

Structural Approaches to understanding Influenza Virus replication and transcription

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Influenza virus causes infections that affect approximately 3 to 5 million people every year, leading to between 250,000 to 500,000 deaths around the world. Key to viral replication is the viral polymerase that copies the viral genome and produces viral messenger RNA which is then used to make building blocks for new virus particles. The polymerase of Influenza has to perform a number of chemical steps in order for the virus to replicate, and, akin to a moving motor, it is increasingly clear that being highly dynamic is key to its ability to work.

We aim is to understand the structural changes that occur in the polymerase at various stages during replication and transcription.

Thus far we have solved the structure of Avian and Human Influenza A virus polymerase as well as Influenza C virus, in an apo-form lacking RNA promoters.

This reveals the polymerase in a closed pre-activation state that is radically different from promoter bound forms. The structure shows the conformation of newly synthesised polymerase but may also be relevant to RNP-associated polymerase and provides additional insight into transcription initiation.

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