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## **Wistar Scientists Develop Single-Dose DNA Method for Delivering Long-Acting Weight Loss and Diabetes Drugs**

**PHILADELPHIA — (JUNE 26, 2026) —** Scientists at The Wistar Institute have shown that a single injection of a small, circular piece of genetic instructions can produce weight loss and blood glucose control in murine models that lasts up to 10 times as long as incretin-mimicking drugs like Ozempic and Wegovy. If shown to be successful in clinical trials, this new method of delivery could eliminate the need for repeated dosing, which currently limits patient access and adherence to these therapies.

Incretin hormones like GLP-1 and GIP, which are naturally produced in the body, regulate blood sugar and appetite. Drugs that mimic them have proven to be extremely effective for treating type 2 diabetes and obesity. However, their native forms break down quickly in the body, so current therapies require weekly injections or daily pills—regimens that demand sustained patient compliance and contribute to the rebound in weight gain and blood glucose dysregulation when patients stop treatment.

“What we’re trying to do here is simple: We want to deliver a drug once and have it work for a really long time,” said [Ebony Gary, Ph.D.](#), a research assistant professor in the laboratory of [David B. Weiner](#) at The Wistar Institute’s Vaccine and Immunotherapy Center and first author of the study.

“The DNA platform has demonstrated it can do that. Instead of delivering a drug that will get cleared by the body, we’re giving cells the instructions to make that drug themselves, and they keep making it.”

Her team’s approach builds on Weiner Lab research already [validated](#) in human patients that showed the human body can function as a “factory” to produce long-lasting antibodies. The lab developed an intramuscular DNA electroporation platform, whereby patients receive a shot of plasmid DNA (the genetic instructions) followed by an electrical pulse to help get the instructions into the nucleus of the body’s cells where they can be read. Weiner and his colleagues used this method to deliver “instructions” for COVID-19-neutralizing antibodies to patients. In a Phase 1 clinical trial, two of the antibodies were expressed continuously in human subjects for more than 72 weeks.

To adapt this platform for metabolic disease, Gary and her colleagues engineered DNA instructions for long-acting incretin hormones GLP-1 and GIP, which they call pLincretins. Importantly, they included an antibody fragment in the instructions that would help prevent the protein from breaking down quickly in the body the way current incretin-mimicking drugs do. When tested in preclinical murine



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models of diabetes using the electroporation method, a single dose of pLincetins produced detectable levels of incretins for up to 70 days and drove sustained reductions in body weight and blood glucose. In a head-to-head comparison with semaglutide (the active ingredient in Ozempic), murine models treated with a single dose of the scientists' DNA construct maintained these metabolic improvements even after the observation period ended, while those treated with semaglutide began regaining weight as soon as dosing stopped.

The scientists then used AI-assisted structural modeling, and an approach called synthetic consensus design to create a new molecule called pSynCretin. The team designed it by identifying the structural elements common across GLP-1, GIP, and existing incretin drugs and then combining those elements into a single protein that could engage the GLP-1 and GIP receptors simultaneously (similar to how Mounjaro works). A single dose of pSynCretin also induced sustained weight loss in murine models.

Gary and others in the Weiner Lab are now pursuing studies on the immunological effects of incretin therapy, including its potential role in modifying cancer outcomes. Clinical data have shown that patients on incretin drugs experience improvements in chronic inflammatory conditions like arthritis and psoriasis. This opens up new questions about the relationship between metabolism and immune function that Gary believes the DNA platform can help to answer.

“What I keep coming back to is how much we still don't know about what these molecules are doing beyond weight loss and blood glucose,” Gary said. “There's lots of data from patients on incretin therapy in the clinic now and just being on these drugs that we think of as weight loss drugs or diabetes drugs has also affected people's chronic inflammatory diseases like arthritis and psoriasis. It's made me start thinking about the immunological implications of incretin therapy.”

Gary also sees potential for the DNA delivery platform to extend well beyond metabolic disease. The same delivery system that enables long-term incretin production in the body could potentially be applied to a wide range of therapeutic proteins needed to treat chronic conditions.

“The really amazing part of this research is that once we have this toolkit, we can think about making novel proteins that didn't exist before and engineering them from the ground up to do exactly what we need them to do,” Gary said. “The possibilities are really exciting.”

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