Gene Therapy Shows Promise for Managing Canine Diabetes

By Susan Chaney
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The signs of type 1 diabetes in five Beagles were controlled after they were injected with two types of genes by researchers at Spain's Universitat Autònoma de Barcelona.

The therapy is minimally invasive, according to lead researcher Fàtima Bosch, Ph.D., a professor at the university. A single session of injections goes into the dog's rear legs, administered with the same needles used for cosmetic treatments like Botox, according to a university press release. "These injections introduce gene therapy vectors, with a dual objective: to express the insulin gene, on the one hand, and that of glucokinase, on the other. When both genes act simultaneously, they function as a 'glucose sensor,'" reducing diabetic hyperglycemia – the excess of blood sugar associated with diabetes.

The hormone insulin, which helps the body use or store glucose and is normally created in the pancreas, is not created in people or dogs with type 1 diabetes. The enzyme glucokinase regulates how much glucose is taken from the blood by the body.

Diabetic Beagles injected with two genes – Insulin and Glucokinase – showed no further signs of the disease, even after four years. Photo © Can Stock Photo.

"We previously demonstrated that it is possible to generate a 'glucose sensor' in skeletal muscle through co-expression of glucokinase (Gck) and insulin (Ins), increasing glucose uptake and correcting hyperglycemia in diabetic mice," reads the abstract of the paper describing the study. "Here, we demonstrate long-term efficacy of this approach in a large animal model of diabetes."

The release states that the study is the "first to report optimal long-term control of diabetes in large animals. This had never before been achieved with any other innovative therapies for diabetes. The study is also the first to report that a single administration of genes to diabetic dogs is able to maintain normoglycemia over the long term."

Injection of the two genes "resulted in normalization of fasting glycemia, accelerated disposal of glucose after oral challenge, and no episodes of hypoglycemia during exercise for [more than] four years after gene transfer," the study states. "This was associated with recovery of body weight, reduced glycosylated plasma proteins levels and long-term survival without secondary complications."

The abstract goes on to state that the insulin or glucokinase gene alone "failed to achieve complete correction of diabetes, indicating that the synergistic action of Ins and Gck are needed for full therapeutic effect."

The treated dogs showed good glucose control, “both when fasting and when fed, improving on that of dogs given daily insulin injections, and with no episodes of hypoglycemia, even after exercise,” the release states.

“Moving from mice to large animals is a big step,” Bosch, director of the Center of Animal Biotechnology and Gene Therapy at the university, told the American Diabetes Association, which publishes the journal, *Diabetes*. “If something works well in large animals, we have reason to believe, based on the previous experience in the field of gene transfer, that it is likely that we will see similar outcomes in humans. For example, gene therapy that worked well in large animals to treat hemophilia is now seeing positive results in clinical trials with humans. We hope that in a few years, we’ll be able to test this therapy for type 1 diabetes in humans as well.”

Many patients – both canine and human – with type 1 diabetes, or diabetes mellitus, require insulin to survive. Despite the use of insulin, patients often develop serious secondary complications like blindness or kidney damage and may require amputation of limbs, according to Bosch. “Moreover, in order to achieve good blood glucose control, insulin has to be injected two or three times a day, which brings a risk of hypoglycemia episodes,” the lowering of blood sugar.

“The excellent results obtained for the first time with large animals lay the foundations for the clinical translation of this gene therapy approach to veterinary medicine and eventually to diabetic patients,” the university concludes.

Bosch also told the American Diabetes Association that her team will next test the procedure on “different breeds of dogs that have type 1 diabetes and live with families,” rather than in a lab. It will allow them to “better adjust the insulin doses in different size and breeds of dogs living in ‘real life’ situations. Once they are able to determine how to adjust the therapy in this context, the investigators will be ready to test the treatment on humans.”

The study involved the UAB Department of Biochemistry and Molecular Biology, the UAB Department of Medicine and Animal Surgery, the UAB Faculty of Veterinary Science, the UAB Department of Animal Health and Anatomy, the Spanish Biomedical Research Centre in Diabetes and Associated Metabolic Disorders, the Children’s Hospital of Philadelphia and the Howard Hughes Medical Institute of Philadelphia. Its results were published in the February 2013 issue of *Diabetes* and discussed in a May 2013 article in the same journal.

Bosch and some of her colleagues designed a video that explains how gene therapy treats and cures disease.

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