Spanish researchers cure type 1 diabetes in dogs

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Fàtima Bosch, Universitat Autònoma de Barcelona, the fifth from the left, and the team of researchers at UAB have developed the gene therapy for the cure of diabetes, with two of the dogs that have followed the new therapy. Credit: Pierre Caufapé

Researchers from the Universitat Autònoma de Barcelona (UAB), led by Fàtima Bosch, have shown for the first time that it is possible to cure diabetes in large animals with a single session of gene therapy. As published this week in Diabetes, the principal journal for research on the disease, after a single gene therapy session, the dogs recover their health and no longer show symptoms of the disease. In some cases, monitoring

continued for over four years, with no recurrence of symptoms.

The therapy is minimally invasive. It consists of a single session of various injections in the animal's rear legs using simple needles that are commonly used in cosmetic treatments. 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. Glucokinase is an enzyme that regulates the uptake of glucose from the blood. When both genes act simultaneously they function as a "glucose sensor", which automatically regulates the uptake of glucose from the blood, thus reducing diabetic hyperglycemia (the excess of blood sugar associated with the disease).

As Fàtima Bosch, the head researcher, points out, "this study is the first to demonstrate a long-term cure for diabetes in a large animal model using gene therapy."

This same research group had already tested this type of therapy on mice, but the excellent results obtained for the first time with large animals lays the foundations for the clinical translation of this gene therapy approach to veterinary medicine and eventually to diabetic patients.

The study was led by the head of the UAB's Centre for Animal Biotechnology and Gene Therapy (CBATEG) Fàtima Bosch, and involved the Department of Biochemistry and Molecular Biology of the UAB, the Department of Medicine and Animal Surgery of the UAB, the Faculty of Veterinary Science of the UAB, the Department of Animal Health and Anatomy of the UAB, the Spanish Biomedical Research Centre in Diabetes and Associated Metabolic Disorders (CIBERDEM), the Children's Hospital of Philadelphia (USA) and the Howard Hughes Medical Institute of Philadelphia (USA).

A safe and efficacious gene therapy

The study provides ample data showing the safety of gene therapy mediated by adeno-associated vectors (AAV) in diabetic dogs. The therapy has proved to be safe and efficacious: it is based on the transfer of two genes to the muscle of adult animals using a new generation of very safe vectors known as adeno-associated vectors. These vectors, derived from non-pathogenic viruses, are widely used in gene therapy and have been successful in treating several diseases.

In fact, the first gene therapy medicine ever approved by the European Medicines Agency, named Glybera®, makes use of adeno-associated vectors to treat a metabolic disease caused by a deficiency of lipoprotein lipase and the resulting accumulation of triglycerides in the blood.

Long-term control of the disease

Dogs treated with a single administration of gene therapy showed good glucose control at all times, both when fasting and when fed, improving on that of dogs given daily insulin injections, and with no episodes of hypoglycemia, even after exercise. Furthermore, the dogs treated with adeno-associated vectors improved their body weight and had not developed secondary complications four years after the treatment.

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 (more than 4 years). As well as achieving normoglycemia, the dogs had normal levels of glycosylated proteins and developed no secondary complications of diabetes after more than 4 years with the disease.

Application in diabetic patients

There have been multiple clinical trials in which AAV vectors have been introduced into skeletal muscle, so the strategy reported in this study is feasible for clinical translation. Future safety and efficacy studies will provide the bases for initiating a clinical veterinary trial of diabetes treatment for companion animals, which will supply key information for eventual trials with humans. In conclusion, this study paves the way for the clinical translation of this approach to gene therapy to veterinary medicine, and eventually to diabetic patients.

Diabetes mellitus

Diabetes mellitus is the most common metabolic disease, and a large number of patients need insulin treatment to survive. In spite of the use of insulin injections to control the disease, these patients often develop serious secondary complications like blindness, kidney damage or amputation of limbs. 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 (lowering of blood sugar): an additional problem that comes on top of the other hardships of the treatment.

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