Children's Mercy KANSAS CITY

CHILDREN'S MERCY RESEARCHER COLLABORATES ON DEVELOPMENT OF NOVEL INSULIN DELIVERY SYSTEM

NIH Funding Helps Advance Innovation to Next Stage

CHALLENGES OF TYPE 1 DIABETES AND INSULIN DELIVERY

According to JDRF, approximately 1.6 million Americans are living with type 1 diabetes, including about 200,000 youth (less than 20 years old) and more than 1 million adults (20 years old and older).

Type 1 diabetes is a 24/7 disease that requires tight management via continuous glucose monitoring in order to reduce the risk of serious complications, including neuropathy, retinopathy and renal damage.

Although insulin injections and insulin pumps are both effective treatments for type 1 diabetes, they are also invasive and not well tolerated by all patients, especially children.

SEARCHING FOR A BETTER WAY TO DELIVER INSULIN

Karen Kover, PhD, researcher with the Division of Endocrinology, Children's Mercy Kansas City and Associate Professor of Pediatrics, University of Missouri-Kansas City School of Medicine, has been collaborating with Simon Friedman, PhD, Professor, University of Missouri-Kansas City School of Pharmacy, trying to develop a new way to deliver insulin via a photoactivated depot, or PAD.

Dr. Friedman originally conceived of the idea for this device several years ago, synthesizing different materials and demonstrating efficacy in vitro. He then enlisted Dr. Kover's assistance for testing the possible treatment in a diabetic rat model. Initial funding was made available internally through Children's Mercy and UMKC.

This innovative device has shown great promise in rat models and is the only one of its kind. With the PAD approach, an insulin-containing material is injected into the skin, just like regular insulin, but takes the place of multiple insulin injections each day. The PAD remains under the skin, inactive until a light source from outside the body passes through the skin and stimulates the release of insulin from the depot.

The first-generation PAD designs linked insulin to a polymer via a light-cleaved linker. When a pulse of light from an LED light source was shined directly on top of the injection site, insulin was released. The amount released was proportional to the amount of light applied.

Research in the diabetic rat model showed that these materials worked to release insulin in the bloodstream and reduced blood glucose. But, it also pointed to several opportunities to improve the device.[1]

A 2019 paper published in *Molecular Pharmaceutics* addressed improvements made to a second-generation PAD, demonstrating effectiveness in the rat model.[2]

Dr. Kover's research focuses on developing a new way to deliver insulin via a photoactivated depot, or PAD, an innovative device that has shown great promise in rat models and is the only one of its kind.

ADVANCEMENTS IN PHOTOACTIVATED INSULIN DELIVERY

Now Dr. Friedman, Dr. Kover and their colleagues have been awarded a $1.5 million R01 grant from the NIH to continue work on this important advancement.

The new grant will help make the technology more reliable to use and easier to manage. For example, the researchers are now creating multiple new PAD materials that eliminate the polymer required in the first-generation materials. These higher-density materials are 90% insulin.

The researchers also are incorporating new light-cleaved linkers that will release insulin using higher wavelengths of light. This will increase the amount of light that reaches the depot and should improve the ease of insulin release.

Dr. Kover will be closely monitoring these new materials for their ability to control blood glucose in the diabetic rats. She will be looking at issues such as light sources, wavelengths, how well the material is released, how stable it is, and how well it reduces the rats' blood sugar levels.

In addition, a similar device is being developed that would release glucagon to control low blood glucose levels and will be studied in a rat model of hypoglycemia.

REVOLUTIONIZING TREATMENT FOR TYPE 1 DIABETES

As this next stage of research begins, Dr. Kover said the stability of these materials is key to further development. "So far, we've only tested the PAD right after the rats have been injected, and we know it does work," Dr. Kover said. "What we don't know is how long the insulin will remain viable at the injection site. We need to demonstrate that when you shine the light over the depot for 5 seconds, for example, the same amount of insulin will be consistently released from dose to dose, day after day," she explained.

Once the researchers have optimized a PAD material and stability can be proven, the next step in the process is to test the PAD in a large animal model, most likely in pigs with type 1 diabetes.

Ultimately, the goal is to create a new and revolutionary method to administer insulin that effectively eliminates most of the injections normally required or the need for an insulin pump.

An insulin delivery system that is less invasive and more user-friendly has the potential to improve both the quality of life and the health of individuals with type 1 diabetes, especially children, who depend on insulin long term to live.

REFERENCES

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