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P-body components LSM1, GW182, DDX3, DDX6 and XRN1 are recruited to WNV replication sites and positively regulate viral replication

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In mammalian cells, proteins involved in mRNA silencing and degradation localize to discrete cytoplasmic foci called processing or P-bodies. These include Sm-like protein LSM1, GW182, 5'-3' exonuclease XRN1, dead box RNA helicase DDX3 etc. West Nile Virus (WNV) infection causes depletion of P-bodies. However, how this P-body depletion occurs and what happens to the P body proteins is not known. WNV infected HeLa cells were analyzed for P-bodies by immunostaining, for protein levels by western blotting. Transient knockdown of P body components was achieved by specific siRNA transfection, WNV replication was measured by FACS analysis and qRTPCR. In WNV infected cells 36 hPI, complete depletion of LSM1, GW182, DDX3 and XRN1 P-bodies was observed but levels of these proteins remained equal in uninfected and infected cells. On the other hand, we found that many P-body components including LSM1, GW182, DDX3, DDX6 and XRN1, but not others like DCP1 and EDC4 are recruited to the viral replication sites as evidenced by their colocalization at perinuclear region with viral NS3. Kinetic studies suggest that the component proteins are first released from P-bodies in response to WNV infection within 12 h post infection, followed by recruitment to the viral replication sites by 24-36 h post infection. These data suggests that in response to WNV infection p body components relocalize to WNV replication complexes and this in-turn might cause depletion of P-bodies. Silencing of the recruited proteins individually with siRNA interfered with viral replication to varying extents suggesting their collective requirement for efficient viral replication. Thus, the P-body proteins might provide novel drug targets for inhibiting viral infection.

Biography

Harendra S Chahar completed his Ph.D from All India Institute of Medical Sciences, New Delhi India-2011. He works in the Center of Excellence in Infectious Disease Research at Texas Tech University, El Paso, Texas in Dr. Manjunath Swamy's group. Their primary area of interest is to understand RNAi mechanism in special reference to flaviviruses and develop novel therapeutics.

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