Liquid glucagon formulation discovered for potential use in artificial pancreas systems

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Researchers at Oregon Health & Science University (OHSU) and Legacy Health have discovered a liquid glucagon formulation that may be useable in standard diabetes pumps. Such a formulation could broaden the use of glucagon to help prevent hypoglycemia in people with type 1 diabetes (T1D) who are treated with insulin. It could also open a path to future-generation artificial pancreas systems that dispense more than just insulin for optimizing glucose control.

"Our previous studies have shown that the injections of small amounts of glucagon prevent hypoglycemia, which is a frequent and serious complication of type 1 diabetes that can lead to seizures, loss of consciousness, and even death," said W. Kenneth Ward, M.D., associate professor of medicine (endocrinology, diabetes, and clinical nutrition) at OHSU School of Medicine and senior scientist at Legacy Health, the two Portland, OR-based organizations that collaborated on the study. The research was presented at the American Diabetes Association's (ADA) 72nd Scientific Sessions on Friday, June 8, and on Sunday, June 10, in Philadelphia.

Dr. Ward continues: "Current forms of glucagon cannot be kept for long periods of time in a portable pump, and therefore could not be used as part of an artificial pancreas system. While it is important to note that additional studies will be undertaken in animals and humans before FDA approval can be sought, we have found that the alkaline glucagon compound we discovered can be kept in liquid form for long periods of time, potentially opening pathways for use in bi-hormonal diabetes

pumps and toward better therapies for people with diabetes."

The research is a key step forward toward the routine delivery of glucagon for people with T1D, and toward the development of a multi-hormonal, fully-automated closed loop artificial pancreas system. Such future-generation artificial pancreas systems would automatically deliver both insulin and glucagon, or other drugs.

Glucagon is a naturally occurring hormone that responds to hypoglycemia (extreme low blood sugar) by raising blood sugars, but its regulation is impaired in people with T1D. It works to complement the function of insulin to provide the natural fine-tuning of blood glucose control. Previous studies have shown that the addition of glucagon to insulin treatment reduces the frequency of hypoglycemia in T1D, more closely mimicking the physiology of someone without diabetes.

Commercially available glucagon does not maintain its liquid form after the powder and solution are combined, making it suitable only for immediate use. Dr. Ward and his team found that raising the pH of the glucagon allowed the hormone to maintain liquid form, and concluded that this formulation could be suitable for use in a closed-loop bi-hormonal pump.

"We have seen very promising results in our studies of artificial pancreas systems that utilize both insulin and glucagon. But for people with diabetes to realize this potential benefit, we need glucagon that is stable and can be used in a pump," said Sanjoy Dutta, Ph.D., JDRF's senior director of treat therapies. "Dr. Ward's research is promising and steers us toward more tangible solutions along the path toward a multi-hormonal, fully-automated closed loop artificial pancreas."

The artificial pancreas combines a continuous glucose monitor (CGM) and an insulin pump via sophisticated computer software, to provide the

right amount of insulin at the right times for people with diabetes. In March, the U.S. Food and Drug Administration approved the first artificial pancreas outpatient trial in the United States. Researchers envision future generations of the device to automatically deliver more than one hormone, in addition to insulin, to more closely perform the functions of a non-diabetic human pancreas.

Provided by JDRF