

W0326

Structural Analyses of Adeno-Associated Virus Serotypes 3B & 6. Q. Xie, S. Murray, J. Hare, M.S. Chapman, Inst. of Molecular Biophysics, Florida State Univ., Tallahassee, FL 32306.

Adeno-associated viruses (AAVs) are SS DNA viruses that depend on helper viruses for replication. There are several human serotypes, for which all have the potential to be developed as transducing vectors, but the vectors in use were almost all derived from AAV2. Infection by wild type AAV results in the production of neutralizing antibodies and 50-80% adults have neutralizing antibodies to AAV, with antibodies against AAV-2 being the predominant type. The presence of high-titer neutralizing antibodies is likely to severely decrease transduction rates on (repeated) vector treatments. This study is directed towards understanding how changes to epitopes have evolved, presumably in response to selection for escape to neutralizing antibodies.

We are working on crystallography to solve the structures of serotype AAV3B & 6. Milligram quantities were prepared with high purity. Crystals were grown that diffracted up to 2.8\AA at CHESS. Molecular replacement and symmetry-averaging will be used to solve the phase problem. Determination of particle orientations through a rotation function search is undertaken. The next step is a translational function to search for the particle position. Phases bootstrapped from the AAV2 structure can then be refined to yield an electron density map for AAV6 & 3B.