Docket #: S21-280

Chemically modified AAVs

Stanford researchers have developed chemically modified AAV vectors through an unnatural amino acid substitution on the capsid surface for post-production vector engineering through biorthogonal copper-free click chemistry.

Adeno-associated viruses (AAVs) are commonly used for in vivo gene therapy. However a major challenge has remained limited targeting to a specific cell type or tissue. To combat this issue, Stanford researchers have developed chemically modified AAV vectors which display an unnatural amino acid on the capsid surface. As a proof of concept, Stanford researchers used an azido-lysine as the unnatural amino acid displayed on the capsid. The azido (N3) group allows for a simple click chemistry reaction with any molecule that contains a dibenzocyclooctyne (DBCO) chemical group. As an example, researchers have successfully conjugated a Folic Acid (FA) molecule on the AAV capsid and have demonstrated that these vectors can transduce cancer cells in which the folic acid receptor (hFOLR1) is expressed at high levels.

Stage of Development
in vitro proof of concept:
1) Demonstration of receptor mediated uptake in cultured cells: successfully conjugate a Folic Acid (FA) molecule on the AAV capsid and demonstrate that these vectors can transduce cancer cells in which the folic acid receptor (hFOLR1) is expressed at high levels.
2) Limited in vivo studies ongoing

Applications

- Gene therapy
- Cancer

Advantages

- Can target specific cell type
- *In vivo* and *ex vivo* applications
- Versatile: theoretically conjugable with any compound to target specific cell receptors
- Compatible with small molecule, antibody, nanobody, aptamer
- Discovering novel AAV vectors with new properties or tropism do not require re-shuffling of rep/cap DNA or several cycles of enrichment

Publications

- Puzzo, F., Zhang, C., et al. (2023). Aptamer-programmable adeno-associated viral vectors as a novel platform for cell-specific gene transfer. Molecular Therapy-Nucleic Acids, 31, 383-397.
- Related Web Links

Patents

- Published Application: WO2024129990

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