VECTOR GLYCOENGINEERING

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Adeno-associated viruses (AAVs) are among the most common vectors used for in vivo gene therapy for gene cargos below 5 kb due to their high transduction efficiency, a good safety profile, broad tropism, low immunogenicity, and general ease of production. Depending on the serotype AAVs bind to cell surface glycans via heparan sulfate, galactose or sialic acid residues, as their primary binding receptor As AAVs show only a low degree of surface glycosylation in contrast to most enveloped viruses which are heavily glycosylated, we were interested in exploring the effect of a pronounced AAV surface glycosylation to modulate vector tropism, improve vector uptake, or avoid immune recognition. To this end, we have prepared a collection of structurally varied synthetic glycans for attachment to the capsid and studied the influence of glycan structure, attachment site, and glycan density on vector internalization, gene transduction, and immune recognition both in vitro and in vivo. We found a strong dependency for the gene transduction capacity of the modified vectors, particularly on glycan capsid density and glycan structure, examples and trends will be given in the talk. As non-viral vector, data on exosome glycoengineering by metabolic and chemical glycoengineering to change exosome tropism in vivo will be presented.