Inhibition of CYP19A1 mediated sex-specific lung inflammation in avian influenza virus infection (FLU-FLAME)

Initiative: Innovative Ansätze in der antiviralen Wirkstoffentwicklung

Bewilligung: 27.06.2022

Laufzeit: 3 Jahre

Avian influenza in humans is associated with pneumonia, inflammation and high case fatality rates. The researchers identified CYP19A1 as a key gene involved in sex-specific lung inflammation in SARS-CoV-2 infected hamsters and humans. CYP19A encodes for the aromatase enzyme that converts testosterone-to-estradiol leading to the activation of various estrogen-regulated pathways associated with lung inflammation. Treatment of SARS-CoV-2 infected hamsters with letrozole, a clinically approved CYP19A1 aromatase inhibitor, recovered impaired lung function and overall lung health in males. The team further found that also avian H7N9 influenza virus infection mediates massive upregulation of CYP19A1 in the lung of infected animals. This project's hypothesis is that estrogen-regulated activation of inflammatory pathways in the lung plays a crucial role in severe viral disease outcome. Therefore, in this proposal, the team will systemically evaluate the impact of compounds that inhibit the synthesis of estrogens (using aromatase inhibitors) or interfere with estrogen-regulated down-stream pathways (using estrogen antagonists) against avian influenza in an in vivo model. Obtained data will provide new insights into estrogen-mediated inflammatory pathways upon infection with respiratory viruses. Moreover, identification of common pathways might result in overarching drug targets to treat inflammatory lung diseases in general.

Projektbeteiligte

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