcome, the global observational Influenza Resistance Information Study (IRIS; NCT00884117) was conducted. Patients that were clinically diagnosed with influenza were enrolled in the study. Nasal and throat swabs taken at baseline and on days 3, 6, and 10 were assessed by semi-quantitative real-time reverse transcription polymerase chain reaction (RT-qPCR) to determine the influenza virus type and subtype. NAI resistance was initially determined by mutation specific RT-PCR, Sanger sequencing and phenotypic susceptibility analysis. Genetic resistance mutations to oseltamivir were detected in 61 patients (43 H1N1pdm [H275Y] and 18 H3N2 [R292K]) by mutation specific PCR. Subsequently, samples of 43 patients were subjected to deep sequencing analysis to characterize both the between- and the within-host diversity and the evolutionary process of the HA and NA proteins of infected patients. The NAI resistance mutations (H275Y and R292K) in the NA protein of the H1N1pdm and H3N2 viruses were either detected in day 3 samples or at later time point. Additionally, viruses in several individuals had mutations that were located across the whole HA and NA proteins. Some low frequency mutations such as D114N, S200P, and D239N, that were located in the antigenic sites or near the receptor binding site of the HA protein, became fixed in the later time point viral samples. Also, some mutations in HA may have occurred in concert with the resistance mutations in NA. Further genetic analyses and phylogeny should provide further insights in the emergence of mutations in individual hosts and the larger population.

**A10 The evolution and molecular epidemiology of epidemic GII.17 noroviruses**

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In past decades, the GII.4 genotype with a higher evolutionary rate predominated in norovirus epidemics globally. In the winter of 2014–5, a novel GII.17 variant emerged, causing large outbreaks in mainland China and sporadic infections globally. The origin, evolution and transmission patterns of this new emerged variant are largely unknown. We generated 103 full capsid and 8 whole genome sequences of GII.17 strains collected

between August 2013 and November 2015 in Guangdong province. Phylogeny reconstruction was performed by including all public available GII.17 sequences. Our evolutionary analysis revealed variable evolutionary rates during GII.17 evolution history. The newly emerged lineage GII.17\_Kawasaki\_2014 most likely originated from Africa around 2001 and evolved at  $5.6 \times 10^{-3}$  substitutions/site/year. In this lineage, a novel variant with series of important amino acids changes emerged around August 2013 and caused epidemics in 2014–5. Through Bayesian skyline plot analysis, we found that the phylodynamics of GII.17\_Kawasaki\_2014 lineage were similar to the epidemic pattern observed during GII.4 evolution. Hong Kong was inferred as the epicenter of local GII.17 outbreaks, and frequent virus transitions were observed among Hong Kong and several coastal cities in Guangdong. In this study, we provide a novel insights into GII.17 noroviruses by inferring virus evolution and local transmission patterns. Our analysis highlights the possibility that a rarely detected genotype of norovirus could rapidly cause local epidemics by replacement with a new variant. As the persistence of GII.17 has been observed in the winter of 2015–6, close monitoring the evolution of GII.17 globally is critical for current norovirus disease control and vaccine development.

**A11 Phylogenetic and phylogeographic analysis of viral surveillance data to inform rabies control programmes in Cambodia**

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Canine-mediated rabies is a serious zoonosis, responsible for at least 60,000 human deaths per year. The disease is caused by Lyssavirus genotype I, which is endemic in domestic dog populations, particularly in Asia and Africa where dogs are free-roaming. There is increasing evidence that the majority of free-roaming domestic dogs are owned; with human-mediated movement of dogs (some of them infected) contributing to the spatial spread of rabies and local persistence through reintroductions. The spatial spread of rabies through the translocation of dogs by people has been demonstrated in South Africa and Thailand using molecular epidemiological techniques. These studies have improved our understanding of the role of human behaviour and interference in conspecific transmission of this important zoonosis. Understanding the transmission dynamics of the virus is essential for its control; however, the spatial dynamics of canine rabies is poorly quantified in Cambodia, where the burden of rabies is substantial. Therefore, we will undertake phylogenetic and phylogeographic analysis of viral surveillance data from Cambodia to inform control programmes. These analyses may be combined with local-level contact tracing and ecological data to generate a more complete picture of conspecific transmission dynamics involving human interference in the region.

**A12 Predictors of treatment failure among Irish individuals infected with hepatitis C virus**

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With the increasing number of licensed direct-acting antivirals (DAA) for the treatment of chronic HCV infection, choosing the right treatment regimen for the right patient has become paramount. We believe baseline sequencing for the presence of