

THE REOVIRUS PLATFORM: NONSTRUCTURAL PROTEIN μ NS AND ITS MULTIPLE ROLES IN VIRAL FACTORIES

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Reovirus-infected cells are notable for large cytoplasmic inclusions, called viral factories, in association with which viral genome replication and assembly of viral core particles occur. Reovirus nonstructural protein μ NS forms structures morphologically similar to viral factories when expressed in uninfected cells, suggesting that μ NS plays a primary role in forming the factory matrix. In addition, μ NS associates with and recruits or retains all of the viral components thought to be necessary for genome replication and core assembly, including parental core particles; newly synthesized core proteins μ 2, λ 1, λ 2, λ 3, and σ 2; and newly synthesized nonstructural protein σ NS. In recent work, we identified discrete regions of μ NS that are necessary for association with each of these components by examining their localizations relative to factory-like structures formed by μ NS deletion mutants. We additionally identified regions of μ NS sufficient for association with each component utilizing a panel of plasmid constructs through which short regions of μ NS were fused to GFP/NSP5, a rotavirus fusion protein that forms similar factory-like structures, called viroplasm in rotavirus-infected cells. We found that short regions within the N-terminal one-third of μ NS are necessary and sufficient to associate with μ 2, λ 1, λ 2, σ 2, and σ NS, whereas λ 3 associates with the C-terminal one-third of μ NS. Additionally, we identified a short region of μ NS necessary for association with core particles and provided evidence that viral transcripts are transcribed within viral factories in infected cells. We propose that in addition to forming the matrix of viral factories and recruiting core proteins, σ NS, and core particles to these structures, μ NS plays a further role as a scaffold protein involved in assembling and organizing structural intermediates for efficient production of genome-containing progeny core particles. The use of μ NS as a generalized platform for studies of protein-protein interactions and evidence that μ NS functions as a clathrin adapter protein will also be summarized. This work was supported in part by NIH grants R01 AI47904 and R56 AI067445 to M.L.N. and F32 AI56939 to C.L.M.