New Results

4 comments

An orally bioavailable broad-spectrum antiviral inhibits SARS-CoV-2 and multiple endemic, epidemic and bat coronavirus

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Abstract

Coronaviruses (CoVs) traffic frequently between species resulting in novel disease outbreaks, most recently exemplified by the newly emerged SARS-CoV-2. Herein, we show that the ribonucleoside analog β-D-N^4-hydroxycytidine (NHC, EIDD-1931) has broad spectrum antiviral activity against SARS-CoV 2, MERS-CoV, SARS-CoV, and related zoonotic group 2b or 2c Bat-CoVs, as well as increased potency against a coronavirus bearing resistance mutations to another nucleoside analog inhibitor. In mice infected with SARS-CoV or MERS-CoV, both prophylactic and therapeutic administration of EIDD-2801, an orally bioavailable NHC-prodrug (b-D-N^4-hydroxycytidine-5'-isopropyl ester), improved pulmonary function, and reduced virus titer and body weight loss. Decreased MERS-CoV yields *in vitro* and *in vivo* were associated with increased transition mutation frequency in viral but not host cell RNA, supporting a mechanism of lethal mutagenesis. The potency of NHC/EIDD-2801 against multiple coronaviruses, its therapeutic efficacy, and oral bioavailability *in vivo*, all highlight its potential utility as an effective antiviral against SARS-CoV-2 and other future zoonotic coronaviruses.

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Sinai Immunol Review Project • 10 days ago

An orally bioavailable broad-spectrum antiviral inhibits SARS-CoV-2 and multiple 2 endemic, epidemic and bat coronavirus

Sheahan et al. 2020

Main Findings: β-D-N4 30 –hydroxycytidine (NHC, EIDD-1931) is an orally bioavailable ribonucleoside with antiviral activity against various RNA viruses including Ebola, Influenza and CoV. NHC activity introduced mutations in the viral (but not cellular) RNA in a dose dependent manner that directly correlated with a decrease in viral titers. Authors show that NHC inhibited multiple genetically distinct Bat-CoV viruses in human primary epithelial cells without affecting cell viability even at high concentrations (100 μM). Prophylactic oral administration of NHC in C57BL/6 mice reduce lung titers of SARS-CoV and prevented weight loss and hemorrhage. Therapeutic administration of NHC in C57BL/6 mice 12 hours post infected with SARS-CoV reduced acute lung injury, viral titer, and lung hemorrhage. The degree of clinical benefit was dependent on the time of treatment initiation post infection. The authors also demonstrate that NHC reduces MERS-CoV infection titers, pathogenesis, and viral RNA in prophylactic and therapeutic settings.

Caveats: Most of the experiments were conducted using MERS-CoV and SARS-CoV and

Jeremy Green • 19 days ago

Could the authors add illustrations of the chemical structures of the EIDD compounds? These are, after all, the subject of the paper.

Grant Jacobs • a month ago

Could the authors add 'in mice' in the abstract, please? Better still, in the title.

Max Sargeson Grant Jacobs • a month ago

"In mice"

Since the ribonucleoside analogue targets the RNA-virus as it replicates, not the mouse, it's probable that it works in humans; moreover the cross-species pharmacokinetics of things like nucleosides are generally comparable between mammals.