Acceptance speech

19 June 2025

Daniel Joshua Drucker, awardee in the Biology and Biomedicine category (17th edition)

I am delighted to be recognized, together with my colleagues, by the BBVA Foundation for our discovery work in GLP-1 science. As a young medical trainee, I was fortunate to have strong academic mentors, Professors Gerard Burrow and Charles Hollenberg, who encouraged me to pursue research training. I was grateful to be offered a position in the laboratory of Dr. Joel Habener at the Massachusetts General Hospital. I had very little prior research experience, but Dr. Habener was generous in giving young MDs a chance to learn science. On arrival, I found myself working in a large laboratory with more than a dozen trainees pursuing many different research questions.

I was extraordinarily fortunate to have been assigned the project to work on the glucagon gene. The gene had just been identified and the DNA sequences predicted the existence of additional glucagon-like peptides, but their production and activity had not yet been interrogated in any biological system. My first project was to characterize the post-translational processing of proglucagon in heterologous cell lines; studies done in collaboration with Dr. Svetlana Mojsov, a peptide chemist, who had just generated antisera and established radioimmunoassays to detect the various glucagon-like peptides. I found that GLP-1 and GLP-2 were not produced in fibroblasts, but could indeed be liberated in cells with endocrine machinery for appropriate post translation processing, such as pituitary cells and islet cells. Interestingly, I detected multiple forms of GLP-1 in our post-translational processing studies, which prompted us to further look at these different forms in my next set of experiments.

Since I already had the cell lines established in the lab, I next interrogated whether I could detect biological activity for some of the GLP-1 forms identified in the post-translational processing experiments. Although I could not detect GLP-1 bioactivity using the fibroblast or pituitary cells, the exciting moments came when I analyzed the islet cells. A short form of GLP-1, GLP-1(7-37) but not the larger form GLP-1(1-37), directly stimulated cyclic AMP accumulation, insulin gene expression and insulin secretion. Notably, the bioactivity in islet cells was detected at very low levels of GLP-1, evident even at 5 pM concentrations. Furthermore, my experiments demonstrated that the activation of insulin biosynthesis and secretion only occurred when the islet

cells were incubated with high concentrations of glucose, whereas GLP-1 did not stimulate islet cells when the glucose was normal.

These experiments launched a new chapter for my scientific career, focused on the study of GLP-1 science; a pursuit I have continued for the last four decades. Upon returning to Toronto in 1987 to establish my own lab, I studied the transcriptional control of glucagon gene expression and I developed new mouse models, including both transgenic mice and GLP-1 receptor knockout mice for interrogation of the actions of GLP-1 in many different systems. I was fortunate to be mentored in Toronto by Dr. Louis Siminovitch, a pioneer in molecular biology who also spent a great deal of effort mentoring young scientists.

The next series of meaningful discoveries with translational impact happened in the mid 1990s. We and others discovered that inhibiting the activity of the enzyme DPP-4 led to effective lowering of blood glucose. In separate experiments, I discovered the first actions of GLP-2, which acted as a powerful gut growth factor. Excitingly, in 1996 we and two other labs demonstrated that GLP-1 acting in the brain was capable of reducing food intake.

These actions of GLP-1 to inhibit food intake were lost in our newly generated GLP-1 receptor knockout mice. These experiments launched the next exciting chapter of GLP-1 science, and we started to see weight loss in people using GLP-1 drugs in clinical studies. Today we know that GLP-1 medicines are useful not only for the treatment of type 2 diabetes and for people living with obesity, but they also reduce rates of atherosclerotic cardiovascular disease, heart failure, liver disease, kidney disease, sleep apnea, osteoarthritis, peripheral artery disease and many additional related comorbidities.

There are an astounding number of new, more powerful GLP-1 medicines being developed, and exciting new indications that are being explored, including neuropsychiatric and neurodegenerative diseases and substance use disorders. The story of GLP-1 science reflects the collective efforts of many talented people working together to move the science forward. We would not be here receiving this recognition if it wasn't for hundreds of basic and clinical scientists in academia and industry, clinical trial experts, nurses, dietitians, and importantly, the tens of thousands of patients who volunteered for all the clinical trials.

Personally, I would like to thank my parents for working so hard to build a life for me in a new country, my wife and best friend Cheryl, and my sons, daughters-in-law and their families for standing beside me all these years and providing me with the support, love and encouragement so important to me as I pursued my research career.

I hope you will agree with me that supporting basic science research can pay enormous unanticipated dividends that meaningfully improve the health of millions of people worldwide. This indeed is one of the most compelling messages of the GLP-1 story, which I believe will resonate with all of us for the years to come. Thank you so much to my nominators, the BBVA Foundation and the awards committee for this honor and recognition, it is deeply appreciated.