

# Cryo-electron microscopy structures of La Crosse orthobunyavirus polymerase in presence and absence of viral RNA

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*Bunyaviridae* is the largest family of segmented negative strand viruses (sNSV) which also include *Orthomyxoviridae* and *Arenaviridae*. Central to their viral cycle is the RNA-dependent RNA polymerase which replicates and transcribes the genome segments within circular ribonucleoprotein particles (RNPs). Here we describe a cryo-electron microscopy reconstruction of the full length La Crosse polymerase in complex with viral RNA, together with a reconstruction of its apo truncated form ( $\Delta$ -Cterminal construct). Combined with the X-ray structure determined in the group, we provide a partial pseudo-atomic model of La Crosse polymerase. Identification of distinct template and product exit tunnels and structural analysis of RNP allows proposal of a detailed model for template-directed replication with minimal disruption to the circularised RNP. The similar overall architecture and vRNA binding of monomeric LACV to heterotrimeric influenza polymerase, despite high sequence divergence, suggests that all sNSV polymerases have a common evolutionary origin and mechanism of RNA synthesis.

## References

[1] - P. Gerlach, H. Malet, S. Cusack, J. Reguera, Structural Insights into Bunyavirus Replication and Its Regulation by the vRNA Promoter. *Cell*. 2015 Jun 4;161:1267-79.