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Eurasian avian-like swine influenza viruses harbor increased pandemic potential due to MxA escape mutations in their nucleoprotein

Inhalt

To cross the human species barrier, influenza A viruses (IAV) of avian origin have to overcome the interferon-induced host restriction factor MxA by acquiring distinct mutations in their nucleoprotein (NP). We recently demonstrated that North American classical swine IAV are able to escape MxA restriction partially. Here, we investigated whether the Eurasian avian-like swine IAV lineage currently circulating in European swine would likewise evade restriction by human MxA. We found that the NP of the isolate A/swine/Belzig/2/2001 (Belzig) exerts increased MxA escape similar in extent to human IAV NPs. Mutational analysis revealed that the MxA escape mutations in Belzig-NP differ from the known MxA resistance cluster of the North American classical swine lineage and human-derived IAV NPs. A mouse-adapted avian IAV of the H7N7 subtype encoding Belzig-NP showed significantly enhanced viral growth in both MxA-expressing cells and MxA-transgenic mice compared to control viruses lacking the MxA escape mutations. Similarly, growth of recombinant Belzig virus was only marginally affected in MxA-expressing cells and MxA-transgenic mice compared to Belzig mutant viruses lacking MxA escape mutations in NP. Phylogenetic analysis of the Eurasian avian-like swine IAV revealed that the NP amino acids required for MxA escape were acquired successively and were maintained after their introduction. Our results suggest that circulation of IAV in the swine population can result in the selection of NP variants with a high degree of MxA resistance, thereby increasing the zoonotic potential of these viruses.

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Kommentare:

Philipp P. Petric and Dominik Dornfeld contributed equally