Norovirus, a small, non-enveloped RNA virus, is the most common cause of acute gastroenteritis in humans (Karst, et. al., 2014). Although pathogenic infection of intestinal epithelial disease is common, repeated attempts at infecting epithelial cells with human norovirus have been unsuccessful (Wobus et al., 2004). Research has shown that murine norovirus demonstrates replication in primary dendritic cells and macrophages (Wobus et al., 2004), and that it replicates remarkably well in STAT1 deficient mice, indicating that a similar system may be relevant in humans. Additionally, intestinal dendritic cells are required for extraintestinal spread of human virus in murine models (Karst, et. al., 2014). However, efforts to induce infection in human dendritic cells have been futile (Lay, et. al. 2010). Our hypothesis is that infection of dendritic cells with human norovirus is dependent on the presence of gastrointestinal stromal factors and signaling pathways, and that infection will occur primarily in STAT1 deficient cells. Previous research in this lab has concerned the identification of gastric stromal factors using gastric stroma-conditioned media, which is a model for the gastric microenvironment. We have thus confirmed SCM-derived immunoregulatory factors as a suitable model for generating dendritic cells with a mucosal phenotype. The proposed project will utilize both gastric and intestinal stroma-conditioned media, as well as H. pylori as a vehicle to suppress STAT1 signaling, to investigate whether mucosal stroma factors render human dendritic cells susceptible for infection with norovirus. This research applies to biomedical in that it concerns the pathogenesis of a prominent human pathogen which is not well understood. Further understanding of this virus could allow for the development of an effective vaccine and more effective antiviral medication (Karst, et. al., 2004), as well as the identification of risk factors associated with coinfection.

**RESULTS cont.**

2. H. pylori suppresses STAT1 signaling in DCs

![Figure 2a: FACS gating strategy for isolating dendritic cells.](image)

**RESULTS cont.**

4. STAT1 suppression is dependent on time post infection with H. pylori

![Figure 2b: FACS histogram showing percent of pSTAT1 after H. pylori stimulation.](image)

**RESULTS cont.**

**CONCLUSIONS**

**H. pylori suppresses STAT1 phosphorylation in peripheral blood derived dendritic cells, primarily at hours 6-8 post infection.**

This suggests that an infection of dendritic cells with HuNoV would be more successful in a coinfection model, and that we have a window in which this would be successful.

Additionally, HuNoV detection is possible through the use of a Human GII plasmid and qPCR. This enables us to successfully detect human norovirus in our samples.

**FUTURE WORK**

The next phase of this research will include DC infections with norovirus, as well as infection using gastric and intestinal S-CM.

This work has applications in public health, in that understanding the way that the virus interacts with the immune system will lead to better vaccines and more effective treatment.

**ACKNOWLEDGMENTS**

Research reported in this publication was supported by the National Institute of General Medical Sciences of the National Institutes of Health under Award Number 1R21GM115347-01. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.