Website address:
https://www.gesundheitsindustrie-bw.de/en/article/press-release/computermodellierung-zur-schnelleren-entwicklung-antiviraler-medikamente

Targeted computer modelling to accelerate antiviral drug development

Effective drugs against viral diseases like COVID-19 are urgently needed now and in the future. The emergence of viral mutants and yet unknown viruses could push vaccines to their limits. The DZIF scientist and bioinformatician Andreas Dräger from the University of Tübingen is working on a computer-based method that can help to accelerate the time-consuming identification and development of antiviral agents. Using a novel analysis technique that applies to any virus and host cell type, the research team around Dräger has now created a model to detect additional host cell targets that allow inhibiting SARS-CoV-2 replication.

"Efficient pandemic preparedness requires new, broadly effective antiviral drugs against which the viruses cannot quickly develop resistance," explains Andreas Dräger, junior professor at the Univer-sity of Tübingen and member of the Tübingen Cluster of Excellence "Controlling Microbes to Fight Infections – CMFI". "But drug development takes too much precious time, which is urgently needed in an emergency."

Dräger wants to remedy this situation through computer modelling. In 2021, the Tübingen research group identified a human enzyme in the model—guanylate kinase 1—indispensable for virus replication and can be switched off without damaging the cell. Now, the bioinformatician has developed a new model with his colleagues to examine the effectiveness of their targets. "Through an improved analysis technique, we can now specifically model viral infection in many different types of tissue," explains Nantia Leonidou, first author of the current study.

Observing host metabolism after viral infection in the model

Using their integrated systems biology model to simulate infection with SARS-CoV-2 in bronchial epithelial cells, the researchers can identify host-based metabolic pathways that can be inhibited to suppress viral replication. "If you know the composition of a virus, you can run different scenarios and see how the biochemical reactions in host cells change during viral infection," Dräger says. The team developed high-quality software to simulate an infection in a cell-type-specific manner.

New targets identified

Applying the model to another cell type, the research group confirmed the previously identified target, guanylate kinase 1, and discovered other new biochemical targets with remarkable antiviral effects. The most promising new hit was CTP synthase 1. Inhibition of this enzyme in the model reduced viral growth by 62 per cent without affecting the maintenance of the human host cells. Both target molecules are closely linked to the structure of genetic material, which requires the same building blocks in both the virus and the host cells. Andreas Dräger's team believes these findings provide a crucial basis for accelerating the development of viral inhibitors.

"Our models could represent a paradigm shift in drug development and accelerate the preclinical phase," emphasises Nantia Leonidou, adding, "The methods are fully transferable to any virus and host cell type and are also commercially viable."

Dräger's group now plans to apply their methods to other viruses. The first inhibitors for their discovered enzymes will be tested in animal models for safety, toxicity, and efficacy.

Publication:
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Further information

- Eberhard Karls University of Tübingen