Larger samples are likely required to fully explore the role of rare coding variation on this phenotype. Additional classes of variation not detected by GWAS or current sequencing technologies may also contribute to host HIV-1 control.

A40 Persistent circulation of highly divergent HIV-1M lineages in the Congo Basin Region

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The evolutionary processes that within a century yielded the nine major HIV-1 group M (HIV-1M) lineages and over 72 circulating recombinant forms (CRFs) remain the most important obstacles to the development of both a cure and an effective vaccine. It is still unknown how global HIV populations will respond over the long-term when confronted with efficiently protective vaccines and drug therapies. It is entirely possible that divergent HIV variants that are presently circulating in diversity hotspots such as Cameroon and the DRC might be the source of future global multi-drug resistant or vaccine evasion re-emergence events. In an effort to discover and characterise more of these highly divergent lineages, we recently performed in-depth characterisation of HIV-1 diversity in Cameroon. We found that 10% of gag sequences and 5% of nef sequences were not easily classifiable into any of the known HIV-1M clades. In addition, the full length characterisation of 24 unique recombinant forms (URFs) from Cameroon showed that these divergent sequences contained large tracts of sequence that could not be credibly classified as having been derived from parental viruses in the known subtypes. Furthermore, we have found that many of the sequence fragments occurring within CRF04_cpx, CRF06_cpx, CRF11_cpx, CRF18_cpx, CRF25_cpx, CRF27_cpx and CRF49_cpx are in fact likely derived from divergent unclassified parental lineages that may pre-date the current subtypes, even though they are presently identified as derived from currently defined HIV-1M subtypes. The highly divergent sequence tracts evident within these various HIV-1M genomes might be the extant descendants of pre-epidemic HIV-1 group M lineages (i.e. they may, in a sense, be evolutionary relics). This suggests that large pools of undiscovered HIV-1M genetic diversity likely exist throughout equatorial West Africa. We hypothesise that viruses belonging to these lineages may have gone largely undetected because of their low pathogenicity and/or transmissibility: characteristics that would be expected to result in the long-term survival of individuals that they manage to infect. This should therefore be manifested by individuals infected with these viruses displaying substantially higher degree of within-individual diversity than is usually displayed by individuals infected by viruses in the main pandemic lineages.

A41 Diversity and evolution of avian influenza (AI) viruses in poultry and wild birds

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Over the past decade, surveillance programs for Avian Influenza (AI) virus infections in the Netherlands have provided extensive information on the spatiotemporal distribution of AI virus infections in poultry and wild aquatic birds. Wild birds are the natural reservoir of AI viruses and suspected to be the source of AI virus infections in poultry. Surveillance focuses mainly on the early detection of AI virus infections of subtypes H5 and H7, which have the potential to mutate from a low pathogenic AI (LPAI) variant into a highly pathogenic AI (HPAI) variant. However, the introduction of AI viruses of other subtypes is also monitored. Here, we provide an overview of all AI virus subtypes that have been detected by virus specific antibody detection or virus isolation in poultry and wild birds in the Netherlands from 2006 to 2015. Results show that poultry as well as wild birds are frequently infected with LPAI viruses. However, the subtype distribution differs between the two groups, indicating that LPAI virus transmission from wild birds to poultry is not random and likely depends on viral factors that determine host range restriction. In multiple cases, LPAI virus infections of the same subtype have been detected on several poultry farms at approximately the same time, suggesting that these viruses have acquired the capacity to be efficiently transmitted from wild birds into poultry and/or between farms. In this study, the whole genome sequences of more than 300 AI viruses isolated from poultry and wild birds have been determined by next-generation sequencing (NGS). Phylogenetic analyses will be performed to understand the evolution of LPAI viruses in the Netherlands. Furthermore, we aim to identify specific mutations in the AI virus genome that correlate with an increased chance of LPAI virus introduction in poultry, within-farm spread of LPAI viruses, and transmission of LPAI viruses to other poultry farms. Increased knowledge of LPAI virus transmission is important to control virus spread and reduce the probability of mutation of LPAI viruses into HPAI viruses.

A42 Evolution and spatial dissemination of the highly pathogenic Asian H5 avian influenza viruses

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After emerging in 1996, the Asian highly pathogenic avian H5Nx influenza viruses had spread to more than sixty countries across Asia, Europe, and Africa through three major transmission waves by 2006. Phylogenetic analysis of all H5 influenza virus sequence data in our long-term surveillance in southern China revealed that the virus was widespread and enzootic in China, continuously developing into different clades and reassortant variants, some of which disseminated to other regions and became enzootic. This indicates that continuous circulation of H5 viruses in China is not only a local risk factor, but also poses a broader threat to birds and humans in other regions. In late 2014, clade 2.3.4.4 of H5Nx viruses emerged and caused sporadic human infections in China and outbreaks in poultry in Eurasia and spread to North America, the first-time Asian highly pathogenic H5 viruses had been detected there. To ascertain how the Asian H5Nx influenza viruses evolved into the wide-spread clade 2.3.4.4 viruses, over 3,000 H5 avian viruses isolated from 2009 to 2015 have been sequenced. I wish to use more sophisticated phylodynamics analysis on our large genomic sequence datasets of H5Nx viruses to examine the emergence of new wide-spreading 2.3.4.4 clade of global concern.