BROAD-SPECTRUM THERAPEUTICS FOR VIRAL DISEASES: A MEDICAL COUNTERMEASURE PLATFORM FOR EMERGING THREATS

Crispr Inhibition And Crispr Activation Pooled Library Screens Offer An Effective Tool For Identifying Therapeutic Targets Against Broad Viral Families

Iris Jones NTESS/Sandia National Laboratories **Sean Lund** Sandia National Laboratories **Nicole Collette** Lawrence Livermore National Laboratory **Pragyesh Dhungel** Sandia National Laboratories **Anupama Sinha** Sandia National Laboratories **Yooli Light** Sandia National Laboratories **Oscar Negrete** Sandia National Laboratories

Epidemics caused by emerging viruses can cause substantial economic and health impacts both globally and within the United States. To prepare for future zoonotic events and prevent future pandemics, a better understanding of host genes associated with viral virulence amongst high-pandemic-risk viral families is necessary. An understanding of such gene networks offers family-specific therapeutic targets, as well as providing a deeper understanding of potential disease mechanisms. The bunyavirales order contains several such high-pandemic risk viruses, including Rift Valley Fever Virus (RVFV), Crimean-Congo hemorrhagic fever virus, and Hantaviruses. These viruses have a high zoonotic risk, especially in regions where livestock and/or pest species exist in close proximity to humans. Here, we present work defining networks of host virulence factors during RVFV infection using CRISPR inhibition (CRISPRi) and CRISPR activation (CRISPRa) pooled library screens. Additionally, we show a reduction in RVFV infection following CRISPR-mediated knock-out of previously identified Heparin-sulfate proteoglycan gene targets in A549 cells, noting, however, that reduction in infection was not as impactful as expected based on previous screen results. Future work will explore the role of identified gene networks in infection by other bunyavirales order members.