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Prof Ralf Altmeyer



Friday 23th July 2021
11am to 12pm (SGT)

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Development of drugs targeting Respiratory Syncytial Virus inclusion body condensates

Biomolecular condensates have emerged as an important subcellular organizing principle. Replication of many viruses, including human respiratory syncytial virus (RSV), occurs in virus-induced compartments called inclusion bodies (IBs) or viroplasm. IBs of negative-strand RNA viruses were recently shown to be biomolecular condensates that form through phase separation. Here we report that the steroidal alkaloid cyclopamine and its chemical analogue A3E inhibit RSV replication by disorganizing and hardening IB condensates. The actions of cyclopamine and A3E were blocked by a point mutation in the RSV transcription factor M2-1. IB disorganization occurred within minutes, which suggests that these molecules directly act on the liquid properties of the IBs. A3E and cyclopamine inhibit RSV in the lungs of infected mice and are condensate-targeting drug-like small molecules that have *in vivo* activity. Our data show that condensate-hardening drugs may enable the pharmacological modulation of not only many previously undruggable targets in viral replication but also transcription factors at cancer-driving super-enhancers.

Prof. Ralf M. Altmeyer obtained his PhD from Institut Pasteur in Paris in 1994 and pursued his research at Institut Pasteur and the Pasteur international network for many years. During his career, Prof. Ralph Altmeyer held various management positions including the position of CEO of the HKU-Pasteur Research Centre in Hong Kong from 2003 to 2006. In 2006 he was President of CombinatoRx-Singapore, the infectious disease subsidiary of CombinatoRx, until the acquisition of the company by Forma Therapeutics in 2009. In 2011, he founded Advance BioChina, a Shanghai-based incubator company that helps global biotech companies access the Chinese market. Prof. Ralf M. Altmeyer also held the Institut Pasteur Shanghai from 2010 to 2014. As a virologist, his research interests include respiratory diseases, Hepatitis C, HIV, and focus on anti-infective therapeutic strategies.