BCCGN
British Columbia Clinical Genomics Network

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BCCGN Newsletter

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BCCGN News and Updates

3rd Annual BC Clinical Genomics Network Conference entitled "GENOMIC MEDICINE IN 2015"to be held on Wednesday April 27th from 8:30 am to 4:30 pm at the Vancouver Convention Centre

Student Competition 2011

BCCGN is pleased to announce its annual Student Research Award competition 2011. The competition aims to assist BC medical students and undergraduates to conduct a genomics related research project under the supervision of experts in the field. Entry deadline is April 01, 2011, with winners being announced by April 15th. The Network is also sponsoring 3 genomics research projects in the CFRI annual summer student research program and one Summer Student Research Project at the Faculty of Medicine, UBC.

Genomics Workshop

BCCGN is holding a series of genomics workshops for physicians. The first one was held on February 24th at the Child and Family Research Institute; Children's and Women's Hospital, Vancouver, BC. The full day CME accredited workshops provide clinicians with a tour through labs involved in microarray technologies, demonstrations of DNA preparation and analysis, and use case studies to apply genomic technologies in clinical situations. If you are interested in attending a future session please let us know. Download Flyer.

Research in Focus

High Throughput Sequencing (HTS) in Intellectual Disability and Epilepsy (IDE)

Disorders causing developmental delay, intellectual disability and epilepsy (IDE) affect up to 3% of the general paediatric and adult populations. However, the underlying cause often remains unidentified due to limited availability of biomarkers and the fact that the currently available "one by one" diagnostic tests are time consuming and costly. Obviously early recognition and treatment of a causal genetic condition can substantially improve a patient's prognosis. BCCGN members, Drs. Sylvia Stockler and Clara van Karnebeek have proposed a novel solution to the problem.

Knowing that inborn errors of metabolism are an important cause of IDE as many of these rare genetic conditions are amenable to causal treatment, they postulated that, using the latest genomics sequencing technology with a creative study design, it might be possible to develop an all-in-one diagnostic screening test for a group of these treatable metabolic IDEs. The doctors approached the BC Clinical Genomics Network and together with Dr. Jan Friedman and Dr. Marion Thomas, they developed a new sample pooling method combined with high throughput sequencing (HTS) to detect treatable inborn errors of metabolism that cause IDE.

The first step was to design a pilot study which allowed for the simultaneous sequencing of over a thousand anonymized DNA samples, to look for mutations in 6 IDE genes. Known positive control samples were also added. A novel method was designed to pool or mix the samples in such a way that if a mutation was found it would then be possible to determine from which individual sample the mutation was detected. This would then prove the technical feasibility of the new HTS-IDE screening protocol. The samples are currently being sequenced at the Genome Science Centre and the results should be known soon. The biggest challenge to come lies in the bioinformatics strategies that will need to be utilized to interpret the results. However if this exciting project is successful, this novel screening protocol can be utilized to allow many different treatable disorders to be screened simultaneously in patients with IDE. Ultimately, this will allow the initiation of early treatment to improve neurodevelopmental outcome and perhaps even prevent developmental delay in a greater number of affected children. Furthermore, the method may also be expanded and applied with great benefit to many other disease areas.

Technology in Focus

High Throughput Sequencing (HTS) – New Pooling Methods

Next generation sequencing (NGS) is about to make another leap forward in revolutionizing medical genetics. Single gene tests have been the standard for identifying treatable disorders including those with genetic heterogeneity such as retinosa pigmentosa. These tests are costly and have been limited by the low throughput of traditional sequencing technologies. A solution to making next-generation sequencing as efficient and affordable as possible involves the use of various pooling methods which take advantage of the extremely large number (up to several hundred million) of sequence reads that can be generated in a single run. The pooling of individual DNA samples prior to sequencing provides a much more cost-effective approach for mutation discovery especially when a large number of targeted genes can be sequenced simultaneously.

This highly-multiplexed sequencing of pooled samples can now be used to determine sequence variation within a single gene, several loci, or even a non-human genome. For some pooling projects it is important to determine exactly which pooled sample has the detected sequence change. To do this individual samples can now be barcoded. This is where a unique sequence identifier is attached to all the DNA fragments in a sample, making it easily identifiable even when mixed in with a number of other DNA fragments. The barcode assures the identification of the original sample after pooling and analysis. Alternatively, a framework of overlapping pool designs without the need for barcoding can be used for even more cost-effective sequencing.

With the new pooling methods currently under development and more specific targeting (protein coding regions or exomes) of the genes known to cause treatable disorders the potential exists that many more individuals may be screened and disease causing mutations identified with potential treatments beginning much sooner than using more traditional step by step gene testing. Studies are underway to develop these new sequencing methods to identify known and novel mutations in heterogeneous genetic diseases such as retinitis pigmentosa which is caused by mutations in over 40 different genes. Even treatable disorders of intellectual delay and epilepsy will soon be able to be screened for known and unknown causes.

However, there are still challenges ahead before these platforms become routine in clinical applications. Issues still to be dealt with include the determination of which pooling strategy optimizes turnaround times, lowest reagent and labor costs and on the bioinformatic analyses side, which of these strategies can reliably reproduce low error rates.

BCCGN Activities

BCCGN News and Updates (Continued)

As part of BCCGN's educational mandate, BCCGN recently sponsored two events, CFRI's Mini-Med School XI and Café Scientifique.

The Mini-Med School XI: Clinical Genomics series was a tremendous success. Over six separate evenings, experts were brought in to talk about various state-of-the-art genomic technologies and to raise important issues surrounding the use of these new technologies. Topics ranged from Human Genomics- what you need to know; Genomics & Medicine – should you be afraid; A Genomics revolution – personalized medicine; Metagenomics – the microbes in you; Up, close and personal with Genetic Counsellors and The great debate – buying genetic tests on the web. High school students and the general public actively participated in many interesting discussions following each presentation. To view these sessions visit: http://www.cfri-training.ca/speakers/minimedfall2010.asp

Last November, 2010 two Café Scientifiques were held in Vancouver for the purpose of inviting a public discussion on unexpected findings from genomic sequencing technology, and what to do about them. Approximately sixty people attended over the two days. The event began with an amusing short film called "Sequence Me", winner of the Gene Screen BC movie competition. After several presentations were made by a panel of experts, there was considerable discussion about a variety of issues. One was the perception that pharmaceutical companies may take advantage of genomic technologies by creating designer drugs based on peoples' incidental findings and fears that result from these findings. Other participants felt that genomic sequencing findings would represent more of the same type of information that had potential to be useful for optimizing health, but likely wouldn't influence people's behavior in the long run

Member Awards:

► BCCGN Co-Founder Dr. Michael Hayden has been named to the Order of Canada for his outstanding contributions as a physician-scientist to the understanding of Huntington disease and other genetic disorders. The Order of Canada is the highest honour that Canada can give its citizens for exceptional achievement, merit or service.

► Dr. Jehannine Austin, was awarded a new Canada Research Chair in Translational Psychiatric Genetics.

► In December, 2010, the Rare Disease Foundation awarded a total of 19 microgrants of $3,500 each. Five of these were given to BCCGN members: Anna Lehman, Christina Dias (x2), Garbriela Horvath, and Patrice Eydoux.

Publications

► Factors associated with experiences of genetic discrimination among individuals at risk for huntington disease. (JM Friedman, MR Hayden, JL Bottorff) Am J Med Genet B Neuropsychiatr Genet 2011 Jan 156(1):19

► Genetic counselors' attitudes towards individuals with schizophrenia: desire for social distance and endorsement of stereotypes. (JC Austin) Patient Educ Couns 2011 Jan 82(1):69

► Cerebrovasculopathy in NF1 associated with ocular and scalp defects. (JM Friedman, LL Armstrong) Am J Med Genet A 2010 Dec

► 19p13.2 microduplication causes a Sotos syndrome-like phenotype and alters gene expression. (AM Lehman) Clin Genet 2010 Dec 13 [Epub ahead of print]

► Hypomorphic temperature-sensitive alleles of NSDHL cause CK syndrome. (C du Souich, M Demos, L Arbour, MI Van Allen, MA Marra, CF Boerkoel) Am J Hum Genet 2010 Dec 10; 87(6):905

► Duchenne muscular dystrophy caused by a complex rearrangement between inton 43 of the DMD gene and chromosome 4. (WT Gibson) Neuromuscul Disord 2010 Dec 4 [Epub ahead of print]

► A different approach to validating screening assays for developmental toxicity. (JM Friedman) Birth Defects Res B Dev Reprod Toxicol 2010 Dec 89(6):526

► Treatment of intractable epilepsy in a female with SLC6A8 deficiency. Mercimek-Mahmutoglu S et al Mol Genet Metab 2010 Dec; 101(4):409