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

Long Non-coding Rnas In Venezuelan Equine Encephalitis Virus Infection

Steven Bradfute University of New Mexico Health Sciences Center **Mahgol Behnia** University of New Mexico Health Sciences Center **Scott Ness** University of New Mexico Health Sciences Center **Yan Guo** University of New Mexico Health Sciences Center **Teresa Bowman** Albert Einstein College of Medicine **Kylene Kehn-Hall** Virginia Tech

Venezuelan equine encephalitis virus (VEEV) causes neurological disorders in humans and equids. VEEV first infects immune cells (such as dendritic cells) in the draining lymph nodes, then spreads to the brain, where it infects neurons and astrocytes and causes encephalitis. Although the disease pattern for VEEV is well- established, nothing is known about the involvement of long non-coding RNAs (lncRNAs) in molecular regulation of pathogenesis. LncRNAs are a diverse set of regulatory RNAs greater than 200 nucleotides long that do not encode for proteins. LncRNA play numerous roles in a cell, such as regulating gene expression at multiple levels by interacting with DNA, RNA, and proteins. Recently, reports have shown that lncRNAs can participate in the regulation of anti-inflammatory responses or directly in antiviral functions in the cell, and that a subset of these may constitute a conserved response against multiple virus types. However, there are few studies that have been conducted with lncRNAs in pathogens with a biowarfare potential. Since VEEV is an important, militarily-relevant pathogen for which no countermeasures are available, we analyzed differential lncRNA responses of relevant primary cells infected with pathogenic Trinidad Donkey (TrD) strain or a non-pathogenic vaccine strain (TC-83) derived from TrD. We found differential expression of lncRNAs in TC-83 infected primary mouse neurons and astrocytes, but not in TrD-infected cells, 16 and 24 hours post-infection. Differential expression of lncRNAs and mRNAs were greatly diminished in TrD-infected neurons and astrocytes compared to TC-83-infected cells. Conversely, in infected dendritic cells, very few differentially expressed lncRNAs were detected after infection with either virus strain, and the level of differential mRNA expression was roughly similar in TrD- versus TC-83-infected cells. Current experiments are focused on modulating expression of selected lncRNAs in target cells to determine their effect on VEEV replication. Together, these data suggest that lncRNAs are differentially induced in pathogenic versus non-pathogenic VEEV infection in certain primary cells, and ongoing experiments will assess their impact on viral replication.

This research is funded by the Defense Threat Reduction Agency (HDTRA-1-20-1-0015). The content of the information does not necessarily reflect the position or the policy of the federal government, and no official endorsement should be inferred