diamond

Drug Discovery

CASE STUDY

The ABCs of flu

Influenza viruses altogether affect 5%-10% of the adult population and 20-30% of children each year. These annual epidemics are estimated to result in about approximately 3 to 5 million cases of severe illness, leading to between 250,000 to 500,000 deaths around the world.

Integral to viral replication, polymerases are enzymes that copy the viral genome and produce messenger RNA which is then used to make building blocks for new virus particles.

UNIVERSITY OF OXFORD

The Challenge

Influenza polymerase, FluPol, is a highly flexible protein complex and it is believed to be able to adopt a number of uncharacterised conformational states. Understanding the nature of the conformation states is critical in understanding how the enzyme is regulated but difficult to achieve using standard biophysical methods.

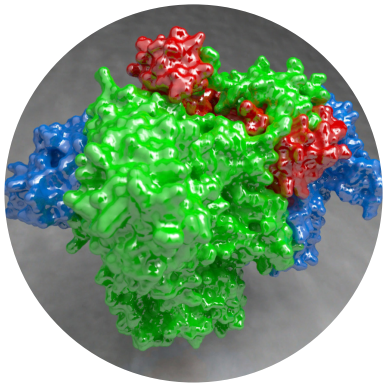
FluPol from influenza C virus in the absence of promoter RNA (apo-FluPol) was crystallised in two different crystal forms to help identify structures not previously known.

The Solution

Scientists from the University of Oxford and Diamond have used the combination of MX (beamlines I03 and I04) to investigate the crystal structure of the apo-FluPolC to 3.9 Å and SAXS (beamline B21) to reveal FluPolC in a “closed” transcription pre-activation state.

This study reveals the conformation of newly made apo-FluPolC in an infected cell, but may also be important in understanding how the activity of FluPol may be influenced by other viral factors and proteins.

The Benefits



Understanding structure and function of the polymerase in influenza C virus could provide insight into polymerases of other viruses in the same family, including the more aggressive and dangerous influenza A and B virus types.

Using this knowledge, the team will also study the polymerases for rabies and Ebola in an attempt to determine their exact structure, so that new avenues for the treatment of these diseases can be opened up in a similar way.

“The polymerase we have mapped is key to the virus’s ability to replicate. If we can understand its structure, we can better understand how it works. This means we could be able to create drugs that target this polymerase to prevent the virus spreading. Understanding the structure also means we may be better placed to understand the processes by which bird flu viruses adapt to infect humans and cause viral outbreaks.” **Prof Ervin Fodor, University of Oxford**

For further information

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