

Mechanisms of SARS-CoV-1 Non-Structural Protein-1 (Nsp-1)-mediated Immune Regulation

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Immune evasion by severe acute respiratory syndrome-associated coronavirus (SARS-CoV) using non-structural protein 1 (nsp1) has been a topic of interest since the 2003 epidemic. It has been suggested that nsp1 is responsible for a delayed and disorganized activation of the immune system leading to worse clinical outcomes. Nsp1's known functions include antagonizing antiviral pathways that would otherwise limit viral replication and blocking eukaryotic translation crucial for host defense. During viral infection, nsp1 localizes in cells to boundaryless aggregates of cell machinery called stress granules. Interestingly, in stress granules, nsp1 may interact with ADAR1, a regulator of retinoic acid inducible gene I (RIG-I)-like receptors (RLRs), which specialize in detecting viral infections. Our lab created mutated versions of nsp1 lacking one or both nsp1 functions or enhanced antiviral activity using site-directed mutagenesis and confirmed our mutants using sanger sequencing. Using fluorescent microscopy, we hope to visualize the effect of distinct nsp1 functions on ADAR cellular localization in human epithelial lung cells. We will assess potential downstream effects via qRT-PCR on RLR-inducible genes and inflammatory cytokines associated with the antiviral response. The results from this study will provide a better understanding of nsp1 function and hopefully provide therapeutic targets to support detection and clearance of SARS-CoV infection by the immune response.