

Tracking adeno-associated virus capsid evolution

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Researchers have used high-throughput screening of adeno-associated viral (AAV) vector capsid libraries to maximize the likelihood of obtaining AAV variants with desired properties. As a result of these experiments, they gained some unexpected insights, reported in an article published in *Human Gene Therapy*.

Mark Kay and colleagues from Stanford University (Stanford, CA) coauthored the [article](#) entitled "Tracking Adeno-Associated Virus Capsid Evolution by High-Throughput Sequencing." The researchers used [high-throughput screening](#) of barcoded AAV capsid libraries to track directed AAV [capsid](#) evolution. The ultimate goal is to be able to more quickly identify improved recombinant AAV vectors for use in clinical gene therapy trials.

Among the most important findings was the following: it is not essential to use multiple rounds of selection, and this may in fact be counterproductive. Functional and efficient AAV variants were obtained after only one round of selection. Additionally, [infection](#) with a high multiplicity of infection (MOI) is preferable to infection with a low MOI, as the use of low MOIs results in more variation between screens and is not optimal at selecting the most desired capsids. Furthermore, competition can take place between AAVs with specific capsids in cells that have been infected with different AAVs. Other key findings are outlined in the article.

"This cutting-edge work by Dr. Kay and his Stanford colleagues is helping to make directed evolution of AAV capsids less of a 'black box'," says Editor-in-Chief Terence R. Flotte, MD, Celia and Isaac Haidak Professor of Medical Education and Dean, Provost, and

Executive Deputy Chancellor, University of Massachusetts Medical School, Worcester, MA. "His insights are likely to result in the discovery of important novel capsids that might otherwise be overlooked."

More information: Gustavo de Alencastro et al, Tracking Adeno-Associated Virus Capsid Evolution by High-Throughput Sequencing, *Human Gene Therapy* (2020). [DOI: 10.1089/hum.2019.339](https://doi.org/10.1089/hum.2019.339)

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