


## Structure of the L protein of vesicular stomatitis virus from electron cryomicroscopy

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**Abstract**

The large (L) proteins of non-segmented, negative-strand RNA viruses, a group that includes Ebola and rabies viruses, catalyze RNA-dependent RNA polymerization with viral ribonucleoprotein as template, a non-canonical sequence of capping and methylation reactions, and polyadenylation of viral messages. We have determined by electron cryomicroscopy the structure of the vesicular stomatitis virus (VSV) L protein. The density map, at a resolution of 3.8 Å, has led to an atomic model for nearly all of the 2109-residue polypeptide chain, which comprises three enzymatic domains (RNA-dependent RNA polymerase [RdRp], polyribonucleotidyl transferase [PRNTase], and methyltransferase) and two structural domains. The RdRp resembles the corresponding enzymatic regions of dsRNA virus polymerases and influenza virus polymerase. A loop from the PRNTase (capping) domain projects into the catalytic site of the RdRp, where it appears to have the role of a priming loop and to couple product elongation to large-scale conformational changes in L.

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