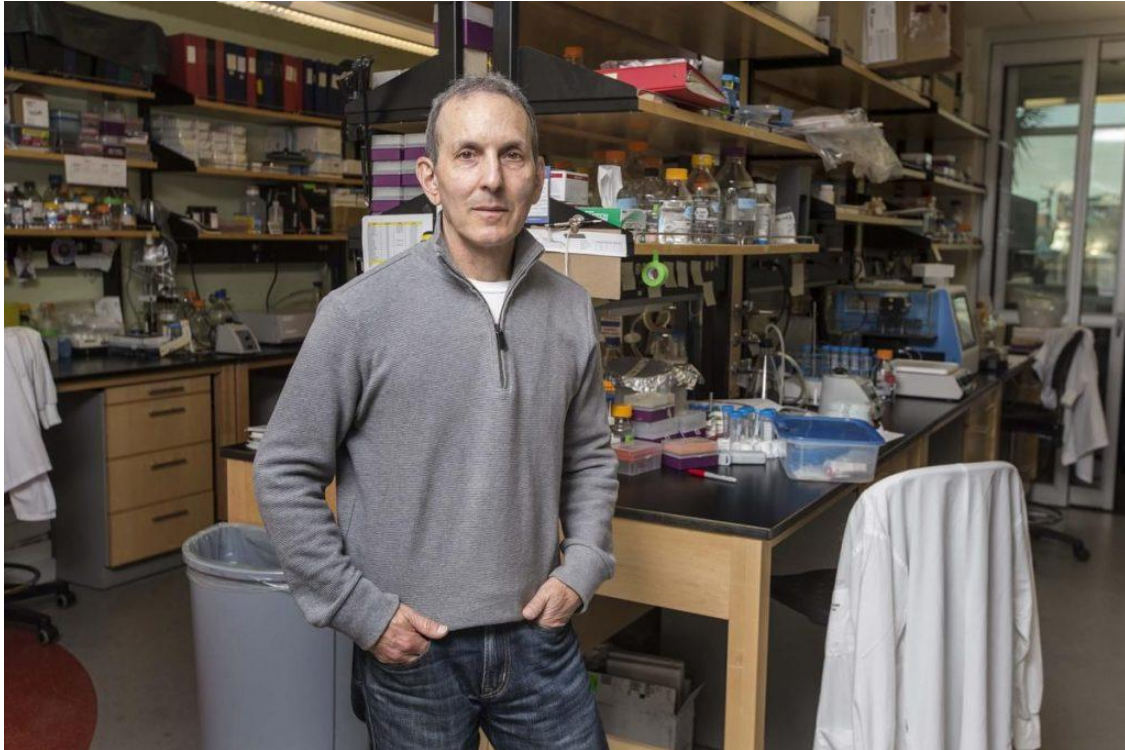


This Toronto doctor is a superstar in the world of diabetes research — and he says it all started as a fluke

By **admin** - February 7, 2020



Dr. Daniel Drucker's gut instincts have made him one of the top diabetes researchers on earth.

In particular, the Toronto physician's early-career insight that hormones in the gut could be key drivers of the Type 2 version of the disease have led to numerous front-line drugs and earned him the most prestigious awards in the diabetes field — including the [\\$50,000 \(U.S.\) Baxter Prize](#) from the international Endocrine Society announced last month.

"The gut is the first place our body comes into contact with the external environment, particularly with regard to nutrients and food," says Drucker, a senior scientist at Mount Sinai Hospital's Lunenfeld-Tanenbaum Research Institute.

And that front-line role gives the gut powerful controls over other parts of the body. These downstream actions are controlled by hormones produced in the digestive tract and include the dispersal and assimilation of nutrients into the growth and metabolic processes of our bodies.

It's when those processes — especially those related to the creation and storage of energy — are out of whack that obesity and the related diabetic conditions epidemic in many parts of the developed world can bloom. Drugs designed from Drucker's discoveries employ those gut hormones to right those metabolic misfires, alleviating the often crippling damage the ailment can cause.

"His contribution is really enormous," says Dr. Ravi Retnakaran, a fellow endocrinologist at Mount Sinai. "He's one of the true world leaders in gut hormone biology."

Retnakaran says research and discoveries are almost always incremental in the health sciences: things build slowly and inch their way toward improved treatments. But Drucker, he says, didn't do incremental.

Rather, the gut-hormone discoveries he's made have led to two entire classes of diabetes drugs that are now standard treatments for the ailment. In particular, injectable medications based on his breakthrough insights into so-called GLP-1 agonists and DDP-4 inhibitors now cram the airwaves with endless loops of diabetes drug commercials.

YOU MIGHT BE INTERESTED IN...

Medications like Ozempic (the Oh, Oh, Oh jingle drug), Trulicity and Victoza are some of the heavily marketed products of his basic hormone research. "If you turn on CNN I know there's commercial airing right now for one of them," Retnakaran says.

Drucker says these drugs — which largely mimic the actions of various gut hormones — have rapidly shifted diabetes treatments. The first was introduced to the market in 2005.

"It's very new. Diabetes has been transformed tremendously in what we can do with medications."

Under healthy circumstances, Drucker says, the gut's job is critical but pretty straightforward.

"Its normal role is to digest the food we eat, send signals to the body that food's coming in, how much food's coming in, rev up the process of digestion and what I call nutrient absorption and assimilation," he says. "It's got to send the glucose and the fatty acids and amino acids to the different parts of the body that can use it to control our metabolism."

With diabetes, he says, your body loses its ability to dispose of glucose; with obesity, it lacks a food intake shut-off switch, making you eat and store more energy than you need.

"And if you think, 'well, what do gut hormones do?' — they normally control how much we eat, they normally control how much energy gets disposed of," he says. "And if we have disorders about how much we eat and where our glucose goes it's natural to use the body's own mechanisms, the body's own gut hormones, pharmacologically to try and reverse those disorders."

But when Drucker began his research and clinical career after post-graduate work at the Harvard Medical School in 1987, such hormonal solutions were not considered natural at all. Few at that time even thought of the gut as a hormone source, let alone a ruling one, Retnakaran says.

"His work (helped lead) to the recognition that the gut is actually a very active endocrine organ in terms of secreting hormones that then go act" on other tissues, he says. "His work has really, really built up that field."

Drucker's hormone work has also led recently to the first effective treatment for short bowel syndrome — a rare disease where inadequate lengths of small intestine prevent the body from absorbing sufficient nutrients.

"Again you're seeing the same story of his basic work leading to a drug that is now contributing to clinical care," Retnakaran says. "It's very unusual for someone over the course of their career see that happen once, let alone multiple times."

In hockey terms, Retnakaran says, Drucker would be a Wayne Gretzky of his field — a generational talent who has already bagged a hat trick of the most prestigious awards available to diabetes



The Montreal native (who grew up a Canadiens fan) is just the second diabetes scientist on the planet to receive the trio of the American Diabetes Association's Banting Medal for Scientific Achievement (2014), Japan's Manpei Suzuki International Prize (2014), and the Claude Bernard Medal from the European Association for the Study of Diabetes (2012).

The Banting award, named for Canadian insulin discoverer Frederick Banting, who did his work at the University of Toronto, is considered the Nobel Prize of the diabetes research field.

Banting's discovery "sort of hangs over all of us who come to work in Toronto to do discovery biology or more particularly diabetes research," Drucker says. "The bar is pretty high for excellence."

Ironically, Drucker's own Toronto work may partially dislodge insulin as a treatment for the Type 2 version of the disease.

For Type 1 or childhood diabetes — where the pancreas just fails to make enough of it — insulin will continue to be the essential treatment.

"For Type 1 diabetes, and that's where insulin started, insulin is the correct thing and it is life-saving," Drucker says. "But for Type 2 ... it basically controls the disease. It doesn't reverse the disease, it doesn't prevent most of the complications."

Type 2 diabetes is strongly linked to obesity, which lessens the ability of insulin to lower blood sugars in the body after eating.

Gut hormone drugs like those based on GLP-1, however, can lower blood sugars as well by effectively raising its native levels and potency in the body. And critically, where obesity causes resistance to insulin — lowering or eliminating its effectiveness in controlling glucose levels — GLP-1 drugs maintain their effectiveness in overweight patients.

“That’s why GLP-1 in fact is an approved therapy for not only diabetes but also for obesity, because it still works,” he says. “Today, it’s the most effective medical therapy for obesity second to bariatric surgery.”

The newest generations of these hormone-based drugs are producing weight losses of 15 to 20 per cent in clinical trials, Drucker says.

“We’re not yet at a level where we can say to a patient ‘you don’t need to consider bariatric surgery, you can try this drug,’ but we’re definitely getting there.”

Drucker says gut hormone drugs help alter the complex feedback mechanisms that make obese patients overly crave food.

“If you say to a person who gets an injection of GLP-1, ‘how do you feel?’ the first thing that people say is ‘wow, for the first time in as long as I can remember, I’m not hungry.’ ”

YOU MIGHT BE INTERESTED IN...

That benefit could affect the multibillion-dollar diet industry, whose TV ads might run even more often than those touting the new hormone drugs.

Drucker says the hormone is part of a “toolbox.” He says physicians facing an obese, diabetic patient will still prescribe diet, exercise and, perhaps, physiological programs to help address the conditions.

“Some people will respond to a supervised diet and lifestyle modifications, and others won’t.”

Drucker concedes 50 to 60 per cent of people would have a “great response” to the drugs and that newer ones coming on line could be even better. He adds that combination therapies like those used in cancer and HIV will likely be common solutions.

Drucker went to med school at U of T — where he is now a professor — graduating in 1980. He did post-graduate endocrinology training at Baltimore’s Johns Hopkins Hospital, the Massachusetts General Hospital and Harvard. Yet three years before he completed that training, he was already doing pioneering work on gut hormones.

Get more of today’s top stories in your inbox

Sign up for the Star’s Morning Headlines email newsletter for a briefing of the day’s big news.

[Sign Up Now](#)

“I started doing my first experiments on GLP-1 in 1984,” he says.

That came as something of a fluke.

In those days the instructors were not questioned, and they’d told him he was to work on the thyroid gland, one of the master hormone producers in the body. When he got to Harvard, however, he was told they didn’t need any more thyroid people.

“They said ... you go figure out what GLP-1 does, and I was pretty upset,” he says. “But my (resulting) paper was the first description of what GLP-1 did, first patent to use GLP-1 for diabetes.”

That 1986 patent, he said, likely fuelled the run of awards, says Drucker, who was named an Officer of the Order of Canada in 2015. But he still has an affection for the thyroid, maintaining a website on the gland three decades later called mythyroid.com.

Like Banting did with insulin, Drucker and his colleagues tried to use natural versions of his gut hormone as a medicine. But they found for reasons unknown that the body broke the natural version down too quickly, so they had to mimic it in a more lasting, synthetic version.

Later drugs that prevent that breakdown of natural GLP-1 in the body — such as Januvia — now sell in the \$10 billion-a-year a range.

One of the toughest aspects of developing new drugs for such abiding conditions as obesity and diabetes is to ensure that they are safe over the long haul, Drucker says. In the normal development of new medications, drug makers search for novel molecules that can block or promote some function in the disease chain and improve outcomes. But often these compounds — never seen by the body before — can have toxic effects.

“If you’re saying I’m going to treat diabetes and obesity for 30 or 40 years, then safety becomes paramount.”

Drucker’s pioneering work with natural hormones has helped alleviate those toxic concerns.

“We all make GLP-1. We have it in our bodies. When we eat, GLP-1 goes up,” he says. “If we make GLP-1 analogues (drugs) that circulate at higher levels that are more powerful, we now know that we have effective treatments for diabetes and obesity.”

As well, Drucker says, there’s a subsequent and “delightful” reduction in diabetes-related heart attacks, strokes and deaths that insulin treatments have failed to produce — combined with the lowered risks of blindness, nerve damage and kidney disease that they have.

In awarding him the Baxter Prize last month, Endocrine Society president Dr. E. Dale Abel said Drucker has helped diabetes patients across the globe.

“Dan Drucker’s work has improved the lives of thousands of patients with diabetes,” Abel, who is also chair of internal medicine at the University of Iowa, said in a release.

His research “has improved the quality of patients’ lives by making treatment more convenient and lowering risks.”

Slender and trim at 63, Drucker is asked if he might be using his own medicines to keep slim.

“No, I’m vain,” he jokes. “I often (thought) if we understood the genetic determinants of vanity, I’m pretty sure that it would have for some people a contribution to how you approach your daily activities.”

For him, that vanity — denied by many who know him — makes Drucker work out every day at his home gym.

“I have three children — they’re all gone and grown up, left the house — and it used to be the kids’ room,” he says. “And I said you know what, I’m just going to convert my basement into a little gym, me and the cat every morning.”

Drucker serves as an adviser and consultant for several of the drug companies that use his research. He lists all his private contributions on his website.

“I think that’s always important when you’re talking to someone who sounds like an evangelist for a particular therapy,” he says.

Drucker lived in Montreal for 13 years before undergraduate studies at the University of Ottawa. He came to Toronto for medical school, where he met his wife — now a dermatologist at Toronto Western Hospital — in their first year.

One of his sons is also a dermatologist, married to a child psychiatrist. Both are assistant professors at U of T. “My other sons are the black sheep of the family,” he says. “One is a corporate lawyer, one is a law MBA ... We don’t know what we did wrong.”

Drucker is currently working on a number of new gut hormone targets as potential bases for future drugs — and at combining two or more in one medication for greater effect.

“It’s very much like chamber music,” he says. “If you have one person playing one instrument that can be petty good.

“Put three people playing three different instruments, even though it’s the same song, probably just brings much more to the table.”



[Source link](#)

admin

FOLLOW US ON INSTAGRAM
[@BESTBROTHERSGROUP](#)