ID der Kurzfassung : **102**

Discovery of a novel influenza A virus inhibitor targeting a distinct pocket at the viral nucleoprotein dimer interface

Inhalt

The Global Viral Infection Research Center (G-VIC), a TOP TIER project of the National Research Foundation of Korea, aims to develop novel antivirals and vaccines through international collaboration. As part of this effort, the VirusBank Platform screened ~100,000 compounds from the Korea Research Institute of Chemical Technology (KRICT) to identify inhibitors of influenza virus using a MUNANA assay on A549 cells.
Here we report compound R91, a novel hit with potent anti-influenza activity (EC50 = 1.3 μM, CC50 > 25 μM). R91 reduced vRNA levels by 5-log10 in the supernatant of MDCK cells infected with A/PR/8/1934 (H1N1) at 6.4 μM. Notably, the activity was restricted to the PR8 strain, with no detectable effects against other influenza A or B viruses.
Selection of resistant variants identified a P283S substitution in the viral nucleoprotein (NP), completely abrogating antiviral activity and identifying NP as the target. Structural analysis of the NP protein placed P283 within a druggable pocket at the NP dimer interface, adjacent to the binding site of nucleozin, a known NP-targeting influenza inhibitor. Interestingly, NPP283S viruses showed increased sensitivity to nucleozin. Moreover, time-of-addition assays revealed similar profiles for R91 and nucleozin, with loss of efficacy when added after ~4 h p.i.
These findings suggest that R91 interferes with NP–NP interactions, impairing ribonucleoprotein complex assembly and thereby inhibiting viral replication and transcription.

Keywords

Registration ID

INF26-42

Professional status of the speaker

Postdoc

Junior scientist status

Yes, I am a junior scientist.

Track Klassifizierung: Antivirals and Vaccines

Typ des Beitrags: Poster presentation