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Studies on the Interaction of Rotavirus Non Structural Proteins NSP5, NSP2 with Host Cellular Factors and their Role in Virus Replication

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Rotavirus (RV) still remains the single most important etiological agent of severe diarrhea in infants and young children worldwide, with an annual mortality of over 200,000 children. It is non-enveloped, segmented, double-stranded RNA virus and belongs to the family *Reoviridae*. The viral genome consists of 11 segments of double-stranded RNA, which encodes 6 structural and six non-structural proteins. In infected cells, rotavirus replicates in the cytoplasm in virus induced inclusion bodies called viroplasms (VMs) which are formed by two essential viral non structural proteins NSP5 and NSP2. VMs are the sites where RNA replication and new immature double layered particle (DLP) assembly take place. Till date, the association of host cellular proteins in rotavirus with NSP5 and NSP2 has remained unexplored. By mass spectrometry analysis we have identified several host proteins showing interaction with NSP5 and NSP2, which were further confirmed by pull down assay using uninfected MA104 cell extracts. Next, we selected three host nuclear proteins hnRNP K, hnRNP D and Fibrillarin for our detailed studies and confirmed their interactions by Co-immunoprecipitation using RNase treated infected cell lysate suggesting the interaction is RNA independent. Immunofluorescence confocal microscopy revealed that these nuclear/nucleolar proteins undergo relocalization to the cytoplasm during virus infection and were sequestered into the VMs where they colocalize with NSP5 and NSP2 through direct interactions. We also observed time dependent nuclear-cytoplasmic redistribution of these proteins by western blot analysis in cytoplasmic and nuclear extracts from infected cells in comparison to that in uninfected cells. The significance of these host proteins in rotavirus infection was elucidated by siRNA-mediated knockdown and over expression in HEK293T cells. Knockdown of hnRNP D, hnRNP K and fibrillarin decreased the expression of NSP5, NSP2 and structural protein VP6 and over expression of hnRNP K and fibrillarin proteins increased the expression of viral NSP5, NSP2 and VP6.

Biography:

Varsha Narayan Tandra is a Ph.D. from Indian Institute of Science working on Molecular virology. Varsha is an enthusiastic and have keen interest in learning and gaining knowledge.