Docket #: S22-152

AAV-LK03 Variant With Enhanced Transduction Properties in Humans and Rodents

Stanford inventors have engineered an adeno-associated virus (AAV) variant on the existing LK03 platform that enables this highly efficient primate-specific serotype for use in rodent preclinical studies. While the previously developed AAV-LK03 is currently in use for human gene therapy clinical trials, this primate-specific serotype is limited in that it requires a surrogate serotype for preclinical rodent studies, adding time and cost to the drug development pipeline. There is little concordance comparing transduction between species when using recombinant AAV vectors, making it difficult to select vectors in the preclinical phase that will behave optimally in human clinical trials. To overcome this limitation, inventors in the Kay lab have engineered an improved AAV-LK03 by altering the capsid codon sequence to both maintain its transduction capacity in primates while also enabling use in rodents. In addition to the expanded capacity of this AAV variant, it also exhibits an increased efficiency in primate hepatocytes over the existing modality and functions in rodents both *in vitro* and *in vivo*. The improved AAV-LK03 modality will not only enable researchers to better understand AAV virology but will also serve as means to better predict more robust AAV vectors for human gene therapy, saving time and money.

Stage of Development
Research - *in vivo*

Applications

- Human gene therapy
- Preclinical gene therapy studies in rodents
- Xenograft liver models
- Research in gene therapy and genome engineering

Advantages

- High efficiency: improvement over previous generation of AAV-LK03 (>100x better in mouse liver; 5-10x better in human hepatoma cells)
- Hepatocyte specific
- Same AAV modality can be used in preclinical and clinical studies
- Cost and time effective
- Low level of neutralization by the human immune system

Publications

- Gonzalez-Sandoval, A., Pekrun, K., Tsuji, S., Zhang, F., Hung, K. L., Chang, H. Y., & Kay, M. A. (2023). The AAV capsid can influence the epigenetic marking of rAAV delivered episomal genomes in a species dependent manner. *Nature Communications, 14*(1), 2448. https://doi.org/10.1038/s41467-023-38106-3
- Gonzalez-Sandoval, A., Tsuji, S., Zhang, F., Hung, K. L., Chang, H. Y., Pekrun, K., & Kay, M. A. (2022). Capsid-mediated chromatin state of the AAV vector genome controls host species range. *bioRxiv*, 2022-10. https://doi.org/10.1101/2022.10.06.511169

Patents

- Published Application: WO2023205751
- Published Application: 20250270261

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