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Smart Insulin

An experimental drug for diabetes dispenses insulin in response to glucose levels.

By Jennifer Chu

Maintaining tight control over blood-sugar levels is a daily challenge for people with diabetes: it requires constant monitoring and multiple insulin injections each day. Now the biotech company SmartCells, based in Beverly, MA, is developing a drug that may do most of the heavy lifting in controlling diabetes. The injectable drug, called SmartInsulin, senses high glucose levels and automatically dispenses insulin on demand. As glucose levels drop off, the drug stabilizes, trapping insulin until the next glucose spike. Such a drug may cut down the number of insulin injections required to once a day.

Todd Zion, founder and CEO of SmartCells, says that such a self-regulating drug may also reduce the risk of hypoglycemia, a potential hazard associated with current diabetic therapies. "You will find with any person taking insulin [that] the most dangerous risk is accidental overdose, or not being able to predict how blood sugar will swing after a meal," says Zion. "From a treatment standpoint, this [drug] would eliminate the risk of dangerously low blood sugar."

Normally, beta cells in the pancreas release the hormone insulin into the bloodstream in response to high glucose levels. The hormone curbs glucose levels by helping the body's cells absorb it as fuel. In diabetes, insulin production is impaired, leading to abnormally high levels of circulating glucose. That results in serious consequences, including blurred vision, changes in metabolism, and sudden weight loss.

Diabetes patients currently take insulin via pens and traditional syringes, which deliver a single dose of the drug, or via insulin pumps, which provide continuous low doses throughout the day and may deliver insulin during periods when it's not needed. SmartCells' alternative is to chemically modify insulin in such a way that the active hormone is released only in the presence of a certain concentration of glucose. Below that level, insulin remains bound and insoluble until the next blood-sugar spike.

Zion developed the technology while working as a doctoral candidate in MIT's Nanostructured Materials Lab, which is led by professor Jackie Ying. In his experiments, Zion modified insulin by chemically attaching it to a biodegradable polymer containing sticky sugar groups. He then mixed it in solution with a sugar-binding molecule, which, in the absence of any other sugars, immediately binds to the sugar groups attached to the insulin. As more binding molecules grab on to more modified insulin, a network forms that holds the insulin in place. When glucose is added to the system, it bumps the insulin-bound sticky sugar group out of the way, grabbing on to the sugar-binding molecule. The more glucose there is, the more insulin is shed from the network, dissolving away. "You can see these particles shrinking and the insulin coming off them, depending on how quickly they're being attacked by sugar from the body," says Zion.

The company has tested the drug on hundreds of rodents and recently moved to studies in pigs that don't produce enough insulin--models that may more closely resemble the diabetic environment in humans. In the experiments, the researchers injected the drug into diabetic animals and followed up with injections of sugar to simulate a meal. They tracked blood-sugar concentrations with continuous glucose monitors and also noted the amount of insulin released in response to increased glucose. So far, Zion's team has observed that the drug is able to sense and adapt to fluctuating glucose levels and deliver insulin as needed, keeping concentrations stable while avoiding insulin overdoses that may lead to hypoglycemia. The group plans to compare the technology with existing insulin-delivery devices in the future.

"The idea of having insulin that responds to glucose, and having an injection once every day, or every three or four days, would be a wonderful advance for diabetics," says Michael Sefton, a professor of chemical engineering and applied chemistry at the University of Toronto. "This could enable them to control blood sugar better and match delivery of insulin to their need for insulin." While the initial data seems promising, Sefton says, it's not yet clear whether the drug works fast enough to be effective in humans.

Zion aims to begin clinical trials within the next two years. Last week, SmartCells received $1 million to fund safety and efficacy studies in preclinical animal trials as part of a partnership with the Juvenile Diabetes Research Foundation.

Before starting clinical trials, the researchers will have to make sure that the drug is, in essence, foolproof--that is, that there aren't any molecular signals other than glucose that could unnecessarily release insulin into the bloodstream, says Frederick Schoen, a

professor of pathology and health sciences and technology at Harvard Medical School. "You have to avoid bursts of insulin, which can be dangerous," says Schoen. "It's an exciting concept, and should be pursued, but lots of questions should be answered along the way."

Upcoming Events

2008 Medical Innovation Summit
Cleveland, Ohio
Monday, November 10, 2008 - Wednesday, November 12, 2008
http://www.clevelandclinic.org/innovations/summit

A2C Access 2 Capital: Exploring Growth Strategies
MIT Campus, Cambridge, MA
Tuesday, November 11, 2008
http://www.cweonline.org/

MITX Awards
Boston, Massachusetts
Wednesday, November 19, 2008
http://www.mitxawards.org/

Academic Enterprise Awards Europe
Stockholm, Sweden
Tuesday, December 02, 2008
http://www.sciencebusiness.net/aces/

11th Annual MIT Venture Capital Conference
Cambridge, MA
Saturday, December 06, 2008
http://www.mitvcconference.com

WHIT 4.0
Washington, DC
Monday, December 08, 2008 - Wednesday, December 10, 2008
http://www.whitcongress.com

South By Southwest
Austin, Texas
Friday, March 13, 2009 - Tuesday, March 17, 2009
http://www.sxsw.com/interactive