Category: Clinical Genomics

Gene-Specific-Candidate-Driven Study to decipher Genetic Predisposition to Rotavirus Infection

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Abstract

Recent report of WHO shows 113000 children in India succumb to death due to Rotavirus diarrhea. Lack of knowledge about pathogenesis of virus has led to lack of therapy for severely infected patients. Previous studies have found that, animal rotavirus requires sialyl glycan moieties on cell surface for pathogenesis. Present study states that human rotaviruses also follows same path and this specificity of virus leads to host genetic predisposition for the infection as well as the disease. Two hundred children less than 5 years of age clinically suspected of viral diarrhea were screened for rotavirus infection. EDTA blood was processed for analyzing DNA sequences of various fucosyltransferase genes. Lewis antigens which are secretory form of ABO Histo Blood Group Antigens were correlated with the genotype of patient. Genetics of HBGA secretion, particularly, basis of Leb expression manifested by fucosyltransferase-2 enzyme was studied in healthy individuals and was compared in cases of rotavirus positive and negative diarrhea. Positive clinical isolates with various genotypes were purified from stool samples and gene for VP4 - surface spike protein was sequenced. Using Bioinformatics interphase, three dimensional protein structures were modeled and their functional domains were analyzed. All these modeled proteins were docked with Leb HBGA (Lewis-b Histo Blood Group Antigens) using molecular docking software. In present study, to investigate possible association of the rotavirus with host genome, we screened highly suspected genes involved in expression of glycoproteins on enterocytes. This study performed for prevalent Indian strains of rotaviruses provides possible evidence that, VP8 domain of VP4 spike protein utilizes Leb surface antigen for attachment and entry to enterocytes in the intestine. The FUT2 and FUT3 gene has been found to show significant association with the rotavirus infection hence can serve as a biomarker for genetic predisposition to Rotavirus diarrhea. Knowledge of molecular biology of the Rotavirus pathogenesis may open up new paths for vaccines and therapy. Data presented here is first of its kind which deciphers Host-Rotavirus interaction by parallel experiments of epidemiological study and In Silico study.

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