THE LIFE SCIENCES INSTITUTE

DIABETES : BIOMARKERS TO CURES

Diabetes expertise at the UBC Life Sciences Institute

As of 2014, 387 million people worldwide suffer with diabetes at a stunning cost of over $450 billion for medical attention. The complexity of this disease – due to its multi-genetic nature and the innate genetic differences of individuals within this population – has perplexed scientists for decades. With advances in our understanding of the mechanisms underlying this disease, we are poised to better understand the complex nature of diabetes and how to more effectively diagnose, treat, and one day cure this devastating disease.

Researchers in the Life Sciences Institute (LSI), the largest institute of its kind in Canada, are positioned to take a lead in unraveling medicine's greatest challenges and providing the data needed by the healthcare system through an evidence-based approach to achieve more precise management of health and treatment of disease. The LSI Diabetes Research Group, with its unique complement of diabetes research programs, has considerable expertise in the areas of molecular biology, genetics, biochemistry, cell biology and physiology. This depth of knowledge, together with private support that is critical to increasing our capacity, enables us to tackle such a complex disease.

Diabetes: genes and the environment

Diabetes results from insufficient levels of the hormone insulin, which is required to transfer consumed sugars out of the blood and into the tissues where they can be used as an energy source. Stable blood sugar levels are required for a healthy life. The most common form of diabetes, or type 2 diabetes, is typically associated with obesity. In that setting, the insulin-producing cells in the pancreas fail to meet the body's need for insulin, resulting in elevated blood sugar levels and diabetes. Seven percent of Canadians live with diabetes, and the annual direct medical costs are expected to reach $16.9 billion by 2020. The indirect costs resulting from related medical complications and loss of productivity are staggering. In addition to financial implications, there is an immense impact on the quality of life of patients with diabetes, who face debilitating complications including damage to multiple organs and life-long dependence

7% of Canadians live with diabetes. Their annual direct medical costs are expected to reach $16.9 billion by 2020.

Only ~50% of conventional therapies are effective in the person for whom they are prescribed and many cause adverse side effects. Personalized diagnosis is key to treatment.

The Life Sciences Institute Diabetes Research Group is a leading team of experts dedicated to tackling diabetes for better diagnosis and treatment.

upon drugs. It has been estimated that diabetes reduces lifespan on average by 15 years. In fact, deaths due to diabetes-related causes approach those of all cancers combined.

While personal, environmental, and lifestyle factors – such as diet and exercise – play a role in whether an individual will become obese or diabetic, biological factors (i.e. individual's genetic makeup) also play an important role in determining their disease risk. This explains why some individuals can eat large, high calorie meals and exercise little yet do not become obese or diabetic, while others have a healthy diet and are physically active but cannot seem to reach their ideal weight. Likewise, while being overweight is a major risk factor for developing diabetes, many people who are overweight will never become diabetic. Knowledge of genetic factors affecting how insulin-producing cells function would help to determine who will be able to cope with the stress of weight gain and who will have their pancreatic cells fail to produce sufficient insulin, ultimately resulting in diabetes.

Personalized diagnosis: key to treatment

Diabetes is the leading cause of heart disease, kidney failure, adult blindness, and limb amputations. The ever-expanding diabetes epidemic costs Canada billions of

dollars and threatens to overrun the world's health care capacity. While some general principles associated with the pathogenesis of type 2 diabetes are well accepted, the precise molecular causes of these interrelated conditions remain unclear despite decades of study. Diabetes is not a single disease but rather a spectrum of individualized conditions, with each person arriving to a similar phenotype via distinct gene-environment interactions. This means that the treatment strategy must also be tailored to the individual in order to be maximally successful and cost-effective. Indeed, clinical and epidemiological studies clearly reveal populations of 'responders' and 'non-responders' to identical pharmacological and lifestyle interventions; only about 50% of conventional therapies are effective in the person for whom they are prescribed and many cause adverse drug responses. The members of the LSI, including those in the Diabetes Research Group, and their academic and industry partners are dedicated to identifying and translating personalized approaches to combating diabetes.

GLP-1R agonists

The launch of the once-daily glucagon-like peptide-1 receptor (GLP-1R) agonist in 2010 boosted the market size to US$ 1.7 billion in 2011. The unique feature of weight reduction associated with the use of GLP-1R agonists clearly differentiates this anti-diabetic drug class from other established anti-diabetics. The profound blood glucose lowering effect without significant hypoglycemia has made GLP-1R agonists a strongly emerging anti-diabetic drug class. The huge potential of GLP-1R agonists in the diabetes market opens opportunities for technology providers and pharmaceutical companies.

Identification of biomarkers that predict personalized responses to type 2 diabetes therapies

Early stage type 2 diabetes can be managed with a combination of diet and exercise, although most patients will require drug therapy. Current pharmacological treatments for type 2 diabetes include approaches to ameliorate insulin sensitivity and improve or replace endogenous insulin release. In the latter category, pioneering work at UBC that includes early work by Dr. Timothy Kieffer helped establish the rationale for blockbuster type 2 diabetes drugs targeting the so-called incretin hormones (GLP-1 and GIP) that are released from the gut to potentiate glucose-stimulated insulin secretion. This class of drugs includes GLP-1 analogues and inhibitors of the enzyme (DPP4) that breaks down GLP-1 and GIP. In some patients the response to these therapies can be dramatic, but in others they are not effective, emphasizing the need for treatment tailored to the individual. To address this issue, we have assembled a unique team of expert clinicians and scientists in diabetes to develop biomarkers that will accurately guide prescribing of GLP-1R agonists. Dr. Tom Elliott, a practicing diabetologist and Medical Director of BC Diabetes has established the largest patient database for diabetic patients in Canada that will be used as the resource to identify accurate biomarkers. Expert input from Drs. Timothy Kieffer and James Johnson will provide insight into biomarker selection. Dr. Susanne Clee will provide her expertise in identifying genetic factors to predict responders/non-responders and adverse drug reactions. Dr. Bruce McManus, CEO of PROOF with his established record will lead in the biomarker signature selection, validation and development. Identifying biomarkers for the development of diagnostics to guide prescription has the potential to reduce adverse drug reactions and improv outcomes while saving the healthcare system and patients in avoidable ineffective prescribing and the treatment of adverse drug reactions.

How you can help

The goal of the LSI Diabetes Research Group is to build capacity to meet the challenges of developing personalized medicine for diabetes. To achieve this, UBC is seeking private support to build core research infrastructure and to expand a comprehensive and advanced diabetes training program to ensure the next generation of scientists are prepared to investigate this disease.

Investment in the LSI Diabetes Research Group will support leading-edge multidisciplinary research, the recruitment and training of scientists and clinical practitioners, and the acquisition of state-of-the-art equipment – all of which would ultimately lead towards improved treatment of this disease and an improved ability to maintain wellness.

For more information, please contact:
Robert Fraser, Associate Director LSI/PMI
1354-2350 Health Sciences Mall
Life Sciences Centre
Vancouver, BC Canada V6T 1Z3
rob.fraser@ubc.ca / 604-827-2088
www.lsi.ubc.ca

For donation enquiries, please contact:
Leanne Denis, Sr Associate Director, Development
317-2194 Health Sciences Mall
Vancouver, BC Canada V6T 1Z3
leanne.denis@ubc.ca / 604-822-2207