Deciphering the Functional Role of Junín virus Nucleoprotein Isoforms

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The limited coding capacities of small RNA virus genomes can be expanded by post-translational modification of existing viral proteins. In this regard, the Junín virus nucleoprotein (NP) produces three additional isoforms lacking various parts of the N-terminal domain. The smaller 47kD and 40kD NP variants are caspase cleavage products, while using mutagenesis studies we found that the 53kD isoform results from alternative translation at position M80. We are now exploring the functional contributions of these alternate NP isoforms in the viral life cycle. Using a minigenome assay, we could show that none of these shorter isoforms support viral RNA synthesis alone, although they also do not inhibit it. Supporting these results, immunofluorescence assays showed a loss of localization with inclusion bodies, which are the sites of viral RNA synthesis. Rather, we observed increased distribution in the cytoplasm, as well as nuclear localization of the 40kD isoform. These results points to a role of these isoforms in accessory NP functions, such as regulating host cell response pathways, and we are now evaluating their ability to influence interferon and NFκB signaling. These results highlight arenavirus strategies to acquire additional protein functionality from their limited coding capacity.

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