# Adeno associated virus

Adeno-associated virus (AAV) is a small virus which infects humans and some other primate species. AAV is not currently known to cause disease. The virus causes a very mild immune response, lending further support to its apparent lack of pathogenicity.

It is an ideal vector for gene transduction into the central nervous system because of its safety and efficiency. While it is currently widely used for clinical trials and is expected to become more widespread, the appropriate combination of viral serotypes and promoters have not been fully investigated.

Gene therapy vectors using AAV can infect both dividing and quiescent cells and persist in an extrachromosomal state without integrating into the genome of the host cell, although in the native virus some integration of virally carried genes into the host genome does occur.

These features make AAV a very attractive candidate for creating viral vectors for gene therapy, and for the creation of isogenic human disease models.

Recent human clinical trials using AAV for gene therapy in the retina have shown promise.

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Adeno-associated virus (AAV) vectors expressing tumoricidal genes injected directly into brain tumors have shown some promise, however, invasive tumor cells are relatively unaffected.

see AAV9.

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Chow et al.e developed an adeno associated virus-mediated, autochthonous genetic CRISPR screen in glioblastoma. Stereotaxic delivery of a virus library targeting genes commonly mutated in human cancers into the brains of conditional-Cas9 mice resulted in tumors that recapitulate human glioblastoma. Capture sequencing revealed diverse mutational profiles across tumors. The mutation frequencies in mice correlated with those in two independent patient cohorts. Co-mutation analysis identified co-occurring driver combinations such as B2m-Nf1, Mll3-Nf1 and Zc3h13-Rb1, which were subsequently validated using AAV minipools. Distinct from Nf1-mutant tumors, Rb1-mutant tumors are undifferentiated and aberrantly express homeobox gene clusters. The addition of Zc3h13 or Pten mutations altered the gene expression profiles of Rb1 mutants, rendering them more resistant to temozolomide. Our study provides a functional landscape of gliomagenesis suppressors in vivo [1].

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Chow RD, Guzman CD, Wang G, Schmidt F, Youngblood MW, Ye L, Errami Y, Dong MB, Martinez MA, Zhang S, Renauer P, Bilguvar K, Gunel M, Sharp PA, Zhang F, Platt RJ, Chen S. AAV-mediated direct in vivo CRISPR screen identifies functional suppressors in glioblastoma. Nat Neurosci. 2017 Aug 14. doi: 10.1038/nn.4620. [Epub ahead of print] PubMed PMID: 28805815.