

W0052

Structure of Adeno-associated Virus serotype 4. Lakshmanan Govindasamy¹, Eric Padron¹, Robert McKenna¹, Nikola Kaludov², John A. Chiorini² and Mavis Agbandje-McKenna¹. ¹Dept. of Biochemistry & Molecular Biology, Univ. of Florida, Gainesville, FL 32601, ²GTTB, NIDCR, National Institutes of Health, Bethesda, MD 20892, USA.

Adeno-associated virus (AAV) serotypes are currently under development as clinical gene delivery vectors for the treatment of human diseases. However, the ubiquitous nature of their cell surface receptors, heparin sulfate (AAV2 and 3) and sialic acids (AAV4 and 5), can preclude specific tissue targeting *in vivo*. Structural studies of AAV4 were initiated to characterize its capsid surface for re-targeting manipulations. Crystals obtained diffracted synchrotron radiation to 3.2 Å resolution. The unit cell is body-centered orthorhombic, I222, with a = 339.6, b = 319.2 and c = 285.0 Å. The structure of AAV4 has been determined by molecular replacement, using the atomic coordinates of feline Parvovirus for phasing. A comparison of the AAV4 structure with that recently published structure of AAV2 clearly shows major differences, on the surface of the viruses, that most likely account for their receptor recognition disparities.