

**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 (N<sub>3</sub>) 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](#)

## Innovators

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