Peptide-based crystallographic fragment screening for fast and efficient discovery of lead structures against zoonotic viral diseases

Initiative: Innovative Ansätze in der antiviralen Wirkstoffentwicklung

Bewilligung: 21.06.2021

Laufzeit: 3 Jahre

The aim of this project is to advance novel strategies for efficient and fast development of compounds for fighting emerging (zoonotic) viral diseases. A key problem in drug development via fragment screening is that the organic chemistry necessary for fragment linking is relatively slow, labor-intensive and not easily accessible. In contrast, synthesis of peptides and many peptidomimetics can be conducted in a highly automated and parallel fashion. In this project, the researchers will establish technologies for fast and efficient development of potent inhibitors of two proteases as targets for antiviral therapy: SARS-Cov-2 main protease and the NS2B-NS3 protease of the Zika virus. This strategy relies on crystallographic fragment screening using fragments that enable inhibitor synthesis via automated parallel solid phase synthesis. Computational tools will be developed for the generation of biased fragment libraries increasing the hit rate, and for fragment linking as well as extension. In addition to the results obtained for the highly relevant viral targets studied, the technology developed in this work will be highly accessible and practicable also for other laboratories, including an academic environment as well as small and medium enterprises.

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