Channel modulators as broad-spectrum antivirals

Brief Description
Calcium channel modulating compounds as antivirals for enveloped RNA viruses.

Inventor
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Problem
Hemorrhagic fever viruses such as Ebola, Marburg, and Lassa fever are serious human pathogens for which there are currently no FDA approved therapeutics or vaccines. These viruses are similar to many other enveloped RNA viruses in that therapeutic efforts are often hampered by their extraordinary mutation rates and ability to evade strategies that target viral proteins. However, transmission of these viruses relies heavily on highly conserved host cell mechanisms. Accordingly, therapeutic strategies targeting these host mechanisms have become an attractive and innovative approach for developing antivirals that circumvent the issue of drug resistance and that can provide broad spectrum activity.

Solution
Calcium signaling is involved in varied mammalian cellular processes and has previously been implicated in viral budding. Budding is a critical step in the enveloped virus life cycle that is required for transmission and spread. Dr. Freedman and his team have demonstrated that matrix proteins from a diverse array of enveloped RNA viruses promote host calcium signaling via a STIM1/Orai activation mechanism. This influx of calcium orchestrates late steps of viral assembly and budding. Indeed, pharmacologically blocking or genetically inactivating the Orai Ca2+ entry channel, significantly attenuates budding and spread of infectious Ebola, Marburg, Lassa Fever, and other related RNA viruses; highlighting the fact that this antiviral approach has broad spectrum activity against enveloped RNA virus budding.

Advantages
- Broad spectrum antiviral activity against enveloped RNA viruses whose budding is orchestrated by virus triggered Orai mediated Ca2+ signaling
- Little to no risk of viruses developing resistance
- Easily accessible therapeutic target