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## The small molecule nucleoside prodrug GS-5734 exhibits broad antiviral activity against pathogenic human coronaviruses and related zoonotic strains

SARS and MERS coronaviruses (CoVs) emerged from zoonotic reservoirs, causing global disease with high mortality rates. Reemergence is likely as viruses very similar to SARS and MERS-CoV are circulating in bat populations. Currently, there are no effective vaccines or therapeutics available to prevent or treat SARS-CoV, MERS-CoV or related zoonotic strain infections. GS-5734, a prodrug of an adenine C-nucleoside analog with known activity against filoviruses is currently undergoing clinical testing for the treatment of Ebola virus infection. We assessed the activity of GS-5734 against SARS-CoV and MERS-CoV-infected human airway epithelial cell (HAE) cultures, a physiologically relevant in vitro human conducting airway model. HAE cultures were infected with either SARS-CoV or MERS-CoV expressing fluorescent reporter genes at a multiplicity of infection of 0.5. Concurrent with infection, cultures were incubated in media containing serially diluted compounds for the duration of the study (48 hours). Levels of infection were assessed using immunofluorescence, viral titration and real-time PCR analysis of replication-specific viral RNA species. GS-5734 was found to have potent activity against SARS-CoV and MERS-CoV with 90% inhibition at less than or equal to 150 nM. In addition, GS-5734 significantly reduced the replication of multiple alpha and beta-coronaviruses (groups 2b and 2c) in HAE cultures including zoonotic ancestors of epidemic coronaviruses. Importantly, GS-5734 has shown low in vitro cytotoxity with 50% cytotoxic concentrations >1 μM in multiple human cell types. These data demonstrate the broad antiviral activity of GS-5734 against human epidemic and novel bat CoV strains that have future pandemic potential.

### Biography

Amy C Sims has completed her PhD in Microbiology and Immunology from Vanderbilt University in 2001 and Postdoctoral studies at the University of North Carolina at Chapel Hill with Dr. Ralph Baric. She is currently a Research Assistant Professor at UNC Chapel Hill. Her work has focused on understanding highly pathogenic human *Coroanvirus* replication in primary human cell types as well as identifying novel drugs and therapeutics that are effective against epidemic *Coronavirus* strains.

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