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cells. On the other hand, some recombinant viruses derived in the mammalian system had low polymerase activity and slow growth in avian cells. Although all the recombinant viruses with different amino acids at PB2-627 replicated in mammalian cells, the virulence of the recombinant viruses in mice vary. It was found that recombinant viruses with isoleucine at PB2-627 led to more significant weight loss and higher mortality in mice than the recombinant viruses with the avian marker at PB2-627, albeit lower than wild-type virus. Conclusions: This study demonstrated that the amino acid identity at PB2-627 is not exclusive to glutamic acid and lysine. Introducing other unnatural amino acid mutations at this position can also lead to viable viruses in mammalian and avian cells. Some of these novel amino acid mutations may also lead to highly virulent virus in mammals. Although the mechanism leading to the role of PB2-627 is yet to be elucidated, more understanding on the effect of this residue on the viral polymerase can surely contribute to the evaluation of the pandemic potential of any novel virus that may emerge in the future.

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Influenza B viruses in swine: virus tropism in swine respiratory organ explant cultures

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Background: Swine has been considered an animal reservoir of pandemic influenza A virus (IAV), for example, the 2009 H1N1 pandemic virus, swine is acting as a “mixing vessel” for the reassortment of swine, human and avian IAVs. Certain influenza B virus (IBV) strains were also found to be readily infecting piglets as early as in 1969. However, tissue tropism of IBV in swine is understudied, at least in 2000s, mainly due to the misconception that IBV causes milder disease than IAV. IBV has in fact circulated in many parts of the world causing regular seasonal epidemics in humans with mortality rates sometimes higher than that in IAV seasons. Here, our research group hypothesizes that swine could be a neglected host of IBV, apart from human and seal, due to the previous infectivity of IBV in this animal, as well as the fact that swine has close contact with human and possesses a similar sialic acid (influenza virus receptor) distribution profile as the human respiratory tract. We aim to examine the characteristics of IBV tissue tropism using swine tracheal and lung explant models, and risk assess swine susceptibility to a panel of IBV strains from both Yamagata and Victoria lineages of different years. Materials and Methods: The tracheal and lung explants were prepared from fresh swine respiratory organs from approximately 6-month-old pigs, and cultured with maximal similarity to the *in vivo* conditions. A panel of IBV strains, from both Yamagata and Victoria lineages and from different years, were used to infect the tissue explants at 37°C or 39°C according to the original physiological temperature of the tissue. The virus replication efficiencies were evaluated through viral titration and immunohistochemistry of the collected supernatant and formalin-fixed tissue explants respectively at 1, 24, 48 and 72 h postinfection. Seasonal IAVs (H1N1 - A/OK/447/08 and H3N2 - A/OK/370/05) were used as controls. Results: Most of the tested IBVs showed productive replication in the swine lung explants. Swine tracheal explants, on the other hand, supported the replication of limited IBV strains. Most of these IBVs belong to the Victoria lineage, which spread across the years from 2005 to 2011. IBVs that could replicate in swine lung explants reached their maxima at 48 hpi or sometimes later. This is comparatively slower than the replication rates of seasonal IAVs (H1N1 & H3N2) used in the study, which usually showed significant increase at 24 hpi with still increasing virus yields at 48 hpi in some cases. However, the overall increase in titres between the IBVs and seasonal IAVs were similar. In swine tracheal explants, both IBVs and seasonal IAVs showed limited replications with similar trends of having maxima being reached at 24 hpi. Conclusions: The successful replication of IBVs in swine explants cultures indicates the possible susceptibility of swine to IBV and provides the essential basis for further investigation on the likelihood for swine to be an animal reservoir of the virus, as well as the threat it may pose to humans. Continuous studies on the replication kinetics of a greater number of IBVs in swine explant cultures across a wider range of years, countries and lineages will probably be our future target.

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