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Characterization of AAV44.9, a Member of the New AAV Clade, with a Tropism Capable of Treating a Broad Spectrum of Genetic Disease

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Recent isolation of novel AAV serotypes has led to significant advances in our understanding of parvovirus biology and vector development for gene therapy by identifying vectors with unique cell tropism and increased efficiency of gene transfer to target cells. AAV44.9 is a natural isolate originally found as a contaminate of laboratory stock of SV15 adenovirus. Its sequence homology places it between clades E and F similar to Rh.8. Recent studies have suggested that AAV44.9 is a promising candidate for photoreceptor-targeted gene therapies. However, its broader biodistribution and cell tropism is not clear. To better understand its activity in other organs and general biodistribution mice were transduced by a variety of routes of transduction. Intracerebroventricular injection showed transduction of the cortex, olfactory bulb, cerebellum, choroid plexus and brain stem similar to AAV9. Like AV9, AAV44.9 also shows transduction of hepatocytes and is able to rescue a neonatal-lethal model of methylmalonic acidemia. Data on the glycan requirements will be presented.