Novel swine influenza reassortant viruses: Risk assessment of their zoonotic potential (funded by the DFG)

(One PhD position)

Influenza A viruses (IAV) are significant human pathogens originating from their natural reservoir represented by wild aquatic waterfowl. Human infection by IAV of animal origin occurs sporadically and is usually restricted to individuals. In rare cases, however, zoonotic animal IAV obtain sufficient adaptive mutations to facilitate sustained human infection chains, incidents that can eventually result in devastating pandemics. The interferon-induced and antivirally active MxA GTPase found in humans represents a major barrier for animal IAV to establish a new lineage in the human population. For the animal-to-human adaptation process, swine seem to play a particularly important role, especially for the emergence of pandemic viruses (Mänz et al. (2013) PLoS Pathog. 9(3):e1003279; Dornfeld et al. (2019) J Virol. 93(2):e00997-18). Thus, swine influenza A viruses (swIAV) may bear a direct zoonotic, and contingently pandemic potential. Yet, the actual flow of IAV of either human or swine origin across the porcine-human interface is not understood. We and others recently showed that diversifying evolution of swIAV in Germany into four distinct lineages produces an ever-increasing spectrum of swIAV genotypes including human pandemic H1N1 and genome segments of avian origin IAV with largely unknown zoonotic potential. These viruses are also antigenically grossly distinct from current seasonal human IAV. However, detailed functional analyses required for a well-founded risk assessment are missing. Together, this seems to increase risks of a re-introduction of antigenically altered and reassorted swIAV into human populations.

Based on a large collection of very recent swIAV isolates from Germany and long standing experience in analyzing viral adaptation processes (Henritzi et al. (2020) Cell Host & Microbes, in press), the proposed project will investigate whether the newly described reassortant swine IAVs (i) can overcome the human species barrier imposed by MxA, (ii) have the propensity for human transmission (ferret model), (ii) have a human-like sialic acid receptor preference, (iv) are already adapted to human airway epithelial cells, (v) are sensitive to the currently available human seasonal influenza vaccines, and (vi) are already transmitted sporadically across the porcine-human interface in Germany. Together, the results are expected to enable a detailed risk assessment of zoonotic properties of currently circulating swIAV.