CANADIAN GENETIC DISEASES NETWORK

Leading Gene Discovery

CANADIAN GENETIC DISEASES NETWORK
RÉSEAU CANADIEN DE MALADIES GÉNÉTIQUES

Annual Report 2003

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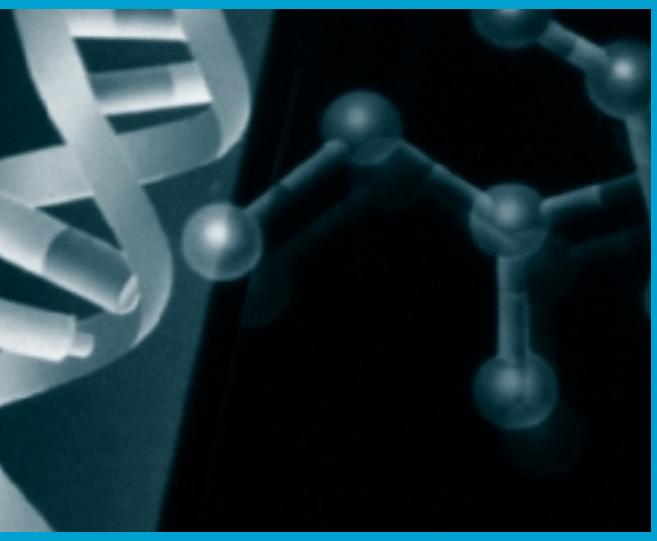

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2003 – A Year of Scientific Excellence

Stakeholders' Letter

In 2002–2003, the Canadian Genetic Diseases Network (CGDN) continued to enhance its well-deserved global reputation for facilitating world-class genetic discoveries. Our ambitious goal of catalyzing scientific excellence continues to be achieved by our foundation of scientific collaboration and innovative training programs. In this reporting period we can see just how significantly both of these founding principles are contributing to our scientific achievements.

Catalyzing partnerships — In Canada and internationally

The spirit of collaboration crossed international borders in 2002 – 03, with CGDN facilitating the creation of memoranda of understanding with other renowned institutions. Our collaboration with the Industrial Technology Research Institute of Taiwan is spawning a new generation of lower cost gene chips, which will make this important technology more widely available in both research and clinical settings.

In Saint Saveur, PQ, the CGDN Annual Scientific Meeting brought together our members for formal scientific presentations and informal discussions, often leading to new collaborations. An account of the discovery of a gene providing resistance to Legionnaire's Disease born out of a conversation at the CGDN's 1996 Annual Scientific Meeting is featured on page 3.

To further solidify our national network of genetic disease researchers, CGDN promotes collaboration by supporting nine core research facilities, which provide services and advice to our members. Training grants are provided to enable Principal Investigators and their students to travel to these facilities and work with the facility scientists.

Increasing Canada's highly-trained personnel

This year, CGDN created the 'Rt. Hon. Ramon Hnatyshyn Youth in Science Initiative — Gene Researcher for a Week' program, enabling 16 high school students to spend their March spring break week in a CGDN laboratory. The goal of the program was to not only encourage the next generation of young Canadians to pursue a career in genetics, but to provide a vehicle to educate Canadians as to the benefits and potential of medical genetics research. As a result of the success of this inaugural year, the program will be expanded to include up to 50 students in March 2004.

Developed in 1999 by Francis Ouellette, a CGDN Investigator and Core Facility Director, the Canadian Bioinformatics Workshop (CBW) program continued to build Canada's bioinformatics capacity by offering a series of intense one and two week courses across the country. Bringing together the disciplines of biology, computer science and mathematics, the CBW series has expanded from one course to five and is now accredited by the University of British Columbia, the University of Toronto and the University of New Brunswick.

In a partnership with the Canadian Gene Cure Foundation and the Canadian Institutes of Health Research, Institute of Genetics, CGDN awarded MD/PhD scholarships to six of Canada's brightest young scientists. Named in honour of Dr. Charles Scriver, an inductee into the Canadian Medical Hall of Fame and his parents, Drs. Walter and Jessie Boyd Scriver, the Scriver MD/PhD Studentship was created to increase the number of clinician-scientists in Canada, those individuals who are able to make discoveries in the lab and translate their new knowledge into improving the health of patients.

Scientific Excellence

Since the creation of CGDN in 1990, Network scientists have discovered more than 50 disease-related genes and many hundreds of clinically relevant genetic mutations. In 2002 – 2003, CGDN investigators discovered genes and gene mutations relating to heart failure, colorectal cancer and diabetes and were especially active in researching genetic conditions affecting

2003 – A Year of Scientific Excellence: Stakeholders' Letter

young children such as Shwachman-Diamond Syndrome, Leigh Syndrome and several inborn metabolic disorders.

CGDN research covers a wide range of disease areas and supports the creation of new, cutting-edge technologies. Some of this research has the potential to increase the efficacy of cancer therapy, as evidenced by the research conducted by Dr. Robert Korneluk at the Children's Hospital of Eastern Ontario. Other research brings the promise of better diagnosis for rare conditions caused by genetic mutations. A discovery in the laboratory of Dr. Michael Hayden at the University of British Columbia suggests a potential therapeutic target for heart disease, while another discovery, by Dr. Peter St. George-Hyslop at the University of Toronto, increases our understanding of neuronal functioning.

Network scientists published more than 250 peer-reviewed articles in 2002 –03 in such prestigious journals as Nature Genetics, Cancer, American Journal of Human Genetics and the New England Journal of Medicine.

World-renowned scientists

CGDN members are dedicated scientists who embrace collaboration. They are influential mentors who take the time to train young scientists with a hope of sparking their interest in genetic research. In this period, CGDN scientists won national and international awards, including the Queen's Golden Jubilee medal (Diane Cox, University of Alberta; David Maclennan, University of Toronto), the Samuel Rosenthal Prize for Excellence in Academic Paediatric Research (Rod McInnes, Hospital for Sick Children, Toronto) and an Honorary Doctorate at the University of British Columbia (Charles Scriver, McGill University, Montreal).

CGDN made important additions to our membership at both principal and Associate Investigator level in 2002 – 03. We are also pleased to welcome Dr. Emőke J.E. Szathmáry to our Board of Directors. Dr. Szathmáry is the President and Vice-Chancellor of the University of Manitoba, an anthropologist with particular expertise in the genetics of native North Americans.

Looking forward

CGDN will continue to build on its successes, as though tremendous progress has been made, there is still much work to be done.

The scientific success of the CGDN has given its Board of Directors the confidence to declare that the Network will continue to operate as a not-for-profit research corporation beyond the end of its NCE funding program in 2005. Over the next year, the Board and management will be working to develop options for continued funding post 2005.

We are able to look forward to an exciting time ahead, knowing that we have a firm foundation in place on which to base our future success.

The Rt. Hon.
Don Mazankowski, PC, OC
Chairman of the Board

Dr. Ron Woznow
Chief Executive Officer

Dr. Michael Hayden
Scientific Director

A CGDN Collaboration

Yielding Clues into Legionnaire's Disease

In collaboration with Dr. Alex MacKenzie, Dr. Philippe Gros and Dr. Sylvia Vidal identified the gene, Naip5 that provides clues into human resistance to Legionnaire's Disease. First occurring at a 1976 Legionnaire's Convention in Philadelphia, Pennsylvania, Legionnaire's Disease (LD) is a severe form of pneumonia caused by infection with Legionella bacteria. The LD bacterium is typically transmitted to humans through air conditioning cooling units, showers and faucets. Approximately 10–15% of LD infections are fatal.

Dr. Alex Mackenzie, a CGDN investigator at the Children's Hospital of Eastern Ontario in Ottawa, first identified Naip5 during his research on Spinal Muscular Atrophy. The collaboration leading to this breakthrough was initiated at the CGDN's 1996 Annual Scientific Meeting, when Dr. Mackenzie and Dr. Gros exchanged ideas.

"The fact that the seed for this discovery was set at our Annual Scientific Meeting speaks to the strength of CGDN's collaborative research program," stated Dr. Michael Hayden, Scientific Director of the Canadian Genetic Diseases Network, "This discovery is an important step towards the development of innovative treatments for Legionnaire's Disease."

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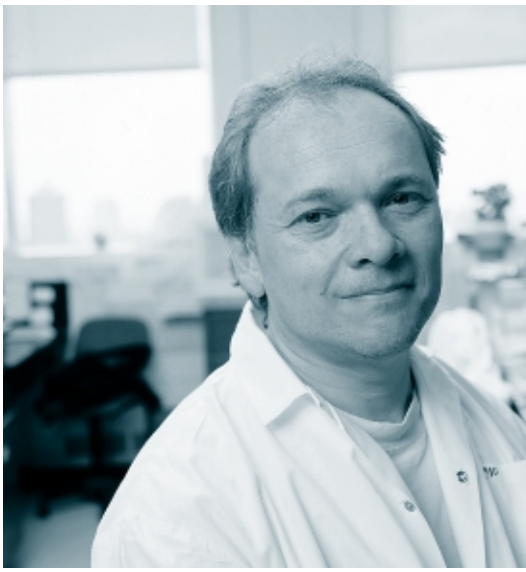

Dr. Philippe Gros, a CGDN Principal Investigator and scientist at the McGill University Health Centre, identified a gene that makes mice resistant to Legionnaire's Disease.

Catalyzing the Wide-Spread Application of Gene Chips

Improving Health Care Services in Canada

Dr. Stephen Scherer, a CGDN Principal Investigator and Scientist at Toronto's Hospital for Sick Children, assisted in the design and testing of the gene chip.

Gene chips, an exciting new technology for health research and clinical diagnostics, have the potential to improve the quality of health care services for Canadians. In 2002–2003, CGDN played a leading role in facilitating the development of low-cost chips, in partnership with leading international researchers.

The Canadian Genetic Diseases Network and the Hospital for Sick Children are collaborating with the Industrial Technology Research Institute of Taiwan (ITRI) to develop gene chips for research and diagnostic applications. This collaboration grew out of a Memorandum of Understanding signed by ITRI and CGDN in 2001. Dr. Stephen Scherer, a CGDN Principal Investigator and Scientist at Toronto's Hospital for Sick Children, assisted in both the design and testing of the new generation of chips. The chips will be manufactured using technology developed by ITRI and are expected to significantly reduce production costs as well as catalyze the widespread application of gene chips in both research and clinical settings.

Gene chips produced through this agreement promise a number of important health benefits for Canadians. Scientists will gain access to an affordable resource for studying disorders such as cancer, diabetes, heart disease, autism and epilepsy. This cost-effective platform for performing diagnostic tests provides a means for doctors to test patients for multiple genetic disorders using a single array, enabling an early diagnosis.

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Global Benefit from Identification of Susceptibility Gene

One Step Closer to Eradicating Leprosy

Leprosy is a chronic infectious disease that affects nearly 1 million people worldwide. While not prevalent in North American communities, it is a significant health concern in Southeast Asia, Africa, and South America. People infected by the Leprosy bacteria develop pigmented skin lesions, nerve damage and gross disfiguration often resulting in the loss of fingers, toes, feet and hands. The leprosy bacteria are transmitted through direct personal contact or contaminated respiratory droplets.

An international research team, led by CGDN scientists Drs. Erwin Schurr and Thomas Hudson, discovered a gene on human chromosome 6 that renders people susceptible to Leprosy. By studying a Vietnamese population, Schurr and his colleagues determined that people with one form of the gene could get Leprosy while those with a different form of the gene could not develop the disease.

This discovery will enable Dr. Schurr to study the gene to determine how it functions and influences the infection process, prerequisites to the development of innovative prevention and treatment strategies for this global health issue.
Scientists will also be looking for ways to apply the gene identification strategies used in this discovery with research into other common infectious diseases such as tuberculosis and malaria.

This discovery will enable Dr. Schurr to study the gene to determine how it functions and influences the infection process, prerequisites to the development of innovative prevention and treatment strategies for this global health issue.

Dr. Erwin Schurr, a CGDN Principal Investigator and Scientist at the McGill University Health Centre, led a team that identified a gene that makes people susceptible to Leprosy.

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A Year of Scientific Excellence

"To be the primary catalyst in advancing Canada's scientific and commercial competitiveness in genetic research."

In 2002 – 2003, CGDN strengthened its capacity for research excellence by inviting new Principal Investigators to join the network and continuing to support its core research program. The scientific output of CGDN members was outstanding in 2002 – 2003 — its scientists published more than 250 scientific research papers in peer-reviewed journals.

Another strength of CGDN is the collaboration among its scientists. By organizing meetings and symposia for Network members, CGDN has created a Canada-wide community of genetic disease researchers with access to Core Facilities and an Annual Scientific Meeting. CGDN-sponsored training grants enable CGDN Principal Investigators and students to travel to other Network labs. The CGDN was pleased to co-sponsor an external networking opportunity on November 9 –10, 2002, the CIHR's first annual New Principal Investigators meeting in Jackson's Point, Ontario. These initiatives provided opportunities for CGDN members to work together to create collaborative relationships, share knowledge and advance genetic discovery in Canada.

Scientific Membership — Members and Scholars 2002

CGDN's scientists are responsible for the Network's research excellence. During the last year, the Network made several additions to its membership, inviting four scientists the CGDN network at the Principal Investigator level after an extensive peer-review process. The CGDN welcomes Moira Glerum (University of Alberta), Elise Héon (Hospital for Sick Children, Toronto), Eric Shoubridge (McGill University) and Wyeth Wasserman (Centre for Molecular Medicine and Therapeutics, UBC). Two scientists were invited to join the network at the Associate investigator level, Daniel Sinnett (Université de Montréal) and Sylvia Vidal (University of Ottawa). In recognition of their scientific abilities, CGDN's Core Facility Directors were invited to compete in a competition to receive funding as Principal Investigators (PI). These new PI's include Blair Leavitt, Francis Ouellette, Johanna Rommens and Stephen Scherer.

CGDN's Scientific Membership

Susan Andrew	Scholar	University of Alberta
Keith Ashman	Core Facility Director	Mt. Sinai Hospital Research Institute, Toronto)
Dennis Bulman	Scholar	Ottawa Health Research Institute
Lorne Clarke	Investigator	CMMT, University of British Columbia
Diane Cox	Investigator	University of Alberta
Jayne Danska	Investigator	Hospital for Sick Children, Toronto
John Dick	Investigator	Hospital for Sick Children, Toronto
Regen Drouin	Core Facility Director	Université Laval

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Leigh Field	Investigator	University of British Columbia
William Foulkes	Investigator	McGill University, Montreal
Brenda Gallie	Investigator	University Health Network, Toronto
Moira Glerum	Investigator	University of Alberta
Roy Gravel	Investigator	University of Calgary
Celia Greenwood	Scholar	Hospital for Sick Children, Toronto
Philippe Gros	Investigator	McGill University, Montreal
Michael Hayden	Investigator, Core Facility Director	CMMT, University of British Columbia
Rob Hegele	Investigator	Robarts Research Institute, Toronto
Elise Héon	Investigator	Hospital for Sick Children, Toronto
Geoff Hicks	Investigator	University of Manitoba
Tom Hudson	Investigator Core Facility Director	McGill University & Genome Quebec Innovation Centre
Frank Jirik	Investigator	University of Calgary
Bob Korneluk	Investigator	Children's Hospital of Eastern Ontario
Blair Leavitt	Investigator, Core Facility Director	CMMT, University of British Columbia
Corrinne Lobe	Core Facility Director	Sunnybrook & Women's College Health Sciences Center
Alex Mackenzie	Investigator	Children's Hospital of Eastern Ontario
David MacIennan	Investigator	University of Toronto
Rod McInnes	Investigator	Hospital for Sick Children, Toronto
Grant Mitchell	Investigator	Hôpital Sainte-Justine, Montreal
Ken Morgan	Investigator	McGill University, Montreal
Steven Narod	Investigator	University of Toronto
Francis Ouellette	Investigator, Core Facility Director	CMMT, University of British Columbia
Christopher Pearson	Scholar	Hospital for Sick Children, Toronto
Brian Robinson	Investigator	Hospital for Sick Children, Toronto
Johanna Rommens	Investigator, Core Facility Director	Hospital for Sick Children, Toronto
Guy Rouleau	Investigator	McGill University, Montreal
Francois Rousseau	Investigator	Centre hospitalier universitaire de Québec
Rima Rozen	Investigator	McGill University, Montreal
Stephen Scherer	Investigator, Core Facility Director	Hospital for Sick Children, Toronto
Erwin Schurr	Investigator	McGill University, Montreal
Charles Scriver	Investigator	McGill University, Montreal
Eric Shoubridge	Investigator	McGill University, Montreal
Kathy Siminovitch	Investigator	Mt. Sinai Hospital Research Institute, Toronto
Emil Skamene	Investigator	McGill University, Montreal
Peter St.George-Hyslop	Investigator	University of Toronto
Barbara Triggs-Raine	Investigator	University of Manitoba
Lap-Chee Tsui	Investigator	Hospital for Sick Children, Toronto
Michael Walter	Investigator	University of Alberta
Wyeth Wasserman	Investigator	CMMT, University of British Columbia
Rachel Wevrick	Scholar	University of Alberta
John Wilkins	Core Facility Director	University of Manitoba
Ron Worton	Investigator	Ottawa Health Research Institute

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Scientific Research Projects – Disease Areas and Core Facilities

CGDN's research areas range from developmental disorders affecting children before birth to genetic diseases of the elderly and involve every part of the body, affecting development, movement, metabolism, cognitive function, eyesight, digestion, cardiac function and respiration. The effects of the diseases range from subtle physical manifestations to life-threatening complications.

The technologies and approaches used by CGDN scientists for their research are broad and include molecular biology and microarrays, transgenic animals and bioinformatics. Bioinformatics, the use and development of tools for computation biology research, is a cutting-edge technology used to manage, analyze and understand enormous data sets and document the presence and impact of gene mutations in large populations over time.

Technology Access

Nine Core Facilities across Canada were supported by the CGDN in 2002 – 2003 which facilitate the development of innovative genetic technologies and provide access to these innovative technologies to its members. A list of the CGDN Core Facilities and their directors is shown below.

Core Technologies	Directors
Bioinformatics	F. Ouellette (Vancouver)
DNA sequence analysis	M. Hayden (Vancouver), S. Scherer (Toronto)
ES Cell-mediated genome alterations	C. Lobe (Toronto)
Genotyping	T. Hudson (Montreal)
Immunoprobes	J. Wilkins (Winnipeg)
In vivo DNA analysis	R. Drouin (Quebec)
Transcribed sequence detection	J. Rommens (Toronto)
Transgenic Mouse	B. Leavitt (Vancouver)
Proteomics	K. Ashman (Toronto)

Technologies and Applications

CGDN scientists are also developing innovative technologies and approaches to study genetic diseases. Some of these innovative approaches include the following: Gene therapy strategies (viral vectors, retrovirus-mediated gene therapy, enzyme substitution), Mutation databases, Mutation analysis in populations, Mutation detection technology, Complex traits analysis in mice, Statistical methodologies, Expression studies using high-density arrays, Bioinformatics applications for novel disease gene associations, gene regulation and ES cell analysis.

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CGDN's 2002 – 2003 Disease Research Areas

Below is a list of the disease research areas studied by CGDN scientists in 2002 – 2003. Because of the nature of disease and the differing approaches taken, some diseases are classified in multiple locations.

Neoplasia	Retinoblastoma, sporatic and inherited breast cancer, ovarian cancer, risk factors for breast cancer, squamous cell carcinoma of the head and neck, epithelial cancer, inherited mitochondrial disorders, understanding cancer causing pathways in cells, cancer risk factors and prevention
Cardiovascular	Atherosclerosis, early onset coronary artery disease, calcium dysregulation, cardiomyopathy, familial polymorphic ventricular tachycardia, HDL/lipids
Cognitive	Schizophrenia
Developmental/congenital defects	Bowen-Conradi syndrome
Gastrointestinal/hepatic	Cystic Fibrosis, inflammatory bowel disease, Crohns disease, colon cancer, liver diseases — North American Indian childhood cirrhosis, hepatorenal tyrosinemia, hemochromatosis, Wilson disease
Hematological/Immune	Fanconi Anemia, SCID, iron deficiency
Metabolic/Endocrine	Type 2 diabetes, Type I diabetes, obesity, homocystinuria, methylenetetrahydrofolate reductase deficiencies, hyperphenylalaninemia, inherited mitochondrial disorders, respiratory chain deficiencies, Tay-Sachs and Sandhoff disease, cobalamin C deficiency, mucopolysaccharidosis types I and IX, deficiencyfamilial partial lipodystrophy, HDL, lipid metabolism
Neurodevelopment and neurodegeneration	Alzheimer disease, dementia, inherited mental retardation, Fragile-X syndrome, Huntington disease, autism, Phonological Coding dyslexia (PCD), neurodegenerative diseases, autism, inherited mitochondrial disorders, cytochrome oxidase deficiency, Leigh syndrome, Shwachman-Diamond syndrome, ACCPN (peripheral neuropathy associated with agenesis of the corpus callosum), Williams-Beuren syndrome, Wilson disease
Neuromuscular	Myotonic dystrophy, muscular dystrophy, spinal muscular atrophy, inherited epilepsy, autosomal recessive ataxia, Brody disease, calcium dysregulation, autosomal recessive ataxia, spinocerebellar ataxia
Ocular	Retinoblastoma, glaucoma, macular degeneration, corneal dystrophies, inherited retinal degeneration, cataracts, developmental eye defects
Reproductive	Infertility
Respiratory	Cystic Fibrosis, asthma
Bone and joint	Rheumatoid arthritis, osteoporosis, hereditary hypophosphatemic rickets
Host response to infection	Vaccine responsiveness, sepsis, cysticercosis, tuberculosis, leprosy, salmonella, Legionnaire disease, CMV, malaria

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Scientific Research Highlights

The research mandate of the CGDN falls into four related research themes: Identification of the Genetic Basis of Human Disease, Pathogenesis and Functional Genomics, Genetic Therapies and Genetics and Health Care. These four themes exist on a continuum, with the discovery of genes and gene mutations contributing to an understanding of disease mechanisms. In turn, this understanding leads to the development of novel therapies, which make a positive impact on patient health care.

CGDN's greatest success has been in the area of gene identification, resulting in international recognition that the CGDN is the leading organization for the identification of the genetic basis of human disease. In the last thirteen years, Network scientists have discovered over fifty disease-related genes and many hundreds of important gene mutations influencing human disease. Below is a selection of the scientific highlights of this reporting period (April 2002 – March 2003), classified according to disease areas.

NEOPLASIA

Evaluation of Prophylactic oophorectomys in carriers of BRCA1 or BRCA2 mutations.

(S. Narod, University of Toronto)

Women with mutations in the BRCA1 or BRCA2 genes have an increased risk of breast and ovarian cancer as compared to the general population. To reduce the risk of ovarian cancer, these women often have a bilateral prophylactic oophorectomy (removal of both ovaries). Previously, there was very little data available to suggest that removal of the ovaries was effective in reducing the risk of developing cancer. This study examined a total of 551 women with BRCA1 or BRCA2 mutations for occurrences of ovarian and breast cancer: 259 patients had a prophylactic oophorectomy and 292 patients had another form of treatment. In these subjects, bilateral prophylactic oophorectomy reduced the risk of coelomic epithelial cancer by 85 percent and breast cancer by 25 percent, in women with BRCA1 or BRCA2 mutations. On the basis of this data, the authors advocate the use of prophylactic oophorectomy to reduce the risk of ovarian and breast cancer in patients with these mutations. *(New England Journal of Medicine, May 2002).*

Understanding how other genes influence the survival of BRCA1 mutation carriers.

(W. Foulkes, McGill University)

A study was conducted in a large group of breast cancer patients to examine how the expression of a tumor suppressor gene and the presence of a cancer-causing mutation influenced the long-term survival of Ashkenazi Jewish women with breast cancer. The *TP53* tumor suppressor gene, which encodes the p53 protein, is one that has been implicated in human malignancies. This study highlighted some of the difficulties in assessing the predictive value of gene mutations on patient prognosis, as many patients had undergone different therapies including chemotherapy, hormonal therapy and oophorectomy, which had influenced the outcome of the disease. The study concluded that both the presence of BCRA1 mutations and p53 expression levels have prognostic and predictive value in breast carcinoma. *(Cancer, February 2003).*

A novel Ubiquitin fusion system generates biologically active Smac/DIABLO protein.

(R.G. Korneluk, Children's Hospital of Eastern Ontario).

One characteristic of cancer cells is that they become immortalized and are unable to respond to the apoptotic signals that would cause normal cells to die. The Smac/DIABLO proteins have a role in the apoptotic signaling pathways, and inhibit the IAP (Inhibitor or Apoptosis) proteins, which in turn inhibit the caspases

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involved in the initiation of the apoptotic cascade. This paper describes the development of a novel ubiquitin-fusion system, which generates biologically active, cytoplasmically localized Smac/DIABLO in transfected cells. The cells containing the expressed Smac protein are sensitized to apoptotic triggers; overexpression of this protein in cancer cells may sensitize these cells to chemotherapy. In the future, this may increase the efficacy of cancer therapies. *(Journal of Biological Chemistry, February 2003).*

CARDIOVASCULAR

Atherosclerosis — increased ABCA1 activity is protective against atherosclerosis.

(M. Hayden, Center for Molecular Medicine and Therapeutics, UBC, Vancouver)

Overexpression of the human ABCA1 protein in transgenic mice has been shown to cause a mild elevation of plasma HDL levels and increased efflux of cholesterol from macrophages. This study examined the effect of ABCA1 in the development of atherosclerosis, by over-expressing the protein in a strain of transgenic mice (ApoE-/-), which spontaneously develop atherosclerotic lesions. Increasing expression levels of ABCA1 in the mice resulted in significant protection against atherosclerosis; the mice developed smaller lesions, and showed a slight increase in both plasma HDL cholesterol levels, and phospholipid levels as compared to controls. This study highlights the value of ABCA1 a potential therapeutic for heart disease in the future. *(The Journal of Clinical Investigation, July 2002).*

GASTROINTESTINAL/HEPATIC

Identifying the cause of a hereditary liver disease, NAIC (North American Indian childhood cirrhosis).

(G. Mitchell, Hôpital Ste-Justine, Montreal; T. Hudson, McGill University and Genome Quebec Innovation Centre)

North American Indian childhood cirrhosis (NAIC) is a severe liver disease occuring in Ojibway-Cree communities. It is often fatal unless a liver transplant can be done in childhood or early adulthood and until now, the causes of this disease were unknown. An analysis of single nucleotide polymorphisms (SNPs) was used to identify a missense mutation (R565W) in a region encoding a hypothetical protein, FLJ14728. This mutation (1741C>T) causes an amino acid change from an arginine residue to a tryptophan, which is likely to result in a conformational and functional change in the protein. This region was named the *cirhin* gene and was shown to be associated with the disease, as all 74 NAIC patients examined had two copies of the mutation. The expression patterns of *cirhin* are consistent with liver development, but a specific function for the protein is not yet established. This is the first time that a cause for this disease has been identified and it promises to lead to new strategies for prevention and treatment of this disease. *(American Journal of Human Genetics, December 2002).*

NEURODEVELOPMENT AND NEURODEGENERATION

Identification of the *SLC12A6* gene mutated in ACCPN (peripheral neuropathy associated with agenesis of the corpus callosum).

(G.A. Rouleau, McGill University

ACCPN (peripheral neuropathy associated with agenesis of the corpus callosum) is an inherited disease affecting every 1/2000 people in Quebec. The symptoms of the disease appear to result from both a developmental defect and a degenerative condition, compromising both mental and physical abilities and dras-

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tically shortening the lifespan of patients. The gene causing this disease, *SLC12A6*, was discovered, and all ACCPN patients examined were found to have mutations in *SLC12A6*. *SLC12A6* is located on chromosome 15 and encodes KCC3, an ion cotransport protein. While the mutations were shown to inactivate the function of the protein, it is not clear how this contributes to the symptoms displayed by ACCPN patients; it is likely that other genes and/or environmental factors are involved. An animal model to study this disease was created by 'knocking out' the KCC3 gene in mice. This will not only allow further work to be done to understand the causes of this disease, but will provide insights into the normal role of KCC3 in development and normal neuronal functioning. *(Nature Genetics, November 2002).*

Discovering mutations in the SBDS gene causing Shwachman-Diamond syndrome.

(J. Rommens, Hospital for Sick Children Toronto)

Shwachman-Diamond syndrome is a rare genetic disease, usually diagnosed in the first few years of life and characterized by a failure to thrive, feeding problems and recurrent infections. The disease involves several organs, but primarily the skeleton, bone marrow and pancreas. Continuing their previous work, Dr. Rommens and her team identified the SBDS gene and identified disease-associated mutations in the SBDS gene. The majority of the Shwachman-Diamond Syndrome patients analyzed had very similar mutations in the SBDS gene, resulting from a nonreciprocal transfer of genetic information from a locally duplicated pseudogene, SBDSP. The protein encoded by the SBDS gene is a member of highly conserved protein family, with no known function and no similarities to any known functional domains. They concluded that these mutations cause Shwachman-Diamond syndrome and suggest that these mutations cause a defect in RNA metabolism. This discovery will allow patients with this syndrome to be diagnosed more readily and will offer hope for a therapy to be developed eventually for these patients. *(Nature Genetics, January 2003).*

Alzheimer disease risk is modified by the nicastrin gene.

(P. St George-Hyslop, University of Toronto)

Alzheimer's Disease (AD) is characterized by the formation of neuritic plaques and lesions in the brain. The neuritic plaques are composed mainly of amyloid ß-peptide, which is generated by the ß- and γ-secretase cleavage of the amyloid precursor protein (APP). Mutations in APP and presenilins have previously been shown to cause a familial early-onset type of AD (EOAD). Nicastrin, a transmembrane glycoprotein, has been shown to regulate the γ-secretase dependent cleavage of the APP. The gene encoding nicastrin (NCSTN) maps to 1q23, a region that has been linked and associated with late-onset Alzheimer disease (LOAD). In this study, the contribution of genetic variations in the NCSTN gene in the occurrence of AD was investigated using mutation screening in AD patients. This research provided evidence that mutations in NCSTN do not frequently lead to EOAD, and that NCSTN itself does not seem to be responsible for the association of the gene region 1q23 with LOAD. However, one specific NCSTN haplotype, or gene variation, significantly modified the risk of developing familial EOAD, particularly in those cases where other genetic mutations were present. These results emphasize the important role of γ-secretase dysfunction in AD, and highlight the complexities of determining the genetic contributions in multi-genetic disorders. *(American Journal of Human Genetics, June 2002).*

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OCCULAR

Identification of the common molecular origin of two corneal disorders leading to blindness (Posterior polymorphous dystrophy and keratoconus).

(E. Heon, University Health Network, Toronto; R McInnes, Hospital for Sick Children, Toronto)

Clear vision depends upon establishing corneal transparency in early development and maintaining it through life. Posterior polymorphous dystrophy (PPD) and keratoconus are two types of corneal disorders leading to visual impairment. A common molecular basis for these two diseases was identified; at least four (and possibly six) mutations were identified in the VSX1 coding region of patients with PPD and/or keratoconus, but not other corneal dystrophies. The VSX1 gene is a member of the Vsx1 group of paired-like homeodomain transcription factors and contains a highly conserved CVC domain of unknown function. The mutations affecting the CVC domain were shown to be functionally important. Since the VSX1 gene was not expressed in the adult cornea, it is either expressed only in the developing cornea, or is expressed in a non-corneal cell type for the production of a signaling molecule essential for normal corneal development and maintenance. Understanding the role of this gene provides insight into the development of the eye as well as provides therapeutic directions for treatment of corneal dystrophies. *(Human Molecular Genetics, May 2002)*.

A sensitive and efficient method for detection of the Retinoblastoma mutation improves care for Retinoblastoma patients and reduces health care costs.

B. Gallie, University Health Network, Toronto).

Retinoblastoma is a tumour of the eye in children, caused by inherited and/or spontaneous mutations in the human retinoblastoma susceptibility gene, RB1. Knowing the molecular nature of RB1 mutations is important for earlier treatment, reducing disease risk and enabling better outcomes for retinoblastoma patients and their families. A sensitive and efficient method to detect RB1 mutation using a combination of sophisticated molecular techniques and statistical programming was developed. Using this method reduced the estimated turnaround time for testing to less than three weeks, reduced the estimated surveillance costs for screening in family members, and has a sensitivity of 89%, the highest yet reported. In addition, more than 450 mutant alleles were identified, world "best practice" standards were set for this gene and the health care quality for the families was improved, in that affected babies avoided loss of eyes with less toxic therapy. To deliver the benefits of this work, affected families and their supporters created a non-profit organization called Retinoblastoma Solutions, which has a goal to promote research and clinical testing for retinoblastoma families internationally. Retinoblastoma Solutions is assisting labs in Germany, Australia and India to improve their retinoblastoma test sensitivity. Our hope is that this information will enable RB1 mutation detection to be more widely implemented in Canada and around the world. *(American Journal of Human Genetics, February 2003)*.

Honor Roll

Recognition Of Excellence In Research

In 2002 – 2003, CGDN scientists and their teams received top Canadian and international awards for excellence in science. A list of those awards received by CGDN PI's, Associates and Scholars is found below.

Academic Women's Association (AWA) Woman of the Year Award
Diane Cox, University of Alberta

Alberta Heritage Foundation for Medical Research
Senior Scholar Independent Investigator Salary Award
Rachel Wevrick, University of Alberta

Association for Research in Vision and Ophthalmology's Cogan Award
Michael Walter, University of Alberta

Burroughs Wellcome Fund
Visiting Professorship in the Basic Medical Sciences Award
Steve Scherer, Hospital for Sick Children
Clinician Scientist Award
Tom Hudson, McGill University
Canada Council Killam Prize
Lap-Chee Tsui, Hospital for Sick Children

Canadian Congress of Neurological Sciences – Penfield Lecturer 2002
Michael Hayden

Canadian Diabetes Association Great-West Life Scientist of the Year
Robert Hegele, Robarts Research Institute

Canadian Institute for Advanced Research Explorer Award
Steve Scherer, Hospital for Sick Children

Canadian Institutes of Health Research Investigator Award
Tom Hudson, McGill University
Michael Smith Prize in Health Research
Tony Pawson, University of Toronto

Canadian Neurological Society Richardson Lectureship
Peter St. George-Hyslop, University of Toronto

Canadian Research Chair in Stem Cell Biology
John Dick, University Health Network

Chair François-Karl Viau in Pediatrics Oncogenomics
Daniel Sinnett, Université de Montréal

Directorship, UBC Bioinformatics Centre (UBiC)
Francis Ouellette, University of British Columbia

Fellow of the Royal Society of Canada
Peter St. George-Hyslop, University of Toronto

Fonds de la recherché en santé du Québec
Senior Investigator Scholarship
Regin Drouin, Francois Rousseau – Centre hospitalier universitaire de Québec

Genetics Society of Canada Young Scientist Award
Steve Scherer, Hospital for Sick Children

Heart and Stroke Foundation of Ontario – Rich Gallop Award
David MacLennan, University of Toronto

Howard Hughes Medical Institute International Scholar
Robert Korneluk, University of Ottawa, Michael Rudnicki, Ottawa Health Research Institute, Steve Scherer, Hospital for Sick Children, Eric Shoubridge, McGill University, Peter St. George-Hyslop, University of Toronto

Leiden University – Netherlands; The 5th Boerhaave Medal
John Dick, University Health Network

Merck Clinician-Scientist Award
Robert Hegele, Robarts Research Institute

McGill University
James McGill Professorship
Eric Shoubridge, McGill University.

President, Board of Directors, National Cancer Institute of Canada
Brenda Gallie, Hospital for Sick Children

Prix du Jeunes Chercheur Club de Recherches Cliniques du Québec 'André-Dupont 2002'
Tom Hudson, McGill University

Prix Fondation Armand-Frappier Prix de la Santé
Tom Hudson, McGill University

Prix Galien Canada
Tony Pawson, University of Toronto

Premier of Ontario's Platinum Medal for Research Excellence
Tony Pawson, University of Toronto

Premier's Research Excellence Award
Dennis E. Bulman, Ottawa Health Research Institute
Jayne Danska, Hospital for Sick Children

Queen's Golden Jubilee Medal
Diane Cox, University of Alberta; David MacLennan, University of Toronto

Samuel Rosenthal Prize for Excellence in Academic Pediatric Research
Rod McInnes, Hospital for Sick Children

Salute to the City of Toronto Award
David MacLennan, University of Toronto

Society for Neuroscience
Gass Traveling Scientist Lectureship
Peter St. George-Hyslop, University of Toronto

University of British Columbia
Honorary Doctorate
Charles Scriver, McGill University

University of Hong Kong
Vice Chancellor
Lap-Chee Tsui, Hospital for Sick Children

University of Western Ontario
Faculty of Medicine and Dentistry Award of Excellence
Robert Hegele, Robarts Research Institute
Kenneth K. Caroll Lectureship
Peter St. George-Hyslop, University of Toronto
World Innovation Foundation
Honorary Member
Lap-Chee Tsui, Hospital for Sick Children

Training Report

Committed to building Canada's capacity of highly trained genetic researchers, the Canadian Genetic Diseases Network coordinates innovative interdisciplinary training programs such as the Canadian Bioinformatics Workshops series. To enhance the expertise of senior researchers and develop the skills of junior scientists, CGDN coordinates an Annual Scientific Meeting and offers summer studentships and scholarships.

Canadian Bioinformatics Workshops

The Canadian Bioinformatics Workshops (CBW) was initiated in 1999 by CGDN in partnership with the Biotechnology Human Resource Council (BHRC) and Human Resources Development Canada (HRDC). CBW is a national, short-course program taught by leading bioinformatics experts with the goal of addressing the critical shortage of researchers with skills in bioinformatics. Since the original workshop in August 1999, more than 580 seats have been filled by biologists and computer scientists from academia and industry.

In 2002 – 2003, with the demand for training high, 172 people registered from across Canada in CBW. The workshops offered were Bioinformatics (50 students), Proteomics (45 students), Developing the Tools (16 students), Genomics (45 students) and Bioinformatics: Intro to Programming (16 students). Twenty-five students completed the "Certificate in Bioinformatics" which is accredited by the Faculties of Science and Medicine at the University of British Columbia and the University of New Brunswick and recognized by the Continuing Medical Education Office of the University of Toronto and the Royal College of Physicians and Surgeons of Canada. To achieve the "Certificate in Bioinformatics", students must successfully complete the Bioinformatics workshop as well as two additional CBW courses: Proteomics, Genomics or Developing the Tools.

In 2002 – 2003, the Burroughs Wellcome Fund, a strong supporter of CBW, contributed $65,000 for student bursaries enabling studentships of between $1200 and $5000 for thirty graduate students. In addition 30 personnel from CGDN labs — graduate students, postdoctoral fellows and Principal Investigators — attended the workshops and received bursaries of $500 from the CGDN.

The CBW series not only increases the bioinformatics capabilities of genetic researchers in Canada and abroad, but it increases the number of trained bioinformatics teaching professionals in Canada. In 2002 – 2003, 4 CGDN PI's and 6 personnel from Network labs participated in the CBW series as instructors, teaching assistants and systems support, the majority of whom have taken courses in the CBW series.

Network Scholars

The CGDN Scholars Program provides young scientists with an opportunity to network and collaborate, with senior Network investigators. Scholars have access to support from CGDN through strategic funds, core facilities, summer studentships, training grants and the Annual Scientific Meeting, but not core research grants. CGDN currently supports five scholars; Susan Andrew (University of Alberta), Dennis Bulman (University of Ottawa), Celia Greenwood (McGill University), Christopher Pearson (Hospital for Sick Children) and Rachel Wevrick (University of Alberta).

Training Report

The Drs. Walter, Jessie Boyd & Charles Scriver MD/PhD Studentship Award

In 2002, in a partnership between the CGDN, the Canadian Gene Cure Foundation and the Canadian Institutes of Health Research, Institute of Genetics, the Drs. Walter, Jessie Boyd & Charles Scriver MD/PhD Scholarship Program was created. The objective of this MD/PhD scholarship program is to increase the number of clinician-scientists in Canada in the areas of genetics and gene-related diseases. Six scholarships were awarded in September of 2002, each one valued at $20,000 per year for six years. Recipients include Christopher George Carlson and Jason Thomas Maynes from the University of Alberta, Sebastien Levesque and Julie St. Pierre from Centre hospitalier universitaire de Québec, Speranza Dolgetta from the University of Calgary and Martin Hyrcza from the University of Toronto. A second group of scholarship recipients will be selected in 2003.

Summer Studentships and CGDN Training Grants

The Network's Summer Studentship Program enables undergraduates to gain hands-on research experience in CGDN laboratories. In 2002 – 2003, the Network awarded fifteen studentships to undergraduate students. Past recipients of the award have gone on to graduate studies, medical school, MD/PhD programs and careers in scientific research. CGDN also provides grants for CGDN members and their staff to travel to other CGDN laboratories for the purposes of training and collaboration.

CGDN's 11th Annual Scientific Meeting

From April 4–7, 2002, 150 members attended the CGDN's 11th Annual Scientific Meeting at Manoir St. Saveur in Quebec. Over the three days, attendees presented their research results, attended lectures from guest speakers, including Canadian director, Anne Wheeler, reviewed posters submissions and networked. More than 70 graduate students were given the opportunity to interact with CGDN scientists and learn about their research and in turn, display a poster detailing their own research. Five students were invited to give a formal presentation of their research and field questions from CGDN scientists and their peers.

New Resources for Network members

Continually looking for opportunities to enhance the capacity of its members, CGDN, on the recommendation of Dr. Charles Scriver, a founding member of the Network, purchased a subscription to the online version of the *Metabolic and Molecular Basis of Inherited Disease* (MMBID). The MMBID is recognized as the definitive resource for genetic disease researchers and physicians and describes the molecular and biochemical basis, pathogenesis and therapeutic approaches to hundreds of diseases.

Nurturing new talent

Strengthening Canada's Bioinformatics Community

February 2003 saw the completion of the fifth annual Bioinformatics course, an integral component of the CGDN's Canadian Bioinformatics Workshops (CBW) Series. Fifty students spent two intense weeks learning computational biology and networking with members of the Canadian bioinformatics community, many of whom act as course instructors and teaching assistants.

Nurturing new bioinformatics talent and building the capacity of geneticists and bioinformatics trainers in Canada are critical goals of the program. As Dr. Joanne Fox, Chief of Training and Support for the UBC Bioinformatics Centre (UBiC) in Vancouver, explained, "I was a student at the first Bioinformatics workshop in Calgary which was my introduction to the field. It was such a positive experience that I changed the focus of my PhD thesis and my career plans. I became motivated to pursue bioinformatics through my exposure to the community of experts who are involved in teaching and running the CBW series. It would be fair to say that my current position with Francis Ouellette at UBiC is due in large part to the training I received through participating in the CBW Workshop series."

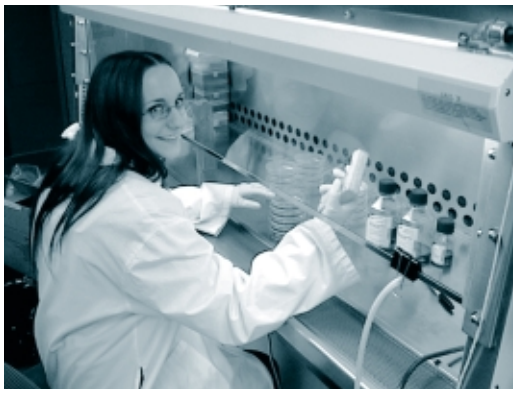
Exposing high school students to genetic research

A New, Interactive Forum for Educating Canadian Youth

Demonstrating it's continuing commitment to training young scientists, in March 2003, CGDN successfully launched the "Gene Researcher for a Week" program. A partnership between the Canadian Genetic Diseases Network and the CIHR, Institute of Genetics, the pilot program placed sixteen high school students from across the nation into the genetic research laboratories of 15 CGDN scientists.

Students were exposed to the leading-edge technology used in health research and performed experiments such as DNA isolation, PCR, gel electrophoresis, SDS-Page, Western blotting, cell culture and ELISA assays. Overwhelmingly, the participating students expressed that "Gene Researcher for a Week" had inspired them to pursue careers in science.

"The program provided real experience for students curious about research careers", stated Dr. Tom Hudson, Associate Scientific Director of CGDN. "Not only did the program inspire young Canadians to choose careers in genetics, but it educated them about the benefits of innovation in health research."



Highschool student Crystal Gennick works in a tissue culture hood at the Manitoba Cancer Research & Treatment Centre under CGDN scientist, Dr. Geoff Hicks.

Commercial Report

Knowledge Exchange and Technology Transfer

Strategic Fund

As a result of CGDN's commercial strategy, the Network provided a strategic grant in 2002 – 2003 to Dr. Moira Glerum at the University of Alberta. Dr. Glerum received $42,679 for the project entitled "*Analysis of mtDNA mutation in Cancer*". The goal of this project is to delineate the role that mitochondria plays in the development of cancer and develop an mtDNA diagnostic microfluidic chip-based assays for cancer.

License agreements

McGill University and Variagenics Inc. – Methionine Synthase

A license agreement between McGill University and Variagenics for the Methionine Synthase diagnostic and therapeutic patent was negotiated by CGDN. This patent provides methods for evaluating patients at risk for Methionine Synthase deficiency and the associated altered risks for neural tube defects, cardiovascular disease and cancer. This collaborative project between Drs. Rima Rozen, Roy Gravel and associates was initially funded through CGDN's core program.

Martinex Inc. and Variagenics Inc. – Methionine Synthase Reductase

CGDN also negotiated a license agreement between Martinex and Variagenics for the Methionine Synthase Reductase diagnostic patent that had resulted from research collaboration between Drs. Roy Gravel, Rima Rozen and associates through the core-funding program. Methionine Synthase Reductase reducing system is required for maintenance of the Methionine Synthase in a functional state.

Development Agreement

CGDN, Hospital for Sick Children, Industrial Technology Research Institute and Phalanx Biotech Group Inc. – The development of high density, commercial-quality and general-purpose microarray chips

Microarray chips, the combination of computer technology and biology, enable researchers to discover medically important genes. An agreement between CGDN, Hospital for Sick Children, Industrial Technology Research Institute (Taiwan) and Phalanx Biotech Group Inc (Taiwan) was executed at a signing ceremony in Taipei on October 16, 2002 and was witnessed by the Honourable Rick Thorpe, Minister of Competition, Science and Enterprise for the Province of British Columbia.

Contract Research

Montreal Children's Hospital and BioMarin Inc – phenylalanine lyase

Early diagnosis of Phenylketonuria (PKU) is currently accomplished by mass screening programs. PKU is a genetic disease resulting in an absence or deficiency of phenylalanine hydroxylase, which leads to the unwanted accumulation of phenylketonurics. If left untreated, this accumulation will lead to severe mental retardation by age one.

The current treatment for PKU is to provide the affected children with a low phenylalanine diet. Since phenylalanine is present in most protein sources, the children are provided with an impalpable diet with little or no variety, profoundly impacting their quality of life.

A one-year research contract between Dr. Charles Scriver (McGill University) and BioMarin for the phenylalanine lyase project resulted from research funded through the CGDN Strategic fund. If successful, a phenylalanine lyase derivative will offer a much-needed therapy to PKU sufferers and allow them to lead a much more normal life.

Networking and Partnerships

National

Symposium – The Clinician-Scientist: A Translator of Knowledge

A symposium entitled "*The Clinician-Scientist: A Translator of Knowledge*" was held in Montreal on April 10th, 2003, in partnership with the Canadian Gene Cure Foundation, the Montreal Children's Hospital

Foundation, Montreal Children's Hospital and the Canadian Institutes of Health Research, Institute of Genetics. The event was organized to honor the Scriver family (Drs. Jessie Boyd, Walter and Charles Scriver) for their contribution to Canadian medical research and healthcare. Guest speakers included Dr. Alan Bernstein, President of the Canadian Institutes for Health Research, Dr. Barton Childs, Emeritus Professor of Pediatrics from the Johns Hopkins University and Dr. Leon Rosenberg, Professor in the Department of Molecular Biology at Princeton University as well as Network members Drs. Michael Hayden, Tom Hudson, Rod McInnes and Rima Rozen.

International

The CIHR, Institute of Genetics and the CGDN International Priorities & Planning Committee

A CIHR, Institute of Genetics and CGDN International Priorities & Planning Committee was created to facilitate collaborations between CIHR, CGDN, Genome Canada and international partners with a goal of furthering basic translational and ethics-related genetic research worldwide.

American Association of Immunologists meeting (FASEB)

The CGDN, in collaboration with the CIHR, Institute of Genetics, sponsored a symposium entitled "*Genomic Approaches to the Immune System*" that took place during the American Association of Immunologists meeting (FASEB) in Denver, Colorado in April 2003.

New Frontiers: Italian/Canadian Genomic Population Genetics and Bioinformatics Collaborations

A meeting between Canadian and Italian researchers was held in Montreal on December 9–10, 2002. It was sponsored and organized by the CGDN, the CIHR, Institute of Genetics, the Department of Foreign Affairs and International Trade and the Italian Embassy to Canada.

Asian Pacific Economic Council (APEC)

The APEC Center for Technology Foresight received funding from the APEC Secretariat for a foresight study entitled *"DNA Analysis for Human Health in the Post- Genomic Era"*. The CGDN was invited to take part in drafting a white paper on gene therapy to be submitted to the APEC Center for Technology Foresight in the fall of 2003. Dr. Ian MacLaughin of Protiva will author the paper on behalf of CGDN.

An Update on Xenon Genetics Inc.

As previously reported, CGDN earned a share position in Xenon Genetics Inc. through the transfer of its intellectual property in 2000.

Xenon's lead programs target the development of therapies to treat the metabolic syndrome (obesity, diabetes/insulin resistance and abnormal lipid levels), neurological disorders, as well as reduce iron stores in the body. In each of these drug discovery programs, Xenon is applying core competencies spanning the range of activities from target discovery and validation to compound screening, chemistry and *in vivo* drug testing to advance small molecule drug candidates into pre-clinical studies and then into clinical trials in humans.

In its Metabolic Syndrome program, Xenon has progressed to the lead optimization stage, with multiple chemical series in development and *in vivo* efficacy studies currently underway. Xenon expects to select candidates for formal pre-clinical development by year-end 2003. In the Iron Metabolism program, Xenon has successfully completed high throughput screening on a library of diverse chemical structures, identifying multiple chemical series. This program is advancing toward *in vivo* efficacy studies. Xenon's Neuroscience program has cultivated many successes with the identification of multiple drug targets, one of which has been selected to advance into drug discovery and has undergone compound screening

Over the longer term, the Company plans to further forward integrate its capabilities to become a leading genomics-based pharmaceutical company, developing and marketing select therapeutics for human health.

Financial Report

Auditor's Report

To the Members of
Canadian Genetic Diseases Network
Réseau Canadien De Maladies Génétiques

We have audited the statement of financial position of Canadian Genetic Diseases Network/Réseau Canadien de Maladies Génétiques as at March 31, 2003 and the statements of operations, changes in net assets and cash flows for the year then ended. These financial statements are the responsibility of the company's management. Our responsibility is to express an opinion on these financial statements based on our audit.

We conducted our audit in accordance with Canadian generally accepted auditing standards. Those standards require that we plan and perform an audit to obtain reasonable assurance whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation.

As described in note 2(a), these financial statements are prepared on a non-consolidated basis.

In our opinion, except for the departure from Canadian generally accepted accounting principles described in the preceding paragraph, these financial statements present fairly, in all material respects, the financial position of the company as at March 31, 2003 and the results of its operations, changes in net assets and cash flows for the year then ended in accordance with Canadian generally accepted accounting principles.

CHARTERED ACCOUNTANTS
Vancouver, Canada
July 11, 2003

Financial Report

Statement of Financial Position
Year Ended March 31, 2003

	2003	2002
ASSETS		
Current assets		
Cash and term deposits	$ 2,527,277	$ 1,519,838
Accounts receivable	134,625	755,150
Prepaid expenses	36,971	55,724
Advances to research institutions (note 3)	693,948	696,348
	$ 3,392,821	$ 3,027,060
Investment in subsidiary (note 4)	13,972	22,061
Capital assets (note 5)	87,908	124,947
	$ 3,494,701	$ 3,174,068
LIABILITIES		
Current liabilities		
Accounts payable and accrued liabilities	$ 67,267	$ 476,769
Deferred contributions (note 6)	1,969,338	1,464,092
	$ 2,036,605	$ 1,940,861
CAPITAL		
Invested in capital assets	$ 87,908	$ 124,947
Unrestricted net assets	1,370,188	1,108,260
	1,458,096	1,233,207
	$ 3,494,701	$ 3,174,068

Approved by the Directors

Director

Director

Statement of Operation
Year Ended March 31, 2003

	2003	2002
Revenue		
Federal government grants (note 8(b))	$ 4,439,371	$ 4,605,682
Provincial government grants	54,976	150,000
Registration workshop fees – Bioinformatics	332,250	435,850
Industry/Foundations – Bioinformatics	–	58,005
Cost recoveries and other	252,624	338,335
	$ 5,079,221	$ 5,587,872
Expenditures		
Amortization	72,544	79,188
Bioinformatics – BHRC	112,435	262,006
– Workshops	328,577	423,315
Commercial research	77,659	789,538
Core research	3,684,164	3,309,705
Administration and general	519,083	470,609
Research training	51,781	50,000
	$ 4,846,243	$ 5,384,361
Excess of operating revenue over expenditures for the year	232,978	203,511
Equity in loss of subsidiary (note 4)	(8,089)	(805)
Net excess of revenue over expenditures for the year	224,889	202,706
Net assets, beginning of the year	1,233,207	1,030,501
Net assets, end of the year	$ 1,458,096	$ 1,233,207

Financial Report

Notes
Year Ended March 31, 2003

1. Nature of activities

Canadian Genetic Diseases Network ("CGDN") is a not-for-profit corporation incorporated on March 3, 1998 under the Canada Corporations Act. The net assets and excess of revenue over expenditures of the corporation are not available for the personal benefit of any member.

The federal government of Canada has selected CGDN to receive core funding under its Networks of Centres of Excellence Program ("NCE") and has charged the Canadian Institutes of Health Research (formerly The Medical Research Council) with administrative responsibility for overseeing CGDN. The Canadian Institute of Health Research, CGDN, and the University of British Columbia ("UBC") have entered into a Funding Agreement dated April 1, 2002 which outlines the terms and conditions pursuant to which the CGDN is to receive core funding of $4,858,000 during fiscal 2003, $4,599,000 during fiscal 2004, and $4,052,000 during fiscal 2005.

CGDN administers the distribution of grant funds directly. Under the Funding Agreement, UBC agreed to provide suitable space and facilities. UBC receives an annual grant from the Province of British Columbia to offset the cost of services provided to the NCE at the University of British Columbia.

2. The Mission Statement of the CGDN is:

To be the primary catalyst in advancing Canada's scientific and commercial competitiveness in genetic research, and the application of genetic discoveries to the prevention, diagnosis and treatment of human disease.

In support of its mission, CGDN will:

- Provide, and continually improve, a framework that supports a network of world-class genetic researchers.
- Develop appropriate intellectual property relationships with strategic partners to facilitate the translation of research into therapeutics and diagnostics.
- Identify appropriate business options to translate genetic research into therapeutics and diagnostics.
- Align with and support organizations that provide Canadians with access to educational opportunities and information on gene-based medicines.
- Provide appropriate training opportunities to continually enrich the network of researchers.
- Identify and develop international relationships that support the mission of CGDN.
- Improve network researchers' understanding of entrepreneurial opportunities arising from genetic research.

The Biotechnology Human Resource Council ("BHRC") had selected CGDN to assist in the development and management of the Building Bioinformatics Capabilities Project which expired on September 30, 2002. For the period April 1, 2001 to March 31, 2004, BHRC will be entitled to receive 10% of any net profit derived by CGDN from the delivery or sale of any bioinformatics training products and services. CGDN derived a net profit of about $10,000 from the delivery or sale of bioinformatics training products and services during fiscal 2003 (2002 – $NIL).

During fiscal 2002 $58,005 was received from a consortium in support of a new Bioinformatics training initiative. During 2003 there was no similar program.

2. Significant accounting policies

a) Subsidiary

The company's investment in CGDN Ventures Inc., a wholly owned subsidiary, is accounted for by the equity method. Generally accepted accounting principles normally require that financial statements prepared for issuance to members be prepared on a consolidated basis. However, in this case, the directors are of the view that since the company's subsidiary is profit-oriented and inactive, the consolidation of the subsidiary provides limited additional information.

b) Capital assets

Capital assets are recorded at cost. Amortization is provided on a straight-line basis over the assets' estimated useful lives, which for furniture and equipment is five years and for computer equipment is three years. Computer software is fully amortized in the year of acquisition.

c) Revenue recognition

CGDN follows the deferral method of accounting for contributions. Restricted contributions including federal grant revenue received under the NCE and BHRC programs are recognized as revenue in the year in which the related expenditures are incurred. Unrestricted contributions are recognized as revenue when received or receivable if the amount to be received can be reasonably estimated and collection is reasonably assured. Endowment contributions are recognized as direct increases in net assets. The benefit of donated services is not recognized in the financial statements.

3. Advances to research Institutions

The advances to research institutions represents the balance of unexpended NCE government grants on hand with the research institutions as at March 31, 2003. These funds are committed to various research projects by the research institutions and will be expended in fiscal 2004.

4. Investment in subsidiary

The investment in CGDN Ventures Inc. is comprised of:

	2003	2002
Shares, at cost (100% owned)	$ 1	$ 1
Note receivable, due on demand	100,000	100,000
Equity in loss	(86,029)	(77,940)
	$ 13,972	$ 22,061

As at March 31, 2003, the subsidiary's liabilities were nominal and the net assets were $13,972. Interest on the note receivable has been waived for fiscal 2002 and 2003 and as at March 31, 2003 the note became non-interest bearing.

5. Capital Assets

	2003			2002
	Cost	Accumulated Amortization	Net Book Value	Net Book Value
Computer software	$ 7,557	$ 7,557	$ –	$ –
Computer equipment	222,596	155,732	66,864	117,441
Furniture and equipment	32,912	11,868	21,044	7,506
	$ 263,065	$ 175,157	$ 87,908	$ 124,947

6. Deferred contributions

Deferred contributions represent unspent funding from NCE and Burroughs Wellcome Fund. The deferred contributions are committed to research and training projects in fiscal 2003.

	2003	2002
NCE – see note 8(b)	$ 1,967,054	$ 1,444,439
Burroughs Wellcome Fund	2,284	19,653
	$ 1,969,338	$ 1,464,092

Financial Report

Notes
Year Ended March 31, 2003

7. Economic dependence and related party transactions:

As described in note 1, CGDN receives substantially all of its funding from NCE.

Under the Funding Agreement, UBC agreed to provide suitable space and facilities. UBC receives an annual grant from the Province of British Columbia to offset the cost of services provided to the NCE at the University of British Columbia.

Substantially all of the core research and research training expenditures are paid to eligible participating research institutions, including UBC, who are members of the corporation in their capacity as researchers. Consistent with NCE guidelines, the scientific director and one other scientist are directors of the company and receive funding in their capacity as researchers.

CGDN acts as a nominee and agent on behalf of the Canadian Gene Cure Foundation ("Foundation"), a registered charitable organization, in connection with certain investments. Substantially all of any share investments or other rights received are held for the endowment fund of the Foundation. The entities are considered related due to certain directors being common to both and their joint activities. During the year-end March 31, 2003, CGDN received a reimbursement of $20,004 from the Foundation (2002 – $18,337). Included in accounts receivable at March 31, 2003 is approximately $69,700 (2002 – $6,400) due from the Foundation.

The transactions between CGDN and the Foundation are measured at the exchange amount, which is the amount of consideration established, and agreed to by each party.

8. Other information

a) Financial instruments

The carrying amounts of CGDN's financial instruments approximate fair value due to their short maturities. CGDN is not exposed to credit or interest rate risks.

b) Federal government grant revenue

	2003	2002
NCE funds	$ 4,858,000	$ 4,500,000
BHRC funds	103,986	263,032
	4,961,986	4,763,032
Add: Deferred contributions, beginning of the year, recognized as revenue in the year NCE	1,444,439	1,287,089
Less: Deferred contributions, end of the year NCE	(1,967,054)	(1,444,439)
	$ 4,439,371	$ 4,605,682

c) Comparative figures

The comparative figures have been reclassified, where applicable, to conform with the presentation used in the current year.

Directors & Officers

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The Rt. Hon. Don Mazankowski, PC, OC
Vegreville, Alberta

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Principal
Abbott Strategies, Vancouver, BC

Mr. David Arkowitz
Controller, Merck Research Laboratories
Merck & Company, Rahway, NJ, USA

Mr. Jean-Michel Halfon
President and CEO
Pfizer Canada Inc., Kirkland, QC

Mr. Noel Hall
President and Co-founder
Aspreva Pharmaceuticals Corp, Victoria, BC

Dr. Michael Hayden
Scientific Director
CGDN, Vancouver, BC

Dr. Tom Hudson
Scientific Director
Genome Quebec Innovation Centre
Montreal, QC

Mr. Louis Lacasse
President
GeneChem Management Inc., Laval, QC

Dr. Heather Munroe- Blum
Principal & Vice-Chancellor
McGill University, Montreal, QC

Mr. Maurice Mourton
Tsawwassen, BC

Dr. Martha Piper
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University of British Columbia, Vancouver, BC

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President & Scientific Director
Professor of Medical Genetics
University of British Columbia, Vancouver, BC

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Co-Director, Scientific Advisory Board
Professor
Banting & Best Department Medical Research
University of Toronto, Toronto, ON

Dr. Lap-Chee Tsui
Co-Director, Scientific Advisory Board
Vice-Chancellor, University of Hong Kong
Hong Kong

Dr. Ron Woznow
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Dr. Louise Desjardins
Manager, Business Development

Ms. Janie Patrick
Manager, Finance

Ms. Megan Airton
Manager, Communications

Ms. Marguerite Caunt
Office Administrator