VectorBuilder Japan Inc

The project of clinical research on rare pediatric Menkes Disease in gene therapy

Purpose of the Project

Custom genetic medicine requires long-term and expensive processes in development. The long-term development failed to rescue the patients in time and expensive drug prices make patients inaccessible to the effective medicine. In general, it is recognized that about 10 years of research and development, and one dose of genetic medicine is worth hundreds of millions of yen. Our company has high technology and experience in the research, development, and quality control of genetically modified custom AAV production. Using our technologies, rapidly development and manufacturing generic drugs is possible. Therefore, the goal of this project was to demonstrate inexpensive and accelerated transition from basic research to preclinical research in the development of gene drugs. We took the Menkes disease, a rare childhood genetic disease, as a model for this study.

Details of demonstration

We have excellent development technology and experience in gene delivery vectors (“vector” deliver gene medicine) and have manufactured adeno-associated virus (AAV) vectors. In Japan, epidemiological studies, and basic research of Menkes disease have been accumulated. Therefore, three bodies collaborated on this project: (1) VectorBuilder Japan Inc. was in charge of project management and animal testing for the entire project, on-site visits to find hospitals and physicians for IIT candidate search, and released projects reports at conferences. (2) VectorBuilder China and Lantu Biopharma, designed and manufactured three kinds of AAVs which carries APT7a gene, and conducted animal experiments using the first line of the Menkes disease model mouse, and (3) the Laboratory of Drug Delivery, Faculty of Pharmaceutical Sciences, Teikyo University, conducted animal maintenance and expansion using the second line of the Menkes disease model mouse.

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Project outcome

The gene of Menkes disease is caused by mutations in ATP7A gene. The gene is very big and exceeds packaging limit into AAV. Therefore, we optimized the gene sequence and regulatory sequences to make the most effective genetic medicine in AAV. In addition, we used tissues and organs expression data of the ATP7A gene products. Eventually we produced three kinds of candidate genetic medicines in AAV. For the drug safety and efficacy study, two animal strains which carry genetic mutations similar to human Menkes disease patients were used. After the AAV administration of AAV, one of the three kinds of AAV was safe and highly effective to rescue the mutant. Only one dose of AAV immediately after birth as well as 2~3 doses of Cu supplement up to 12 days of after the birth dramatically prolonged survival and further increased body weight. The results highlight the potential of AAV genetic medicine in a rare inherited disease. These results were presented by Bruce Lahn, the founder and principal scientist of our company, at the 14th International Cooperation Genetic Disease Gene Therapy Forum.

Challenges and Solutions

We searched for existing Menkes disease patients and cooperate physicians and hospitals who collaborate with the development of genetic medicine for personalized therapy. However, at this time we did not find any Japanese patients who could be candidates for dramatic improvement in symptoms. We keep searching for physicians, hospitals, as well as AMED grant, to perform investigator-initiated clinical trials. In addition, if genetic abnormalities can be detected at the neonatal stage, early treatment with genetic medicine is possible. Therefore, we keep appealing to include the APT7A gene in neonatal genetic screening panel.

Future plans

Regarding gene therapy for Menkes disease, we will consider conducting GLP trials, Orphan drug designation by FDA, and IIT in Japan. In addition to this we keep working to add APT7A gene is in the neonatal diagnosis to enable early diagnosis of Menkes disease. Our Menkes disease program is a good model to accelerate research and development to clinical transition of gene therapy. we hope this study accelerates development of other genetic medicines with our hands, eventually increase drugs developed in Japan export overseas to help healthier world.