Aim: To begin to determine the antigenic differences between and within human norovirus genotypes and to compare neutralization with the carbohydrate blocking assay (a surrogate for neutralization).

Experimental Scheme

Carbohydrate blocking assays suggest that norovirus genotypes are antigenically distinct. Variant A of GII.6 was antigenically distinct from variants B and C.

Carbohydrate blocking activity of GII.4/GI.1 and GI.1/GII.4 sera against GI.1 and GII.4 VLPs. Sera were produced against chimeric VLPs presenting the shell domain of GI.1 virus and the P-domain of GII.4 virus (GII.4/GI.1) or vice versa (GI.1/GII.4). Bars represent means and standard deviation of duplicate values from hyperimmune sera produced by two guinea pigs. (B) Neutralization of a GII.4 Sydney variant. Sera produced from different VLPs are color-coded by genotype. Replication in human intestinal enteroids in the presence of hyperimmune sera was compared to replication in the absence of sera (3 d.p.i.) and to cells infected with virus incubated with pre-immune sera isolated from guinea pigs before VLP immunization. The bars represent the geometric mean (in genome copies/well of a 96-well plate) using hyperimmune sera samples from the GI.1 and GII.4 VLPs. The dots represent individual values as calculated by RT-PCR. The replication per well at 1 h.p.i. was set as the neutralization threshold and is denoted with a dashed line. Samples with undetectable norovirus RNA were set as half the limit of detection (LOD50 = 2700 genome copies/well of a 96-well plate). All infections were performed in the presence of 0.5 mM GCDDA (bile acid component).

Conclusions

- Human intestinal enteroids can potentially be used to determine norovirus serotypes
- Carbohydrate blocking assays and neutralization exhibited similar patterns in antibody responses
- Antigenic differences between genotypes and even within some variants of the same genotype (i.e. GII.6) could complicate vaccine design

Acknowledgements: We would like to thank Kim Green for providing the sera produced against the chimeric VLPs and Mary Estes for providing the sera produced against the chimeric VLPs. This work was supported by the Food and Drug Administration intramural and the OCS Challenge Grant 414. K. Tohma is a recipient of a CBER/TDA-sponsored Oak Ridge Institute for Science and Education (ORISE) Fellowship. Nothing to disclose.