Abstract

Viral RNA-dependent RNA polymerases (RdRps) are enzymes essential for viral multiplication. The general function of RdRp is universal for all RNA viruses: to recognise viral RNA, bind it and synthesize the complementary RNA strand. This series of steps is absolutely crucial for viral infection.

It is important to mention that the non-infected cell is incapable of replicating any RNA. The host cell thus does not naturally express any RdRps. I chose RdRps for my research because these enzymes are key to viral replication and thus an excellent target for antivirals.

This study characterises polymerases from *Picornaviridae* and *Flaviviridae* families, in depth. Picornaviral replication takes place in viral-induced membrane structures called Replication Organelles (ROs), where the polymerase is localised to the membrane. In this study, we investigated the recruitment of picornaviral polymerase membrane. Subsequently, we focused on the activation of picornaviral RdRp induced by the insertion of the very first residue into the protein core.

Next, we focused on the flaviviral RdRps specifically from yellow fever virus (YFV) and Zika virus (ZIKV). This study reports the first structure of a full length YFV polymerase and a model of ZIKV polymerase in complex with RNA. The model of ZIKV RdRp in complex with RNA provides the information needed for ligand docking.