CANADIAN GENETIC DISEASES NETWORK
RÉSEAU CANADIEN DE MALADIES GÉNÉTIQUES

Newsletter of the Canadian Genetic Diseases Network

OPEN READING FRAME

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In This Issue

CGDN 12th Annual Scientific Meeting a Success

Researchers and science meet in the Rockies.

The CGDN's 12th Annual Scientific Meeting was held May 15–18 at the Kananaskis Mountain Lodge in Kananaskis, Alberta. Among the 150 attendees were 37 CGDN investigators and core facility directors, 85 students and post-doctoral fellows and 25 guests. The international guests included CGDN scientist, **Dr. Lap-Chee Tsui**, Vice-Chancellor of the University of Hong Kong (HKU) and Chair of the Steering Committee of the Genome Research Centre at HKU, **Prof. Paul Tam**, Associate Dean of the Faculty of Medicine and Chair Professor and Head of Paediatric Surgery at HKU, **Prof. Kathryn Cheah**, Chair Professor and Head of Biochemistry at HKU and **Dr. Yu Lung Lau**, Head and Chair Professor of the Department of Paediatrics and Adolescent Medicine at HKU. Attending from the UK was **Dr. Helen Middleton-Price** from the North West Genetic Knowledge Park in Manchester.

Once again, the CGDN's Annual Scientific Meeting fostered networking and collaboration among Canada's

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An example of the stunning beauty that surrounded the 2003 CGDN Annual Scientific Meeting held in Kananaskis, Alberta.

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The Other Side

A Profile of Dr. Moira Glerum of the University of Alberta

Dr. Moira Glerum, one of CGDN's newest Investigators, researches mtDNA in cancer at the University of Alberta.

Dr. Glerum is one of the newest CGDN scientists, invited to join the network in 2002. Her research focuses on mtDNA mutations in cancer and her lab is located at the University of Alberta, Department of Medical Genetics.

Q: Where are you from originally?
A: I'm from a small village in Ontario, just north of Toronto, called King City.

Q: What made you go into science?
A: My main influence was my father, who was a tree physiologist. He taught me to love the rigor of science and investigation.

> "You never know enough. Every time you think that you've got a handle on something, in or out of the lab, something happens… and it changes everything. There are always ten more questions."

Q: Who has been your greatest role model?
A: I would have to say that I've had two role models: the first was my post-doctoral supervisor, Alex Tzagoloff of Columbia University. He taught me to be a yeast geneticist. The second was my PhD supervisor, Brian Robinson at the University of Toronto as it was during this time that I became interested in inborn errors of metabolism.

Q: What has been one of your biggest challenges in your career?
A: To have the confidence to know that you can do it!

Q: What is the most important life lesson that you've learned?
A: That you never know enough. Every time you think that you've got a handle on something, in or out of the lab, something happens — you read an article or someone tells you something you didn't know — and it changes everything. There are *always* ten more questions.

Q: If you could be anywhere in the world right now, where would you be?
A: I would be in a chalet in the mountains with Internet access. I love the mountains and with Internet access, I could stay current and write my papers.

Q: Finish this statement: If I wasn't a scientist, I would be……
A: …a musician. I took piano lessons from grade 2 until the 2nd last year of my graduate school.

Q: Do you have any interesting idiosyncratic lab quirks?
A: I don't have any yet, but if I had a wish, it would be that CBC Radio Two would be the only station that's played in the lab. If I get more crotchety as I get older, maybe I'll impose this as a rule. ▲

Alex Mackenzie appointed VP Research of Genome Canada

Dr. Alex Mackenzie, a CGDN Investigator, is Genome Canada's Vice-President, Research.

Dr. Alex Mackenzie has been appointed Vice-President, Research of Genome Canada as of July 1, 2003. Dr. Mackenzie is an internationally recognized researcher in the field of cell apoptosis and the study of Spinal Muscular Atrophy. He is also a Principal Investigator of the Canadian Genetic Diseases Network.

Dr. Mackenzie is currently the Director of the Children's Hospital of Eastern Ontario's (CHEO) Research Institute in Ottawa and a professor in the Faculty of Medicine at the University of Ottawa. He has been the recipient of the Scientist of the Year Award from the Muscular Dystrophy Association of Canada (1999) and the Burroughs Wellcome Clinical Translational Award (1998). ▲

Students Recognize Importance of CBW Bioinformatics Workshop

CGDN hosted workshops open doors to "future of biology"

If you were to ask **Dominique Verlaan** why she took the recent CBW Bioinformatics course, her answer would be simple — because bioinformatics is the future of biology.

The Canadian Bioinformatics Workshops (CBW) Series held its sixth Bioinformatics workshop from May 26th to June 7th, 2003 at the School of Information Technology and Engineering at the University of Ottawa. The workshop provides a comprehensive introduction to the use and development of tools for computational biology research.

Verlaan and **Anastasia Levchenko**, PhD students in the lab of Dr. Guy Rouleau of the Montreal General Hospital, spent the two weeks with fifty individuals from academia, industry and government learning about biological databases, gene prediction, microarrays and structure prediction for RNA and proteins.

In her research on the genes responsible for Restless Leg Syndrome, Levchenko saw the need for a greater understanding of bioinformatics tools, in particular gene prediction software and how to leverage the resources available in public biological databases.

Verlaan echoed her sentiment, "There are so many bioinformatics tools available on the Internet and it is difficult to learn how to use each of them individually as well as in combination with others. The CBW Bioinformatics Workshop shows how to integrate the various tools into a single application."

Both students left the workshop with a more detailed understanding of how to retrieve and interpret biological information from their research and from public databases such as GenBank. They believe that they will apply the skills learned at the workshop to their research.

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Another benefit of the workshop is the opportunity for people with life science careers to network in a learning environment, with a focus on bioinformatics. "I wondered initially about the value of bringing people together from such different fields. But I soon realized that valuable exchanges of knowledge were taking place every day," said Levchenko.

"It was interesting to get a first-hand look at the diversity of career paths available to someone with training in bioinformatics," stated Verlaan. "I think that gaining an understanding of computational biology is important to my career growth." ▲

Gene linked to Schizophrenia Discovered

NPAS3 gene may be associated with schizophrenia susceptibility

Research done in the laboratory of **Dr. Diane Cox** has identified an important genetic flaw linked to schizophrenia. Dr. Cox is a Professor and Chair of the Department of Medical Genetics at the University of Alberta and a Principal Investigator for the Canadian Genetic Diseases Network. The work was carried by **Deepak Kamnasaran**, a graduate student of Dr. Cox's, who recently completed his PhD studies. The discovery was published in the Journal of Medical Genetics on May 13, 2003.

"Much further research needs to be done to identify the gene targets and determine their potential role in schizophrenia. This discovery has opened the way for new and exciting research directions for this very complex disease."

Schizophrenia is a complex biochemical brain disorder that may be associated with many genes. The disease causes delusions, hallucinations, thought and speech impediments, and lack of motivation and energy. Affecting 1% of the population, symptoms usually start appearing between the ages of 15 and 25, although in some cases, there is evidence for associated changes in early brain development.

The discovery of this genetic flaw was made through studying the DNA from a mother and daughter in Scotland who were both afflicted with schizophrenia. While searching for genes related to another developmental brain disorder, holoprosencephaly, a region of chromosome 14 was mapped, and chromosome breakpoints and deletions were determined in a series of patients. Both of the Scottish women were found to share the same chromosomal rearrangement, causing a disruption of the neuronal PAS3 gene (NPAS3). This disruption affects the DNA binding ability of the corresponding NPAS3 transcription factor, which is predicted to interfere with its ability to control the expression of other genes.

The NPAS3 gene is part of a family of genes involved in behavior, memory and regulating day/night cycles. Although the specific targets of the NPAS3 gene product are not known yet, links to schizophrenia can be made based on studies where knockout mice of the closely related NPAS2 gene exhibit altered behavior and memory.

The identification of specific causative genes for schizophrenia has been elusive, but isolating this member of a group of genes involved in the disease opens many new pathways for research. "Much further research needs to be done to identify the gene targets and determine their potential role in schizophrenia. This discovery has opened the way for new and exciting research directions for this very complex disease," said Dr. Cox. ▲

12th Annual Scientific Meeting

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genetic research community, with animated scientific discussions taking place even in Woody's Pub until the early morning. The program included presentations by scientists and guests as well as a student and postdoctoral fellow poster session, which allowed them to present and discuss their research with attendees. Five of the six Scriver MD/PhD Studentship recipients had the opportunity to meet for the first time.

The CGDN's Annual Scientific Meeting fostered networking and collaboration among Canada's genetic research community, with animated scientific discussions taking place even in Woody's Pub until the early morning.

Meeting highlights included an address by the **Right Honorable Don Mazankowski**, CGDN's Chairman of the Board who discussed the importance of translating discoveries into improved health outcomes and keynote speaker, **Brian J. Cohen**, who discussed his experiences representing Canadian patients seeking access to genetic testing services.

CGDN's Scientific Director, **Dr. Michael Hayden**, highlighted the scientific and commercial achievements of the network in a presentation entitled "Celebrating 13 years of success". Saturday night's immensely popular Genomic Karaoke challenged CGDN's scientists to spontaneously provide scientific commentary to a series of random and unrelated slides.

The dates and location of the 2004 ASM will be announced this summer. ▲

Bioinformatics Tool Developed to help Decode Genome

Dr. Wyeth Wasserman, a Principal Investigator with the CGDN, has developed a new bioinformatics tool that is publicly available to the global research community.

The publication of the complete sequence of the human genome left many wondering "What next?" Although the linear sequence of the genome is delineated, there are still many mysteries to be solved. Many important genes have yet to be identified and the regulatory or 'control' signals of the known genes are undetermined. This information is important as control signals determine when, where and how a gene will be expressed.

The publication of the complete sequence of the human genome left many wondering "What next?"…there are still many mysteries to be solved.

Dr. Wyeth Wasserman and his collaborative team have provided a new computational approach to help unlock some of the information that is encoded in linear sequence. The combination of the knowledge about evolutionary relationships between genes with sophisticated bioinformatics resources provides researchers with a powerful tool to identify regulatory elements in the DNA sequence.

Wasserman and his team took a three-step approach to the problem of identifying regulatory elements. First, they compiled the JASPAR Database, a library of information about known transcription factor binding sites. The team then created a bioinformatics tool for aligning long stretches of genomic DNA to facilitate the examination of the evolutionary relationships between the sequences. This approach, known as "phylogenetic footprinting", is used to help identify biologically relevant sequences that have been conserved through evolution. Finally, the database was combined with the genome-alignment tools in a user-friendly manner to create ConSite http://www.phylofoot.org/consite.

ConSite was tested with well-characterized gene sequences and was found to work very well. It is expected that this resource will be modified and upgraded as more information is made available and will be used extensively by researchers around the world.

Most notable is that Dr. Wasserman is providing the ConSite web interface as a resource for the global bioinformatics community, thus making it widely available without restriction. A recent notice from PubMedCentral reported that the ConSite paper was the most widely reviewed report from June 2003 with over 2200 downloads of the PDF file.

This information was published in the May 22nd issue of the Journal of Biology and received comment in a "News & Views" article by **Zhaolei Zhang** and **Mark Gerstein**, published on June 6th. The Journal of Biology is part of BioMedCentral, a growing effort to create free, unrestricted access to the scientific literature. Wasserman's paper can be accessed at: http://jbiol.com/content/2/2/13. The "News & Views" article written is available at: http://jbiol.com/content/2/2/11/abstract. ▲