CANADIAN GENETIC DISEASES NETWORK

The first generation…

ANNUAL REPORT 1999

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…with hopes of a healthier future?

We are working to make it a reality.

About the Canadian Genetic Diseases Network: Profile

We are a not-for-profit nation-wide institute committed to research excellence in human genetic disease, training young scientists, and to strategic partnerships to commercialize discoveries.

The institute's research programs focus on the molecular and cellular causes of common diseases such as cancer, heart disease, and Alzheimer's.

Our scientists and their teams are based in universities, hospitals, and research centres across Canada (see page 16). The institute succeeds through dynamic collaboration among scientists, industrial partners, academic institutions, and core technology facilities. CGDN corporate headquarters provides leadership in training, partnerships and business development based on technology transfer.

We build partnerships with biotechnology, pharmaceutical and diagnostics companies to move research discoveries out of the laboratory and into the health care sector...so that the next generation can be the first with hopes of a healthier future.

"A Reality in the Making"

The mission of CGDN is to research the diagnosis and treatment of genetic diseases and to help move the resulting discoveries into the health care system.

In 1998/1999 the Canadian Genetic Diseases Network proudly entered its tenth year as a leader in human genetic research – newly incorporated as a not-for-profit R & D corporation.

Excellence in research

The mission of CGDN is to research the diagnosis and treatment of genetic diseases and to help move the resulting discoveries into the health care system. The process requires exceptional human and financial resources. CGDN's excellence in discovery research and scientific training is reflected in the fact that the Network earned unprecedented support from the private and public sectors in 1998/1999.

The reporting year was the first period in our third and final phase of funding (1998-2005) from the federal Network of Centres of Excellence program. Phase 3 funding was awarded on the basis of CGDN accomplishments in phase 2 (1994-1998), and in 1998/1999 the Network was awarded $4.5 million. In addition, our partners in industry and the non-for-profit sector contributed leveraged cash and in-kind support during the year of over $13 million. In total, CGDN attracted over $17.5 million in 1998/1999 in support of research for human genetic disease.

CGDN beyond 2005

The NCE funding program provides 14 years of core support for centres of excellence. As a result CGDN, which began operations in 1990, needs to identify new sources of revenues by 2005. Last year, we launched a sustainability plan to grow an endowment fund for genetic research that will help ensure that CGDN continues beyond 2005 in working towards an improved quality of health for Canadian families. The goal of the fund, which is currently valued at close to $2 million in cash and equities, is to raise a minimum of $20 million over 5 years in support of collaborative human genetic research in Canada.

An important step in this process was taken in March 1999: the Canadian Gene Cure Foundation was formed and incorporated as a federal charity. The Board of the Foundation, chaired by Mr. Maurice Mourton, a CGDN Director, approved a strategic study, to be completed in 1999, which will determine the capacity of fund raising for medical genetic research in Canada. Meanwhile, as a pilot fund raising event, the Foundation will hold a corporate *Jeans for Genes* week in Montreal in October, 1999 with the support of selected companies in the biotechnology industry. In 2000, it is planned to take the campaign national.

In January 1999, CGDN incorporated a for-profit company, CGDN (Ventures) Inc., whose mission is to be a leader in the commercialization of genomic and proteomic technology. An active Board drawn from the investment and biotechnology industries is working towards the goal of generating additional revenues for genetic research in Canada.

Growing technology and equity

During the year, CGDN's successful *Strategic Investment Fund* provided approximately $300,000 to Network projects with high commercial potential in the following areas: schizophrenia, heart disease, disease susceptibility, protein interaction, nucleic acid analysis, and prenatal abnormalities. These investments earn CGDN an interest in the intellectual property resulting from the research. For example, in 1998/1999, CGDN earned approximately $500,000 in license fees, royalties, and other revenues and negotiated over $500,000

Mr. Graham Strachan
Chairman

Dr. Michael Hayden
Scientific Director

Dr. Ron Woznow
Chief Executive Officer

in equity in two spin-off companies, SignalGene and Xenon (see Commercial Report).

Last year was another exciting period for CGDN scientific discoveries. Network scientific teams published over 400 collaborative manuscripts in peer-reviewed journals, filed 3 patent applications, and were issued two patents. Some of our major science success stories were reported in newspapers and biotechnology organs across the country and internationally. The Science section of this report describes CGDN discoveries and breakthroughs in a number of disease areas including cystic fibrosis, bone tumors in children, human blood disease, epilepsy, Huntington disease, and cardiovascular disease.

Training for the future

In the Spring of 1999, CGDN entered into a unique initiative with the Biotechnology Human Resource Council and Human Resources Development Canada to create the first national training environment in the country for bioinformatics, i.e. training highly qualified personnel in the use of powerful new tools in computer science and biology. The Training section of this report describes the exciting pilot program of short courses which will be given throughout 1999 and 2000.

CGDN also introduced a new research fellowship and studentship program in partnership with universities and not-for-profit disease societies, and sponsored the Network's annual undergraduate summer studentship program. In April, the Network held its eighth Annual Scientific Meeting at Blue Mountain Inn in Collingwood, Ontario. Each year this forum for scientific exchange provides over 100 of our students and post doctoral fellows additional exposure to some of the country's leading genetic researchers for a 4-day program of plenary sessions and workshops.

Looking ahead to 2000

The 1999/2000 year will take CGDN into the millenium on a high note. Our scientists and management have laid the groundwork for major achievements in genetic research and sustainability over the next twelve months. We also look foward to CGDN scientists playing a significant role in organizing and participating in the Human Genome Meeting 2000, to be held in Vancouver April 9-12.

In summary, it is a pleasure to report that CGDN partnerships and links with the national and international scientific communities and industry have never been stronger. We are working hard to make a brighter and healthier future a reality for the next generation of Canadians.

Graham Strachan
Chairman

Michael Hayden
Scientific Director

Ron Woznow
Chief Executive Officer

Network scientific teams published over 400 collaborative manuscripts in peer-reviewed journals, filed 3 patent applications, and were issued two patents.

"From Genes to Therapies"

Gene Identification

Researchers

L. Field (Calgary); D. Cox, M. Walter (Edmonton); G. Ebers, R. Hegele (London); B. Triggs-Raine (Manitoba); P. Gros, T. Hudson, K. Morgan, G. Rouleau, E. Schurr (Montreal); F. Rousseau (Quebec); R. McInnes, J. Rommens, S. Scherer, K. Siminovitch, P. St George-Hyslop, L-C. Tsui (Toronto); M. Hayden (Vancouver)

Projects

Craniofacial diseases	Nonsyndromic cleft lip with or without cleft palate
Gastrointestinal diseases	Cystic fibrosis, inflammatory bowel disease, colorectal cancer, liver disease
Diabetes	IDDM, NIDDM
Cardiovascular diseases	HDL deficiency, intracranial aneurysm
Neurological disorders	Dyslexia, familial dementia, multiple sclerosis, attention deficit/hyperactivity, Tourette syndrome
Bone & joint disorders	Rheumatoid arthritis, psoriasis
Modifier genes	Cystic fibrosis, triplet expansion diseases
Susceptibility to infection	Legionnaires' disease, CMV, malaria, salmonella, tuberculosis
Ocular diseases	Glaucoma, retinitis pigmentosa, developmental eye defects

Pathogenesis & Functional Genomics

Researchers

N. Dovichi (Edmonton); R. Gravel (Calgary), T. Hudson, G. Mitchell, K. Morgan, G. Rouleau, R. Rozen (Montreal); A. MacKenzie, R. Korneluk (Ottawa); F. Rousseau (Quebec); B. Gallie, D. MacLennan, B. Robinson, P. St George-Hyslop (Toronto); M. Hayden, P. Hieter, F. Jirik (Vancouver)

Projects

Cancer	Retinoblastoma, folate metabolism & tumours
Neurological disorders	Apoptosis, Alzheimer's disease, Huntington disease, fragile X syndrome
Metabolic disorders	Tay-Sachs & Sandhoff diseases, respiratory chain defects, obesity
Neuromuscular disorders	Calcium regulation & muscle disease, myotonic dystrophy
Functional genomics	SAGE analysis, DNA chips, gene trapping in embryonic stem cells, methylation patterns in genomic DNA

Genetic Therapies

Researchers

C. Scriver (Montreal); R. Worton (Ottawa); J. Dick, R. McInnes, C. Roifman, L-C. Tsui (Toronto); L. Clarke, P. Cullis, M. Hayden, F. Jirik, F. Tufaro (Vancouver)

Projects

Technology development	Viral vectors: HSV, liposomes, stem cells
Applications	Murine tumour models, LPL deficiency, murine Hurler's syndrome, cystic fibrosis, Duchenne muscular dystrophy, human immunodeficiency diseases, retinal degeneration, enzyme substitution for phenylketonuria

Genetics & Health Care

Researchers

N. Dovichi (Edmonton); C. Scriver (Montreal); B. Gallie, D. MacLennan, S. Narod, L-C Tsui (Toronto)

Projects

Technology development	DNA diagnostics
Mutations	Detection, databases
Impact/Evaluation	Meta-analysis of treatment of hereditary diseases, retinoblastoma, malignant hyperthermia, breast & ovarian cancer

Core Technologies

Facilities & Directors

Genotyping	T. Hudson, K. Morgan (Montreal)
Complex traits analysis	E. Skamene (Montreal)
DNA sequence analysis	M. Hayden (Vancouver), B. Koop (Victoria), S. Scherer (Toronto)
Bioinformatics training	F. Ouellette (Vancouver)
DNA FISH mapping	J. Squire (Toronto)
Transcribed sequence detection	J. Rommens (Toronto)
Genome alteration in mice	F. Jirik (Vancouver), A. Nagy, J. Rossant (Toronto), M. Rudnicki (Hamilton)
Genome alterations in *C. elegans*	J. Culotti (Toronto)
In vivo DNA analysis	R. Drouin (Quebec)
Protein-protein interactions	J. Friesen, J. Greenblatt, A. Pawson (Toronto)
Immunoprobes	J. Wilkins (Winnipeg)

Since 1990, CGDN's scientific program has led to many significant discoveries and research advances into the causes of genetic disease. Together these have contributed to a better understanding of the genetic and environmental factors underlying the disease process and the development of novel therapeutic approaches. This report covers the first year of CGDN's Phase 3 research program which focuses on the genes involved in common disorders such as diabetes, cancer and heart disease.

Many common disorders are caused by a complicated interplay of genetic and environmental factors. CGDN uses advanced molecular research techniques to uncover the genetic basis of these diseases. Discovery of the underlying action of genes on physiology and environmental interactions allows CGDN and its partners to plan therapeutic approaches to prevent or ameliorate these diseases. While CGDN still supports research into relatively rare disorders such as Phenylketonuria (PKU) and Hurler's syndrome, the current program relates these investigations to studies of genes involved in common diseases.

To maintain its strong leadership position, CGDN supports the research activities of its investigators through direct funding of novel research, interaction through scientific retreats, cross-country collaborations among researchers and advanced training of young scientists. Importantly, CGDN maintains core technology facilities at laboratories around the country in support of its research activities.

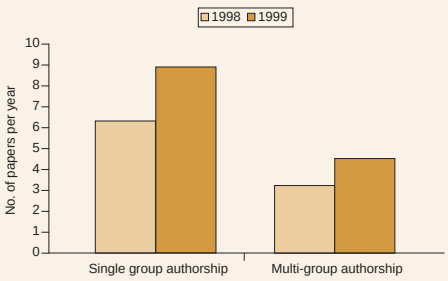
The program shows progress in scientific discovery and health care application in each of its four theme areas: gene identification associated with common disorders, pathogenesis and functional genomics (how genes contribute to the cause and mechanism of common disorders), new approaches to genetic therapies, and genetics and health care where CGDN and its partners apply research advances for the benefit of health care and disease prevention.

This report covers the first year of CGDN's Phase 3 research program which focuses on the genes involved in common disorders such as diabetes, cancer and heart disease.

Publications and patents

A key measure of scientific excellence is the quality and number of peer reviewed papers published in scientific journals. CGDN investigators rank highly with 661 papers in the last year in high-impact journals such as Cell, Nature Medicine, Nature Genetics and Proceedings of the National Academy of Sciences. The total number of papers is up 40% over the previous year. It is noteworthy, among these papers that more than half come from enhanced collaborations between two or more CGDN research groups. In addition, CGDN research generated 3 patent applications in the last year (see Commercial Report).

CGDN peer-reviewed publications per research group



Discoveries and advances

In 1998/1999 CGDN investigators made a number of significant world-leading advances including:

- Discovery of a gene responsible for two genetic diseases that result in low levels of 'good' cholesterol and a highly elevated risk of cardiovascular disease (M. Hayden, Centre for Molecular Medicine and Therapeutics, Vancouver)
  Dr. Hayden led an international consortium involving CGDN spin-off company, XENON Bioresearch Inc., to discover the ABC1 gene. The gene provides a target for novel therapeutics against cardiovascular disease. Says Dr. Hayden, "Although medical science has developed effective methods to lower LDL or 'bad' cholesterol, until now we have not understood crucial mechanisms which elevate levels of HDL or 'good' cholesterol." (Nature Genetics, August 1999).
- Discovery of new mutation in a gene causing early onset type 2 diabetes mellitus in Canadian aboriginal population (R. Hegele, John P. Robarts Research Institute, London)
  Dr. Hegele's team discovered a mutation that is

present in 40% of Oji-Cree with type 2 diabetes mellitus. Dr. Hegele comments, "It is possible that a large number of Canadian aboriginal people are carriers of this mutation, which appears to place them at increased risk of diabetes in the context of a sedentary lifestyle." (Diabetes Care, March 1999; Journal of Clinical Endocrinology and Metabolism, March 1999).

- Gene responsible for debilitating muscle disease, oculopharyngeal muscular dystrophy (OPMD)(G. Rouleau, Montreal General Hospital)

  Dr. Rouleau headed an international team which discovered the gene and defined a previously unknown mutation responsible for OPMD. It is also the first time a mutation is reported where there is an expansion of a short GCG repeat in the coding region of DNA leading to an enlarged polyalanine tract in the protein. There is a high incidence of OPMD carriers in Canada: it is the most frequent muscular dystrophy in Quebec, affecting 1 in 1,000 people. Almost 100% of the carriers of the gene eventually develop the disease and pass the condition on to half of their children. Says Dr. Rouleau, "Within a few months, a simple blood test will be available to diagnose accurately and easily if a person is a carrier of the OPMD gene. We will be able to offer a pre-symptomatic diagnosis which was not previously available." (Nature Genetics, February 1998).
- Structure and function of enzyme responsible for specific bone tumor (F. Tufaro, University of British Columbia, Vancouver)

  Dr. Tufaro identified the structure and function of a tumor suppressor protein which is encoded by the gene which, when mutated, leads to the formation of bone tumors in children – a disease called Hereditary Multiple Exostoses. His team found that the protein is located in the endoplasmic reticulum where it contributes to the biosynthesis of an important biological regulatory molecule, heparan sulfate. Dr. Tufaro said, "The discovery brings us one step closer to understanding the cause of this devastating bone cancer." (Nature Genetics, June 1998).
- Discovery of mutations in gene that cause some forms of congenital blindness (M. Walter, University of Alberta, Edmonton)

  Dr. Walter led an international team which discovered mutations in a gene called FKHL7, responsible for glaucoma in some patients. In addition to blindness, alterations of the mouse version of FKHL7 cause brain defects as well. It is likely that at least one more gene in the same chromosomal region as FKHL7 is involved in heritable blindness. Says Dr. Walter, "We will be able to determine the function of FKHL7 in eye and brain formation, and test whether alterations in FKHL7 have a role in other forms of glaucoma." (Cell, June 1998; American Journal of Human Genetics, November 1998).
- Towards stem cell gene therapy for leukemia, thalassemia and sickle cell anemia (J. Dick, Hospital for Sick Children, Toronto)

  By transplanting human blood cells into special immune-deficient mice called NOD/SCID mice, Dr. Dick's team has generated the human blood system in mice. Key to this technological advance is the identification of stem cells into which specific genes can be inserted. These altered cells then begin to produce blood containing the normal gene. Dr. Dick's discovery indicates that a particular type of stem cell which was previously discarded in cell transplantation therapies may, in fact, provide a good target for stem cell gene therapy. (Nature Medicine, August 1998).
- Gene responsible for a specific form of epilepsy, Lafora disease, (S. Scherer, Hospital for Sick Children, Toronto)

  Dr. Scherer led an international team to identify the gene that causes one of the most severe forms of epilepsy which occurs during late childhood or early adolescence. Sufferers have seizures and progressive neurological degeneration, leading to death within a decade of onset of the first symptoms. The causative gene produces a signalling protein which is thought to be involved in the brain's breakdown of carbohydrates. (Nature Genetics, October 1998).

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- New enzyme substitution approach to treat phenylketonuria (PKU) (C. Scriver, McGill University, Montreal)
  Dr. Scriver's team collaborated with IBEX Technologies Inc. of Montreal to develop a new therapeutic approach to the treatment of PKU which will relax the stringent, lifelong controlled diet and dependence on nutritional supplements presently used by PKU sufferers. Researchers produced a replacement enzyme that reduces phenylalanine in laboratory mice by up to 50%. PKU is caused by the absence of an enzyme which is normally present in the liver for the purpose of degrading phenylalanine ingested in foods such as milk, cheese, meat, fish, bread and nuts. (Proceedings of the National Academy of Sciences USA, March 1999).
- First mouse model to reproduce the cardinal features of Huntington disease (M. Hayden, Centre for Molecular Medicine and Therapeutics, Vancouver)
  An international team led by Dr. Hayden produced the first genetically engineered mouse that truly mimics the disease. The mouse shows electrophysiological abnormalities and selective degeneration of the specific neuronal cells that die in patients with Huntington disease. (Neuron, June 1999).
- Locus of human gene found which modifies the severity of cystic fibrosis (L-C. Tsui, Hospital for Sick Children, Toronto)
  A team led by Dr. Tsui identified a region on chromosome 19 that contains a gene which modifies the severity of cystic fibrosis (CF). The CF gene has over 800 different mutations, all causing variations in the disease. However, not all clinical variations are attributable to mutations in the gene. As a result, researchers have suspected that other factors are involved such as the activity of other genes that have a modifying effect on the disease. Dr. Julian Zielenski, the lead author explains: "The area we have pinpointed contains a gene that modifies the severity of a common intestinal obstruction that affects 20% of patients with CF. We now know that the obstruction is not caused by a mutation in the CF gene itself, but by the activity of a modifying gene." (Nature Genetics, June 1999).
- Discovery of a cellular mechanism controlling a powerful suppressor of apoptosis in programmed cell death (R. Korneluk, Children's Hospital of Eastern Ontario, Ottawa)
  Dr. Korneluk led a team involving CGDN spin-off company, Apoptogen Inc., in the discovery of a cellular mechanism that controls XIAP expression, a protein that inhibits cell death. Disregulation of apoptosis occurs in cancer, autoimmune disorders, immunodeficiency and neurodegenerative disorders. Dr. John Gillard, CEO of Apoptogen comments "The sequence is also an important target for pharmaceutical intervention." (Nature Cell Biology, July 1999).

An ongoing strength of CGDN is its core technology facilities.

Core technology facilities

An ongoing strength of CGDN is its core technology facilities. These state-of-the-art facilities are designed to provide CGDN researchers and partners with rapid and cost efficient access to leading-edge technologies that are not readily available elsewhere. In the past year, 48 network members from 13 institutions used CGDN's core facilities which have proven invaluable in the quest for new genes and understanding the molecular mechanisms involved in the disease process. Network industry partners also can access core facilities with spare capacity. This is an effective means for small biotechnology companies to gain access to leading edge technologies.

CGDN has made it possible for researchers in one part of Canada to make use of core facilities that are thousands of miles away, eliminating the need to duplicate technologies around the country. Says Dr. David MacLennan, Banting and Best Institute for Medical Research, University of Toronto, "We've had a superb collaboration with Dr. Frank Jirik and the CGDN Transgenic Core Facility at UBC to make animal models for diseases resulting from defects in calcium regulation. Our first joint paper has just been submitted for publication."

Recognition of Excellence in Research: Science Honors

In 1998/1999 CGDN scientists and students received some of the top Canadian and international awards for excellence in science.

Awards received by senior researchers

Alberta Heritage Foundation: Scientist Award
Roy Gravel, Uni. of Calgary

American Assoc. for Cancer Research/Pezcoller Foundation:
International Award for Cancer Research
Anthony Pawson, MSHRI

Bayer/CSACI: Distinguished Scientist
Chaim Roifman, HSC

Burroughs Wellcome Trust:
Visiting Professor, 1998
Emil Skamene, MGHRI

Cdn Federation of Biological Societies:
PMAC keynote lecture
Rima Rozen, MCHRI

Cdn Foundation for Innovation: Researcher
Stephen Scherer, HSC

Cdn Rheumatology Assoc. & Sanofi Canada:
Distinguished Investigator
Frank Jirik, CMMT

Cdn Society for Chemistry: Fisher Scientific Award 1998
Norman Dovichi, Uni. of Alberta

Cdn Society for Clinical Investigation:
Henry Friesen Award
Anthony Pawson, MSHRI

Fonds de la recherche en santé du Quebec
Chercheur boursier senior:
Erwin Schurr, MGHRI
Scholarship junior II:
Régen Drouin – Laval Uni.

Genome Canada Interim Board: Co-Chair
Lap-Chee Tsui, HSC

Gov't of Ontario:
Premier's Research Excellence Award
Michael Rudnicki, McMaster Uni.
Stephen Scherer, HSC

Graham Boeckh Chair for Schizophrenia Research
Guy Rouleau, MGHRI

H.E. Sellers Chair in Cystic Fibrosis
Lap-Chee Tsui, Uni. of Toronto & HSC

Hospital for Sick Children:
Burton Lectureship 1999
John Dick, HSC

Howard Hughes Medical Institute:
International Research Scholar
Roderick McInnes, HSC

Huntington Disease Society of America:
Guthrie Humanitarian Award 1999
Michael Hayden, CMMT

Leo-Pariseau 1999 Prize in Biological & Health Sciences
Guy Rouleau, MGHRI

Leukemia Research Fund (UK):
Guest lectureship
John Dick, HSC

Medical Research Council of Canada
Clinician Scientist (Phase II):
Tom Hudson, MGHRI
Distinguished Scientist:
Jospeh Culotti, MSHRI
Research Scientist:
Michael Rudnicki, McMaster Uni.

Montreal General Hospital: Phil Gold Award
Erwin Schurr, MGHRI

Ontario March of Dimes & Pasteur Merieux Connaught Laboratories Ltd:
Dr. Jonas Salk Award
David MacLennan, Uni. of Toronto

Ottawa Life Sciences Council: Career Achievement
Ronald Worton, Ottawa Hospital Research Institute

Royal Netherlands Academy of Arts & Sciences:
Dr. H.P. Heineken Prize for Biochemistry & Biophysics
Anthony Pawson, MSHRI

Royal Society of Canada: Flavelle Medal
Anthony Pawson, MSHRI

Society for Pediatric Research:
E. Mead Johnson Award
Chaim Roifman, HSC

Le Téléthon de la recherche sur les maladies infantiles: Prix d'excellence 1998
François Rousseau, Laval Uni.

University of Calgary:
Izaak Walton Killam Memorial Chair
Roy Gravel, Uni. of Calgary

University of Toronto:
Dales Award for Medical Research
Chaim Roifman, HSC

Utrecht University: DSc (Hon)
Charles Scriver, MCHRI

Awards received by research team members

Alberta Heritage Foundation
Incentive Award:
Tracey Petryshen, Uni. of Alberta
Studentship:
Ramsey Saleem, Uni. of Alberta
Aaron Wilson, Uni. of Calgary
Fellowship:
Rachel Szilard, HSC

Studentship & G.H. Woods Graduate Student Award:
Deepak Kamnasaran, Uni. of Alberta

American Society of Human Genetics:
Student Award
Jonathan Horsford, HSC

Canadian Cystic Fibrosis Fellowship
Mark Van Oene, HSC

Canadian Diabetes Association:
Post Doctoral Fellowship
Ketan Badiani, Uni. of Manitoba

CGDN Joint Training Award
CGDN/Institution:
Cynthia Coffill, Véronique Tanay – CHEO; David Sinasac, Maja Popovic, Jonathan Horsford – HSC; Karen Berg – Samuel Lunenfeld Research Institute
CGDN/Arthritis Society:
Catherine Taylor – MSHRI
CGDN/B.C. Children's Research Institute:
Vikramijit Chopra, CMMT
CGDN/Huntington Society:
Emond Chan, CMMT

CGDN Summer Studentship 1999:
Robert Adam – MSHRI; Andrea Stewart – OCI; James Kennedy, Matthew Roberts – CHEO; Robert Shih, Jennifer Jabalee, Graeme Bocock, David Lam – HSC; Inge Meijer, Michael Ward, Jacques Moisan – McGill; Mark Gillespie – McMaster; Nicole Martin – Eye Research Inst.; Martin Labuda – Uni. Montreal; Micah Simcoff – U. Manitoba; Catherine Murray, Ayman Yassa – U.B.C.; Alyssa Boyd – U. Toronto; Tayna Chandra – OGH

Cdn Liver Foundation: Studentship
Steven Moore, Uni. of Alberta

Federation of American Socities of Experimental Biology: Summer Research Conference Student
Zhoutao Chen, McGill Uni.

Fight for Sight Summer Studentship
Kathy Kozlowski, Uni. of Alberta

Gov't of British Columbia: GREAT Award
Christian Smith, Uni. of Victoria

Gov't of Canada: Employment Challenge Award
Daniel Shiff, MGHRI

Gov't of Ontario
Graduate Scholarship:
Suzana Drmanic, CHEO
Maja Popovic, HSC
Ministry of Health Training Award:
Jean Jordan, CHEO
Studentship in Science and Technology:
Claire Palmer, McMaster Uni.

Governor General's Gold Medal: Top graduate in Natural Sciences & Engineering
Bernard Brais, MGHRI

Hospital for Sick Children:
Restracom Student Fellowship
Martina Puchyr, HSC

Huntington Society of Canada:
Studentship/Fellowship
Elizabeth Almqvist, Miriam Torchinsky – CMMT

Huntington Disease Society of America:
Fellowship
Cheryl Wellington, CMMT

INSERM: Post Doctoral Fellowship
Sandrine Marquet, McGill Uni.

Medical Research Council of Canada
Centennial Fellowship:
Peter Liston, CHEO
Doctoral Research Award:
Aaron Wilson, Uni. of Calgary
Postdoctoral Fellowship:
Celia Greenwood, MGHRI
Martin Holcik, CHEO
Blair Leavitt, Abagail Hackam – CMMT
Robert Chow, HSC
Studentship:
John Forbes, Uni. of Alberta
Zhoutao Chen, McGill Uni.
Ryan Brinkman, CMMT
Ted Erclik, HSC

McGill University
Mary Louise Taylor Fellowship:
Pamela Tran
MSc Dean's Honor List:
P. Nowacki

Montreal Children's Hospital: Studentship
Ilan Weisberg, Manuel Chan, Perpetual Pereira, Sahar Sibani

NSERC
Post Graduate Scholarship:
Tracey Petryshen, Uni. of Alberta
Studentship:
Gloria Hsi, Uni. of Alberta
Patrick Seale, McMaster Uni.
Scholarship:
Sharan Goobie, HSC

The A. and R. Pietrangeli Memorial Travel Award 1998
Samantha Gruenheid, MGHRI

Prix d'Excellence de l'Academie des Grands Montrealais
Ron Lafrenière, MGHRI

University of British Columbia:
Graduate Fellowship
Vikramijit Chopra, CMMT

An important part of CGDN's mission is to commercialize CGDN-funded intellectual property. This is done in close collaboration with the Network's scientists and stakeholders – universities, medical institutions, and industry partners.

Commercialization process

The key steps from discovery to marketplace are as follows:
Funding discovery research
Disclosure of invention
Patent protection
Licensing
Development and marketing of product

Funding discovery research: strategic grants

CGDN provides strategic grants of up to $75,000 to support projects with the potential to lead to an invention together with results to support a patent application within one year. These awards are incremental to core research funding.

In 1998/1999, as in previous years, strategic grants played a key role in funding patentable research, with $271,000 being awarded to six CGDN scientists. Table 1 lists the grant recipients and the patent applications resulting from these projects.

Disclosure of invention and patent protection

Following a scientific discovery, CGDN researchers notify their institutions, and a joint CGDN-university assessment of the value of the intellectual property is made. If it has commercial value, a patent application will be filed.

During 1998-1999, CGDN scientists disclosed six new inventions of which three resulted in the filing of patent applications led by CGDN (see Table 1). The inventions are described below:

Dr. Régen Drouin's non-invasive method for detection of Trisomy 21 has the potential to provide a faster, safer, less expensive test for Down's syndrome than the amniocentesis test currently used.

Dr. Frank Jirik's protein interaction and transcription factor trap invention is a platform technology that facilitates the functional analysis of genes and protein-protein interactions. This technology will facilitate the discovery and functional characterization of novel targets for small molecule drug development.

Dr. Jeremy Squire's invention – nucleic acid analysis by comparative particle hybridization – complements existing micro array chip technology which has broad applicability in all phases of medical research and disease management.

During the year, PCT patent applications were filed for Dr. Michael Walter's glaucoma gene technology and Dr. Frank Jirik's complementation gene trap technology.

Licensing of invention

All pending patents and issued patents have the potential to be licensed. Pursuant to the Internal Agreement between CGDN scientists and their host institutions, the lead role in commercialization is negotiated among CGDN, the host institution/s where the research is conducted, and the scientists.

In 1998/1999 CGDN participated in negotiations to license intellectual property relating to research developed by the following scientists:

Dr. François Rousseau (Laval University)
Research area: osteoporosis and psoriasis
Licencee: SignalGene Inc. of Montreal
CGDN received 800,000 shares in SignalGene for its interest in the licences.

Dr. Guy Rouleau (McGill University)
Research area: epilepsy
Licencee: RGS Genome Inc., a CGDN spin-off company based in Montreal.

Dr. Frank Jirik (Centre for Molecular Medicine & Therapeutics)
Research area: gene trapping technology
Licencee: Under negotiation

Dr. Michael Hayden (Centre for Molecular Medicine & Therapeutics)
Research area: low HDL cholesterol
Licencee: XENON Bioresearch Inc., a CGDN spin-off company based in Vancouver.

CGDN's reputation for negotiating licensing agreements for DNA-based technology was evidenced when it was asked by the University of Saskatchewan to partner in the commercialization of a conductive nucleic acid patent. CGDN has entered into an agreement with the university whereby it will earn an interest in patent royalties for negotiating licence agreements.

Development of product

The development of commercial products from patents requires significant capital investment by the biotechnology and pharmaceutical industries. In 1998-1999, companies that licensed technologies based on CGDN projects raised over $10 million to develop commercial products from these licences.

Table 1: Strategic funding & patent applications filed in 1998/1999

Researcher	Project Area	Strategic Funding	Patent Application
Dr. Régen Drouin Laval University	Down's syndrome	$45,000	Non-invasive method for detection of Trisomy 21
Dr. Michael Hayden Centre for Molecular Medicine & Therapeutics	Identification of novel genes associated with low HDL cholesterol in Familial HDL deficiency & Tangier disease	$45,000	
Dr. Frank Jirik Centre for Molecular Medicine & Therapeutics	Genome-wide functional analysis of genes	$34,500	Protein interaction and transcription factor trap
Dr. Guy Rouleau McGill University	Identifiction of a gene predisposing to schizophrenia	$50,000	
Dr. François Rousseau Laval University	Identification of disease susceptibility genes in the French-Canadian population	$50,000	
Dr. Jeremy Squire University of Toronto	Research and management of disease	$46,865	Nucleic acid analysis by comparative particle hybridization

"Tomorrow's Innovators"

CGDN's successful training initiatives are designed to prepare the next generation of researchers in a number of innovative ways. Trainees acquire advanced technology skills such as bioinformatics and gain experience in working with industry. In the past year, CGDN more than doubled the number of trainees in its various programs.

For example in 1998, CGDN established a core training facility in bioinformatics to address a critical shortage in bioinformatics skills in Canada. With the successful recruitment of Francis Ouellette to direct the Bioinformatics Core Facility, CGDN developed the Canadian Bioinformatics Workshops in partnership with the Biotechnology Human Resource Council and the Sectoral Partnerships Program of Human Resources Development Canada. These workshops are a series of one and two-week courses offered nationally to researchers in life sciences and in computational sciences. More information on the pilot series of workshops can be found at www.bioinfomatics.ca

The first workshop was a great success, attracting more than twice the number of students than seats available. CGDN is working with the University of British Columbia, the University of Toronto and the University of New Brunswick to offer a formal certificate in Bioinformatics to workshop participants. Other workshop sponsors include the Burroughs Wellcome Fund, Merck Genome Research Institute and the Alberta Heritage Foundation for Medical Research.

CGDN is an ideal environment in which to introduce undergraduates to careers in research. In 1999 CGDN selected 19 top undergraduate students to spend a summer working in CGDN laboratories.

CGDN recognizes the importance of investing in the long-term training of graduate students and post doctoral fellows. In the past year, 139 graduate students and 70 post doctoral fellows worked on CGDN projects. CGDN expanded its shared funding agreements with research institutes and foundations to support 9 graduate students and post-doctoral research fellowships across Canada.

To better prepare our students and trainees for careers in academic and industry-based research, CGDN sponsored a number of workshops over the past year. Successful entrepreneurs held a session on "Creating your own company." Other sessions covered emerging technologies such as "microarray technologies."

Bioinformatics	University of Calgary	August 1999
Genomics	University of British Columbia	January 2000
Proteomics	University of Toronto	May 2000
Developing the Tools	Université de Montréal	July 2000

Bioinformatics Workshop, University of Calgary, August 2 -14, 1999

"The Bioinformatics workshop series organized by the Canadian Genetic Diseases Network is invaluable and timely. As an Industrial Technology Advisor for National Research Council's Industry Research & Assistance Program in St. John's, Newfoundland, I am taking the skills I learned in the first workshop home. They will be used as an essential part of our strategy to assist high technology companies in Newfoundland explore the commercial frontiers of genomics." Ronda Dillon, NRC IRAP, St John's.

Summer student:
Alyssa Boyd, Queens University
"Thank you for the CGDN summer studentship. It enhanced my knowledge of both biochemistry and cell biology and greatly stimulated my enthusiasm for science." CGDN Supervisor: Dr. Peter St. George-Hyslop, Centre for Research in Neurodegenerative Disease, University of Toronto.

CGDN Joint Training Award:
Cynthia Coffill, Children's Hospital of Eastern Ontario
"My CGDN /CHEO studentship has enabled me to acquire advanced skills in molecular methodologies. Although my project studying the consequences of upregulation of anti apoptotic protein is still in its early stages, I plan to move on to gene profiling using DNA chip technology as well as protein sequencing – methodologies which would not be as available to me without CGDN.
At the CGDN annual scientific meeting this year I enjoyed learning about world class work done on the many genetic diseases by Network investigators.

REVIEW ENGAGEMENT REPORT

To the Members of
Canadian Genetic Diseases Network

We have reviewed the statement of financial position of Canadian Genetic Diseases Network as at March 31, 1999 and the statements of activities and changes in net assets and cash flows for the year then ended. Our review was made in accordance with generally accepted standards for review engagements and accordingly consisted primarily of enquiry, analytical procedures and discussion related to information supplied to us by the company.

A review does not constitute an audit and consequently we do not express an audit opinion on these financial statements.

Based on our review, nothing has come to our attention that causes us to believe that these financial statements are not, in all material respects, in accordance with generally accepted accounting principles.

COLLINS BARROW
CHARTERED ACCOUNTANTS
Vancouver, Canada
July 8, 1999

Statement of Financial Position
for the year ended March 31, 1999
(Unaudited)

ASSETS		
Assets		
Cash	$	48,342
Due from administrator (note 3)		831,059
	$	879,401
LIABILITIES		
Current liabilities		
Accounts payable and accrued liabilities	$	31,981
Deferred contributions (note 4)		822,907
		854,888
CAPITAL		
Unrestricted net assets		24,513
	$	879,401

Approved by:

Ron Woznow
Chief Executive Officer & Director

Statement of Activities and Changes in Net Assets
for the year ended March 31, 1999
(Unaudited)

Revenue		
Federal government grants (note 6(a))	$	3,755,093
Provincial government grants		20,000
Cost recoveries and other		28,513
		3,803,606
Expenditures		
Administration		514,460
Bioinformatics workshops		32,152
Commercial research		179,500
Core research		2,906,939
Research training		146,042
		3,779,093
Excess of revenue over expenses for the year and net assets, end of the year	$	24,513

Notes to the Financial Statements
for the year ended March 31, 1999
(Unaudited)

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 corporation commenced its operations on April 1, 1998. The net assets and excess of revenue over expenses 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 Medical Research Council with administrative responsibility for overseeing CGDN. The Medical Research Council, CGDN, and the University of British Columbia ("UBC") have entered into a Funding Agreement dated April 1, 1998 which outlines the terms and conditions pursuant to which the CGDN is to receive core funding of $4,500,000 during each of fiscal 1999, 2000, 2001 and 2002.

Under the Funding Agreement UBC, on behalf of and as directed by CGDN, has agreed to: a) provide suitable space and facilities; b) receive and distribute grant funds to eligible participating institutions; and c) provide ongoing accounting and annual financial reporting for the NCE funds.

The specific objectives of CGDN are to:

- promote advances in genetics research related to common diseases;
- provide scientific participants with access to technology to derive insights on the molecular mechanisms of disease;
- develop the basis for novel therapies and related diagnostics;
- foster the application of genetic discoveries in health care;
- provide new Canadian venture investment opportunities and jobs;
- provide trainees with new skills related to emerging employment opportunities; and
- build an endowment fund to support Canadian Genetic Diseases Network research and development after the current NCE mandate is completed.

The Biotechnology Canada Human Resource Council ("BHRC") has selected CGDN to develop and implement a Canadian bioinformatics capability development program in Canada. CGDN will receive funding from BRHC to manage, implement, and administer the program for a 22 month period.

BHRC and CGDN have entered into a contract dated February 17, 1999 which outlines the terms and conditions pursuant to which CGDN is to receive a total of about $400,000 during fiscal 1999, 2000 and 2001 to fulfil the terms of the contract.

2. Significant accounting policies

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. Due from administrator

The amount due from UBC represents the balance of unexpended NCE and provincial government grant funds and other funds on hand as at March 31, 1999. These funds are committed to various research projects and will be expended in fiscal 2000.

4. Deferred contributions

Deferred contributions represent unspent NCE, BHRC and provincial government grant funds. The deferred contributions are committed to research and training projects in fiscal 2000.

NCE funds	$	777,059
BHRC funds		17,848
Provincial government funds		28,000
	$	822,907

5. Economic dependence and related party transactions

As described in note 1 CGDN receives substantially all of its funding from the NCE and BHRC.

CGDN is dependent upon UBC for its administration of the NCE and provincial government grants and for the provision of office premises and certain capital assets on a rent-free basis. UBC does not receive fees for administrative services.

Substantially all of the core research and research training expenditures are paid to eligible participating institutions, including UBC, who are members of the corporation in their capacity as researchers.

6. Other information

a) Federal government grant revenue

NCE funds received	$	4,500,000
BHRC funds received		50,000
		4,550,000
Deferred contributions		(794,907)
	$	3,755,093

b) Financial instruments

The carrying amounts of CGDN's financial instruments, which include due from administrator, and accounts payable approximate fair value due to their short maturities. CGDN is not exposed to credit or interest rate risks.

c) Uncertainty due to the Year 2000 Issue

The Year 2000 Issue arises because many computerized systems use two digits rather than four to identify a year. Date-sensitive systems may recognize the year 2000 as 1900 or some other date, resulting in errors when information using year 2000 dates is processed. In addition, similar problems may arise in some systems which use certain dates in 1999 to represent something other than a date. The effects of the Year 2000 Issue may be experienced before, on, or after January 1, 2000, and, if not addressed, the impact on operations and financial reporting may range from minor errors to significant systems failure which could affect an entity's ability to conduct normal business operations. It is not possible to be certain that all aspects of the Year 2000 Issue affecting the entity, including those related to the efforts of customers, suppliers, or other third parties, will be fully resolved.

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Eye Research Institute
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MDS Health Group Ltd.
MDS-SCIEX
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Visible Genetics Inc.

Industrial Affiliates:

Affymetrix
Alcan Aluminum Ltd.
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Base4 Bioinformatics Inc.
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Non-profit Affiliates:

Amyotrophic Lateral Sclerosis Society
Armaurer Hansen Institute
Arthritis Society of Canada
Association Française contres les myopathies
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Canadian Breast Cancer Foundation
Canadian Breast Cancer Research Initiative
Canadian Cystic Fibrosis Foundation
Canadian Diabetes Association
Cancer Research Society
Foundation for Fighting Blindness
Glaucoma Research Foundation
Heart & Stroke Foundation of Canada
Heart & Stroke Foundation of Ontario
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Huntington Disease Society of America
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Muscular Dystrophy Association (USA)
Multiple Sclerosis Society of Canada
National Cancer Institute of Canada
National Cancer Institute (USA)
National Institute of Health
National Parkinson Foundation
Retinis Pigmentosa Eye Research Foundation
Scleroderma Association
Terry Fox Foundation
University of Alberta Hospital Foundation

Government Affiliates:

Biotechnology Human Resource Council
Fonds de recherches en santé du Québec
Human Resources Development Canada
Japan Science and Technology Council
Medical Research Council of Canada
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Province of British Columbia
US Department of National Defense
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