

UF makes gene therapy breakthrough in treating severe genetic disorder

GAINESVILLE, Fla. — A dog born with a deadly disease that prevents the body from using stored sugar has survived 20 months and is still healthy after receiving gene therapy at the [University of Florida](#) — putting scientists a step closer to finding a cure for the disorder in children.

Called glycogen storage disease type 1A, the genetic disease stops the body from being able to correctly store and use sugar between meals. In order to survive, children and adults with this disease must receive precise doses of cornstarch every few hours. The disease is even more dire in dogs, which must be fed sugar every 30 minutes to survive.

“Without treatment, these dogs all die,” said Dr. David Weinstein, director of the [UF Glycogen Storage Disease Program](#) and co-investigator on the study. “People usually survive because they are fed so much as infants. But by 4 to 6 months of age, they will have developmental delays and a big liver. If it is diagnosed at that point, the kids can do fine. If it is not diagnosed, then the kids get exposed to recurrent low sugars, and they will end up with brain damage, seizures or they will die.”



Cathryn Mah, Ph.D.

UF researcher [Cathryn Mah](#), a member of the [Powell Gene Therapy Center](#) and [UF Genetics Institute](#), will present the findings at an American Society of Gene Therapy meeting this weekend in San Diego.

About one in 100,000 children have this severe form of glycogen storage disease. Children receive doses of cornstarch at scheduled intervals throughout the day because it metabolizes more slowly than other carbohydrates. Until this therapy was discovered about 30 years ago, most children born with this disease did not survive past infancy.

Glycogen storage disease type 1A stems from a faulty enzyme that doesn't convert stored sugar, or glycogen, to glucose, the type of sugar the body uses for energy. This prevents the body from getting the energy it needs and causes glycogen to build up in the liver.

The goal of gene therapy is to restore the faulty enzyme so the body uses sugar properly, said Mah, a UF assistant professor of [pediatric cellular and molecular therapy](#) and a co-investigator on the study.

The dog, which comes from a line of dogs genetically prone to the disease, received its first dose of gene therapy the day after it was born, Mah said. The dog improved at first, often going as long as two to three hours without needing additional glucose to supplement its diet. But several weeks later the progress stopped.

When the dog was 5 months old, the researchers administered another dose of gene therapy, this time using a different type of AAV. Six weeks after the therapy, the dog was completely weaned off glucose supplements.

“We have never had to use any glucose supplementation since we weaned her off,” Mah said. “She just gets fed normal dog food. That is a huge improvement in quality of life.”

A few years ago, when Weinstein, Mah and other UF and [National Institutes of Health](#) collaborators began discussing the project, the longest a dog with the disease had lived was 28 days. The dog treated at UF is now 20 months old.

“The success is beyond what I would have imagined at this stage,” Weinstein said. “To have a dog off treatment for 14 months that is clinically doing great with outstanding lab results is beyond what I even dreamt about.”

Researchers hope to eventually establish a clinical trial in humans, but for now would like to test gene therapy in dogs again within the next year, Weinstein said.

"This is very exciting work and holds great promise for treatment of the disease in humans," said Joseph Wolfsdorf, a pediatric endocrinologist at [Children's Hospital Boston](#) and professor of pediatrics at [Harvard Medical School](#) who studies glycogen storage disease in children.

Finding better treatments for the glycogen storage disease is crucial because the disorder is still associated with multiple complications, and care remains a challenge. As a result of the lack of expertise in this condition, children and adults also must travel to special centers for care. With more than 300 patients from 18 countries, UF's Glycogen Storage Disease Program is the largest in the world.

Aside from Weinstein and Mah, other collaborators include Catherine Correia and Laurie Fiske, research coordinators for the UF Glycogen Storage Disease Program; John Verstegen, of the [UF College of Veterinary Medicine](#); Thomas Conlon, associate director of the Powell Gene Therapy Toxicology Core; Travis Cossette; Sean Germain; Andrew Specht, of the UF College of Veterinary Medicine; Maggie Struck and Harvey Ramirez, of [UF Animal Care Services](#); Karine Onclin-Verstegen, of the UF College of Veterinary Medicine; Stacy Porvasnik, of the [UF College of Medicine](#); Darin Falk, of the UF College of Medicine; Janice Y. Chou, of the National Institutes of Health; and Dr. Barry J. Byrne, director of the Powell Gene Therapy Center.

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Contact: April Frawley Birdwell, afrawley@ufl.edu, 352-273-5817

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