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(54) **Title**: COMPOSITIONS AND METHODS FOR ALTERING TISSUE SPECIFICITY AND IMPROVING AAV9-MEDIATED GENE TRANSFER

(57) **Abstract**: A method of altering the targeting and/or cellular uptake efficiency of an adeno- associated virus (AAV) viral vector having a capsid containing an AAV9 cell surface binding domain is described. The method involves modifying a clade F cell surface receptor which comprises a glycan having a terminal sialic acid residue and a penultimate β-galactose residue. The modification may involve retargeting the vector by temporarily functionally ablate AAV9 binding in a subset of cells, thereby redirecting the vector to another subset of cells. Alternatively, the modification may involve increasing cellular update efficiency by treating the cells with a neuraminidase to expose cell surface β-galactose. Also provided are compositions containing the AAV9 vector and a neuraminidase. Also provided is a method for purifying AAV9 using β-galactose linked to solid support. Also provided are mutant vectors which have been modified to alter their targeting specificity, including mutant AAV9 in which the galactose binding domain is mutated and AAV in which an AAV9 galactose binding domain is engineered.