Towards better understanding of the human adenovirus pVII protein interactome

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Viruses need to access various cellular mechanisms to be able to infect and survive within the cells. One of the most studied mammalian viruses is human adenovirus, which has been extensively used to study different molecular biology processes, epidemiology, immune system and infection mechanisms. The knowledge gained from these studies has been instrumental to reveal the basic mechanisms of virus infections.

Human adenoviruses are classified in the *Mastadenovirus* phylogeny of the *Adenoviridae* family. Adenoviruses are worldwide and can cause several diseases, such as conjunctivitis, gastroenteritis, myocarditis and pneumonia (mostly in children). Adenoviruses are non-enveloped viruses of approximately 80 to 90 nm of diameter containing linear double stranded DNA genome. Adenovirus genes are classified according to the onset of viral DNA replication into early (before DNA replication) and late (after DNA replication) genes.

My project was focused on adenoviral protein VII (pVII), which is responsible for packing of adenovirus genomic DNA. The pVII protein wraps the viral DNA so it can be transported to the cellular nucleus. The pVII's role during early infection is to prevent viral DNA from the cell's DNA damage response. Thereafter, as the adenovirus life-cycle proceeds, the pVII protein has an essential role in the virus gene expression regulation and viral genome packaging. However, it is currently unknown how the pVII protein accomplishes its functions during different stages of infection. Considering the multiple functions of the pVII protein is likely that it establishes a variety of protein-protein interactions, which are essential for its biological functions.

Recent study has identified 12 novel pVII interacting proteins. Inspired by this finding I have biochemically analysed some of the pVII interacting proteins in mammalian cells. To characterise the pVII interacting proteins, I confirmed their interaction with pVII *in vivo* and *in vitro*. To define the specific region where the pVII binds on identified proteins I performed mutagenesis analysis. Finally, I followed the identified proteins through adenovirus infection and found that the virus is regulating the target proteins in the early stage of infection. This suggests that the interaction between pVII and the target protein is essential to regulate cellular mechanisms at key time points during infection. This process may prevent detection of the virus by the immune system, or could allow the virus to take over cellular mechanisms.

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