THE LIFE SCIENCES INSTITUTE

Poised to become a major global contributor to the implementation of personalized medicine, The Life Sciences Institute at UBC is home to more than 85 principal investigators and their research labs from 10 different departments across 5 faculties.

Multidisciplinary teams work closely with practicing physicians to focus on the delivery of personalized medicine solutions to patients suffering from cancer, diabetes, cardiac arrhythmias, autism spectrum disorders, and major immune disorders and infectious diseases.

What is Personalized Medicine & how does it affect you?

More than 50% of prescribed drugs don't work on the person for whom they are prescribed. Adverse drug reactions are the 5th leading cause of death in North America. These and many other reasons are forcing healthcare to adopt new technologies to characterize individual patients at the molecular level in order to predict drug efficacy and safety and to detect, monitor, and treat disease.

The advent of health care based on the molecular makeup of individuals – commonly called "personalized medicine" – will allow more effective preventive care and improve the safety, efficiency and effectiveness of the healthcare system while potentially reducing healthcare costs.

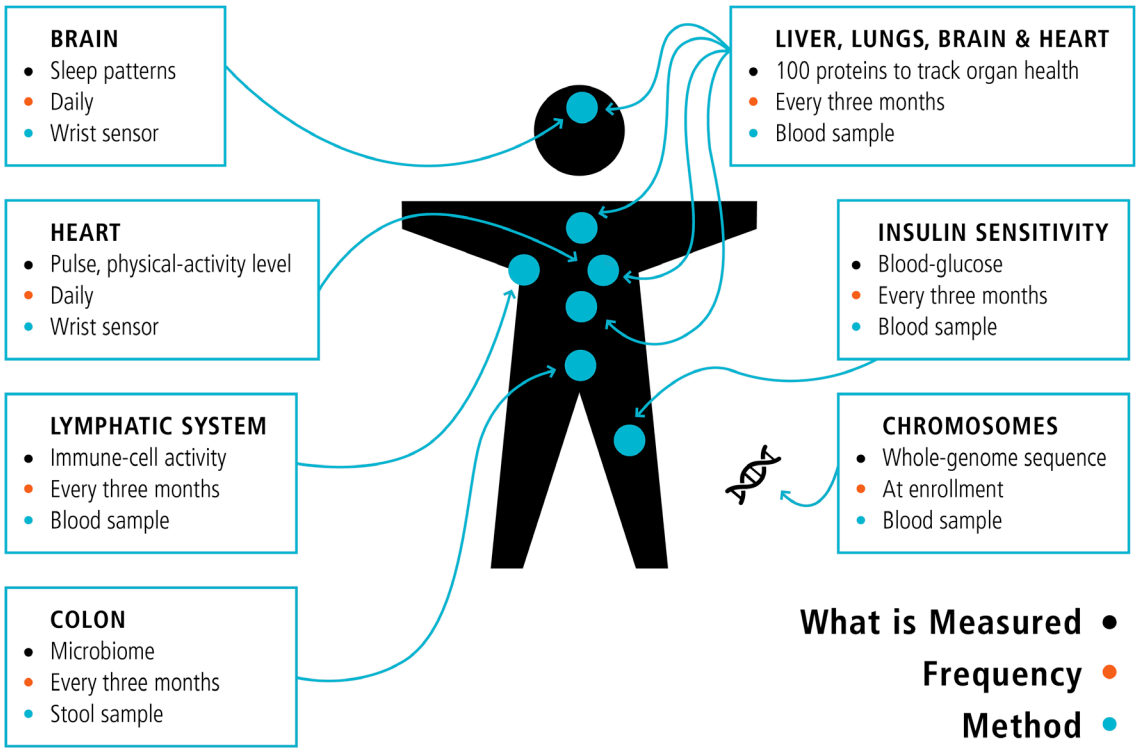
A personalized medicine approach to health care can reduce adverse drug reactions, provide more accurate diagnoses and better matching of treatments to disease and ensure patients are treated only with medications that work with their unique molecular makeup.

Personalized medicine also offers enormous economic opportunities. In their 2009 report on "The New Science of Medicine," PriceWaterhouseCoopers projected that the market for a personalized approach to health and wellness will grow to as much as $452 billion world-wide by 2015, thus identifying tremendous opportunities to grow and diversify Canada's economic base through a personalized health care industry.

UBC is ranked #1 in Canada in life science research by the London Times; the LSI is the largest life science institute at UBC. As the technological hub of the Personalized Medicine Initiative, the LSI is poised to take a lead in introducing molecularly based, personalized medicine in the front lines of medical care in BC and Canada. It is anticipated that this will lead to dramatically improved abilities to diagnose and treat disease and will enable preventive medicine to be practiced more effectively.

Current Projects

To exploit the personalized medicine theme, investigators at the LSI are initiating translational projects that have the aim of changing clinical practice by implementing an individualized approach to treatment. These projects are being developed and conducted in collaboration with the Personalized Medicine Initiative, industry, leading clinicians and the BC healthcare system. Currently over 10 proj-



ects (see below) are being planned and initiated that have the aims of changing clinical practice to improve healthcare outcomes and potentially reduce healthcare costs for a wide range of diseases and preventive health.

Implementation and Evaluation of Pharmacogenomics in Primary Care

The rapid expansion in the quantity and range of drugs prescribed by family physicians, coupled with the wide variation of individual, genetically determined, response to medications, has led to an urgent need for a medication decision support system that incorporates genetic information, and displays it in a way that can be used easily within the normal 10 minute family practice consultations. This project will develop and implement a genetic test that predicts response to drug therapies and incorporates this pharmacogenomic information into a computerized decision support tool for family practice that utilizes this genetic information to enable safer and more effective prescribing for patients at high-risk of an adverse drug reaction.

National Cancer Hot Spot Test

Improvements in cancer care will need to embrace the concepts that each patient is different, each cancer is unique and cancers are clonally diverse populations of cells that obey evolutionary principles. There are about 90 known mutations to which a treatment is available or the treatment is in late stage clinical trial. This project aims at establishing equitable access across Canada to state-of-the-art cancer diagnostic test that surveys these 90 "actionable" mutations. Such a test will enable clinicians to prescribe available drug therapies based on the presence of the mutations and match the cancer and patient with the highest likelihood of success in the shortest time possible improving outcomes in a cost and time efficient manner.

Personalized Oncogenomics (POGS)

Understanding the causes of cancer can lead to effective interventions. Until recent breakthroughs in genomic sequencing technologies, using the tissue of origin as a guide in the treatment of cancer was the best course of action. Now with affordable accurate detailing of genomic sequences, it is feasible to study individual cancers and personalize care at the molecular level. Extending from the analysis of known mutations with "actionable" therapeutics, this project provides a comprehensive genetic characterization of human tumors. This project will provide a basic understanding of the changes that contribute to and drive the cancer causing processes, and in certain cases insights into guiding individualized therapeutic action to stop cancer growth,

proliferation and metastasis. Collectively this information has the potential to provide more accurate diagnostics and validated therapeutic targets.

iTARGET ASD; Individualized Treatments for Autism Recovery using Gene-Environment Tools for Early Diagnosis

The Autism Spectrum Disorders (ASDs), defined by significant deficits in communication, social reciprocity and behaviour, are the most common childhood neurodevelopmental disorder and a rapidly growing public health concern. ASDs are complex and research suggests a strong genetic link. Most experts agree that signs of ASDs are evident in the first year of life in nearly 50% of affected children, yet most are not diagnosed until they are much older. Research implicates that earlier treatments lead to significantly better quality of life. Our team of scientists, clinicians and trainers will construct an integrated phenomic-genomic-microbiomic database to develop diagnostics that will enable early characterization of ASD, identify patients at high risk of developing certain clinical symptoms (co-morbidities), and guide the management and support strategies that best-fit individual patients and their families for the greatest possible therapeutic benefit.

Biomarkers for Precise Prescribing for Diabetic Patients

Diabetes is a multigenetic disorder arising from poorly understood interactions between genes and the environment and is predicted to affect one in three children born today. In 2012, 371M people suffer from diabetes that costs over $450 billion to treat. The multi-genetic nature of diabetes and the innate genetic differences of individuals within this population give rise to a variable response to diabetic treatment regimes (approximately 50% of therapies are effective). Delivering an effective treatment immediately following diagnosis of the disease can be vital to the health of the patient and make the healthcare system more cost effective. We have assembled a unique team of expert clinicians and scientists in diabetes to develop biomarkers that will accurately guide two emerging classes of therapeutics aimed at increasing insulin sensitivity and lowering blood cholesterol, glucagon-like peptide-1 receptor agonists (GLP-1) and Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, respectively.

Approximately 50% of prescribed drugs, costing over $30 billion/yr in Canada, do not work on the patients they are prescribed for due to genetic differences.

Adverse drug reactions to prescribed drugs are the fifth leading cause of death in North America.

Adverse drug reactions cost approximately $50 billion/yr to the Canadian healthcare system.

Molecular Diagnostics of Viral and Non-Viral Liver Fibrosis Progression

Liver fibrosis is a process of replacing healthy liver tissue with scar tissue, caused by inflammation or injury. The last stage of fibrosis is called cirrhosis and it is the 12th leading cause of death by disease (more than 1.5 Million per year) and the resulting economic burden is over $20 Billion in the U.S. alone. Fibrosis is reversible, but reversibility is easiest during the early stages of liver damage, with progression of fibrosis leading to liver failure, cancer and ultimately death. As fibrosis is asymptomatic, diagnosis heavily relies on clinical tools, but no accurate non-invasive test is available. This project will develop a comprehensive suite of three non-invasive molecular diagnostic blood tests (genomics-, proteomics-, and metabolomics-based) that can rapidly and accurately distinguish various stages of fibrosis, especially the early stages where treatments and interventions are most efficient and critical.

Asthma and the Personalized Microbiome

Asthma is a major problem in Canada, with 8.3% of the Canadian population aged 12 and over and 11.7% of Canadian children, aged 12-19 having asthma. This number has quadrupled in the past 20 years. There is a growing body of evidence that the microorganisms that we host influence our health and disease. This project will establish how the microorganisms in the gut impact immune function and asthma development, and define which microorganisms are associated with either resistance or susceptibility to asthma development. This information will provide accurate diagnostic tests to identify asthmatics before onset with the potential to guide

effective therapeutic interventions that can prevent or better treat young children at risk.

Personalized Treatment of Cardiac Arrhythmias

Inherited cardiac arrhythmias adversely affect the lives of about 1 in 2000 people. Too often the first symptom is sudden death and when the arrhythmia is detected earlier, the response to accepted therapies is highly variable due to the nature of the individual and the genetic mutation. The aim of this project is to employ genome-sequencing technologies to identify the primary disease mutation and stem cell technology to empirically determine an effective therapeutic regime for each individual. The genetic profiles of patients will be compiled to create a clinical registry linking the type of arrhythmia and functional activity, so that future patients can benefit from a rapid and effective diagnostic paired to the therapeutic.

As the largest institute of its kind in Canada, the LSI is positioned to take a lead in unraveling medicine's greatest challenges.

Preventive Medicine; Molecular You

Early detection of disease risk and early intervention would dramatically improve health and decrease health costs. However, previous efforts have been hampered by a lack of strong science to guide intervention. Our effort will revolutionize effective prevention. Traditionally medicine has had difficulty in identifying people at risk of developing a disease or in the very early stages of disease. Population based approaches such as screenings have had variable success.

In contrast, a comprehensive innovative approach designed to detect early signs of potential disease would allow early stage intervention before serious consequences occur. The only way to map the natural history of diseases and understand etiology is through longitudinal studies of a large patient population. A preventive medicine program aimed at maintaining health is being planned in partnership with the Institute for Systems Biology in Seattle. Participants will be extensively studied utilizing the most up-to-date and validated tools available. Their genomes will be sequenced and analyzed to identify genetic risk factors for disease. Plasma proteins will be comprehensively evaluated by proteomic and computational biology approaches. Their physical activity, heart rate, sleep patterns will be regularly monitored. Analysis of microbial species present in the gut and about 100 organ-specific proteins will also be monitored. Data will be analyzed for health status and transitions from health to disease (see figure above). Participants will receive regular consultation with a healthcare professional to interpret data and discuss potential options. Data will be presented using a totally new graphical interface to produce a "dashboard for health".

In addition to the health maintenance benefits to participants, the large database created from this study will be a powerful source of information to develop biomarkers indicating health status and early indications of transition to disease. Such data will be the basis of new intellectual property and proprietary opportunities to create industries focused on maintaining wellness and the early personalized prevention of diseases before they become dangerous.

Fueling Innovation

Additional resources are required to advance our understanding and capabilities in the personalization of medical care. Investments in the LSI will support leading-edge multidisciplinary research, the recruitment and training of scientists and clinical practitioners and generation of new commercial opportunities – all of which would ultimately lead to improved innovative treatment of disease and ability to maintain wellness.

As the largest institute of its kind in Canada, the LSI is 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.

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