ANNUAL REPORT
2001-2002

Building a Foundation for
New Technologies and Therapies

Our Vision and Mission

The Stem Cell Network is a unique collaboration by leading Canadian biological scientists, social scientists, clinicians and engineers, with the mandate to investigate the therapeutic potential of stem cells for the treatment of diseases currently incurable by conventional approaches. The Network's ultimate goals are a) to be the catalyst for development of new therapies for a wide variety of chronic degenerative diseases; b) to contribute to the training and education of specialists competent in these technologies; and c) to facilitate the transfer of technologies to the marketplace. The Network recognizes the concerns of Canadians regarding the source of stem cells and their use in research and, while operating under the highest legal and ethical standards, will promote an informed debate on ethical, legal, social and policy matters related to stem cell research.

The Networks of Centres of Excellence of Canada

The Stem Cell Network is one of 22 networks funded by the Networks of Centres of Excellence, Canada's flagship science and technology program. Industry Canada provides funding to the federal government's three granting councils (the Natural Sciences and Engineering Research Council, the Canadian Institutes of Health Research and the Social Sciences and Humanities Research Council) to support and oversee this initiative. For information, visit www.nce.gc.ca.

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Building a Foundation for
New Technologies and Therapies

Stem Cell Network

Network of Centres of Excellence
Réseaux de centres d'excellence

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The Network.
has quickly emerged as the voice of Canada's stem-cell researchers

Judy Birdsell

Report from Judy Birdsell

Chair of the Board of Directors

With this annual report, we mark the first year of the Stem Cell Network, launched in April 2001 as one of Canada's Networks of Centres of Excellence.

The Stem Cell Network is a unique collaborative effort, drawing together more than 50 of the country's best and brightest scientists, ethicists, bioengineers and clinicians.

In the first year, researchers from all fields have come together to work in novel ways for collective benefits. As a result, the Network has quickly emerged as the voice of Canada's stem-cell researchers, a repository of scientific expertise, and the hope of health charities and thousands of Canadians who live with chronic and debilitating disease.

The Stem Cell Network's first year been a year of promise for a new area of medicine, a year of reflection as politicians and the public explore the moral and scientific implications of the research, and a year of debate as scientists await a legislative framework for their work.

The Network is honoured to have at its helm Scientific Director Dr. Ron Worton, a respected researcher and CEO of the Ottawa Health Research Institute, and stem-cell pioneer Dr. Connie Eaves, Associate Director of UBC's Terry Fox Laboratory, who serves as Associate Scientific Director. Ron and Connie, along with Executive Director Drew Lyall, provide a clear direction and energetic commitment to this new area of research.

The Stem Cell Network is led by a very strong Board of Directors. The Board understands that this research holds enormous potential, but requires great care going forward. And, because the public looks to stem cell research with high expectations, the Network faces an uncharacteristic level of scrutiny.

Dr. Howard Alper, Vice-Rector, Research, of the University of Ottawa, sits on the board as a representative of our Host Institution, one of the most important fully bilingual universities in the world. Also from the research community is Dr. Alain Caillé, Vice-Rector, Research, at the Université de Montréal. And, from the not-for-profit sector, the board has Dr. Francine Décary, Executive-Director of Héma-Québec.

Frank Gleeson, President and CEO of MDS Proteomics, Tom Caskey, President of Cogene Biotech Ventures Ltd., Bill Ringo, former President and CEO of Eli Lilly (Canada), and Milton Wong, Chairman, HSBC Asset Management Canada and Chancellor of Simon Fraser University, are well-suited representatives of the business community.

Dr. Rebecca Eisenberg, Professor at the University of Michigan Law School, Dr. Eric Meslin, Director of the Indiana University Center for Bioethics, and Kent Plumley, who is a partner with the legal firm Osler, Hoskin and Harcourt, represent the ethics and legal community. And, from the Networks of Centres of Excellence Program, we have Dr. Richard Snell as our program officer.

Fuelled by the hope of lifesaving therapies, the Stem Cell Network looks to the future with optimism and a strong sense of purpose. Three years after the prestigious journal *Science* declared stem cell research the "Breakthrough of the Year," the potential of these remarkable cells continues to resonate around the world. In Canada, we hope to lead a research revolution that will create treatments for some of humanity's most tragic diseases.

Our Goal
is to move stem cells from the laboratory to the bedside

Ronald Worton

A Word from Dr. Ronald Worton

Scientific Director

Canada's Stem Cell Network was created a year ago to unite research scientists, clinicians, bioengineers and ethicists along medicine's new frontier — a frontier that may one day bring revolutionary treatments for a wide variety of incurable diseases.

Our goal is to move stem cells from the laboratory to the bedside, while contributing to debate on the ethical controversies surrounding research, and to accelerate all types of stem cell research by enabling collaboration among investigators.

Most scientists now believe that the potential of stem cell research is real, although cures will only follow years of painstaking work. Within this context, the Network's role is to promote collaboration among multidisciplinary research teams; probe the social, legal and ethical aspects of stem cell research; create a supportive and rewarding research environment; train and educate specialists; and foster informed debate on a field of science that is widely discussed, but often misunderstood.

In its first year, the Stem Cell Network — the world's largest network of stem cell researchers — has drawn leading thinkers from across Canada to its Board of Directors, chaired by Dr. Judy Birdsell, past president of the Canadian Cancer Society. We have put in place an exceptional management team, under the direction of Executive Director Drew Lyall, created an efficient administrative structure, incorporated and moved into permanent offices at our host institution, the University of Ottawa.

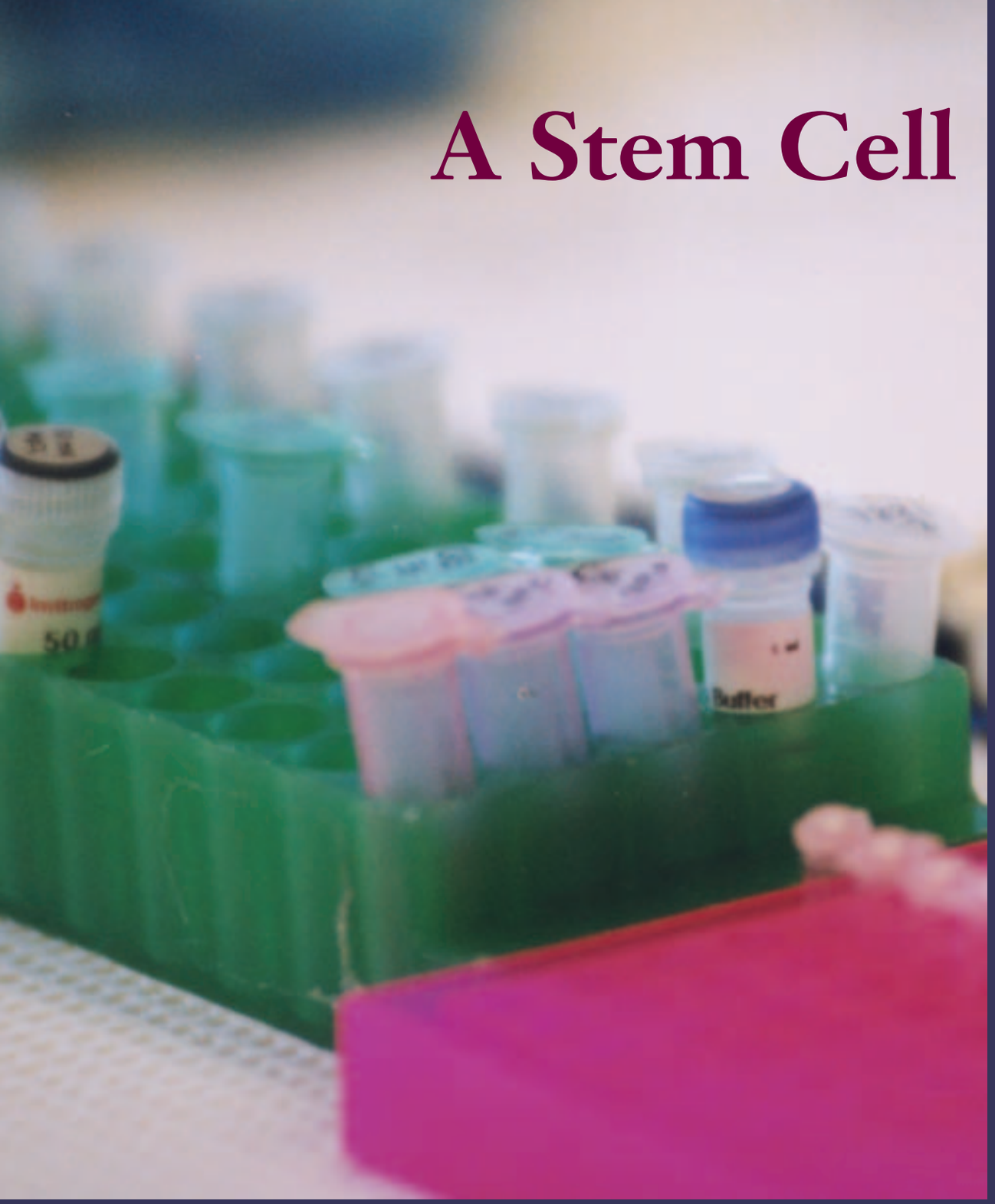
We have organized research into four themes: ethics, law and social policy; basic biology; bio-engineering; and clinical applications of research. Each of these themes is discussed in more detail in this annual report.

The Network's management committee obtained consensus among investigators on an integrated research strategy for the coming years. A number of highly successful workshops were held throughout the year to advance science, and a top-flight training program was established to engage researchers from across the country. Investigators participated in and presented at a number of international conferences and, from the earliest days, the Network developed a profile in the media as a recognized source of solid scientific information.

During the debate over Canada's stem cell legislation, the Network took an active role. Many of our members were called before the Standing Committee on Health as it discussed proposed stem cell legislation; a scientific workshop was organized on Parliament Hill; and we were regularly consulted by policy-makers who identified the Network as the voice of stem cell scientists in Canada. We participated in public forums and developed an extensive website and newsletter with the latest educational material.

It's clear that the Network's first year has been full and productive. It has been a year in which we have converted the privilege of being a Network of Centres of Excellence into useful and practical results. We have created an innovative, accessible and responsible research network, which is helping to advance science and stimulating informed debate.

Based on the foundation we have developed, and on increasing collaboration with partners in the public and private sectors, we look forward to exciting new scientific developments. The potential is tremendous.



A Stem Cell Primer

Stem cells are present from the earliest stages of embryonic development and provide the starting material for every organ and tissue. In humans, embryonic stem cells are found at the blastocyst stage, four to five days after the union of the sperm and the egg, before the embryo implants into the uterus. The blastocyst consists of a hollow ball of cells containing a pool of about 20 undifferentiated stem cells clustered in an inner cell mass. These cells are said to be pluripotent — capable of forming all embryonic tissues, but unable to form a complete organism without placental support. Embryonic stem cell lines that can grow and divide indefinitely are created by culturing the cells derived from the inner cell mass. These can be frozen in small batches for future experiments and distribution to other scientists.

Stem cells are also present in the fetus, child and adult. These so-called “adult” stem cells are found in many tissues throughout the body, such as blood, brain, intestine, skin and muscle, and are responsible for repair and regeneration in the body. Until recently all the evidence suggested that adult stem cells had less flexibility than embryonic stem cells, normally forming only cell types specific to the tissue of origin. However, recent research breakthroughs have shown that adult-derived stem cells appear to be capable of developing into cell types outside of the tissue of origin (e.g. human blood stem cells have been shown to differentiate into liver cells). However, while scientists now believe that some adult stem cells from one tissue can develop into cells of another tissue, no adult stem cell has been definitively shown to be completely pluripotent.

The hope of stem cell researchers is that they will be able to turn stem cells into repair tissue for diseased or aging hearts, livers and other organs. In order to develop treatments that are both efficient and precise, scientists need first to fully understand at a molecular level how stem cells of all kinds work — how they renew themselves, how they differentiate into other cell types and how they can be coaxed or manipulated into turning into cells with a specific function.

Theme I

stem cells have the potential to **lead** revolutionary treatments

Bartha-Maria Knoppers

Ethical, Legal, Social and Policy Issues

Most scientists believe that stem cells have the potential to lead to revolutionary treatments for a host of degenerative diseases. But how those stem cells are obtained is highly controversial.

Groups that believe human life begins at the moment of conception want to ban the creation of embryos for research purposes and the use of stem cells collected from early embryos left over after *in vitro* fertilization. But early scientific evidence suggests embryonic stem cells have the greatest versatility and potential to lead to therapies for a range of diseases, including diabetes, Alzheimer's, muscular dystrophy, Parkinson's, heart disease and stroke.

This is where seven of Canada's top ethicists and lawyers — the Stem Cell Network's research Theme I — provide insight and leadership. Their job is to guide scientists and the public through a rapidly unfolding world of research, creating a unique opportunity to help policy development in Canada.

One way they're helping to do this is through a newly developed website that draws together all relevant international policy documents on stem cell ethics, gene therapy, cloning and relevant laws and policies.

Accessed via **www.humgen.umontreal.ca** or at **www.stemgen.org**, this unique and comprehensive database makes it easier for people to obtain information and to consider issues relevant to new these technologies.

StemGen includes position papers and reports on stem cell research, gene therapy (germline/somatic), reproductive cloning, and therapeutic cloning. It will also include a review of current literature on these topics.

Through looking at where research is now, and where it is headed, clarifying the ethical issues surrounding the use of stem cells, and providing some reflection, legal and socio-ethical experts hope to provide information that will enable scientists to design ethical experiments.

In addition, by exploring the strengths and weaknesses of different policy-making approaches that have worked, or not, with other technologies, the hope is to help guide researchers and policy-makers before, or when, developments occur.

Areas of study in Theme 1 include research into chimeras; the impact of novel biotechnologies on specific communities; moral obligations to present and future generations; the regulation of stem cell research and cloning; and, the commercialization of research.

Theme II

stem cells have huge potential for medicine

Michael Rudnicki

Janet Rossant

Biology of Stem Cells

In the emerging world of stem cells — the powerful building-block cells that your body can turn into anything from muscle to brain to fingernails — scientists still understand very little about how the stem cell chooses its final shape.

Stem cells have huge potential for medicine. The hope is to turn them into repair material, rebuilding diseased organs or deteriorating brains. But while many biologists can point out these building-block cells and tell you what is in them and how they behave, the guidance system in a stem cell's genes remains a mystery.

In other words, what makes a stem cell a stem cell? Is it one gene or a pattern of thousands of genes?

The Stem Cell Network's gene expression project—the most extensive program of its kind in the world—is trying to answer these questions by identifying the genes responsible for telling a stem cell when to wait for instructions, and when to get to work.

Considerable detective work is involved because each cell in the human body has thousands of genes. In any one cell, only about 40 per cent of those may actually be "switched on" and working. Scientists call this "expressing" a gene. For instance, a cell in your stomach needs to switch on one set of genes to digest your food, but cells in your blood or bones don't need to use those genes at all, and express different ones instead. So which ones are switched on in stem cells? The first task is to look at all different kinds of stem cells. Researchers will study stem cells in blood, in nerve tissue, in muscles and other tissue, and compare the genes in them all, looking for similar patterns that will show the spectrum of genes, anywhere from a few dozen to many thousand, controlling stem cells. Researchers will also look just "downstream," at those cells that have already begun to differentiate, or turn from stem cells into the final product — finished bone, nerve or muscle cells.

Besides this overall pattern, this project is hunting for the important genes that regulate major steps in a stem cell's life. Which ones make it decide to reproduce itself, and which make it decide to turn into a particular cell type such as muscle or blood cells?

Most of the network's investigators are contributing samples of material for analysis.

And when scientists find answers there's a huge potential for insight that could lead to novel therapies and use of stem cells for treating human disease.

Theme III

stem cells play a critical and essential role in the human body

Stem Cell Bioengineering

Stem cells play a critical and essential role in the human body not only by providing the starting material for organs and tissues, but also for their continual maintenance, growth and renewal. As the embryo and fetus develop, stem cells are seeded into the various tissues and organs where they remain throughout life.

While scientists are discovering the effectiveness of these cells for gene, cellular, and regeneration therapies, they face a pressing problem: Stem cells are in short supply.

How do scientists grow enough cells for research and clinical purposes? How do they take 10 cells and make them 10 billion?

That's where the Stem Cell Network's Theme III comes into play. It's the job of this group to respond to the supply problem and to deliver cells for research and therapies.

As it stands, there are no effective ways to cultivate or stimulate most types of stem cells to grow to large numbers.

Stem cells are rare, they have complex requirements for growth, and they have to be cultured in a way specifically suited to each type of stem cell.

Not only that, bioengineers have to create processes to enhance the growth of rare cells in hopes of being able to more efficiently target their growth.

Among research projects underway in Theme III are the development of optimum culture conditions for embryonic, neural, pancreatic, blood, muscle, and other types of stem cells using tools such as microarray analysis; the development of serum-free media; the development of processes for large-scale culture of specific stem cell types; the development of culture conditions to selectively grow particular stem cell types or direct stem cells to specialize in particular directions; the development and production of viral vectors for engineering expression of new genes introduced into stem cells; and, the development of methods for studying gene and protein expression (genomics and proteomics) in single cells.

Theme IV
a number of diseases could benefit from stem cell research

Samuel Weiss

Freda Miller

Clinical Applications of Stem Cell Research

Two years ago, an islet transplantation procedure created at the University of Alberta provided remarkable hope for diabetics in Canada and around the world.

The "Edmonton Protocol" made national and international headlines when researchers described their success in reversing insulin dependence by transplanting islet cells, harvested from cadaver donors, into patients with type 1 diabetes.

Type 1 diabetes, a debilitating disease that requires rigorous monitoring and daily injections, occurs when the body's immune system mistakenly attacks the pancreas and destroys its ability to produce enough insulin to regulate blood glucose levels.

Diabetics with uncontrolled blood sugar may lose consciousness or fall into a coma. Some can't drive because they fear passing out at the wheel; others can't work because they don't have the energy to even sit at desk.

Complications of diabetes include blindness, heart disease, kidney failure, nerve damage and death. In Canada, the incidence of diabetes is rising dramatically.

While the Edmonton Protocol has been heralded around the world as a medical breakthrough, serious limitations restrict its widespread use. The biggest problem? There aren't enough donor pancreases for transplant.

Doctors need to transplant 800,000 islets to treat one patient. At the best of times, they can harvest 400,000 from a single pancreas. That means two to three cadaver donors are required for each treatment procedure. And, 40 per cent of the time, the procedure to retrieve islets is unsuccessful.

In Canada, where there are about 300 donor pancreases a year, fewer than 100 of the 100,000 diabetics who could potentially benefit from the procedure can receive treatment annually.

Researchers are looking at two possible solutions for the short supply of islet cells.

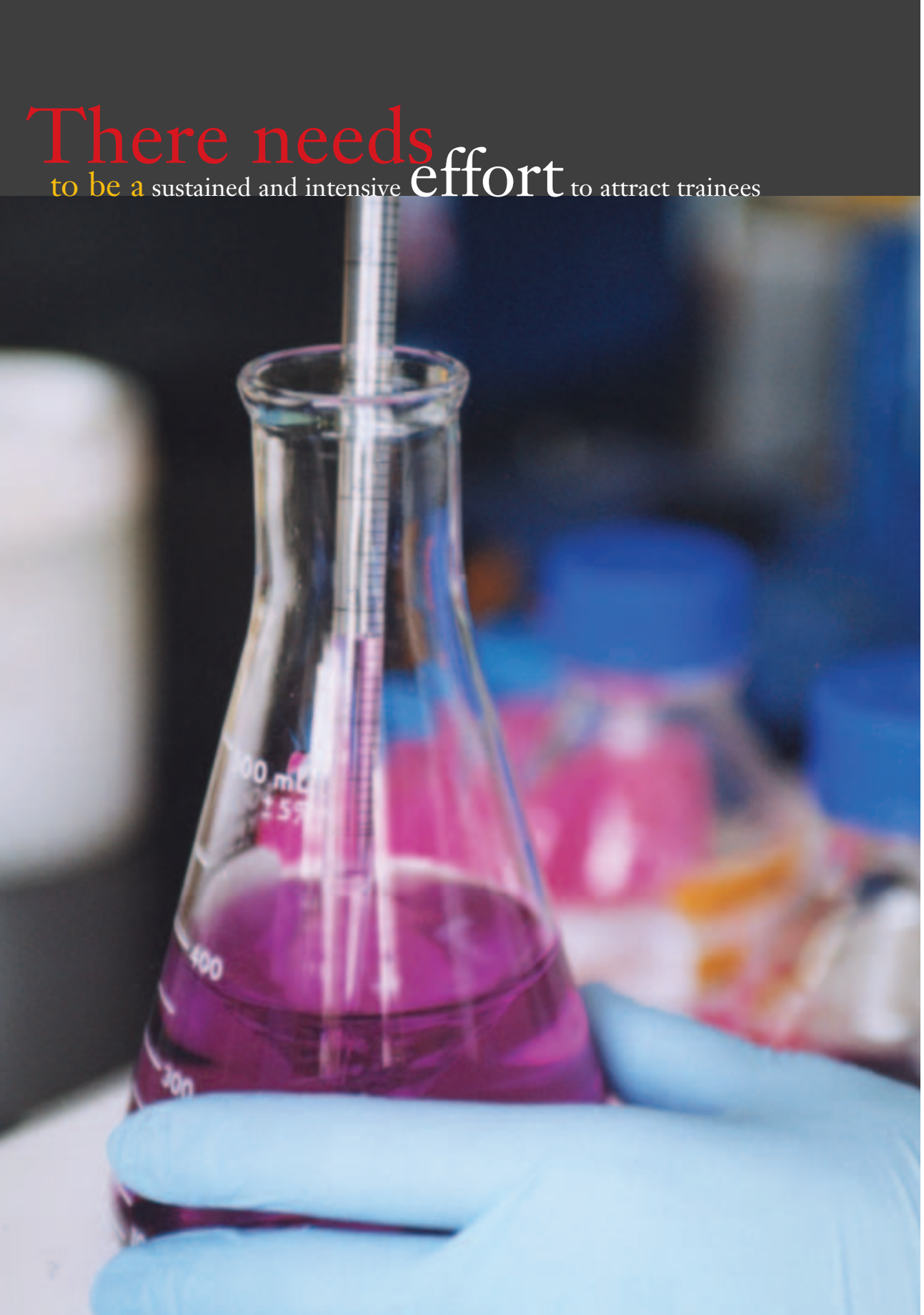
One is xenotransplantation, which is the use of animals — in this case, the pig — as a source of transplant material. However, there are myriad legal and ethical issues around xenotransplantation, including a fear that animal viruses could be transferred to humans.

The other possible solution lies with stem cells. Researchers want to try to stimulate stem cells — cells that are capable of growing into any other type of cells — to provide a potentially unlimited supply of islets.

Researchers in Theme IV hope to use embryonic stem cells to learn more about developmental biology to determine why diabetes develops and how to treat it. If they can understand how certain cells become insulin-producing, they will apply that knowledge to get diabetics' own cells to begin producing insulin.

Other Theme IV researchers are looking at potential therapies for diabetes using adult stem cells derived from the pancreas and the gut.

Diabetes is just one of a number of diseases that could benefit from stem cell research. In addition to diabetes, the Stem Cell Network is currently focusing on Parkinson's disease, hemophilia and muscular dystrophy.



Building Canada's Research Capacity

Recruiting and retaining trainees in Stem Cell Network laboratories, and making the training experience as worthwhile and enjoyable as possible, is a very high priority of the Network. In an area as competitive as stem cell research, there needs to be a sustained and intensive effort to attract trainees not just from Canada but also from other parts of the world.

The Stem Cell Network training program funds postdoctoral fellows, graduate students at the Master's and Ph.D. levels, undergraduate co-op students, summer students, and "research students" who have finished a Bachelor's degree and want a year of laboratory experience to help them decide whether to pursue a graduate degree. These trainees are funded through two programs:

1) a training program that considers applications for postdoctoral fellowships, graduate studentships and research studentships four times a year, and

2) a networking and training fund that supports co-op and summer students and provides funding for trainees to visit other laboratories to learn or teach techniques or to attend conferences. Funding for the latter program is available to all investigators at any time without a formal application process.

From October 2001 to spring 2002, the training program funded 31 trainees from 25 different laboratories in 17 institutions across the country. Eight postdoctoral fellowships, 21 graduate studentships, and 2 research studentships have been awarded for a total of $381,000 committed.

Plans are underway for other projects that will help to recruit and retain trainees, and enhance both the traineeship and mentorship experiences. These new initiatives include creation of promotional material, advertising, having a presence at strategic international meetings attended by students, creating more opportunities for trainee involvement in Network activities at all levels, and promoting some ideas at the national level that would make graduate and postdoctoral training more attractive.

Financials

STATEMENT OF FINANCIAL POSITION

Year ended March 31

	2002
ASSETS	
Current assets	
Cash	$ 2,801,469
Other receivables	6,516
Grant receivable	449,125
Prepaid research	1,355,470
Prepaid expenses	11,963
	4,624,543
Capital assets	84,577
	4,709,120
LIABILITIES AND NET ASSETS	
Current liabilities	
Accounts payable and accrued liabilities	97,962
Research commitments payable	281,543
Contributions received in advance	4,245,038
	4,624,543
Deferred capital contribution	63,200
	4,687,743
Commitments	
Net assets	
Invested in capital assets	21,377
Unrestricted	—
	21,377
	$4,709,120

STATEMENT OF OPERATIONS

Year ended March 31

	2002
REVENUES	
Network Centres of Excellence grant	$ 2,958,962
Services in-kind	21,000
Deferred capital contribution recognized	15,800
Gain on disposal of capital asset	22
	2,995,784
EXPENSES	
Research grants	2,306,662
Salaries and benefits	266,721
Conferences, seminars and meetings	223,326
Professional and consulting fees	59,490
Communications	56,702
General and administration	36,231
Amortization of capital assets	25,275
	2,974,407
Excess of revenues over expenses for the year	**21,377**

Universities

University of Calgary
University of Alberta
University of British Columbia
B.C. Cancer Agency
Dalhousie University
McMaster University
Queen's University
John P. Roberts Research Institute
Lawson Health Research Institute
Western University
University of Ottawa
Ottawa Health Research Institute
University of Toronto
Hospital for Sick Children
Samuel Lunenfeld Research Ins.
Sunnybrook & Women's College HSC
University Health Network
University of Waterloo
University of Montreal
McGill University
Jewish General Hospital
Institut de Recherches Clinques de Montreal
Centre du Recherche en droit public
Laval University

Industries

OnManagament Inc.
Neurostasis
HSBC Asset Management Group
StemCell Technologies
MDS Proteomics
Osler Hoskin & Harcourt
Aegera
CellGene
Q-Biogene
Cogene Biotech Ventures Ltd.
Immunex
The Island Group Health Care Consulting

Federal departments and agencies

Biotechnology Research Institute/NRC

Not-for-profit groups

ALS Society of Canada
Canadian Blood Services-Bayer
Juvenile Diabetes Research Foundation
Muscular Dystrophy Association of Canada
Parkinson's Society of Canada
Hema-Quebec
HumGen
Centre for Genetics and Society
Indiana University
University of Michigan Law School

Investigators

Aubin, Jane	University of Toronto
Baylis, Françoise	Dalhousie University
Behie, Leo	University of Calgary
Bhatia, Mickie	Robarts Research Institute
Caulfield, Tim	University of Alberta
Clarke, Lorne	University of British Columbia
Dick, John	University Health Network
Dube, Ian	Sunnybrook & Women's College Health Science Center
Eaves, Connie	B.C. Cancer Agency
Ellis, James	Hospital for Sick Children
Galipeau, Jacques	Jewish General Hosp.
Garnier, Alain	Université Laval
Glass, Kathleen	McGill University
Hassell, John	McMaster University
Hayden, Michael	University of British Columbia
Hill, David	Lawson Health Research Institute
Humphries, Keith	B.C. Cancer Agency
Iscove, Norman	Ontario Cancer Institute
Jervis, Eric	University of Waterloo
Jirik, Frank	University of Calgary
Karpati, George	McGill University
Kieffer, Timothy	University of British Columbia
Knoppers, Bartha	Université de Montréal
Korbutt, Greg	University of Alberta
Lansdorp, Peter	B.C. Cancer Agency
Lemmens, Trudo	University of Toronto
Leroux, Therese	Université de Montréal
Lillicrap, David	Queen's University
Lorimer, Ian	Center for Cancer Therapeutics
Massie, Bernard	NRC, Montreal
McBurney, Mike	Center for Cancer Therapeutics
McInnes, Rod	Hospital for Sick Children
Megeney, Lynn	Ottawa Health Research Institute
Mendez, Ivar	Dalhousie University
Miller, Freda	Hospital for Sick Children

Nagy, Andras	Samuel Lunenfeld Research Institute
Piret, Jamie	University of British Columbia
Power, Chris	University of Calgary
Rancourt, Derrick	University of Calgary
Rosenberg, Lawrence	McGill University
Rossant, Janet	Samuel Lunenfeld Research Institute
Rudnicki, Michael	Ottawa Health Research Institute
Sabourin, Luc	University of Ottawa
Sauvageau, Guy	IRCM
Schuh, Andre	University of Toronto
Stewart, Keith	University of Toronto
Till, Jim	University of Toronto
Tremblay, Jacques	Universite Laval
Underhill, Michael	University of Western Ontario
van der Kooy, Derek	University of Toronto
Weiss, Sam	University of Calgary
Worton, Ronald	Ottawa Health Research Institute
Zandstra, Peter	University of Toronto

Board of Directors

Birdsell, Judy, PhD, (Chair), past-president, Canadian Cancer Society
Alper, Howard, PhD, Vice-Rector, Research, University of Ottawa
Caillé, Alain, PhD, Vice-rector, research, Université de Montréal.
Caskey, Tom, MD, President of Cogene Biotech Ventures Ltd.
Décary, Francine, MD, PhD, MBA, Executive Director, Héma-Québec
Eaves, Connie, PhD, Assoc. Scientific Director, Stem Cell Network; Associate Director, Terry Fox Lab
Eisenberg, Rebecca, PhD, Professor, University of Michigan Law Schools
Gleeson, Frank M., MBA, President and CEO, MDS Proteomics
Lyall, Drew, Executive Director, Stem Cell Network
Meslin, Eric, PhD, Director, Indiana University Center for Bioethics
Plumley, Kent, Partner, Osler, Hoskin and Harcourt LLP
Ringo, Bill, MBA, former President and CEO, Eli Lilly (Canada)
Snell, Richard, PhD, Networks of Centres of Excellence
Wong, Milton, Chairman, HSBC Asset Management Canada; Chancellor, Simon Fraser University
Worton, Dr. Ron, PhD, Scientific Director, Stem Cell Network; CEO, Ottawa Health Research Institute

Management Committee

Lyall, Drew	Executive Director, Stem Cell Network
Beckett, Barbara	Manager of Scientific Affairs and Training, Stem Cell Network
Knoppers, Bartha	Université de Montréal, Faculté de Droit
Rossant, Janet	Samuel Lunenfeld Research Institute
Piret, Jamie	University of British Columbia
Galipeau, Jacques	Lady Davis Institute for Medical Research
Eaves, Connie	Terry Fox Laboratory
Worton, Ron	CEO and Scientific Director, Ottawa Health Research Institute; Scientific Director, Stem Cell Network