

Synergistically targeting pyrimidine metabolism and RNA integrity for the treatment of respiratory diseases caused by zoonotic influenza A viruses and henipaviruses

Initiative: Innovative Ansätze in der antiviralen Wirkstoffentwicklung

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Recent pandemics were caused by zoonotic RNA viruses, mainly leading to respiratory diseases with high transmission rates. To counteract these pathogens, the project team is exploiting antiviral drug combinations without relying on particular viral targets, thus making them broadly applicable. The researchers have combined a nucleoside analogue, N4-hydroxycytidine (active compound of Molnupiravir), with inhibitors of pyrimidine synthesis targeting the enzymes DHODH and CTPS, to achieve exquisite synergy against virus propagation. The approach was successfully demonstrated first for SARS-CoV-2 and recently also for influenza A virus. Now, the team proposes to systematically explore the antiviral activity of pyrimidine-based antivirals with inhibitors of pyrimidine synthesis against two virus families with zoonotic and pandemic potential, in cell culture and appropriate animal models. Firstly, avian and swine influenza A viruses will be targeted, bearing the potential of rapid reassortment and human infection while leaving insufficient time for the development of vaccines. In addition, this approach will be evaluated against infections with henipaviruses, especially the highly pathogenic Nipah virus.

Projektbeteiligte

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