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Determination of Sialic Acid Binding Region of Adeno-Associated Virus 5. M DiMattia¹, L Govindasamy¹, B Whitaker¹, R McKenna¹, S Zolotukhin², N Muzyczka³, M Agbandje-McKenna¹, ¹Dept. of Biochem. & Mol. Bio., ²Dept. of Pediatrics, ³Dept. of Mol. Genetics and Microbiology, COM UF Gainesville, FL 32610.

Adeno-associated virus 5 (AAV5) is under development for gene-therapy applications for treatment of cystic fibrosis. Belonging to the *Dependovirus* genus of the ssDNA *Parvoviridae*, this non-lytic virus is highly applicable for packaging and delivery of recombinant therapeutic DNA into target tissues due to its non-pathogenic nature and ability to establish long-term expression. Different AAV serotypes have distinct cell surface tropisms mediated through differential recognition of cell surface carbohydrates. AAV5, known to bind sialic acid (SA), is significantly more effective at transducing the apical surface of airway epithelia than AAV2. Crystals of AAV5 soaked with SA have been used to determine the structure of the AAV5-SA complex to 3.5 Å resolution. F_o-F_c density observed at the icosahedral 3-fold axis is consistent with ordered SA. The structure determination of the complex and the analysis of receptor-capsid interactions will be presented. Mapping of this receptor attachment site represents another step toward our understanding of the AAV5 structure and will lead to engineering of novel vectors, expanding the repertoire of tissues that can be targeted by AAV5 vectors.