Calgary NGS Symposium: Improving Genomics through Collaboration and Innovation

2014

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D-MARK Biosciences, and Integrated DNA Technologies

April 22

Calgary NGS Symposium: Improving Genomics through Collaboration and Innovation

Tues April 22, 2014
8:30am – 3:45pm
3:45-6pm Poster Session / Wine and Cheese Social
Libin Lecture Theatre - 3330 Hospital Drive Northwest, Health Science Centre

Alberta Children's Hospital Research Institute, D-MARK Biosciences, and Integrated DNA Technologies are proud to welcome you to this Next Generation Sequencing Symposium, hosted at the Libin Lecture Theatre (HSC) on **Tuesday April 22nd.**

Overview

Next generation sequencing holds great promise for advancing the understanding the genetics of all organisms. Advances in this area continue to come at an increasing rate, and there are now several platforms to choose from. For the uninitiated this can create confusion and make planning for an initial experiment difficult. In order to help demystify NGS as an application, we have assembled a panel of academic and industry speakers experienced in the field. The objective of this symposium is to provide an overview of NGS, move on to a more detailed look at instrumentation and methods, and then hear directly from academics putting local NGS platforms to work. The symposium is open to anyone who is interested in or is already using NGS in their research or diagnostic programs. Each talk will last 20-30 minutes, and ample time will be made available for discussion.

Poster Competition

A poster session will be held from **3:45-6 PM** on each day following the symposiums, featuring NGS research from industry and academia. Refreshments will be provided, and **prizes** will be awarded for the best 3 posters. Judges will be selected from the main workshop speakers.

If you would like more information, please contact:

- **Jeffrey Seitz** (Jeffrey.seitz@d-markbio.com)
- **Bob Setter** (rsetter@idtdna.com)

Invited Speakers:

Francois Bernier, M.D.,
ACHRI, University of Calgary

Dr. Bernier is an Associate Professor in the Department of Medical Genetics at the University of Calgary. He is also the Head of the department and Clinical Director of the R.B. Lowry Genetics Unit, which serves Southern Alberta. After obtaining his MD from the University of Manitoba, he completed his residency training in Medical Genetics at the University of Calgary. He is a Fellow of the Canadian College of Medical Genetics and a member of the American Society of Human Genetics. His research interests include the application to genomic technologies in order to elucidate the genetic basis of rare disorders as well as complex traits. He has an ongoing interest in the clinical and molecular delineation of a novel autosomal recessive disorder (dilated cardiomyopathy, cerebellar ataxia and 3-methylglutaconic aciduria) described in Hutterite populations. Recent work has also focused on the genetics on childhood neurodevelopmental disorders including developmental coordination disorder and autism. A large prospective cohort study of women and children is being established to explore the relationship between maternal environment and nutrition on maternal and child mental health as well as neonatal and infant health including congenital anomalies. The establishment of the cohort as well as a biobank will provide ample opportunities to explore the relationship between the maternal environment and genes.

Genomic Medicine….the revolution begins

Genomic medicine promises innovative gains in both the accuracy and timeliness of diagnostic and treatment approaches to health care. For many patients their health care journey is characterized by lengthy and expensive diagnostic or treatment odysseys, during which delays to arrive at a diagnosis are common or multiple rounds of ineffective or even harmful therapeutic interventions are attempted. Increasingly, it is becoming apparent that incorporating knowledge of an individual's personal genome can feasibly address many of these concerns. The revolutionary speed, cost and throughput of next generation sequencing (NGS) has brought genomic medicine to the doorstep of the clinic. The implementation of genomic medicine though will require addressing issues such as consent, privacy, return of results, incidental findings and clinical utility.

Marc Strous, Ph.D.
University of Calgary

I am a microbiologist and a chemical engineer and I try to use naturally selected communities of bacteria to do new and useful things. My aim is to make a contribution to a greener energy ecosystem, renewable energy sources and mitigation of greenhouse gases.
Prof. Strous, who recently held roles at the Max Planck Institute for Marine Microbiology, Bremen, Germany and the Center for Biotechnology, University of Bielefeld, Germany, will focus his research on the energy and environment theme and more specifically, reservoir biogeoscience. During his PhD project, Strous identified new bacteria that were previously considered unknown and successfully applied them in industrial wastewater treatment. Later, he discovered other "impossible" bacteria that couple methane oxidation to denitrification, a process which reduces nitrogen to a more usable form that is less detrimental to the atmosphere. His scientific discoveries received national and international recognition in the form of many papers in high impact journals, a membership in the young academy of sciences of the Netherlands, a prestigious European Research Grant and the ISME young investigators award. One of the projects he'll be championing at the University of Calgary is focused on significantly reducing carbon dioxide (CO_2) emissions and diminishing the environmental impact of electricity power plants and oilsands mining operations. Apart from his academic achievements, Strous has also worked as a process engineer at Paques (The Netherlands) and has filed three patent applications.
Marc Strous is a Professor of Microbiology and Campus Alberta Innovates Chair at the Department of Geoscience and joins a successful University of Calgary team of microbiologists and microbial ecologists, petroleum geoscientists and petroleum engineering researchers committed to achieving transformative results in the study and application of the petroleum reservoir biosphere to the solution of large-scale problems in the unconventional energy, carbon management areas and related areas. For example, in Calgary he is developing a new process for bioenergy production with microbes from extreme environments.

"In search of the nuts and bolts of the microbiome"

Next generation sequencing enables the complete characterization of microbial communities. Assembly of millions of short sequencing reads into contigs, followed by binning and annotation of the assembled contigs, yields provisional whole genome

sequences of the abundant microbial populations. In combination with transcriptomic, proteomic and metabolomic approaches the microbial interactions that define overall communal metabolism can be resolved. This approach has already been used successfully on relatively simple microbial communities. In this presentation I will show how simplification of microbial communities by cultivation in engineered laboratory habitats can be used together with omics approaches to resolve basic questions as to how competition and cross feeding can shape microbial communities.

Scott D. Rose, Ph.D.,
Director of Product Development/Integrated DNA Technologies

Dr. Scott Rose was recently appointed Director of Product Development at Integrated DNA Technologies with special emphasis being placed on developing: improved Nucleic Acid Capture and Enrichment technologies, Synthetic Biology tools, RNase H2 based detection technology, and functional genomics. He previously served as Director of Molecular Genetics at IDT under Dr. Mark Behlke, Chief Scientific Officer. He carried out his post-doctoral work at the University of Texas Southwestern Medical Center in the laboratory of Dr. Raymond MacDonald in the department of Molecular Biology and Oncology studying transcriptional based gene regulation using the pancreas as a model system. He received his Ph.D. in Biochemistry from Rice University in 1988 under the supervision of Dr. Susan Berget. His thesis work focused on RNA processing, looking at mRNA splicing and polyadenylation. His undergraduate degree in Biochemistry was from the University of Michigan-Dearborn.

xGen® Lockdown® Panels-Stocked Enrichment Panels for Targeted Next Generation Sequencing

Genomic target selection enables faster development of clinical sequencing tests for disease diagnosis, stratification, and informed therapy selection by allowing smaller, specific regions of the genome to be sequenced and analyzed at high depth in a cost-effective manner. Faster, targeted sequencing could also accelerate development of effective therapies for various diseases. Currently available commercial target capture reagents use biotinylated, array-synthesized oligonucleotides to generate DNA or RNA probes, often referred to as “baits”. However, baits that are generated by these methods often present performance challenges. IDT has developed an improved bait synthesis methodology known as xGen® Lockdown® Probes that meet those challenges. Based on the superior performance of the Lockdown Probes, IDT has launched two hybridization enrichment panels. The first one targets genes documented to be involved in Acute Myeloid Leukemia. The AML panel is comprised of 11,743 xGen® Lockdown Probes targeting regions within 260 genes. The second xGen® Inherited Disease Panel, which was based on the HGMD® (Human Gene Mutation Database) repository of known inherited disease-causing mutations and was refined by the Emory Genetics Laboratory at Emory University for clinical significance and relevance. The xGen® Inherited Disease Panel, is comprised of 116,355 xGen® Lockdown Probes, targeting 4503 genes and 180 SNPs. In addition to performance data, improved rapid capture protocols that have been validated with the enrichment panels will be detailed as well.

Paul Gordon, Ph.D.
Alberta Children’s Hospital Research Institute

Paul Gordon is the Bioinformatics Support Specialist for the ACHRI next generation sequencing facility. Dr. Gordon has been doing bioinformatics since 1996, starting at the National Research Council of Canada with the programmatic analysis and visual representation of the first archaeal genome, *Sulfolobus solfataricus*. He was lead programmer of the Genome Canada Bioinformatics Platform before joining ACHRI, developing software for a wide range of projects, from detecting kidney transplant rejection to fungal gene prediction for biofuel development to next generation Web infrastructure for sharing biological data. He is an author of 44 peer-reviewed journal and conference papers (12 as first author) with over 2000 citations. Dr. Gordon’s focus since joining ACHRI has been on optimizing analysis methods for high-throughput NGS data, from genomic variant prediction through to genotype-phenotype association.

Bioinformatics for NGS: from benchmarking to bedside and beyond

In this talk, I will outline the capabilities of the ACHRI NGS platform, the software developed in-house to aid in results interpretation, and examples of the types of projects being performed. NGS is opening up new basic research and applied healthcare opportunities, the informatics challenges these present going forward will be explored.

Joe Harrison, Ph.D.,
Department of Biological Sciences, University of Calgary

Dr. Harrison is an Assistant Professor in the Department of Biological Sciences at the University of Calgary and holds a Canada Research Chair (Tier II, CIHR) in Biofilm Microbiology and Genomics. He obtained his PhD in Microbial Biochemistry at the University of Calgary where he investigated the metal resistance and tolerance of biofilms in the laboratories of Raymond J. Turner and Howard Ceri. He subsequently undertook a postdoctoral fellowship in the laboratory of Mathew R. Parsek at the University of Washington, Seattle, USA, where he studied the cystic fibrosis pathogen *Pseudomonas aeruginosa*. His research interests include ecology and evolution in biofilms, signal transduction networks, and the mechanisms of biofilm antimicrobial resistance and immune evasion.

A bacterial thermosensor modulates biofilm formation in response to human body temperature

Pseudomonas aeruginosa is the principal pathogen of people suffering from the genetic disease cystic fibrosis (CF). This bacterium builds biofilms in the airways of CF patients, causing chronic infections that slowly destroy the lungs. Bacterial biofilm formation is controlled by a second messenger molecule called c-di-GMP. Low levels of c-di-GMP upregulate motility and acute virulence factors, whereas high levels promote biofilm development. While much is known about the diguanylate cyclase (DGC) and phosphodiesterase domains that synthesize and degrade c-di-GMP, respectively, very few signals to which these proteins respond have been identified. Here we sought these signals by searching for conditions that could trigger or suppress the *P. aeruginosa* rugose small colony variant (RSCV) phenotype, which is expressed when c-di-GMP is elevated. This identified a temperature-dependent RSCV phenotype for *P. aeruginosa* CF39S, a CF sputum isolate. Using data from whole-genome optical mapping and single-molecule real-time sequencing, the 7.3 megabase CF39S genome, which harbors a 500 kilobase megaplasmid, was finished *in silico*. Using genetic, biochemical and bioinformatics-based comparisons of a closely related isolate that did not respond to temperatures, we linked this phenotype to a transposon encoded DGC, which we have named the **t**hermosensing **d**iguanylate **c**yclase A (TdcA). This enzyme possesses a hallmark GGDEF-domain that catalyzes the synthesis of c-di-GMP, and purified recombinant TdcA displays a 140-fold increase in activity when shifted from room temperature (25°C) to body temperature (37°C). Acquisition of TdcA confers thermal control of biofilm formation to laboratory *P. aeruginosa* strains. RNA-seq of *P.aeruginosa*CF39S revealed that TdcA activity not only regulates genes for extracellular polymers and motility, but also several genes of unknown function in the accessory genome. Altogether, this work identifies a signal that directly regulates a DGC, suggests that c-di-GMP may control genes outside the core genome, and provides insight into a mechanism for temperature-sensing that may modulate biofilm formation in response to the human host.

Adam Morris, Ph.D.,
Senior Scientist Genomics, Bioo Scientific

Dr. Adam R. Morris is currently a Senior Scientist of Genomic Research at Bioo Scientific where he directs the development of Next Generation Sequencing technologies. During his career, Dr. Morris has applied genomic technologies to study various aspects of posttranscriptional regulation of gene expression, including mRNA binding and regulation by RNA-binding proteins, microRNA-mediated regulation of mRNAs, alternative polyadenylation of mRNAs, and simultaneous identification of mRNA transcription start sites and polyadenylation sites.

Dr. Morris received his Ph.D. from Duke University in 2010 under the supervision of Dr. Jack D. Keene. He then went on to perform postdoctoral research with Dr. Reuven Agami at the Netherlands Cancer Institute (NKI) and with Dr. Vishy Iyer at the University of Texas before joining Bioo Scientific in 2013.

Innovations in library preparation methods lead to superior data quality and streamlined workflows

Most current Next Generation Sequencing (NGS) library prep methods introduce significant sequence bias. The use of enzyme processing and fragmentation steps can introduce errors in the form of incorrect sequence and misrepresented copy number. Conventional RNA sequencing library construction involves the ligation of a population of DNA or cDNA molecules to adapters prior to PCR amplification and sequencing. An inherent weakness of conventional library prep methods is that DNA fragments that amplify more efficiently will unavoidably result in a higher number of reads than fragments that do not amplify as well during the library construction PCR step. Therefore, when multiple reads mapping to the same sequence are encountered, it is not possible to determine whether sequenced reads originate from the same or different DNA molecules. Molecular Indexing is used in library preparation to "tag" nucleic acid molecules before PCR amplification, allowing reads arising from PCR duplicates to be accurately distinguished from reads arising from distinct starting molecules. The use of Molecular Indexing in RNA-Seq will be described, as well as recent improvements and additional applications of Molecular Indexing.

Nizar Jacques Bahlis, MD.,
Department of Hematology, Southern Alberta Cancer Research Institute

Dr Bahlis is an Associate Professor of Medicine at the University of Calgary in the division of Hematology and Bone Marrow Transplantation and a member of the Southern Alberta Cancer Research Institute (SACRI). Dr Bahlis received his medical degree in 1995 from St Joseph University - French Faculty of Medicine in Beirut. He then completed his internal Medicine residency at the State University of New York in Syracuse followed by a Hematology-Oncology fellowship at the University of Miami, Florida. Dr Bahlis also completed a postdoctoral fellowship in cancer biology at the University of Miami under the mentorship of Dr Lawrence Boise. Dr Bahlis' clinical and laboratory research focus on the study of plasma cell dyscrasia, with particular interest in multiple myeloma genomics and the development of novel therapeutics. He has received several awards and research funding from numerous agencies including the ASCO young investigator award, the Multiple Myeloma Research Foundation, The Leukemia and Lymphoma Society of Canada, Alberta Cancer Foundation, the National Institute of Health, the Terry Fox Foundations and the Canadian Institute of Health and Research (CIHR). His research work was published in many peer-reviewed journals including Blood, Molecular Cancer Research and Clinical Cancer Research. Dr Bahlis also serves on the editorial board for the journal Blood and on the review panels of several funding agencies. He is a member of the American Society of Hematology, the International Myeloma Society and a board member of Myeloma Canada.

Genomics and precision medicine in multiple myeloma

Daniel Gregson, M.D.
Department of Pathology and Laboratory Medicine, University of Calgary
Medical Microbiology, Calgary Laboratory Services, Alberta Health Services

Dr. Gregson graduated with a medical degree from the University of Toronto and has specialty training and Royal College certification in Internal Medicine, Infectious Diseases, and Medical Microbiology. He was the Associate Microbiologist and Director of the Regional Virology Laboratory in London Ontario for 10 years prior to moving to Calgary in 2000. In addition to being a Medical Microbiologist for CLS and Infectious Diseases consultant for the Calgary Zone of AHS, he is an Associate Professor of Pathology and Laboratory Medicine at the University of Calgary.

Currently Dr. Gregson is President of the Association of Medical Microbiology and Infectious Disease Canada. He also is a member of the Laboratory Accreditation Committee for the College of Physicians and Surgeons of Alberta. His research interests are primarily in the area of rapid diagnostics in the microbiology laboratory including the use of mass spectrometry.

A father of 4, Dr. Gregson enjoys travelling, skiing, running, and cycling in his spare time.

NGS Sequencing in the Diagnostic Microbiology Laboratory

To discuss the uses of NGS in the Diagnostic Microbiology Laboratory and the impact of this technology on infection control. These will be highlighted through case studies currently underway by investigators in the Section of Medical Microbiology in the Department of Pathology and Laboratory Medicine at the University of Calgary.

Sean Rogers, Ph.D.,
Department of Biological Sciences, University of Calgary

Dr. Sean Rogers is an Assistant Professor, Department of Biological Sciences at the University of Calgary. He is a molecular evolutionary biologist with a diverse set of interests in ecology and environmental genomics, an emerging field that seeks to predict how organisms will respond, at the genomic level, to changes in their environment. Dr. Rogers explores [1] the genetics of adaptation, [2] the genetics of reproductive isolation and speciation, [3] the molecular ecology of invasive species, and [4] conservation genetics of fishes.

From snails to salmon: a role for genomics in the environmental monitoring, conservation, and enhancement of wildlife

Ecological and environmental genomics is an emerging field that seeks to predict how organisms will respond, at the genomic level, to changes in their environment. The objective of my research is to understand how genetic variation enables organisms to adapt to environmental change. The tight fits between form and function in organisms suggests the influence of adaptive evolution; however, the prevalence of adaptive traits, the mechanisms by which they arise and the corresponding phenotypic and molecular responses to selection (including human induced selection) are subjects of extensive debate. My research focuses on understanding the proximate (genetic mechanisms) and ultimate (strength/agent of selection) causes of evolutionary change to explain phenotypic effects stemming from interactions between genes and their environment. I address these questions using unique process-oriented experiments that directly test the fitness consequences of selection on genes underlying adaptive traits in nature. Consequently, this research framework enables the identification and explanation of evolutionary outcomes for adaptation and ecological diversification, a novel and innovative means to mitigate environmental monitoring methods that can understand and predict how populations will respond to environmental change. In this talk I will discuss the role of new genomic technologies that are being used in my lab to find answers to questions that translate into conservation biology and government policy initiatives related to environmental monitoring, environmental sustainability, and ecosystem integrity and management.

Jillian Parboosingh, Ph.D.
Molecular Diagnostic Laboratory, Alberta Children's Hospital Research Institute
Department of Medical Genetics, University of Calgary

Dr. Jillian Parboosingh is an Associate Professor in the Department of Medical Genetics at the University of Calgary, member of ACHRI and a Molecular Geneticist, head of the Molecular Diagnostic Laboratory located at the Alberta Children's Hospital. She has over ten years of experience performing human genetics research and running a molecular diagnostic lab. She has been involved in over 50 different exome sequencing projects. Over the years, many of her research discoveries have been translated into diagnostic testing. Dr. Parboosingh's primary research area is Clinical and molecular characterization of autosomal recessive disorders in the Hutterite population; identification of genetic risk factors for cardiovascular and cerebrovascular disease (and other complex disorders).

The highs and lows of exome sequencing-based gene discovery

Exome sequencing for gene discovery has gained popularity over the past 5 years leading to the identification of the underlying defect in over 100 diseases. Some diseases have proven easy to solve while others remain intractable. This talk will highlight study designs that have been both successful and unsuccessful and will present alternative approaches.

About the organizers:

D-MARK Biosciences

www.d-markbio.com

D-MARK Biosciences specializes in providing solutions to Molecular Biology and Protein Biology laboratories. The company was founded in 2008 by the former Canadian General Manager of a top 15 Multinational Life Sciences supply company, with an emphasis on PCR/qPCR and sequencing. D-MARK works with small manufacturers of advanced solutions for molecular and protein biology, allowing cutting edge research to be performed faster, more accurately, and at a lower cost.

D-MARK Biosciences is the premier Canadian distributor of advanced solutions for Molecular Biology. It has a unique focus on Genetic Technologies surrounding key applications such as Next Generation Sequencing, Microarrays, qPCR, PCR, nucleic acid preparation and Sanger Sequencing. Using a solution focused consultative approach; we will exceed your expectations and build a long lasting scientific relationship with your laboratory.

For more info, please contact Jeffrey Seitz: Jeffrey.seitz@d-markbio.com

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IDT DNA

www.idtdna.com

Integrated DNA Technologies (IDT) is a leader in manufacturing and developing products for the research and diagnostics life science market. IDT serves the areas of academic research, biotechnology, and pharmaceutical development. IDT was founded by Dr Joseph Walder in 1987. Since then, its development has been guided by an uncompromising approach to quality, a belief in the value of good service, and a determination to minimize consumer costs.

Serving over 80,000 life sciences researchers, IDT is widely recognized as the industry leader in custom oligonucleotides due to its capabilities in:

Analytical Sophistication – IDT pioneered the use of high throughput quality control (QC) methods and is the only oligonucleotide manufacturer to offer purity guarantees and 100% QC. Every oligonucleotide is analyzed by mass spectrometry and purified oligonucleotides receive further analysis by CE and HPLC.

Design Engineering – IDT maintains an engineering division dedicated to advancing synthesis, processing technology, and automation. An in-house machine shop provides rapid prototyping and custom part design/control.

Customer Support – IDT received over 100,000 calls last year with an average wait time of only 8 seconds.

Reagent and Input Control – IDT receives all solvents in large bulk containers, runs QC on all incoming materials, and performs bulk reagent formulation and functional QC on all reagents.

For more info, please contact Bob Setter: rsetter@idtdna.com

Alberta Children's Hospital Research Institute

research4kids.ca

The Institute is a partnership between Alberta Health Services, the University of Calgary and the Alberta Children's Hospital Foundation. By harnessing the collective strengths of their researchers from the hospital and the University of Calgary Faculties of Medicine, Nursing, Science, Arts, Kinesiology and Education, they focus on three priority areas:

- Behavior and the Developing Brain
- Optimizing Health Outcomes
- Genes and Development

The Institute's goal is to conduct world-class basic, translational, clinical, population and health outcomes research to optimize health and healthcare for children and their mothers. The Institute will excel by international standards in the creation of knowledge and training of scientists and health professionals for the development of state of the art health care of mothers, children and communities. Thanks to community support, the Institute has more than 200 leading experts in research, education, clinical care and community health working together to solve today's most pressing child and women's health problems. Working together, with an incredible breadth of expertise, Institute members are determined to find root causes, advance medical treatments and ultimately prevent illness and injury in children. Scientists at the laboratory bench team up with specialists at the hospital bedside and in the community backyard to establish a clear picture of urgent health issues requiring disciplined examination.

A big thank you to our sponsors!!