

PaVe-GT: Paving the Way for Rare Disease Gene Therapies

A new program at the National Institutes of Health (NIH) will test whether the efficiency of gene therapy clinical trials can be increased by using the same gene delivery system and manufacturing methods. The program, Platform Vector Gene Therapy (PaVe-GT), holds promise to streamline clinical trials by examining the use of an increasingly common platform, adeno-associated virus (AAV) gene therapy, in treating four different rare genetic diseases. PaVe-GT is led by the NIH's National Center for Advancing Translational Sciences (NCATS), in collaboration with the National Human Genome Research Institute and the National Institute of Neurological Disorders and Stroke.

Only about 5 percent of rare diseases have a treatment approved by the U.S. Food and Drug Administration (FDA). While many rare diseases can potentially be treated by gene therapy, thousands are so rare that many companies are reluctant or unable to invest the years of research and millions of dollars necessary for development and testing to bring a gene therapy to market.

PaVe-GT researchers are looking for ways to reduce redundancies and implement standardization in the gene therapy development process. They will publicly test if the clinical trial startup process for AAV gene therapies for distinct diseases can be streamlined by using the same manufacturing methods to make the four gene therapies, and using the same viral delivery system to carry a gene to the right place in the body. The PaVe-GT approach may be significantly more efficient than using different manufacturing and testing processes for each gene therapy. Key questions in preclinical testing like biodistribution — how an investigational therapy is distributed in the body — might only need to be answered once for a given method of manufacturing a gene therapy for a particular AAV delivery system. This has the potential to save time and resources in developing and testing a gene therapy. PaVe-GT will also test if gene therapy clinical trials could be streamlined through use of master protocols. PaVe-GT will conduct the four clinical trials under two master protocols.

“The focus of the PaVe-GT program is not on the specific diseases, but rather on improving the efficiency of the process,” said NCATS program officer P.J. Brooks, Ph.D., who is one of the leaders of the program.

PaVe-GT will be carried out using NIH investigators and facilities, and project data will be shared with the public. “PaVe-GT will test important questions in the translation of gene therapies from lab to clinic,” said Donald Lo, Ph.D., director of the NCATS Therapeutic Development Branch. “The pilot project's results could speed and streamline subsequent efforts to develop AAV gene therapies, and to help make gene therapy more accessible to rare disease patients and communities.”

The four diseases under study include two inherited muscle weakness diseases and two inherited metabolic diseases. The muscle weakness diseases are Dok7 deficiency and ColQ deficiency. The metabolic diseases are propionic acidemia (caused by PCCA deficiency) and isolated methylmalonic acidemia (MMAB deficiency/cobalamin type B methylmalonic acidemia). These are serious diseases with well-characterized natural histories that are amenable to AAV gene therapy and are currently under study by investigators at the NIH Clinical Center. None of the diseases have effective treatments or therapies available. Ultimately, the focus of PaVe-GT is not on the rare diseases included in this pilot project: PaVe-GT will test an important question in translational science and make the results publicly available to benefit subsequent efforts to develop AAV gene therapies.

For more information on PaVe-GT, visit <https://pave-gt.ncats.nih.gov/>.