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X-ray Structure of AAV5, A Gene Therapy Vector for Cystic Fibrosis. L. Govindasamy¹, M. DiMattia¹, H. Levy¹, B. Gurda-Whitaker¹, J.A. Chiorini², R. McKenna¹, N. Muzyczka³, S. Zolotukhin⁴, M. Agbandje-McKenna¹, ¹Dept of Biochem. and Mol. Biol., ³Dept. of Mol. Genetics and Microbiology, ⁴Dept. of Pediatrics, COM, UF, Gainesville, FL 32610; ²GTTB, NIDCR, NIH, Bethesda, MD 20892.

Adeno-associated virus serotype 5 (AAV5), is a small, nonpathogenic, non-enveloped icosahedral capsid of ~260Å in diameter. This virus, belonging to the *Dependovirus* genus of the *Parvoviridae* is under development for gene therapy applications to treat cystic fibrosis. To identify the structural features of AAV5 that contribute to its enhanced transduction of the apical surface of airway epithelia compared with other AAV serotypes, we have determined its capsid structure by X-ray crystallography. AAV5 crystals belong to the orthorhombic space group $P2_12_12_1$, with unit-cell parameters $a = 264.7$, $b = 447.9$, $c = 629.7$ Å. There is one complete $T = 1$ viral capsid per asymmetric unit. The structure of the capsid was determined to 3.2 Å resolution by molecular replacement. Structural comparison of AAV5 with those already available for AAV2, AAV4, and AAV8 clearly shows structural re-arrangements in surface loop regions of the capsids that co-localize with regions identified as being important for AAV2 receptor attachment, transduction efficiency, and antigenic reactivity.