Summary of: Lack of norovirus replication and histo-blood group antigen expression in 3-dimensional intestinal epithelial cells.pdf

Key Findings and Quantitative Results:

- **NV Replication and CPE:** - **No Evidence of Replication:** Real-time PCR of viral RNA and immunocytochemical detection of viral structural and nonstructural proteins showed no evidence of NV replication. - **No Detectable Histo-Blood Group Antigens:** No detectable presence of histo-blood group antigens that participate in NV binding and host tropism. - **LPS Treatment:** Treatment with highly purified NV induced morphologic changes consistent with CPE, suggesting the CPE-like effects were not due to viral replication.

- **NV Genotyping and Binding:** - **FUT2 Genotyping:** The INT-407 cell line showed the genetic determinants to express a functional FUT2, indicating the cells are likely secretor-positive. - **HBGA Expression:** Confocal microscopy showed no expression of H-type antigens on the surface of the cells, indicating the cells lack the putative NV receptors.

- **NV Binding and Pathogenesis:** - **Binding Pattern:** NV binds to H-type antigens on the surface of mammalian cells, hypothesized to be the mechanism for NV entry into cells. - **Pathogenesis:** In Caco-2 monolayers, NV VLPs were found to preferentially bind to A and H type 1 and Leb carbohydrates, consistent with the binding pattern observed in human cells.

- **In Vivo and In Vitro Studies:** - **In Vivo Studies:** Human volunteers infected with NV were resistant to the virus, as evidenced by the FUT2 genotype. - **In Vitro Studies:** The 3-D INT-407 model did not support NV replication, as evidenced by the absence of detectable viral RNA and proteins.

- **Statistical Analysis:** - **qRT-PCR Analysis:** qRT-PCR showed no significant increase in viral RNA levels over time, indicating no productive replication. - **LPS Treatment:** LPS at ≈1 μg/mL induced morphologic changes equivalent to those induced by NV addition, suggesting the CPE-like effects were not due to viral replication.

Summary: - The 3-D INT-407 model did not support NV replication. - NV VLPs preferentially bind to H-type antigens on the surface of the cells, consistent with the binding pattern observed in human cells. - The FUT2 gene is expressed on the surface of the cells, indicating the cells are likely secretor-positive. - The model lacks the HBGA carbohydrates necessary for NV binding and entry into cells. - LPS treatment induced morphologic changes consistent with CPE, suggesting the CPE-like effects were not due to viral replication.