Biodistribution of AAV gene transfer vectors in nonhuman primate

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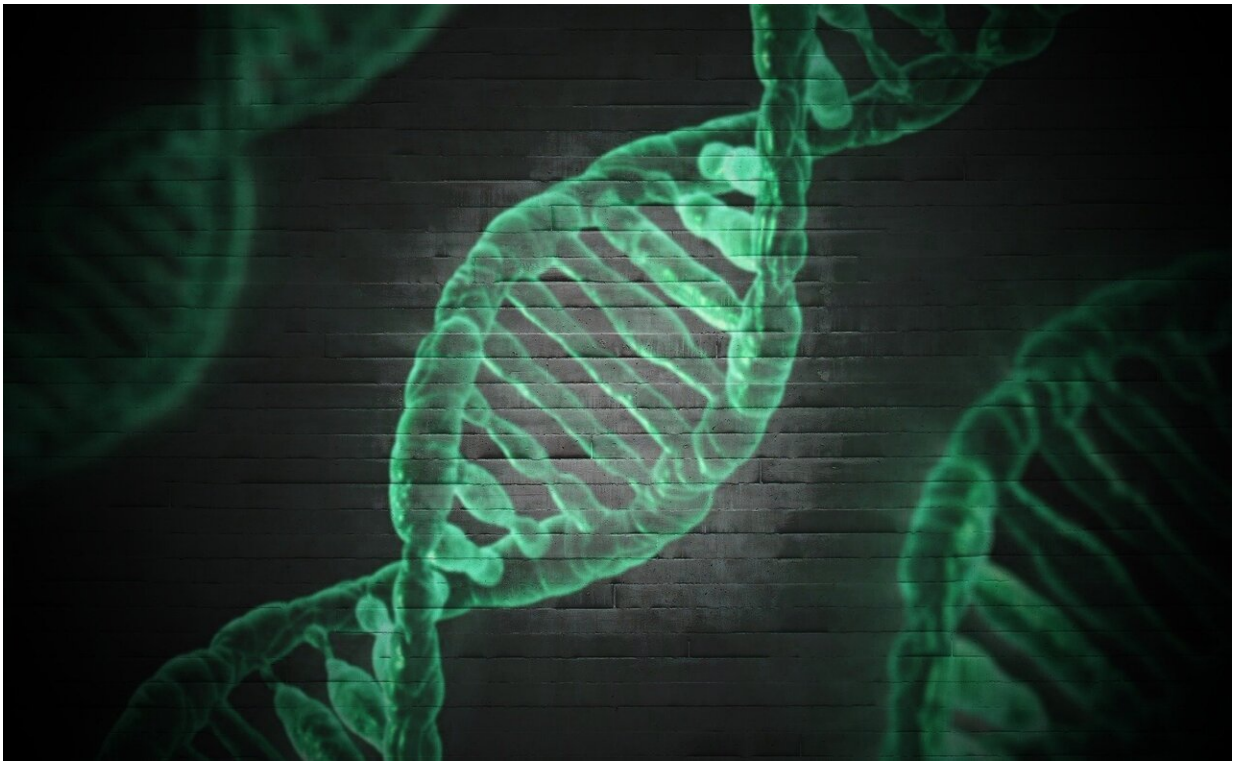

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The biodistribution of adeno-associated virus (AAV) gene transfer vectors can be measured in nonhuman primates using a new method. The method quantifies whole-body and organ-specific AAV capsids from 1 to 72 hours after administration. Study design and results are presented

in the peer-reviewed journal *Human Gene Therapy*.

AAV capsids were labeled with I-124 and delivered using two routes of administration: intravenous and directly into the cerebrospinal fluid (CSF). Biodistribution was measured by quantitative positron emission tomography (PET) at 1, 24, 48, and 72 hours after AAV administration. Two AAV vectors—AAVrsh.10 and AAV9—were compared.

"Following intravenous administration, both vectors behaved in a similar fashion, distributed primarily to the liver and to a lesser extent heart. Neither were detected at significant levels in the brain. Both vectors administered intravenously also distribute to the vertebrae," state Ronald Crystal, Weill Cornell Medical College, and coauthors. About 50% dispersed throughout the body, in part in skeletal muscle.

Following administration into the CSF, the labeled capsid had a half-life of approximately 10 hours, suggesting the possibility of slow diffusion into the brain.

In animals with pre-existing immunity, compared to naïve animals, there was a 10-fold increase in biodistribution to the spleen.

"PET imaging is a powerful tool to track biodistribution, which is a critical property affecting the safety and efficacy of gene therapy," according to Editor-in-Chief of *Human Gene Therapy* Terence R. Flotte, MD, Celia and Isaac Haidak Professor of Medical Education and Dean, Provost, and Executive Deputy Chancellor, University of Massachusetts Medical School.

More information: Douglas J. Ballon et al, Quantitative Whole-Body Imaging of I-124-Labeled Adeno-Associated Viral Vector Biodistribution in Nonhuman Primates, *Human Gene Therapy* (2020). DOI: 10.1089/hum.2020.116