Prophylactic autophagy-inducing therapies to tackle coronaviruses (ProATTaC)

Initiative: Innovative Ansätze in der antiviralen Wirkstoffentwicklung

Bewilligung: 21.06.2021

Laufzeit: 3 Jahre

The lack of medical treatment options is a major challenge during the current COVID-19 pandemic. SARS-CoV-2 is a newly emerged highly pathogenic zoonotic coronavirus, causing mild to severe respiratory symptoms but also embolisms, pneumonia, and neurological disease through enhanced inflammatory and autoimmune responses. The research team previously showed that human pathogenic CoVs limit autophagy, the cellular recycling system of cells involved in the inflammatory response, and found that compound-driven autophagy induction inhibits replication of highly pathogenic CoV. To generate improved future treatments, the team intends to develop minimally toxic, broad-range dual antiviral, anti-inflammatory drugs suitable for long-term and prophylactic use. Within a newly established high throughput platform, antiviral activity of N=355 autophagy-inducing compounds will be analyzed with SARS-CoV, newly generated MERS-CoV and SARS-CoV-2 replicons in novel CoV-susceptible autophagy-reporter cells. Minimally toxic, efficient compounds will be further tested in CoV-infected cell cultures, primary airway epithelial cells, and organoids. Antiviral and anti-inflammatory activity of the most potent compounds will be confirmed in a CoV-susceptible autophagy-reporter mouse line. The reporter mice will serve to characterize compound-induced effects, and enable to monitor autophagy and inflammation during CoV infection. The project could pave the way for developing a new class of broad-range dual antiviral and anti-inflammatory drugs.

Projektbeteiligte

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