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Tropism and neutralisation studies on bat influenza H17N10

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The diversity of subtypes within Influenza A recently expanded with identification of H17N10 and H18N11 from bats. To study the tropism and zoonotic potential of these viruses, we successfully produced lentiviral pseudotypes bearing haemagglutinin H17 and neuraminidase N10. We investigated a range of cell lines from different species for their susceptibility to infection by these pseudotypes and show that a number of human haematopoietic cancer cell lines and the canine kidney MDCK II (but not MDCK I) cells are susceptible. Using microarrays and qRT-PCR we show that the dog leukocyte antigen DLA-DRA mRNA is over expressed in late passaged parental MDCK and commercial MDCK II cells, compared to early passaged parental MDCK and MDCK I cells, respectively. The human orthologue HLA-DRA encodes the alpha subunit of the MHC class II HLA-DR antigen-binding heterodimer. Small interfering RNA- or neutralizing antibody-targeting HLA-DRA, drastically reduced the susceptibility of Raji B cells to H17-PV. Conversely, over expression of HLA-DRA and its paralogue HLA-DRB1 on the surface of unsusceptible HEK293T/17 cells conferred susceptibility to H17-PV. The identification of HLA-DR as an H17N10 entry mediator will contribute to understanding the tropism of the virus and help to elucidate its zoonotic transmission. We also show that H17 pseudotypes can be efficiently neutralised by the broadly-neutralizing HA2 stalk monoclonal antibodies CR9114 and FI6. The lentiviral pseudotype system is a useful research tool, amenable for investigation of bat influenza tropism, restriction and pandemic preparedness, without safety issues of producing a replication-competent virus, to which the human population is naïve.

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