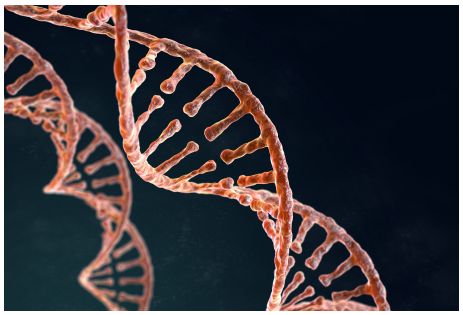
Gene therapy for long-term treatment of Pompe disease

Unmet Need

Pompe disease is a rare heritable disorder impacting heart and skeletal muscle function with an estimated incidence rate of 1 in 40,000 births in the US. Of these affected births, a third take the form of infantile-onset disease, occurring within the first few months of life and more severe than late-onset disease. Treatment for Pompe disease currently uses enzyme replacement therapy (ERT) to provide a recombinant version of the acid alpha-glucosidase (GAA) enzyme to the patient, restoring the ability to covert glycogen in the body to simple sugar molecules. While ERT prolongs survival in Infantile-onset disease, residual motor weakness remains. Alternative treatment methods using viral vector delivered gene therapy are being developed for adults. However, these approaches lose efficacy in patients with infantile-onset disease due to a growing liver and the formation antibodies to the viral vectors which prevent re-administration of therapy. There is a need for effective and long-term genetic therapies for early life treatment of Pompe disease to prevent the progressive loss of muscle function in patients with infantile-onset Pompe disease.

Technology

Duke inventors have developed a novel gene therapy for Pompe disease. This is intended to be used as the first long-term and effective treatment for infantile-onset Pompe disease. Specifically, the technology uses CRISPR-Cas9 mediated genome editing, delivered via a single adeno-associated virus (AAV) vector, to insert a GAA liver depot. This genetic transduction of the liver enables long-term expression of functional GAA. The selection of the genetic insertion site for the liver depot further allows treatment of any disease-associated



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Meet the Inventors

Koeberl, Dwight
Arnson, Benjamin "Benjamin"
Cullen, Bryan

Contact For More Info

Thomas, Dennis
919-681-7580
dennis.thomas@duke.edu

Department

Pediatrics (Dept. & CRU)

Publication(s)

External Link(s)

- From the lab of Dr. Dwight D. Koeberl
- Duke To Begin Clinical Trials For Pompe Disease Gene Therapy This Fall (Duke Health, 2018)

causative mutation. The researchers have demonstrated this technology using *in-vitro* experiments in human cells as well as *in-vivo* experiments in GAA-knockout adult and infant mouse models.

Other Applications

This technology could also be used for adult-onset Pompe disease. The method for this gene therapy could also be adapted to other heritable metabolic disorders characterized by deficiency in enzymatic activity such as Gaucher disease, Hunter syndrome, Metachromatic leukodystrophy, and Tay-Sachs disease.

Advantages

- Long-term and effective treatment for infantile-onset Pompe disease using liver-depot gene therapy
- Enables treatment of any Pompe disease causative mutation, presenting a universal therapy
- Rare disease status can classify gene therapy as orphan drug, fast-tracking FDA approval