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Review

A structural view of the RNA-dependent RNA polymerases from the *Flavivirus* genus

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Highlights

- A structural overview of the flavivirus RNA-depedent RNA polymerases (RdRPs).
- The flavivirus RdRP global architecture and elements related to polymerase function.
- The flavivirus RdRP autoregulation by its natural fusion partner methyltransferase.
- Characteristic features in conformational dynamics in flavivirus RdRPs.

Abstract:

The RNA-dependent RNA polymerase (RdRP) from the *Flavivirus* genus is naturally fused to a methyltransferase (MTase), and the full-length protein is named nonstructural protein 5 (NS5). Similar to other polymerases from other RNA viruses, the flavivirus RdRP has an encircled human right hand architecture with palm, fingers, and thumb domains surrounding its polymerase active site. In contrast to primer-dependent RdRPs that have a spacious front channel to accommodate the template-product RNA duplex, the flavivirus RdRP has a priming element as a thumb domain insertion, partially occupying the front channel to facilitate the *de novo* initiation process. Seven catalytic motifs A through G