Type 2 diabetes drug discovery and development

As part of this month's special focus on diabetes, our two interviewees discuss their complementary roles in the discovery and development of new anti-diabetic drugs.

David E. Moller, MD.

Vice President, Endocrine and Cardiovascular Research and Clinical Investigation, Lilly Research Laboratories, Indiana, USA.

A deeper understanding of the links between diabetes and cardiovascular disease highlights the potential value of developing medicines that might target multiple cardio-metabolic risk factors. "Diabetes, obesity and cardiovascular disease — three areas of disease with obviously interrelated pathogenesis with respect to clinical outcomes — are part of an integrated discovery approach at Lilly. We have also added musculoskeletal research into the mix, given the common themes related to the endocrine system and regulation of body composition," says David E. Moller, Vice President of Endocrine and Cardiovascular Research and Clinical Investigation at Lilly.

While working as a resident in medicine at George Washington University Medical Center, Washington DC, USA, a clinical mentor, Robert Ratner, steered Moller towards a Harvard Medical Area Combined Endocrinology Fellowship at Beth Israel Hospital, Brigham and Women's Hospital, and the Joslin Diabetes Center in Boston, Massachusetts, USA. "My postdoctoral training at Harvard [1986–1988] in the laboratory of Jeffrey Flier ignited a spark in me around metabolic research *per se* and this translated rapidly into a successful career as an academic researcher," he says.

For the following 8 years, Moller's research at Harvard Medical School focused on the molecular and genetic basis of insulin resistance and type 2 diabetes, but the desire to further pursue ideas 'from bench to bedside' led him into industry. "As a physician–scientist I am most excited by the ability to develop a concept in preclinical cell-based and animal models and then to rapidly see these novel hypotheses tested in early clinical studies. In other words, what is known today as translational medicine," says Moller.

In 1995 he joined Merck Research Laboratories as Director of the Department of Molecular Endocrinology in the division of Biochemistry and Physiology, progressing to become Vice President, Metabolic Disorders in 2003. "At Merck, I saw a unique opportunity to create a new research area in the context of a company with great science. One of the most valuable experiences was having the privilege to lead the division at Merck which discovered sitagliptin [the first in a new class of diabetes drugs that inhibit dipeptidyl peptidase 4, which is involved in the regulation of endogenous glucoregulatory peptides]," he says.

After leading diabetes and obesity drug discovery for 10 years at Merck, Moller moved to Lilly in 2006 because of the opportunity to broaden his therapeutic area experience to include cardiovascular and musculoskeletal research and also oversee early clinical development. "In addition, I was excited to leverage Lilly's biotechnology expertise (large molecule platforms) in order to maximize its potential impact on clinical outcomes," he explains. To this role Moller brings the most important lesson he has learnt in the pharmaceutical industry: the value of humility. "Things you are most bullish about may not succeed in the end. It's important to listen to a wide range of opinions before rendering a judgement about where to place a bet."

Daniel J. Drucker, MD.

Director, Banting and Best Diabetes Centre, University of Toronto, Ontario, Canada.

The incretins are endogenous glucoregulatory peptide hormones that are important targets for the treatment of obesity, diabetes and intestinal disease. Daniel Drucker's research team focuses on the molecular biology and physiology of the incretins glucagon-like peptide 1 (GLP1) and GLP2. As well as being Director of the Banting and Best Diabetes Centre, Drucker is Professor of Medicine at Mount Sinai Hospital, University of Toronto, and a scientist in the Samuel Lunenfeld Research Institute at Mount Sinai Hospital.

Following training in clinical medicine and endocrinology at the University of Toronto, Canada, Drucker's mentors, Gerard Burrow and Charles Hollenberg, encouraged him to pursue research training with Professor Joel Habener, Director of the Laboratory of Molecular Endocrinology at the Massachusetts General Hospital, Boston, USA. "Through the guidance, support and direction provided by Dr Habener, I was able to begin my studies of molecular endocrinology, with a focus on understanding the biology of the glucagon gene and the proglucagon-derived peptides," he explains.

It is the training experience and mentorship that Drucker received in Habener's laboratory that he credits, in part, for the success he enjoys today. "The opportunity to learn science and the art of enquiry from Joel was a real privilege. He taught us to never accept current thinking, and he was always quick to conceptualize new pathways. His boundless imagination and talent for innovation produced many novel discoveries and patent filings and has made a huge impact on molecular endocrinology and diabetes research. He taught us the importance of persistent hard work and innovation, and his infectious curiosity and high scientific standards served as wonderful paradigms for how to succeed in science," he says.

From Habener's laboratory in Boston, Drucker started to look for faculty positions. Having trained at the University of Toronto, he was familiar with the tremendous breadth and depth of the clinical and basic science faculty there and was offered a junior faculty position as an assistant professor in 1987.

Now, over 20 years later, Drucker enjoys the challenge of combining patient care, teaching and basic science research with administrative activities. "As a physician, one is always trying to provide excellent clinical care while mindful of the resource and time challenges associated with clinical medicine. As a scientist, pursuing adequate grant support for funding our research remains an ongoing challenge, and does not seem to get much easier over time. As an administrator, I am mindful of the need to identify and secure additional financial resources so we can expand the range of terrific activities currently underway in the Banting and Best Diabetes Centre." Among these challenges lies Drucker's greatest pleasure: "… participating in those moments of discovery when we realize that, for the first time, we understand a new aspect of biology that previously was unknown or obscure."

WEBSITE

Career snapshots:
http://www.nature.com/drugdisc/nj/nj_dd_arch.htmlhtml