

## **Title**

The FACTs Project: Fabry disease Clinical research and Therapeutics

## **Project Description**

Fabry disease is an inherited disorder due to a deficiency of an enzyme that breaks down fats in the body. It is a rare disorder - with just over 300 patients identified so far in Canada - that affects many organ systems and results in a reduced life expectancy. As the disease progresses, patients develop heart problems, kidney problems, and strokes in mid-life. Treatment for Fabry disease is mostly directed at lessening symptoms - although enzyme replacement therapy (ERT) has now been developed. Unfortunately, ERT only really shows a benefit in slowing progression of the disease and does not treat the core genetic defect itself. It is also very costly, dependent on availability, and often requires patients to travel biweekly to drug infusion sites. Patients also have to receive this therapy for the rest of their lives with many developing immune reactions against the drug itself.

For many years we have been working to develop gene therapy for Fabry disease. Gene therapy seeks to supplement expression of absent or defective genes with the actual corrective factor. We use viruses to transfer the correct DNA sequence into cells, which then generates the corrective factor in the host. Fortunately, in Fabry disease once that corrective protein is generated it circulates in the body and can even then impact cells at a distance. We have tested this therapeutic strategy in a number of pre-clinical models including a new strain of Fabry mice that we generated that can harbor human hematopoietic (blood) cells.

Based on our pre-clinical success we are progressing towards a clinical trial in gene therapy for Fabry disease. We are planning to direct the therapy to the Fabry patient's own blood stem cells, which can then circulate and distribute the corrective factor throughout the body. To do this we will take blood stem cells from Fabry patients using a standard technique that is routinely used for patient care. The virus containing the correct DNA sequence will then be used to infect the patient cells which will then be returned to the individual.

This grant provides resources to assemble the Canada-wide Team of researchers and clinicians needed to bring this gene therapy approach from the laboratory bench into the clinic. Success here will not only impact Fabry disease but serve as a platform for this type of therapy to be applied to other rare and not-so-rare inherited disorders.

## **Principal Investigator**

Jeffrey Medin, University Health Network