

Adenoviruses are common viruses that can cause a variety of diseases, such as respiratory, stomach and eye infections. In healthy individuals, these infections are usually mild or unnoticeable. However, in young children, the elderly and those with weakened immune systems, adenoviruses can lead to serious complications and even be life-threatening. These viruses are difficult to control because they can survive for long periods of time in the environment and are resistant to many commonly used disinfectants. This makes them easy to spread in hospitals, schools and other places.

In order to multiply, adenoviruses need to create copies of themselves inside host cells. They take over cellular mechanisms and use them to build new virus particles. A key element in this process is the virus's machinery, which copies its genetic material. It consists of three viral proteins:

- DNA polymerase (Ad Pol), which performs the actual duplication of the genetic material (DNA),
- preterminal protein (pTP), which helps start the process,
- DNA binding protein (DBP), which stabilizes genetic material and keeps DNA duplication running smoothly.

In addition, the virus uses host proteins such as NFI and Oct-1 to aid replication.

Although much is already known about adenovirus multiplication, detailed three-dimensional images of the virus proteins and their interactions are still lacking. Without such images, it is difficult to fully understand how the machinery that multiplies the virus' genetic material works and why it is so effective. The goal of this project is to solve this puzzle by studying the spatial atomic structures of key proteins involved in adenovirus replication and their interactions with host proteins. Using advanced imaging techniques, we want to get an accurate picture of how these proteins work.

The project will use cryo-electron microscopy (cryo-EM), a modern technology that allows us to see molecules at the level of individual atoms. Cryo-EM allows us to freeze proteins in their natural state and obtain detailed spatial images of their shapes and the contacts between them. We will also use the classical approach, in which, to acquire images of proteins, their microcrystals are obtained and X-rays are refracted on them. These techniques will allow us to visualize, among other things, how Ad Pol binds to pTP at the beginning of replication, how pTP assists the first steps of the process, and how DBP helps organize genetic material. Using these techniques, we will also show how host proteins, such as NFI and Oct-1, support viral proliferation.

The main goal of the research is to discover how the adenovirus machinery works at the level of individual atoms. This knowledge will be the basis for designing antiviral drugs. Although this project is not focused on developing new therapies, the data obtained in this study will be helpful in creating drugs that target key components of the virus machinery, such as the interactions between Ad Pol and pTP, for example.

This research is important because it fills one of the biggest gaps in our knowledge of adenoviruses: understanding how their machinery that duplicates genetic material works at the atomic level. In the long term, this research may help develop more effective methods to combat adenoviral infections and protect susceptible groups, such as children and immunocompromised individuals, from severe disease.