CANADIAN GENETIC DISEASES NETWORK
RÉSEAU CANADIEN DE MALADIES GÉNÉTIQUES

P1

Newsletter of the Canadian Genetic Diseases Network

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CANADIAN GENETIC DISEASES NETWORK
RÉSEAU CANADIEN DE MALADIES GÉNÉTIQUES

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Network Collaboration Yields Clues into Legionnaire's Disease

Resistance Gene Discovered in Mice

Dr. Philippe Gros and **Dr. Silvia Vidal**, working in collaboration with **Dr. Alex MacKenzie**, have identified a gene (Naip5) that makes mice resistant to Legionnaire's Disease. "This study demonstrates that a mouse gene, Naip5, can prevent Legionnaire's Disease in mice that would otherwise be susceptible to disease. With this new information, we hope to determine whether human Naip-related genes play a role in the pathogenesis of Legionnaire's Disease in people", stated Dr. Philippe Gros.

Legionnaire's Disease (LD) is a severe form of pneumonia, caused by infection with the *Legionella* bacteria. The first outbreak of LD occurred during a 1976 Legionnaire's Convention in Philadelphia, Pennsylvania. Since then, numerous outbreaks have been reported in Canada and the United States.

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The collaboration that led to this breakthrough began when Dr. MacKenzie and Dr. Gros exchanged ideas at the Network's 1996 Annual Scientific Meeting in Vancouver, BC.

Strengthening Relations with Taiwan and Hong Kong

Dr. Ron Woznow (left), CEO of the Canadian Genetic Diseases Network, **Dr. Johnsee Lee** (middle), Vice-President of the Industrial Technology Research Institute of Taiwan, and **Dr. Lap-Chee Tsui** (right), Vice-Chancellor at Hong Kong University, met in Taipei to discuss additional collaborative projects between ITRI, Hong Kong University, and the Canadian Genetic Diseases Network. ▲

Gene Linked to Leprosy

Gene on Chromosome 6 Renders People Susceptible to Disease

Network scientists **Dr. Erwin Schurr** and **Dr. Thomas Hudson** have identified a gene on human chromosome 6 that renders people susceptible to Leprosy. "This discovery will now allow us to study how the gene works and how it influences the infectious process. This is an important step toward the development of innovative prevention and treatment strategies for leprosy", stated Dr. Schurr.

Affecting nearly 1 million people worldwide, Leprosy is a chronic disease caused by infection with the bacteria *Mycobacterium leprae*. The disease causes pigmented skin lesions, nerve damage, and gross disfiguration such as loss of fingers, toes, feet, and hands. The disease is not prevalent in North American communities, but is a significant health concern in Southeast Asia, Africa, and South America. "Leprosy has plagued humans for many centuries and it continues to be a concern in many countries," stated **Dr. Marcel Behr**, Infectious Disease Specialist at McGill University.

Using a sophisticated technique called "whole genome scanning", Dr. Schurr and his colleagues mapped the gene to human chromosome 6. They analyzed DNA samples from nearly 100 families who were susceptible to the disease, and found that the individuals affected by the disease shared a common gene variant. To confirm their findings, the researchers analyzed an additional 200 Vietnamese families with leprosy. "In the last few years advances in technology have made complex genetic analyses, such as those used in this study, possible, "stated Dr. Thomas Hudson. "Without these advances and the cooperation of the families, this research would not have been possible."

> This discovery will now allow us to study how the gene works and how it influences the infectious process. This is an important step toward the development of innovative prevention and treatment strategies for leprosy.

Dr. Schurr and his team showed true compassion, determination and persistence in finding this gene. "Some of my team members were nearly injured during a flash flood while we were in Vietnam. Luckily, we only lost some of our equipment and a motorcycle", remarked Dr. Schurr.

And as his research moved forward in that instance, it moves forward now. Having established a genetic link, the research team will now focus on studying how the gene works and why it makes people susceptible to the disease. With a little bit of luck and a lot of hard work, the research will provide new insights into developing a vaccine or new therapies that will help eradicate the disease. ▲

Continued from page 1

"This is very exciting. In particular, the seeds for this discovery were set at our Annual Scientific Meeting. It is an important step toward the development of innovative treatments for Legionnaire's Disease. It also demonstrates the strength of our collaborative research program", stated **Dr. Michael Hayden**, Scientific Director of the Canadian Genetic Diseases Network.

The Naip5 gene was initially identified in a screen for the Spinal Muscular Atrophy gene by Dr. Alex MacKenzie, a CGDN investigator at the Children's Hospital of Eastern Ontario in Ottawa, and important early collaborator in this work. Indeed, the collaboration that led to this breakthrough began when Dr. MacKenzie and Dr. Gros exchanged ideas at the Network's 1996 Annual Scientific Meeting in Vancouver, B.C.

Gros and his collaborators used a technique called "functional complementation" to identify Naip5. They inserted pieces of mouse chromosome 13 into mice that were susceptible to infection. When a piece of DNA containing the Naip5 gene was inserted into these same mice, they became resistant to infection. "Many viruses such as HIV and CMV rely on host genes to replicate and cause infection. This study shows that in mice Legionella replication is also regulated by a host gene", stated Dr. Silvia Vidal, a co-author in the study. The researchers now intend to study human Naip-related genes. ▲

Canadian and Italian Researchers Meet to Discuss Collaborations

Dr. Steve Scherer, Chair of CGDN-Institute of Genetics,CIHR International Collaborations in Human Genetics Committee, talks with the participants of a meeting between Canadian and Italian genetic researchers. The meeting was hosted by the CGDN, Institute of Genetics,CIHR, and the Italian Embassy

The Canadian Genetic Diseases Network, CIHR Institute of Genetics, and the Italian Embassy hosted a scientific meeting entitled "New Frontiers: Italian/Canadian Genomic Population Genetics and Bioinformatic Collaborations" in Montreal on December 9-10, 2002. The meeting was attended by 30 leading Canadian and Italian researchers, representatives from Xenon Genetics, Newfound Genomics, Genome Canada, Industry Canada, and the Italian Trade Commission.

The participants were welcomed by **Dr. Louise Desjardins**, Business Development Manager of the Canadian Genetic Diseases Network, **Dr. Rod McInnes**, Scientific Director, CIHR Institute of Genetics, and **Dr. Giuseppe Martini**, Scientific Attaché to the Italian Embassy.

Over the course of the two-day meeting, Canadian and Italian researchers presented their work and discussed potential new collaborations. "The meeting was an excellent venue for the scientists to meet, exchange ideas and develop opportunities for research collaborations. The participants were committed to finding infrastructure and support mechanisms to ensure successful outcomes with these collaborative efforts", stated Dr. Desjardins. Eight CGDN members participated in the meeting: **Dennis Bulman, Thomas Hudson, Ken Morgan, Steven Narod, Guy Rouleau, Francois Rousseau, Steve Scherer,** and **Peter St. George-Hyslop**.

"The level of interest displayed over the course of the meeting was impressive", remarked **Dr. Steve Scherer,** Chair of CIHR-CGDN International Collaborations Priorities and Planning Committee, "There were many common projects and we have much to learn from each other." A follow up meeting, hosted in Italy by **Dr. Graziella Persico** of the National Research Council in Naples, is scheduled for September 2003. ▲

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CGDN Delegation Visits the UK Genetic Knowledge Parks

Drs. Michael Hayden, **Brenda Gallie** and **Chrystal Palaty** recently visited the Genetics Knowledge Parks (GKP) Network in the United Kingdom. The GKP network, a joint venture between the Department of Health and the Department of Trade and Industry, aims to create centres of clinical and scientific excellence and to promote advances in human genetics in the UK, by bringing together academic, clinical and industrial communities. The network consists of five GKPs located in England (London, Oxford, Cambridge, Newcastle and the Northwest) and one GKP located in Wales. While the GKPs have some overlap in their mandates, each has its own unique program for research and development, education and training, ethical, legal and social issues, commercialization and public engagement.

The trip included visits to the Genetic Knowledge Parks in London, Newcastle and Oxford. CGDN delegates had an opportunity to meet with **Dr. Peter Greenaway** from the Department of Health, and the various group leaders from the London IDEAS (Innovation, Dissemination, Evaluation and Application Strategy for genetics) Park, which focuses on four main projects (Familial Hypercholesterimia, Hypertrophic Cardiomyopathy, breast cancer and smoking cessation). Drs. Gallie and Palaty also visited the Genetic Knowledge Parks in Newcastle, which included a tour of the Learning Labs and the International Center for Life. They concluded their visit at the Oxford Genetic Knowledge Park, which focuses on research into single gene disorders (sudden cardiac death syndrome), complex gene disorders (cardiovascular disease and colorectal cancer), and ethical, legal and social implications of genetics research and public understanding.

Besides a strong Scientific Research mandate, other GKP initiatives include creating a standardized system for genetic testing by incorporating diagnostic tests for predisposing genes in the health care system, education programs for family doctors, patients and families with rare genetic disorders, educating the public about how genetic and lifestyle risk-factors may affect health, and assessing the influence of genetic testing on health outcomes. With many shared goals and values, CGDN looks forward to a strengthening of its relationship and continuing collaborations with the GKP. For more information, please contact Dr. Chrystal Palaty at cpalaty@cgdn.ca. ▲

The Wellcome Trust Centre for Human Genetics, part of the Oxford Genetics Knowledge Park. Photo courtesy of the Wellcome Trust Centre for Human Genetics.

Researchers Discover Gene for Shwachman-Diamond Syndrome

Dr. Johanna Rommens, a Principal Investigator of the Canadian Genetic Diseases Network and Director of the Network's Transcribed Sequence Detection Faciility, has identified a gene that causes Shwachman-Diamond Syndrome. Dr. Rommens is an Associate Professor of Medical Genetics at the University of Toronto and Senior Scientist at The Hospital for Sick Children in Toronto.

The identification of the gene is important because it will allow for accurate diagnosis and screening of Shwachman-Diamond Syndrome. Understanding this new gene will also help us understand how leukemia develops.

Shwachman-Diamond Syndrome (SDS) is a rare genetic disease and patients affected by it experience digestive, blood, and bone problems. Patients with SDS are also susceptible to potentially fatal infections and bone marrow failure leading to leukemia. "The identification of the gene is important because it will allow for accurate diagnosis and screening of Shwachman-Diamond Syndrome. Understanding this new gene will also help us understand how leukemia develops", stated Dr. Rommens. The discovery will also make possible the development of therapies that will benefit SDS patients. ▲

Collaborative Bioinformatics Training Aids Search for Retinoblastoma Defect

Stuart Lithwick,a graduate student working with Dr. Brenda Gallie, received bioinformatics training from Dr. Wyeth Wasserman. Stuart will now use his newly developed skills to search for retinoblastoma gene defects.

Retinoblastoma is a rare form of eye cancer that is observed in children. Much effort has been spent on understanding the disease, testing patients for the disease, and developing effective treatments. **Dr. Brenda Gallie's** team has just published results which indicate that clearly defined mutations in the RB1 gene can be observed in 90% of patients with retinoblastoma. No precise RB1 mutations can be found, due to limitations in technology, in the remaining 10% of patients, even though they are likely to carry a defective RB1 gene. This observation posed a mystery to Dr. Gallie, a CGDN Investigator located in Toronto. She and her graduate student, **Stuart Lithwick**, wanted to know why 10% of RB1 gene defects could not be detected.

Dr. Gallie theorized that in the absence of a detected mutation, regions surrounding the gene that control how much RB1 is produced by retinal cells may be causing the disease. "The idea for the project emerged when I attended the CBW Genomics Workshop in Montreal. I was very excited when I realized that we could use bioinformatics to address this important problem. We decided to use bioinformatics in our approach to identify regions that control RB1 expression. Stuart approached me at just the right time and he was in a position to gain the benefit and fun of bioinformatics", commented Dr. Brenda Gallie, a CGDN Investigator located at the Ontario Cancer Institute in Toronto.

At the time, neither Lithwick or Gallie had applied experience with bioinformatic tools. So in December 2002, Stuart traveled to Vancouver for an intensive, one-week training session in the lab of **Dr. Wyeth Wasserman**, a CGDN investigator who specializes in bioinformatics. "We helped Stuart get going with the basics and pointed him to the resources needed for his analysis. We also game him access to some early stage tools we were developing in our group", stated Dr. Wasserman.

Stuart is presently using his newly developed skills to compare human RB1 sequences to those of mice and rat, and to determine which regions of DNA around the gene are involved in controlling RB1 expression. "The experience I received in the Wasserman lab has been invaluable to my research and I continue to consult with the group on a regular basis", remarked Lithwick.

While still in the early stage of their research, Lithwick and Gallie have identified two potentially important regions near the RB1 gene. They will be assessing whether these regions play a role in disease. They will also be looking to take on new projects in collaboration with Dr. Wasserman, as the two lab groups have established a strong and positive working relationship. ▲

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CGDN Hosts 5th Annual CBW Bioinformatics Workshop

The CGDN recently hosted its fifth annual CBW Bioinformatics workshop from February 17 to March 1 in Vancouver. This intensive 12-day training program was attended by 50 participants from across Canada and the United States. Selected from a pool of over 100 applicants, the class was comprised of researchers from academia, government and industry.

Francis Ouellette (left), CGDN Investigator and Director of the UBC Bioinformatics Centre, stands with keynote speaker Mark Boguski (centre) of the Fred Hutchinson Cancer Research Center and CGDN Associate Investigator Phil Heiter (right).

Held at the UBC's Robson Square, the workshop was coordinated by **Francis Ouellette** (Director, UBC Bioinformatics Centre and CGDN PI / Core Facility Director) and featured lectures and practical lab sessions designed and delivered by a team of leading Canadian experts. Each student was provided with a laptop computer for the duration of the course, and all laptops were given a high speed internet connection and a suite of bioinformatics software and tools. This enabled students to follow along with instructor-led exercises, explore a variety of bioinformatics applications, and complete a number of marked assignments designed to consolidate their understanding of the material.

The primary goal of the workshop was to provide a broad overview of the methodologies, software, tools and databases currently used in bioinformatics. Those who successfully completed the coursework will be eligible for CBW's follow-on courses including Genomics and Proteomics.

The CBW program is a successful collaboration involving more than 40 Canadian bioinformatics experts and up-and-coming experts. Organized by the Canadian Genetic Diseases Network with the leadership of Francis Ouellette, the program has an alumni network of more than 400, with over 600 seats filled since the first workshop in 1999. "Bioinformatics has become a key enabling technology for research in biotechnology, and there is an overwhelming demand for individuals with these skills. CGDN is actively addressing that need with the CBW program" said **Keri Gammon**, Manager of the CBW series.

In response to the tremendous interest in the two-week workshop, CGDN is planning a second offering of Bioinformatics for May 26 – June 7 in Ottawa. The application deadline is March 20, and CGDN members are reminded of their eligibility for tuition bursaries. For more information on the CBW series and the Bioinformatics landscape in Canada please visit www.bioinformatics.ca ▲

ANNOUNCEMENTS

Canadian Genetic Diseases Network
12th ANNUAL SCIENTIFIC MEETING 2003

WHEN: Thursday, May 15th 2003 4:00 p.m. to Sunday, May 18th 2003 noon.

WHERE: Kananaskis Mountain Lodge situated in the beautiful Alberta Rockies. Website: www.kananaskismountainlodge.com

WHO: Network Principal Investigators & Core Facility Directors, Network Associate Investigators & Scholars, Post Doctoral Fellows, Graduate Students, Collaborators, Board Members, Industrial partner scientists and invited guests

WHAT: Scientific presentations, poster sessions and networking. CGDN Annual General Meeting.

Email: jpatrick@cgdn.ca
Fax: 604-221-0778 ▲

Scriver Scientific Symposium and Dinner

The Drs. Walter, Jessie Boyd, and Charles Scriver Scientific Symposium and Dinner will be held on April 10, 2003. The Symposium will take place at the Montreal Children's Hospital, and will feature several invited speakers from both the Network and from the scientific community at large. A no-host dinner, chaired by **Arnold Steinberg**, will take place at the Hôtel Omni Mont-royal. ▲

Vancouver Core Facility Expands
Now offering ES Cell work and Frozen Embryo Implantation

The CGDN Transgenic Mouse Core Facility is now offering 2 new services, ES cell work and frozen embryo implantation. The facility serves both academic and commercial clients, and offers quality service and competitive prices. For more information, access the website (http://cmmt.ubc.ca/core_fac/transgenic/) or contact Dr. Blair Leavitt (bleavitt@cmmt.ubc.ca), L. Munro or T. Davidson (cgdn@cmmt.ubc.ca), phone (604) 875-3837. ▲

bioinformatics.ca

Canadian Bioinformatics Workshops

Organized by the CGDN and hosted nation-wide, this highly acclaimed workshop series is now in its 5th year. Join us in 2003 for one or more of the following:

Bioinformatics
May 26 – June 7, 2003, Ottawa.
Apply by March 20, 2003.

Proteomics
July 7 – 12, 2003, Vancouver.
Apply by May 16, 2003.

Bioinformatics: Introduction to Programming
June 16 – 28, 2003, Vancouver.
Apply by April 26, 2003.

Genomics
August 18 – 23, 2003, Calgary.
Apply by June 20, 2003.
For details, visit
www.bioinformatics.ca ▲