

Adeno-associated Virus 5 Bound to Its Cellular Receptor AAVR

Yuan, Zhengjia (School: Capital Normal University High School)

Adeno-Associated Virus (AAV) is an ideal vector for gene therapy, but it still has some challenges. Based on AAV, more efficient and more tissue-specific recombinant vectors are needed. In a previous work, it was found that the cell entry of AAVs is determined by their binding with a transmembrane protein, KIAA0319L (hereafter termed AAV receptor-AAVR), which contains 5 polycystic kidney disease (PKD) repeat domains. Different AAV serotypes might use different PKDs during cell entry process. AAV5 only required PKD1 and other serotypes required PKD2 or 3 for binding and infection. However, the molecular detail of the interaction is still unclear. I determined the physical structure of AAV5-AAVR complex. I used different software to process the cryo-EM images of AAV5 and AAV5-AAVR complex, obtaining the physical structure of AAV5-AAVR. The structure shows that PKD1 is bound at the opposite side of the spike of the AAV5 capsid and residues in strands F/G and the CD loop of PKD1 interact directly with AAV5, which is strikingly different from the interaction of AAV2-AAVR and AAV1-AAVR. Moreover, by introducing point mutations, I tested each amino acid residue involved in the interaction on AAVR using surface plasmon resonance, and obtained the essential, inessential, and inhibitive residues in AAV5-AAVR binding. This discovery provides us a new sight to design more effective AAV vectors with high efficiency on receptor binding. Based on this project, it will be more convenient for us to control the infection of adeno-associated virus, so that the virus can be better used in gene therapy. The results also give us the evidence that different serotypes might able to share the tissue tropisms through surface recombination.

Awards Won:

