

Sendai virus recruits cellular villin to remodel actin cytoskeleton during fusion with hepatocytes

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Reconstituted Sendai viral envelopes (Virosomes) are well recognized for their promising potential in membrane fusion mediated delivery of bioactive molecules to liver cells. Despite the known function of viral envelope glycoproteins in catalyzing fusion with cellular membrane, the role of host cell proteins remains elusive. Here, we used two-dimensional differential in-gel electrophoresis (2D-DIGE) to analyze hepatic cells in early response to virosome-induced membrane fusion. Quantitative mass spectrometry together with biochemical analysis revealed that villin, an actin-modifying protein, is differentially up-regulated and phosphorylated at Threonine-206 (T206), as an early molecular event during membrane fusion. We found that villin influences actin dynamics which, in turn, promotes membrane mixing through active participation of Sendai viral envelope glycoproteins. Modulation of villin in host

cells also resulted in a discernible effect on the entry and egress of progeny Sendai virus. Taken together, these results suggest a novel mechanism of regulated viral entry in animal cells mediated by host factor villin.

Speaker Biography

Sunandini Chandra is trained in the field of virus-host interactions, especially in the field of viral fusion with host cell membrane. After a Master's in Biotechnology, she recently completed her Doctoral research work in Sendai virus-host cell interactions, with special emphasis on the role of actin modifying proteins in fusion. Her work employed proteomic approaches and is the first to result in identifying a host cell protein- villin, implicated in virus induced membrane fusion with the host cell membrane. This work provides an insight into the mechanism of membrane fusion mediated entry of enveloped viruses and may be exploited for therapeutic interventions for other related pathogenic viruses. Also, this information could be exploited to improve fusion efficiency of Sendai virosomes, for efficient targeted delivery to liver cells.

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