
STEM CELL NETWORK | ANNUAL REPORT
IMPACT
2003-2004

Building on historic leadership and current collaboration and discoveries, Canada is poised to play a pivotal role in the future of stem cell science.

The Stem Cell Network is making an impact – an impact evident in the remarkable discoveries coming out of research laboratories across the country and in the energetic spirit of collaboration that is driving those discoveries. Only in its fourth year of operation, the SCN is securing a key Canadian role in a future in which stem cell science may unlock the doors that hide the cures to some of the world's most devastating degenerative diseases. In this Annual Report, we profile several initiatives that highlight the impact the SCN has had, is having and will have as scientists strive to better understand the role of the stem cell in the regeneration of the human body, the relief of human suffering and the improvement of our quality of life.

One major impact was the passage of Bill C-6, an *Act respecting assisted human reproduction and related research*. The landmark law received Royal Assent in March, allowing the use of surplus human embryos derived from *in-vitro* fertilization for scientific research. Through almost three years of debate, the SCN led the way in keeping the public, politicians and media informed to ensure discussions were fairly balanced. The SCN website became a trusted source of information while Network researchers appeared as key witnesses at Commons and Senate committee hearings to supply the scientific underpinning to what was a highly-charged emotional issue. In providing briefing materials to every MP and Senator, holding workshops and encouraging the enlightened exchange of ideas, the SCN played a major role in helping Canada create a legal framework in which this important work will proceed.

While those efforts were underway, the SCN also was busy building consensus on how to transform successes in the lab into successful therapies that not only defeat diseases but provide a return on the millions of dollars taxpayers have invested in research. As is explained further in this report, the SCN is creating a single biotechnology company to commercialize university and hospital-based stem cell research. As envisioned, this company will secure investment, develop product lines and create long-term economic benefit. Endorsed by eight key universities and hospitals, 45 senior stem cell scientists and major funding organizations, the company will be the first of its kind and could become a model for commercializing intellectual property in Canada and across the world.

In addition to bringing stakeholders together to support the idea of a single company, the SCN's championing of collaboration is paying dividends in the high levels of success achieved by Network investigators. As described in the pages that follow, the discovery of insulin-producing multipotent cells in the pancreas – a remarkable development that offers new hope for a cure for Type 1 Diabetes – is the direct result of expertise exchanged by SCN scientists in labs in Calgary, Edmonton, Vancouver and Toronto. Meanwhile, the establishment of a world class centre for the study of brain repair in Halifax can be traced to the SCN's role as a catalyst to attract investments

Judy Birdsell,
Chair, Board of Directors

Ron Worton,
Scientific Director

Drew Lyall,
Executive Director

in stem cell research and encourage the free flow of ideas and innovations. That story is told here too, as is the tale of how the SCN "de-isolated" a bright researcher at the University of Waterloo whose cell-imaging work is now creating a better understanding of how stem cells behave.

Beyond the lab, the SCN had a big impact in schools across the country, helping students weigh the potential benefits against the ethical/religious issues concerning the use of embryonic stem cells. As explained in this report, ***ENGAGE: Stem Cells,*** the first national-scope outreach program of its kind, was undertaken in partnership with Genome Canada and the University of Toronto's Joint Centre of Bioethics to encourage young people to engage in the complex issues they will face in the future. With the SCN providing the scientific content and creating and maintaining the website that supported the five-day teaching module, it succeeded far beyond organizers' expectations.

The SCN will reach out even further in November when it hosts the world's researchers and major granting councils in Montreal. More than 500 researchers and trainees are expected to attend the International Stem Cell Symposium, where the world's leading researchers will present their work, and the International Stem Cell Forum, where stem cell networks from Germany, Australia, Israel, the United Kingdom and Sweden will share insights on research, ethical issues and the protection of intellectual property.

The coming year will also see a change in leadership as Ron Worton follows through on his plans to retire as Scientific Director of the SCN after leading the organization from its inception. Michael Rudnicki, Director of the Molecular Medicine Program at the Ottawa Health Research Institute, was selected to become the new Scientific Director by a search committee composed of four Board members and four scientists and chaired by the Board Chair. We are confident he will provide strong leadership to the Network as it continues to champion the cause of collaboration to overcome diseases that have baffled medical science. The SCN is poised to build on its successes and make an even stronger impact in the future.

With SCN seed money and collaboration with labs across the country, Halifax is becoming a world-class centre for brain repair.

Dr. Ivar Mendez
Department of Surgery (Division of Neurosurgery) Dalhousie University

When the enemy is stroke, Parkinson's Disease or spinal cord injury, working together is the best approach, says Dr. Ivar Mendez.

"Repairing the brain is a very complex thing," says Dr. Mendez, a Stem Cell Network investigator and the head of neurosurgery at Dalhousie University and Queen Elizabeth II Health Sciences Centre in Halifax. "I believe that task can only be accomplished by putting all of our efforts together. Individual efforts in isolated labs will be less likely to come up with therapies. The best expertise from people around the country has a higher chance of finding those cures."

When it comes to collaboration, Dr. Mendez truly walks the talk. He asks for help from – and gives it back in return to – some of the best minds in medical research across the country.

"It's true collaboration," says Dr. Mendez. "Neural stem cells from Dr. Samuel Weiss's laboratory at the University of Calgary arrive in Halifax and our team travels with these cells to St. John's, Nfld. to work with Dr. Dale Corbett's lab at Memorial University, where the cells are transplanted into animals with stroke for testing of brain repair. Afterwards, the tissue comes to Halifax and we do further analysis. So, this is not just on-paper collaboration. There is movement of cells, of people, of tissue, from lab to lab across the country."

But what about the fear that sharing secrets will cost you glory? That the big guys in the larger labs in bigger cities will steal your research thunder?

With the SCN encouraging the free flow of ideas, that hasn't been the case for Dr. Mendez. He routinely exchanges his discoveries with Dr. Freda Miller at Sick Kids Hospital in Toronto, Dr. Derek van der Kooy at the University of Toronto and Dr. Leo Behie at the University of Calgary. Graduate students and post-doctoral researchers shift between each other's labs, spreading biotechnical innovation as they go. And instead of draining research away from Halifax to larger centres, collaboration has helped Dr. Mendez build the Brain Repair Centre in the Nova Scotia capital, creating a centre of neurological expertise where none existed before.

"The SCN was the spark for a critical mass of individuals to come together to support work on brain repair and stem cells," says Dr. Mendez. "And we have been able to leverage about $20 million for programs and infrastructure for brain repair research."

He used $500,000 in SCN project money to generate about $5 million in funding for the Stem Cells for Brain Repair project to be operated out of the Brain Repair Centre. Money for the project has come from the Atlantic Innovation Fund, the Queen Elizabeth II Health Sciences Foundation, the Dalhousie Medical Research Foundation and a variety organizations and institutions.

He also secured $8-million in infrastructure from the federal government for the Brain Repair Centre, and has built a brain imaging research laboratory, allowing a team of investigators to study neuronal circuitry in patients with Parkinson's, ALS, Huntington disease, multiple sclerosis, spinal cord and optic nerve injury. The centre, which works in partnership with the Atlantic Canada Opportunities Agency, Dalhousie University, the Government of Nova Scotia and the National Research Council, has one of the more powerful MRIs in the world. "It allows us to look at the structure of the brain and the function of the brain."

The centre has also opened a telemedicine and telerobotics centre. "We communicate through video and audio links. We have routine communication with all the neurosurgeons in Atlantic Canada. If there is a difficult case in Newfoundland, we can exchange information, look at the X-rays, even look at the patient and discuss the case and consult. With robotics, we are finishing the first phase so that we can help neurosurgeons to operate on a complex case with experts in Halifax. The surgeon in Halifax has control of the robotic arm."

It all comes back to collaboration. "It's a no-brainer," says Dr. Mendez, no pun intended. "We need to work together. The Stem Cell Network has been crucial in putting all these people and all these laboratories together."

"The SCN was the spark for a critical mass of individuals to come together to support work on brain repair and stem cells"

Dr. Ivar Mendez, Department of Surgery (Division of Neurosurgery), Dalhousie University

The discovery of insulin-creating multipotent cells in the pancreas brings stem cell science another step closer to defeating Type 1 Diabetes.

Dr. Derek van der Kooy
Department of Medical Biophysics
University of Toronto

A team of Canadian scientists has taken a big step forward in the journey to find a cell-based therapy to defeat diabetes.

Work at the University of Toronto by Drs. Raewyn Seaberg, Simon Smukler and Derek van der Kooy and team members across the country, has identified what has eluded scientists until now: a single cell in the pancreas capable of creating insulin-producing beta cells.

The findings, to be published in the September 2004 edition of *Nature Biotechnology*, represent a fresh new hope for diabetics in Canada and across the world who must undergo regular injections of insulin to compensate for defective pancreatic islet cells that regulate the body's blood sugar levels.

"This represents a potential cure for a deadly disease," says Dr. van der Kooy. "It wouldn't have happened – at least it wouldn't have happened in Canada – without the Stem Cell Network. This is an example of bringing together people with different expertise. And it worked out wonderfully."

In fact, the discovery could be a case study in cross-Canada collaboration. Dr. van der Kooy used "essentially the same assay" for identifying neural stem cells developed by Samuel Weiss at the University of Calgary. Because Dr. van der Kooy was unfamiliar with pancreatic cells (his expertise is retinal and neural stem cells), Timothy Kieffer, now at the University of British Columbia in Vancouver, and Gregory Korbutt, a University of Alberta professor who worked on the Edmonton Protocol for islet transplants, provided the needed help.

"Their work was spectacular," said Dr. van der Kooy. "We had the techniques available, but we simply didn't have any background in studying pancreases. They provided the tissue that allowed us to proceed."

The discovery offers considerable new hope, as it contradicts a recently published paper that suggested no such cell exists in the pancreas.

"It's very exciting," says Joel F. Habener, Professor of Medicine at Harvard Medical School and Associate Physician at Massachusetts General Hospital. "An earlier paper in *Nature* said, essentially, there are no stem cells in the pancreas. So this is a highly important paper in the field. This paper shows there is a rare cell that has the property to be a precursor, be multipotent and create insulin cells."

Many researchers have claimed there are adult stem cells in the pancreas, says Dr. van der Kooy. "They saw some new pancreatic cells being generated, but they didn't know which cells were doing it. We've shown that a single cell cultured from a pancreas can produce all the cells in the pancreas, including insulin-producing ones."

Dr. van der Kooy is careful to call the cell "a multipotent precursor cell" and not a stem cell. "If a stem cell is defined by its ability to proliferate and produce all the cells, then we've done that. But to truly show it's a stem cell, we have to show it can renew itself. We haven't shown that yet. We're working on it."

The discovery builds on a proud history of diabetes research in Canada, from the 1920s' discovery of insulin by Frederick Banting and Charles Best, to the development of the Edmonton Protocol for islet transplantation in 2000 by U of A researchers that has freed some diabetics from insulin injections. Given that donor organs used in the protocol are in such short supply, this discovery could be a key to the future treatment of diabetes.

"If this process can be replicated in human tissue, and scaled up, it could provide a means of making the islet transplant protocol that was developed in Edmonton more widely available as a therapy for Type 1 (Juvenile) Diabetes," says Dr. Kieffer. The next step, says Dr. van der Kooy, will be testing the cells in mice to see if they can rescue diabetes, a step that would bring them ever closer to a cure.

Robert R. Hindle, Chairman of the Board of the Juvenile Diabetes Research Foundation of Canada, calls the discovery, "a tremendously encouraging step forward for everyone affected by juvenile diabetes."

"This is a very tangible demonstration of how the SCN has rapidly moved forward stem cell and stem cell-related research which offers a wide array of therapeutic potential. At the same time, this discovery shows how rapidly specially-focused research can zone in on the target. The SCN has created a unique forum to permit widespread multidisciplinary research across the world. It is worth noting that, once again, a major step forward in diabetes research has occurred in Canada."

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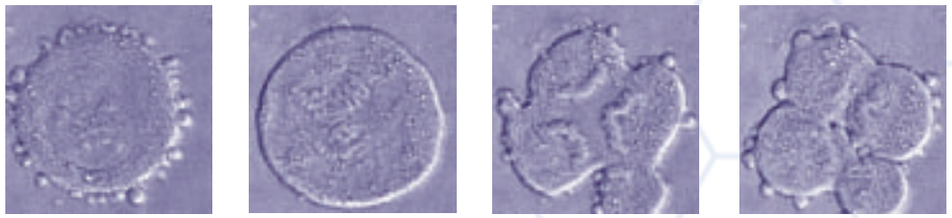
Dr. Derek van der Kooy, Department of Medical Biophysics, University of Toronto

Tucked away in a lab, Dr. Eric Jervis' world-class work on cell imaging was going unnoticed until the Stem Cell Network brought him into the loop.



Dr. Eric Jervis
Department of Chemical Engineering
University of Waterloo

For Dr. Eric Jervis, the turning point was a Stem Cell Network annual general meeting.

Still six months away from tenure at the University of Waterloo, he was a chemical engineer doing innovative work on the imaging of cells. But few biomedical researchers knew his work existed, let alone could solve some of their most vexing problems.

The five-minute "home movie" he showed – weeks of cell activity recorded every three minutes, played backwards to show how masses of cells had proliferated from single cell origins – changed his life forever and helped stem cell researchers in Canada look at things in a new way.

"That was the big break, having five minutes of floor time and showing a little movie of cell lineage trees run backwards. I was amazed at the response. When I went over and looked at the 'Sticky Notes of Intent' – indications of interest to work together – I could not believe the people who had signed their names. Dr. Janet Rossant and Dr. Derek van der Kooy in Toronto. Dr. Connie Eaves in British Columbia. Dr. Leo Behie in Calgary. Suddenly the top stem cell researchers in Canada wanted to work with me. Dr. Lawrence Rosenberg at the Montreal General Hospital invited me onto his project. He saw that I could contribute the cell lineage understanding they needed."

Dr. Jervis calls SCN "the best thing that has happened to my career." He was doing world-class work. But, toiling at a university without a hospital or medical research centre, he was out of the loop.

"At a small university like Waterloo you very easily become geographically isolated. You're not running into people in the hall. A lot of important information gets shared in lining up for coffee. I didn't have that. I could go to Toronto for a day trip, but I wouldn't have access to everyone. They wouldn't know me because Waterloo is not known for its biomedical research."

"The SCN de-isolated me. It brought me into a family of researchers, with the support and structure to allow collaboration to happen. Now the interaction is just like it would be if I was at the same larger schools as these researchers. I was quite isolated before I got involved in the SCN. Now I have the opportunity to speak to these people."

The benefits flow both ways. Stem cells hold the potential to cure currently untreatable degenerative diseases. The hope is that transplanted cells capable of repairing diseased tissue could cure diabetes, muscular dystrophy, Parkinson's Disease or repair spinal cord damage. But for that to happen, the properties of transplant cells must be completely understood. With Dr. Jervis using the microscope image as "a behaviour morphological sensor" to trace stem cells back to their origins, a clear picture of their properties emerges.

"It's a rational approach to producing cells for transplantation," says Dr. Jervis. "You want to give transplant recipients only what they need and exactly the function they need. Fully customized, free of extraneous cells."

To make that happen, Dr. Jervis is working with Dr. Cindi Morshead, an Assistant Professor in the Department of Surgery at the University of Toronto. The fact that they are working together is another indication of how the SCN brings highly qualified personnel together.

"We come from totally different backgrounds," says Dr. Morshead. "I'm a cell biologist, he's a chemical engineer. We both have our strengths, but we both need each other. Those are the best collaborations to be in. If it wasn't for the SCN, we never would have got together on this project to do lineage analysis of single cells to see how they grow. The SCN brought us together."

The benefits of collaboration continue. A donor, impressed by the work Dr. Morshead and Dr. Jervis are doing, has contributed $200,000. Dr. Morshead is seeking matching grant money to buy more microscope equipment to expand the process of tracking the activities of the elusive stem cells. "It's important work," says Dr. Morshead. "It's a big leap forward to understanding how these stem cells work."

Dr. Jervis, happy not be toiling in isolation, concurs. "The SCN is one of the few programs that helps people not be tucked away in labs. It doesn't just encourage collaboration – it's built in. It's money specifically targeted to getting these things started."

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Dr. Eric Jervis, Department of Chemical Engineering, University of Waterloo

In an effort to foster "citizen engagement," an innovative nation-wide project brought the ethical debate over stem cells into 4,300 high schools.

While Members of Parliament were locked in a highly-charged emotional debate in the House of Commons this past year, an interesting phenomenon was underway in high schools across the country.

Students were tussling with the very same thing, trying to sort through the passion and pragmatism that engulf the arguments for and against the use of embryonic stem cells to fight diseases.

"It was the major issue of science and social policy of the day – and we had parallel processes," says Dr. Peter Singer, Director of the University of Toronto's Joint Centre for Bioethics. "It's in the national interest for young people to be well-informed and have opinions. That's what democracy is all about: citizen engagement."

ENGAGE: Stem Cells was the first national outreach program of its kind. The five-day teaching module, which balanced the science behind stem cell research with the ethical/religious issues that surround it, was sent to some 4,300 high schools – English and French, public and private, religious and non-denominational – across the country. Students did role-playing exercises to decide how they would make their own laws governing reproductive technology.

Funded by Genome Canada through the Ontario Genomics Institute, ***ENGAGE: Stem Cells*** was part of the Canadian Program on Genomics and Global Health based at the University of Toronto's Joint Centre of Bioethics. It emerged from concerns by students themselves that a lack of informed debate about the crucial issue of using stem cells was hampering sound decision-making. To make the project a reality, the Stem Cell Network supplied the scientific content and built and maintained the website that accompanied the in-class instruction.

"SCN was a key partner in this exercise," says Dr. Singer. "They had a lot of impact on the scientific issues. They had a good understanding of the policy and legislative issues. They supported the website. It would have been impossible to do it as well without them."

By all accounts, the project has been a significant success.

The SCN-built website for ***ENGAGE: Stem Cells*** has had 70,000 hits. More important, says Rick Levick, President of the Canadian Biotechnology Education Resource Centre, are statistics showing different internet provider visits, indicating some 15,000 different people used the site. "We are kind of astounded by the statistics. This is well beyond our expectations," said Mr. Levick, who helped make the module materials classroom-ready.

Teachers who used the module were also enthusiastic. "The project was excellent," says Rosemary Evans, who, with a biology teacher, taught the unit to Grade 11 students at Branksome Hall, a private, non-denominational girls' school in Toronto. "One student told me that the entire experience, from serving as a member of the team charged with drafting the legislation through to the press conference, was one of the most significant learning opportunities she had this year."

Shauna Nast, who was involved in creating the module, said young people need this kind of thoughtful approach to difficult issues. "I think a lot of students are eager to burst out of the classroom and use their talents and passion to make the world a better place. This module simulates that experience, but also shows them along the way how challenging these issues are. Black and white fade into grey. Issues are complex. Governance is not a straightforward business. I would hope that this module sensitizes students to the delicacy of the issues, and engenders respect for those in our society who wrestle with these issues."

ENGAGE: Stem Cells will continue to be used and be relevant to students for years. "It has a long shelf life for understanding the ethics and approach of science and biotechnology," says Mr. Levick. "It is tailor-made for the pan-Canadian curriculum requirement of science, technology and society. It is very timely."

Beyond which, it will help broaden the base of understanding of what will continue to be a controversial issue for the 21st century. "This is absolutely the kind of project the Stem Cell Network should be involved in," says Dr. Singer. "Any science group that focuses narrowly on medical technology issues, to the exclusion of ethical issues, is painting itself into a corner. Science is a public trust, supported through tax dollars by citizens. Citizens have every right to be engaged. The SCN is a good example of a group that follows that principle."

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Dr. Peter Singer, Director of Joint Centre for Bioethics, University of Toronto

The creation of a single company to manage intellectual property will transform innovation into economic benefit and bring cures to clinics.

James Price
Director of Partnerships and Corporate Development
Stem Cell Network

Canada's innovation in stem cell research could soon be converted into an equally innovative economic reality – one in which Canadians benefit from the strategic development and delivery of disease-fighting therapies.

Over the past year, the Stem Cell Network has brought together the key players in finding cures – the scientists themselves, the universities that support them and the funding agencies and charities that drive research in Canada – to build a vehicle to turn Eureka moments into economic benefits.

In what could become a model for commercializing research, the SCN has brokered an unprecedented agreement among Canada's top scientists and major universities and hospitals to collectively manage intellectual property and create a globally competitive Canadian stem cell company. This company will be better positioned to realize value from the more than $40 million annual investment in stem cell research.

For more than 40 years – from Drs. Ernest McCulloch and James Till proving the existence of stem cells in the early 1960s to Dr. Derek van der Kooy's 2004 discovery of multipotent insulin-creating cells in the pancreas – Canadians have led the way in a field that offers potential cures for degenerative disorders from Alzheimer's to Parkinson's, muscular dystrophy to heart disease, diabetes and cancer. Building on this history of scientific innovation, Canada is well positioned to take advantage of this transformative field of technology to generate significant health benefits and economic opportunity.

While there has been a proliferation of start-up biotech firms in Canada over the last decade, most remain small operations in which the CEO-scientist lacks sufficient time or business experience to move his or her innovation from lab bench to hospital bed. And with only small pools of capital to support the early stages of research and little follow-through financing available to get the product to the public, securing funding has been the highest hurdle of all.

Also, each university and hospital in Canada has its own policies on IP and technology transfer. This has made the much-needed bundling of patents, protected procedures and technologies to create a single product – be it a drug, a transplantation protocol or a therapy – too large an endeavour for most start-ups to manage.

"We do great research and a good job of protecting our IP, but we don't see it through to the technology and product development stage," says James Price, Director of Partnerships and Corporate Development at the SCN. "We have lots of start-ups, but few large biotech companies that have enough critical mass to get a product to market."

The company, as yet unnamed, will have that critical mass. It will have a world-class management team that not only understands stem cell research but can raise money, develop product lines and clear the innumerable legal and administrative hurdles that stand between research and results.

Mr. Price and Drew Lyall, Executive Director of SCN, travelled the country to talk to stem cell scientists, university technology transfer officers, biotechnology business managers, disease-fighting charities and government funding agencies to sound them out on applying the single-company approach to the business of moving stem cell research out of the labs and into the clinics.

They found an unprecedented willingness to collaborate.

"From our own 65 scientists, we have 45 letters of intent to found a single company – and we anticipate a lot more," says Mr. Price. "We have a working IP agreement with eight key universities/hospitals including the University of British Columbia, the B.C. Cancer Agency, the University of Toronto, the Hospital for Sick Kids, the University Health Network, the Robarts Research Institute, the Ottawa Health Research Institute and McGill University. The major granting councils and charities have all been very supportive."

John Challis, the U of T's Vice-President of Research and Associate Provost, says it "makes sense to create a company that can both protect and develop Canadian research results in this important field. It also makes sense to build such a company on the foundation of scientific collaboration that is the mandate of the SCN … The SCN has performed a real service in taking this initiative."

To make sure it is on the right path, the SCN engaged Dr. Jim Murray, a Canadian technology transfer pioneer, who helped put together the tech transfer office working group and develop the IP transfer agreement. The SCN hired Canadian expatriate Helen Becker, former head of technology transfer with the Institut Pasteur in France, to compile an inventory of some 200 patents, more than 150 of which are stem cell-related. Graham Strachan, former CEO of Allelix Biopharmaceuticals Inc. and a leader in the biotechnology sector since its birth some 25 years ago, has been brought in to investigate the commercial potential of various stem cell technologies to develop potential products.

The company will be structured like a mutual fund, to attract significant and non-traditional financing by diversifying the risk for investors and inventors. Instead of betting on one horse in the biotech race, investors will have a stake in the entire field.

"I think it's brilliant," says Cal Stiller, Chairman and CEO of the Canadian Medical Discoveries Fund. "When you are dealing with very early science, such as stem cell research, finding a way to generate value for everyone, while not creating unrealistic expectations, is very difficult. What this very creative initiative does is spread the risk and the value in an equitable way."

"When you are dealing with very early science, such as stem cell research, finding a way to generate value for everyone, while not creating unrealistic expectations, is very difficult. What this very creative initiative does is spread the risk and the value in an equitable way."

Dr. Cal Stiller, Chairman and CEO, The Canadian Medical Discoveries Fund

The Stem Cell Network's record for publications shows researchers at the top of their game, in the most competitive league in the world.

Dr. Janet Rossant
Winner of 2004 Killam Prize in Health Sciences

Stem Cell Network scientists published 139 times in peer-reviewed journals during 2003-2004.

What is even more impressive than the sheer volume of publishing is the very high quality of the work done: 35 papers authored or co-authored by SCN appeared in prestigious high-impact journals, including *Nature*, *Science* and *Cell.*

That roughly a quarter of SCN-related papers are receiving this kind of world-wide scrutiny is the clearest indicator possible that discoveries made in the past year alone are among the most influential among academics trying to unravel the mysteries of the stem cell.

Among the dozens of papers from 2003-2004 here are a few of particular noteworthiness:

- Stem cells: Self-renewal writ in blood. *Nature,* Dr. John E. Dick
- Contribution of hematopoietic stem cells to skeletal muscle. *Nature Medicine,* Dr. Fabio Rossi
- Is it ethical to transplant human stem cells into non-human embryos? *Nature Medicine,* Dr. Derek van der Kooy
- In vitro expansion of hematopoietic stem cells by recombinant TAT-HOXB4 protein. *Nature Medicine,* Dr. Keith Humphries, Dr. Guy Sauvageau
- Stem cells. Setting standards for human embryonic stem cells. *Science,* Dr. Janet Rossant
- Pregnancy-stimulated neurogenesis in the adult female forebrain mediated by prolactin. *Science,* Dr. Samuel Weiss
- Hematopoietic stem cells engraft in mice with absolute efficiency. *Nature Immunology,* Dr. Norman Iscove
- Wnt signaling induces the myogenic specification of resident CD45+ adult stem cells during muscle regeneration. *Cell,* Dr. Michael Rudnicki
- Rapid myeloerythroid repopulation after intrafemoral transplantation of NOD-SCID mice reveals a new class of human stem cells. *Nature Medicine,* Dr. John Dick
- Site-specific cassette exchange and germline transmission with mouse ES cells expressing phiC31 integrase. *Nature Biotechnology,* Dr. Andras Nagy
- Somatic cell nuclear transfer--how science outpaces the law. *Nature Biotechnology,* Dr. Tim Caulfield
- Bone marrow-derived stem cells initiate pancreatic regeneration. *Nature Biotechnology,* Dr. Mick Bhatia

Given widespread interest over the past year, it is worth wondering where Canadians would have got their information if the SCN did not exist.

Over the course of the past year, the Stem Cell Network became the trusted source for stem cell news and background materials for everyone from members of the public to Members of Parliament, from students to senators.

Our online presence is particularly impressive. From April 1st 2003 to March 31st 2004, more than 88,000 people visited the Network's website (www.stemcellnetwork.ca), resulting in almost 500,000 hits. There were more than 60,000 hits in the month of March alone when Bill C-6, *An Act respecting assisted human reproduction and related research,* was passed by the House of Commons and the Senate after almost three years of debate. A special Web feature on the bill proved hugely popular, with more than 35,000 hits in 2003-2004.

Also, the SCN's role in creating and maintaining a website link for ***ENGAGE: Stem Cells,*** an outreach program with 4,300 schools across Canada, was a complete success. The site has had 70,000 hits from 15,000 visitors, surpassing all expectations.

"I used to believe that I would never see a cure for blindness. Now, we're getting close and my outlook for the future has changed."

Donna Green, President, The Foundation Fighting Blindness-Canada

The SCN's proactive approach to engage the mainstream media helped make the Network the first stop for journalists seeking information. In the space of a year, there were more than 150 newspaper articles and hundreds of broadcast reports relied on the Stem Cell Network as an information source. The SCN was also featured in specialty publications, such as *Ottawa City, Hospital News,* and *Biotechnology Focus* and *Research Money.*

The Network is reaching people in other ways, too. Twice a year, 7,000 copies of the SCN news magazine are distributed to and through health charities, SCN partners, research institutes, patient groups, health leadership organizations and scientific researchers across Canada. Articles from the magazine are offered for reprint in other publications – a frequent occurrence.

And, the Network is developing strong links among its researchers in all parts of the country, facilitating work on large-scale collaborative projects. Through a monthly newsletter, called CELL*lines,* researchers are kept current on discoveries, meetings, events and partnership possibilities.

The Network's next big outreach effort will be the International Symposium on Stem Cells, as part of the annual general meeting in Montreal in November. While somewhat larger in scale – more than 500 scientists are expected to attend – it reflects the Network's approach in promoting an understanding of stem cell research, whether at high school forums, biotech conferences or through workshops for politicians and policymakers.

"Overall, there is some really terrific science. If even 25 percent of it reaches fruition, I think the field of stem cell research will yet again be changed by Canadians."

Dr. Ihor Lemischka, Department of Molecular Biology
Princeton University

AUDITORS' REPORT

To the Directors of the
Stem Cell Network / Réseau de cellules souches

We have audited the statement of financial position of the **Stem Cell Network / Réseau de cellules souches** as at March 31, 2004 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 Network'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.

In our opinion, these financial statements present fairly, in all material respects, the financial position of the Network as at March 31, 2003 and the results of its operations and its cash flows for the year then ended in accordance with Canadian generally accepted accounting principles.

Ernst & Young LLP

Ottawa, Canada,
May 7, 2004.

Chartered Accountants

ERNST & YOUNG

STATEMENT OF FINANCIAL POSITION

Year ended March 31, 2004

	2004 *(in dollars)*	2003 *(in dollars)*
ASSETS		
Current assets		
Cash	**2,916,056**	3,082,185
Other receivables	**20,332**	93,635
Grant receivable	**580,000**	1,220,049
Prepaid research	**—**	133,466
Prepaid expenses	**109,022**	5,320
Total current assets	**3,625,410**	4,534,655
Capital assets *(notes 3 and 5)*	**40,277**	63,884
	3,665,687	**4,598,539**
LIABILITIES AND NET ASSETS		
Current liabilities		
Accounts payable and accrued liabilities *(note 5)*	**76,867**	77,703
Research commitments payable *(note 5)*	**358,176**	10,000
Contributions received in advance *(notes 4 and 6)*	**3,094,495**	4,435,134
Total current liabilities	**3,529,538**	4,522,837
Deferred capital contribution *(note 5)*	**31,600**	47,400
	3,561,138	**4,570,237**
Commitments *(note 4)*		
Net assets		
Invested in capital assets	**8,677**	16,484
Unrestricted	**95,872**	11,818
Total net assets	**104,549**	**28,302**
	3,665,687	**4,598,539**

See accompanying notes

On behalf of the Board:

Director

Director

STATEMENT OF OPERATIONS

Year ended March 31, 2004

	2004 *(in dollars)*	2003 *(in dollars)*
REVENUES		
Network Centres of Excellence grant *(note 6)*	**6,095,639**	4,305,904
Services in-kind *(note 5)*	**65,580**	61,915
Contributions	**91,354**	46,000
Deferred capital contribution recognized	**15,800**	15,800
Interest	**3,650**	356
	6,272,023	**4,429,975**
EXPENSES *(note 5)*		
Research grants	**4,923,348**	3,447,860
Salaries and benefits	**575,172**	457,708
Conferences, seminars and meetings	**377,966**	268,586
Professional and consulting fees	**148,224**	61,126
General and administration	**76,173**	71,924
Communications	**69,258**	90,790
Amortization of capital assets	**25,635**	25,056
	6,195,776	**4,423,050**
Excess of revenues over expenses for the year	**76,247**	**6,925**

See accompanying notes

STATEMENT OF CHANGES IN NET ASSETS

Year ended March 31, 2004

	Invested in Capital Assets *(in dollars)*	Unrestricted *(in dollars)*	Total *(in dollars)*
Net assets, beginning of year	**16,484**	**11,818**	**28,302**
Excess of revenue over expenses	(9,835)	86,082	76,247
Investment in capital assets	2,028	(2,028)	—
Net assets, end of year	**8,677**	**95,872**	**104,549**

See accompanying notes

STATEMENT OF CASH FLOWS

Year ended March 31, 2004

	2004 *(in dollars)*	2003 *(in dollars)*
OPERATING ACTIVITIES		
Excess of revenue over expenses	**76,247**	6,925
Amortization of assets not involving cash	**25,635**	25,056
Deferred capital contribution recognized	**(15,800)**	(15,800)
Increase *(decrease)* in other receivables	**73,303**	(87,119)
Increase *(decrease)* in grant receivable	**640,049**	(770,924)
Decrease in prepaid research	**133,466**	1,222,004
(Increase) decrease in prepaid expenses	**(103,702)**	6,643
Decrease in accounts payable and accrued liabilities	**(836)**	(20,259)
Increase *(decrease)* in research commitments payable	**348,176**	(271,543)
Increase *(decrease)* in contributions received in advance	**(1,340,639)**	190,096
Cash provided by *(used in)* operating activities	**(164,101)**	**285,079**
INVESTING ACTIVITIES		
Capital assets acquired	**(2,028)**	(4,363)
Cash used in investing activities	**(2,028)**	(4,363)
Net increase *(decrease)* in cash and cash equivalents	**(166,129)**	280,716
Cash and cash equivalents at beginning of year	**3,082,185**	2,801,469
Cash and cash equivalents at end of year	**2,916,056**	**3,082,185**

See accompanying notes

1. GENERAL

The Stem Cell Network / Réseau de cellules souches [the "Network"] brings together more than fifty leading Canadian scientists, clinicians, engineers, and ethicists, with the mandate to investigate the immense therapeutic potential of stem cells for the treatment of diseases currently incurable by conventional approaches.

It is one of Canada's twenty-two Network Centres of Excellence ["NCE"]. The NCE program is administered and funded by the Natural Sciences and Engineering Research Council ["NSERC"], the Canadian Institute of Health Research ["CIHR"], and the Social Sciences and Humanities Research Council ["SSHRC"], in partnership with Industry Canada. The goal of the federal NCE program is to mobilize Canada's research talent in universities, industry and government to create new economy jobs, stimulate growth and improve the quality of life for Canadians.

The Network research programs are focused on four areas: the ethical, legal and social implications of stem cell research; basic stem cell biology; bioengineering of stem cells; and clinical applications.

The Network has been approved for funding for the years ending March 2002 to March 2005.

2. SIGNIFICANT ACCOUNTING POLICIES

These financial statements have been prepared by the Network in accordance with Canadian generally accepted accounting principles. The preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the year. Actual results could differ from those estimates.

Revenue recognition

The Network follows the deferral method of accounting for contributions, which include government grants. Funds are received from the Canadian federal government as well as anticipated private and public sector partners.

Grants and other contributions which have external restrictive covenants governing the types of activities that they can be used to fund are deferred until such time as the actual spending is incurred. Consequently, unspent grants having restrictions will be recognized as revenue in future periods when the spending occurs. Grants approved, but not received at the end of the accounting period, are accrued.

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.

Contributions and services in-kind

Many organizations and individuals contribute a significant amount of volunteer effort in each year. The fair value of these services is often difficult to determine. Contributed services are not recognized in the financial statements unless a fair value can be reasonably estimated, such services are used in the normal course of operations and the provider of the services has explicitly defined the value of the services to the Network. The Network is dependent on such contributors to appropriately report the value of all contributions and services in-kind to its administrative centre.

Capital assets

Purchased capital assets are recorded at cost. Donated capital assets are recorded on the balance sheet at their estimated fair value, and recognized in the statement of operations based on their related amortization policy.

Capital assets are amortized on a straight-line basis using the following annual rates:

Software	50%
Computer equipment	33%
Office equipment	20%
Leasehold improvements	20%

Research grant expenses

Research grant expenses are recorded as expenses when they become payable. Research grants that will be payable in future periods are summarized and disclosed as commitments in the notes to the financial statements.

3. CAPITAL ASSETS

	2004		2003	
	Cost	Accumulated Amortization	Cost	Accumulated Amortization
	(in dollars)	*(in dollars)*	*(in dollars)*	*(in dollars)*
Software	**4,167**	**2,361**	2,139	1,523
Computer equipment	**19,342**	**17,641**	19,342	11,193
Office equipment	**12,745**	**7,575**	12,745	5,026
Leasehold improvements	**79,000**	**47,400**	79,000	31,600
	115,254	**74,977**	**113,226**	**49,342**
Less: accumulated amortization	**74,977**		49,342	
Net book value	**40,277**		**63,884**	

4. COMMITMENTS

At March 31, 2004, the Network has specifically committed to the future expenses set out below. The commitments for 2006 are to be funded by the contributions received in advance as described in note 6 as well as being contingent on the Network securing additional funding from the NCE Program.

	2005 *(in dollars)*	2006 *(in dollars)*
Approved research grants	**5,728,300**	—
Approved training	**518,000**	125,000
Total committed to date	**6,246,300**	**125,000**

5. RELATED PARTY TRANSACTIONS

Under an agreement with the University of Ottawa ["University"], the University provides accounting and administrative support services as well as office space without charge to the Network. The value of the in-kind contribution received for services in fiscal 2004 is $65,580 [2003 - $61,915]. Leasehold improvements included in note 3 were contributed by the University of Ottawa.

The Network has expensed during fiscal 2004 a total of $40,000 [2003 - $166,666] in research grants to the University and $830,083 [2003 - $160,000] to the Ottawa Health Research Institute, of which $nil [2003 - $10,000] due to the University is included in research commitments payable as at March 31, 2004. Included in accounts payable and accrued liabilities is $ nil [2003 - $186] due to the University.

6. CONTRIBUTIONS RECEIVED IN ADVANCE

	2004 *(in dollars)*	2003 *(in dollars)*
BALANCE, BEGINNING OF YEAR	**4,435,134**	**4,245,038**
Contributions from the Network Centres of Excellence	**4,640,000**	4,496,000
Less: amount recognized as government assistance in year	**6,095,639**	4,305,904
Balance end of year, government funds	**2,979,495**	**4,435,134**
Other funds	**115,000**	—
Balance, end of year	**3,094,495**	**4,435,134**

Other funds of $115,000 include monies received from Foundation Fighting Blindness [$52,500] for the Retinal Stem Cell Project, and a partnership effort with the INMHA and the ICRH [$62,500] for Adult Stem Cells to treat Stroke.

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