BCCGN
British Columbia Clinical Genomics Network

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IN THIS ISSUE:

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BCCGN Newsletter

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BCCGN News and Updates

Dr. Mojgan Yazdanpanah joins BCCGN.

BCCGN proudly announces that Dr. Mojgan Yazdanpanah, a genetic epidemiologist was recruited to join our team to assist clinicians and researchers across B.C. in the areas of genetic epidemiology and statistics. She has a MD from Azad Medical University in Tehran, and a PhD on "Genetic determinants of macrovascular complications and mortality in type 2 diabetes" from the Genetic Epidemiology Unit of Erasmus Medical University, NDL. She continued her Postdoctoral work at Erasmus, Department of Internal Medicine working on the genetics of cardiovascular disease and diabetes using a variety of methods including a candidate gene approach and genome wide association studies. Dr. Yazdanpanah will most certainly increase the genetic epidemiology capacity in BC.

BCCGN is supporting summer studentships

BCCGN is pleased to announce its **annual student award competition 2010**. 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. Entries will be accepted until April 15th 2010, with winners being announced at the end of April. The Network is also sponsoring 3 genomics research projects in the **CFRI annual summer student research program**.

Research in Focus – Chromosomal Imbalance in Heart Disease

Congenital heart defects (CHD) are the most common birth defects of all human malformations. In most affected individuals no underlying cause can be identified. Genetic factors are thought to play an important role and recent studies implicate submicroscopic chromosomal imbalances or pathogenic copy number variants (CNVs) in 5- 25% of cases.

Dr. Harinder Gill, a medical geneticist at **C&W** teamed up with cardiologist, Dr. George Sandor and BCCGN to investigate the contribution of pathogenic CNVs in children with moderate to severe left-sided CHD (LCHD). Since LCHD has been shown to cluster in families, the team hypothesized a genetic etiology would be evident in this group. Recruited subjects were clinically assessed and a blood sample obtained from the patient and biological parents. Micro**a**rray-based **C**omparative **G**enomic **H**ybridization (aCGH) was performed using a Nimblegen whole-genome microarray.

The study included 32 children (20 males; 12 females), aged 1-19 with conditions such as coarctation of the aorta (23), aortic stenosis (7), interruption of the aorta (1) and hypoplastic left heart (1). All lesions were moderate to severe and required intervention by surgery or cardiac catheterization.

14 *de novo* CNVs were identified in 7/32 subjects. To see if they were pathogenic the team analyzed their size, prior association with a phenotype and if they contained genes expressed in the heart. They also used phenotypic databases to look for overlapping regions that would indicate a CHD phenotype. None of these CNVs were thought to be pathogenic. Analysis of the inherited CNVs revealed 257/355 recurrent CNV's that could be pathogenically important. Two regions that contain genes (*GATA4* and

SYT15) known to be expressed in the heart were observed in 9 individuals. Deletions involving transcription factor, *GATA4*, have been shown to be associated with CHD, in particular septal defects. Synaptotagmin (*SYT15*) is expressed in the developing heart of vertebrates and may be involved in membrane trafficking. This study concluded that pathogenic *de novo* CNVs do not appear to contribute significantly to the etiology of isolated of LCHD.

Technology in Focus – Array Genomic Hybridization

A big advance in genetic testing has recently been developed that allows a more detailed examination of the genome when compared to standard chromosome analysis. Micro**a**rray **G**enomic **H**ybridization or AGH uses a specially designed microchip to detect missing or extra pieces of chromosomes called microdeletions and microduplications that are too small to be seen under the microscope.

Two important factors ultimately influence the outcome of a deletion or duplication, gene dosage and breakpoint location. Duplication or deletion of DNA regions containing genes will ultimately impact the quantity or dose of the affected gene(s). An increase/decrease in gene dose may transcribe into problems due to an excess/deficiency in the relative amounts of a protein. Secondly, if a gene spans the breakpoint this may affect that gene's expression and ultimately its function.

The BCCGN provides clinical investigators access to AGH technologies and the expertise needed to use them effectively. Read more about AGH on our website and AGH fact sheet

BCCGN Activities

Publications

► Variants in two genes predict deafness from cisplatin chemotherapy: show BCCGN scientists (Drs. Ross, Carleton, Hayden) in new research published in Nature Genetics.
► Misunderstood skin disease can disfigure, isolate victims: The Canadian Press interviewed BCCGN Co-Leader, Dr. Jan Friedman about a genetic condition called neurofibromatosis.

Member Awards

► BCCGN researchers du Souich, Creighton, Rupps, Boerkoel, Gibson, Stockler & van Karnebeek were awarded microgrants by the Rare Disease Foundation to use genomic technologies in their projects.
► BCCGN investigators Drs. Jan Friedman, Marco Marra and Neal Boerkoel were awarded a CIHR operating grant to study "Massively Parallel Genomic Sequencing for Clinical Identification of Mutations that Cause Intellectual Disability".
► BCCGN investigator, Dr. Gibson was awarded a 1 year bridging grant by the CIHR for his study "Rare Obesity Disorders Informing Common Disease."

Announcements

► The BC Newborn Screening Program is expanding the number of disorders it screens from 6 to 18; they are all treatable and include metabolic, endocrine, blood disorders and cystic fibrosis. Their early identification allows treatment that may prevent severe mental handicap, growth problems and more.
► CFRI's Genetics & Health and Developmental Neurosciences & Child Health research clusters host Site-Wide Research Rounds, 2nd Tuesday of the month. BCCGN investigators, Drs. Friedman, Boerkoel, van Karnebeek and Lehman are among those who either have presented or will be presenting.

Events Calendar

► BCCGN and Genome BC are launching their first annual Gene Screen BC video competition, Monday, March 22nd at the Museum of Vancouver. The inspirational speaker will be Marianne Kaplan, who directed "The Boy Inside" an award winning film about her 12 year old son with Asperger Syndrome.
►BCCGN 2nd Annual Conference: "GenOMICS - Today and Tomorrow's Medicine" will be held on Friday, April 30th at the Fairmont Hotel Vancouver. Keynote speaker, author James Reston Jr. will discuss challenges he faced when his daughter was born apparently healthy but later developed a rare, undiagnosed disease. There is no charge for the conference, but registration is required.
► The Future of Genomic Medicine III: March 5-6, 2010. San Diego, California. BCCGN investigators Dr. Michael R. Hayden (Pharmacogenomics) and Dr. Marco Marra (Cancer Genomics) will be presenting.
► Keystone Symposia-Diabetes; April 12-17, 2010, Whistler, BC Session: Genetics of Diabetes