



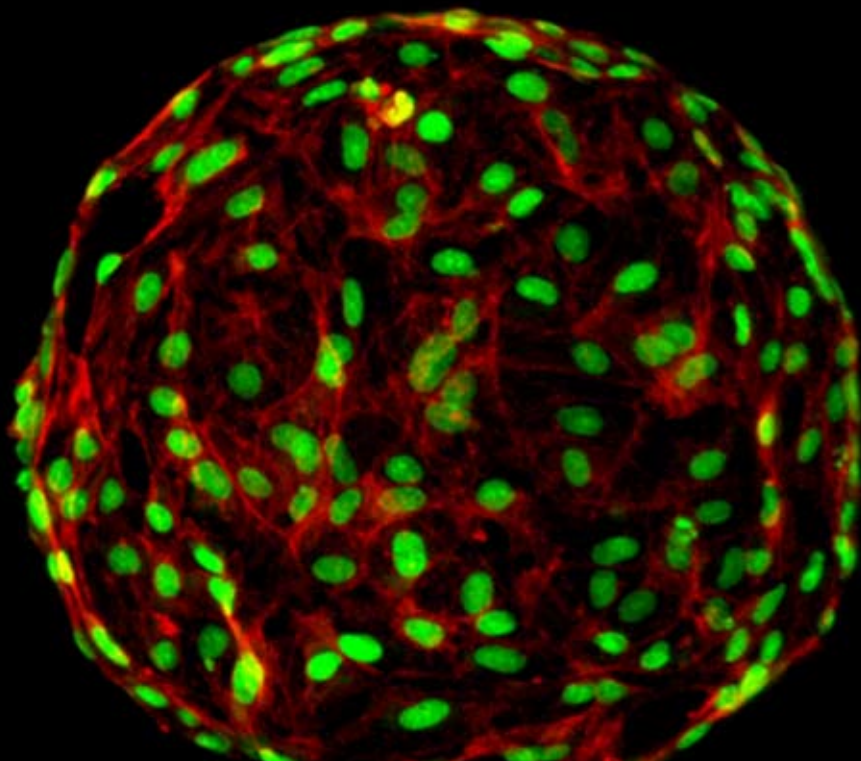
Canadian Institutes
of Health Research

Instituts de recherche
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CIHR IRSC
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Health Research Instituts de recherche
en santé du Canada

Regenerative Medicine & Nanomedicine



Investing Today in the Promise of Tomorrow

Second Edition

Canada

Regenerative Medicine & Nanomedicine

Investing Today in the Promise of Tomorrow
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Canadian Institutes of Health Research

160 Elgin Street, 9th floor, Address Locator 4809A, Ottawa, Ontario K1A 0W9 www.cihr-irsc.gc.ca

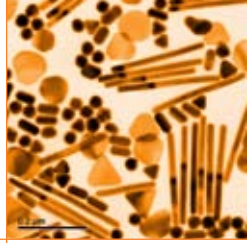
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Cover photo: Cells growing on a polymer sphere, as imaged by composite fluorescence and confocal microscopy.

Photo courtesy of Dr. Christopher Yip, University of Toronto.

Inset corner: Image of nanorods and other nanostructures. Photo courtesy of Dr. Warren Chan, University of Toronto.

Regenerative Medicine and Nanomedicine



Message from the President



Canada is entering a critical time in its development. We must identify and capitalize on our strengths to help create a stable, healthy future. Science and innovation hold the greatest promise for producing long-term benefits, such as a highly skilled workforce, new intellectual property and entrepreneurial opportunities.

In 2007, the Government of Canada announced a new S&T Strategy, *Mobilizing Science and Technology to Canada's Advantage*. Each of CIHR's 13 Institutes is helping realize the priorities identified in the S&T Strategy and the sub-priorities identified by the Science, Technology and Innovation Council.

One of those sub-priorities is regenerative medicine. This field of research, along with nanomedicine, holds the potential to dramatically change the way we diagnose and treat disease. As you will read in these pages, researchers across the country have already begun to translate advances in regenerative medicine and nanomedicine into innovative health solutions for Canadians.

Dr. Alain Beaudet
President, Canadian Institutes of Health Research

CIHR at a glance

The Canadian Institutes of Health Research (CIHR) began in 2000 with a mandate to create new health knowledge and translate that knowledge into improved health, a strengthened health-care system, and new health products and services for Canadians.

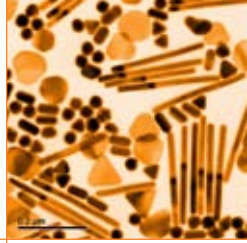
During that time, the world has witnessed some tremendous advances in health research. CIHR has helped shape this rapidly changing environment by removing barriers to collaboration across research disciplines, building national and international partnerships, and training a new generation of researchers.

While the majority of CIHR funding supports investigator-initiated research, a proportion is set aside for strategic initiatives in areas of research where the need is great and the likelihood of results is promising. Regenerative medicine and nanomedicine are two such areas that hold tremendous potential for Canadians.

Through the hard work and vision of the researchers CIHR funds, we are already beginning to realize some of that potential. With each new discovery, the course of regenerative medicine and nanomedicine research shifts, and new possibilities are born.



Building on Partnerships



Since its inception, the Regenerative Medicine and Nanomedicine Initiative (RMNI) has been closely aligned with the priorities of CIHR and a large number of external organizations. RMNI's goals and activities have been set through close collaboration with these partners. This integrative model ensures that RMNI's goals and objectives remain focussed on the most relevant activities, while reducing overlap and duplication in funding programs through multi-partner collaborative efforts.

RMNI has partnered with a number of CIHR Institutes, branches, and divisions on joint funding programs and collaborative workshops, meetings and symposia, including:

- Institute of Neurosciences, Mental Health and Addiction (co-lead)
- Institute of Genetics (co-lead)
- Institute of Aboriginal Peoples' Health
- Institute of Aging
- Institute of Cancer Research
- Institute of Circulatory and Respiratory Health
- Institute of Infection and Immunity
- Institute of Musculoskeletal Health and Arthritis
- CIHR Ethics Office
- CIHR Knowledge Synthesis and Exchange Branch

RMNI also has served as a nucleus for engaging external partners. A number of voluntary health organizations (VHOs), non-governmental organizations (NGOs), government agencies, and Networks of Centres of Excellence (NCEs) have joined in sponsoring joint funding opportunities, including:

- ALS Society of Canada
- Canadian Space Agency
- Canadian Stroke Network
- Foundation Fighting Blindness
- Heart and Stroke Foundation of Canada
- Jacob's Ladder

- Juvenile Diabetes Research Foundation International
- Neuroscience Canada
- Ontario Neurotrauma Foundation
- Stem Cell Network

In addition to funding research, RMNI has worked closely with a large number of government departments and agencies to sponsor workshops and meetings on topics of common interest. These meetings bring together experts and stakeholders from different domains, aligned along common themes, to form connections between fields, disciplines and backgrounds. CIHR's partners in these planning and development activities include:

- Alberta Heritage Foundation for Medical Research
- Alberta Ingenuity
- Canadian Federation of Biological Societies
- Environment Canada
- European Research Area and Canada Initiative
- Health Canada
- Industry Canada
- National Research Council Canada – National Institute for Nanotechnology
- Natural Sciences and Engineering Research Council of Canada (NSERC)
- Social Sciences and Humanities Research Council of Canada (SSHRC)

RMNI is also part of CIHR's contribution to the Cancer Stem Cell Consortium (CSCC). The CSCC is designed to enhance research into cancer stem cells, and its partners include the Ontario Institute for Cancer Research, Genome Canada, the Canadian Foundation for Innovation (CFI), the Stem Cell Network and research organizations in Canada and California.

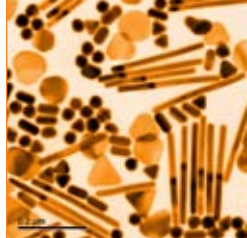
As of December 2008, RMNI has committed a total of \$65M in grants and awards funding. Additional funding opportunities are ongoing.



“Canadian medical researchers are at the forefront of regenerative medicine. The window of opportunity is open to create a tremendous new industry in Canada and to improve the health and quality of life of our citizens. That's why Canada's Science, Technology and Innovation Council advised the Government of Canada, and the latter agreed, that regenerative medicine is a key theme, or sub-priority, within the Government's Science and Technology Strategy.”

Dr. Howard Alper
Chair, Science, Technology
and Innovation Council

The Promise



Knee implants that encourage the re-growth of healthy joints. Tiny sensors that can detect the earliest signs of illness. Viruses designed to stimulate insulin production in people with type 1 diabetes. These are just a few of the innovative projects receiving support from CIHR's Regenerative Medicine and Nanomedicine Initiative – a visionary program that promises to change health care.

Science moves forward step by step, with each new discovery building on past accomplishments that make the next innovation possible. In regenerative medicine and nanomedicine, however, researchers are advancing what we know and what we can do at a rapid pace.

Regenerative medicine encompasses a wide range of health research fields that share the goals of stimulating the renewal of bodily tissues and organs or the restoration of function through natural and bioengineered means. Regenerative medicine also focusses on strategies that promote health and prevent disease. The overarching goal is to develop innovative treatments to improve quality of life.

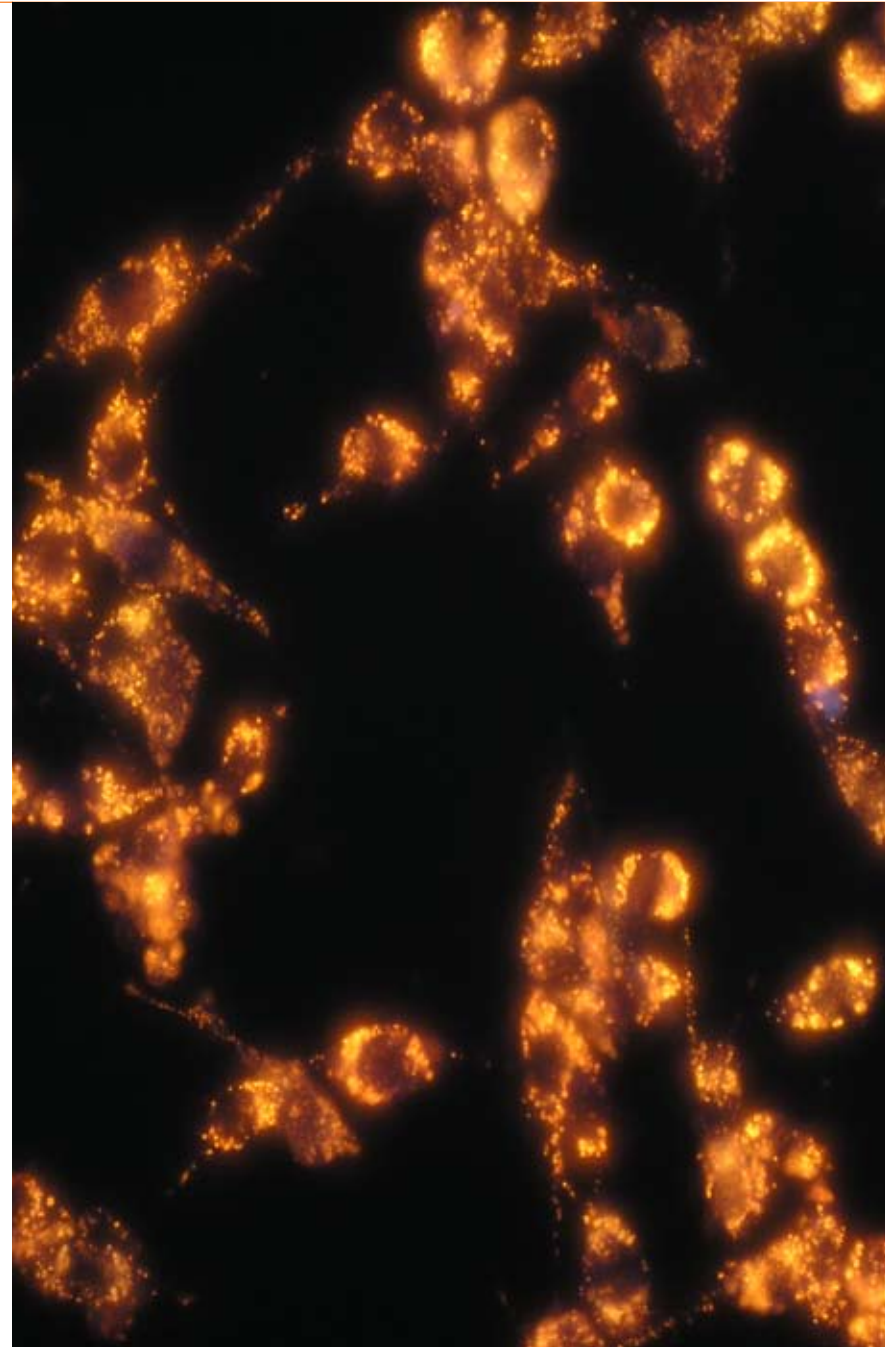
Nanomedicine is the application of nanotechnology to health research. Many materials have unique properties at the nanometre scale – one-billionth of a metre, or one-80,000th of a human hair. These properties have given rise to nanotechnology – which encompasses the technologies used in the design and manufacture of extremely small materials and devices built at the molecular level of matter, as well as the resulting materials and products themselves. These tiny materials can be used to diagnose and treat diseases or repair damaged tissues.

This brochure describes the work of some of the creative CIHR-funded researchers and research teams that are advancing the fields of regenerative medicine and nanomedicine, changing health care and creating new opportunities for economic growth.



“Integrating new technologies into health research that have not previously been applied has been a fundamental success of RMNI. This achievement has been driven heavily by the physical and applied sciences community. A challenge for CIHR will be to ensure that our efforts build on these early successes that hold the promise of significant social and economic benefit for Canada.”

Dr. Roderick McInnes
Scientific Director, CIHR's
Institute of Genetics



*Image of macrophages ingesting quantum dots.
Photo courtesy of Dr. Warren Chan, University of Toronto.*

Realizing the Promise

Changing the face of health care together

To realize the full potential of regenerative medicine and nanomedicine, CIHR and its partners in RMNI have developed a strategy of partnership, multidisciplinary and commitment to responsible use of technology. We're not just funding promising researchers; we're building an integrated research environment in which they can succeed.

RMNI's partnerships are breaking down barriers between research institutions, funding agencies, government departments, industries and countries. For example, in May 2006 CIHR embarked on an international partnership with the Juvenile Diabetes Research Foundation, an American non-profit organization that is the world's largest charitable funder of research into type 1 diabetes. This partnership, worth approximately \$2 million over five years, combines Canadian and American research capacity to develop strategies for regenerating or repairing insulin-producing cells in the body.

RMNI is also uniting researchers across many fields and helping ensure that the technology emerging from today's research is in Canadians' best interests.



*Operating theatre with integrated femtosecond laser system.
Photo courtesy of
Dr. Isabelle Brunette,
Maisonneuve-
Rosemont Hospital.*

Commitment to multidisciplinary research in nanotechnology

In January of 2008, RMNI co-sponsored the Canadian Workshop on Multidisciplinary Research on Nanotechnology: Gaps, Opportunities and Priorities. Organized by the three federal funding agencies (CIHR, NSERC and SSHRC), along with Health Canada, the National Research Council, Environment Canada and Industry Canada, the workshop brought together researchers and representatives from government, industry and citizens' groups. The participants identified emerging issues in nanotechnology, including its ethical and economical implications, potential impact on the environment and public health, and gaps in regulation and policy.

A summary report of this workshop is available from RMNI, detailing the key research gaps and needs identified in all areas, including: basic science gaps; ethical, legal, economic and social gaps; health and environmental risks; governance, regulatory and policy gaps; public engagement and communication needs; and challenges for interdisciplinary collaborations.

In addition, a number of short- and long-term research priorities were identified at the workshop, and are included in the report. Based on these, the major players in Canada's nanomedicine community now have a clearer picture of the state of nanotechnology research, key concerns about the technology, and ideas for future targeted funding programs.

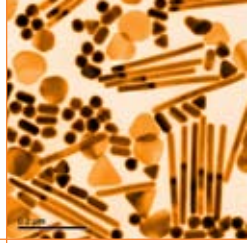
While the promise of regenerative medicine and nanomedicine belongs to tomorrow, CIHR and its partners are building towards it today. And we're already beginning to see progress.



"The advantage of a wide-ranging and flexible multi-partnered initiative like RMNI is the ability to rapidly respond to changing needs and priorities – both from our funding partners and from the research community itself. Supporting dialogue and interactions at all levels of the research enterprise is key to translating research excellence into meaningful health benefits."

Dr. Eric Marcotte
Associate Director, CIHR
Regenerative Medicine and
Nanomedicine Initiative
(RMNI)

Excellence in Research



A clear vision

With the support of RMNI, Dr. Isabelle Brunette and her team at the Maisonneuve-Rosemont Hospital of the University of Montreal created the BioFemtoVision research program to improve corneal transplants. This multidisciplinary program includes collaborators at the Institut national de la recherche scientifique (INRS) and at the Laboratoire d'organogenèse expérimentale (LOEX).

Traditional corneal transplants involve removing the entire cornea from a patient's eye and replacing it with one from a donor. The donor's cornea must be shaped by hand to match the recipient's eye and sewn into place. Patients must wait for a suitable donor cornea to become available and, once they receive their transplant, face a life-long risk their body will reject it.

Dr. Brunette and her team are adapting existing laser technology and harnessing the potential of regenerative medicine to address these challenges. They are testing a device, called a femtosecond laser, to remove the diseased layers of a patient's cornea and prepare the donor cornea. Similar to the laser used commercially in laser eye surgery, the device has a deeper reach and is more efficient in cloudy, thickened corneas.

The ultimate goal is to eliminate waiting lists by using tissue engineering technology to build new corneas from a patient's own endothelial cells. The team has already demonstrated that endothelial cells can be successfully grown in the lab and transplanted back into a living eye.

According to Dr. Brunette, targeted funding opportunities like RMNI have been the key to her success. "It's very simple – if this funding opportunity hadn't been there, we wouldn't be where we are today."



Dr. Isabelle Brunette
Maisonneuve-Rosemont
Hospital
University of Montreal

Promoting development in emerging economies

Regenerative medicine is usually considered high-tech and expensive – more suitable for the developed world. But the ability to repair or regenerate tissue may be of even greater benefit in the developing world, where the incidence of diseases such as diabetes or heart disease and accidents and burns is greater than in the developed world. Dr. Abdallah Daar of the McLaughlin-Rotman Centre for Global Health, the University Health Network and the University of Toronto, is leading a research network called RMethnet that seeks to maximize the potential and minimize the risks of regenerative medicine and nanomedicine worldwide.

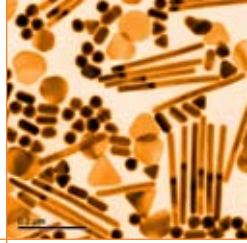
Dr. Daar's research team includes lawyers, ethicists, philosophers, social scientists and biomedical researchers from across Canada and the United States. They recently completed a study of the most promising applications for regenerative medicine in the developing world. Dr. Daar and his colleagues found that strategies for pancreatic islet regeneration, cardiac cell regeneration, and engineered immune cells would prove the most beneficial for easing the burden of chronic disease in developing countries. The study follows on the heels of a similar investigation of the top nanotechnologies for addressing urgent global health needs.

Dr. Daar's team is now looking at how low-to-middle income countries are using regenerative medicine. In a recent article, they documented regenerative medicine innovations in India. The team has also completed a similar study in China and has another underway in Brazil. Additionally, they are investigating the challenges associated with the application of neuro-regenerative medicine, with a focus on understanding these technologies in emerging economies.



Dr. Abdallah Daar
University of Toronto

Excellence in Research



A molecular approach to treating heart disease

Angioplasty to inflate the vein or artery, accompanied 80% of the time by the insertion of a stent to maintain the wider passageway, has greatly reduced deaths due to heart disease. However, the procedure itself can leave the surface of the vein or artery vulnerable to the deposition of blood proteins, further narrowing it.

Dr. Maryam Tabrizian of McGill University is working at the molecular level to minimize these problems. She and her team are using biomaterials such as polyelectrolytes, which are basically sugars, as lubricant coating and vehicles to deliver drugs and other substances directly on the stent. Because stents aren't used in all procedures, the team is also using the same principle to treat the surface of the arterial wall, delivering the biomaterials by perforated catheter.

Through her layer-by-layer assembly model, Dr. Tabrizian can deliver multiple substances, including anti-coagulant drugs, directly where they are needed. As a result, patients don't have to take the drugs themselves and the drugs are not generalized to all blood throughout the body. Other drugs, such as vascular growth factors that promote the formation of the first smooth cell layer, can also be delivered in this way. Among many other potential applications, a contrast agent can be introduced so physicians can monitor the stent once inserted in the patient's body.

"Cardiovascular disease is a multifactorial problem," says Dr. Tabrizian. "The versatility of this application means we can address many questions at the same time."



Dr. Maryam Tabrizian
McGill University

A better way to fight type 1 diabetes

Treatment options are limited for people with type 1 diabetes. Because their immune system destroys pancreatic beta cells and leaves them unable to produce insulin, they must take injections – sometimes as many as seven a day – to survive. They can wait for a donor pancreas to become available and undergo islet cell transplantation, but the relatively new procedure isn't always successful in the long term and requires the use of immunosuppressive drugs to prevent rejection of the foreign cells.

Dr. Timothy Kieffer of the University of British Columbia is taking a two-pronged, virus-based approach to improving the odds.

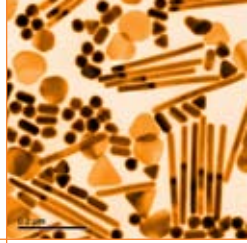
Gene therapy uses vectors, such as viruses, to deliver healthy genes and other materials to diseased sites in the body. Dr. Kieffer and his collaborators are using a viral vector shown to succeed in reaching the beta cells scattered throughout the pancreas while leaving other cells alone. Using this vector, Dr. Kieffer hopes to stimulate the growth of insulin-producing beta cells and stop the immune system from attacking those cells without having to shut down the entire immune system. He is investigating how cancer tumour cells evade immune system attacks to see if the same factor could provide protection to beta cells.

"Before we had this viral vector, we didn't have the tools to do this," he says. "Now, we're only limited by our imagination."



Dr. Timothy Kieffer
University of British Columbia

Excellence in Research



Building a better knee

For those suffering from joint disease, artificial knees can turn a painful walk into a pleasure. But patients must wait until the knee degenerates to justify the replacement and there's always the risk that the body will reject the foreign object. Dr. Rita Kandel of Mount Sinai Hospital at the University of Toronto and her team have a better idea. They are developing a substitute knee replacement that combines cartilage engineered in the lab with a degradable porous biomaterial that functions like bone. When implanted, the bone gradually grows through the porous holes while the biomaterial biodegrades – leaving a functioning, natural joint.

The advantages are manifold. This approach can be used for localized damage as soon as a defect is identified, or as a knee replacement when the damage is more diffuse. The replacement is natural, not artificial. And, says Dr. Kandel, the biomaterial can be shaped and customized to fit each recipient's knee, rather than using an "off-the-shelf" prosthesis. Once perfected, the technique will be applicable to other joints such as hips, shoulders and elbows. This means fewer people could be waiting for conventional joint replacements, resulting in shrinking waiting lists.

There's still a long way to go to make the new technique a reality. Developing cell sources to form the tissue and shaping and machining techniques to customize the replacement are just two areas Dr. Kandel's team of engineers, cell biologists, surgeons, radiologists and veterinarians are addressing.

"It is so important to have all these different perspectives to facilitate the development of this approach into a clinical treatment," says Dr. Kandel.



Dr. Rita Kandel
Mount Sinai Hospital
University of Toronto

First steps

Training on a treadmill can help people with spinal lesions regain some of their ability to walk, but little is known about the underlying mechanisms. The spinal cord has circuits that can generate basic functions such as locomotion even after an accident or degenerative disease creates a lesion. While some of this functional recovery happens naturally, Dr. Serge Rossignol of the University of Montreal has observed that the use of a specific noradrenergic drug initiated patterns of locomotion much earlier.

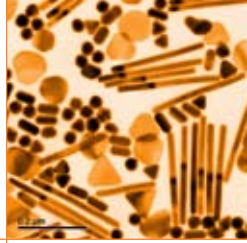
Dr. Rossignol and his team of researchers from the basic and clinical sciences at the University of Montreal, McGill University and Laval University are investigating whether sensory enhancements such as muscle reinforcement, tactile stimulation or visual virtual reality motivate people to work harder on treadmills. The goal is to provide further evidence of the benefits of treadmill training in regaining some ability to walk after a spinal lesion and to determine what works best to encourage that recovery. Dr. Rossignol and his team hope to provide evidence to support the development of guidelines on how to provide training that achieves the best results. They are also using electrophysiology and magnetic resonance imaging (MRI) to measure changes in the nervous system before and after training to better understand the mechanisms involved in the regeneration of locomotion.

The implications are far reaching. "We're not talking about miracles here," says Dr. Rossignol. "But if you can improve someone's ability to walk from 0.2 metres per second to 0.5, it can mean the difference between being able to cross a street or not."



Dr. Serge Rossignol
University of Montreal

Excellence in Research



Safer, gentler gene therapy

Gene therapy is a revolutionary concept with the potential to change the way we treat disease, but getting therapeutic genes into malfunctioning cells isn't easy. Dr. Marianna Foldvari and a team of researchers at the University of Waterloo are harnessing the power of nanotechnology to deliver genes and other therapeutic molecules painlessly to the sites of disease in the body.

Researchers have so far focussed on using modified viruses to deliver healthy versions of defective genes to ailing cells. However, viruses pose health risks and must have their disease-causing genes removed before they can be used safely. Dr. Foldvari's approach involves producing microscopic delivery molecules specifically designed for gene therapy that are safer for patients and easier to mass produce than viral delivery systems.

Dr. Foldvari's team is working on topical treatments for scleroderma of the skin, a debilitating disorder. By using creams and adhesive patches applied directly to the skin to deliver the gene therapy, Dr. Foldvari is eliminating the need for painful injections and giving doctors greater control over the treatment. This technology is also being tested for needle-free administration of disease-fighting vaccines and could be adapted to target cancer cells.



Dr. Marianna Foldvari
University of Waterloo

Detecting the subtle signs of disease

The human body sends out silent warning signs when health is failing. It could be a change in gene activity or the sudden presence of a tell-tale chemical in the blood. With the help of nanotechnology, Dr. Peter Grutter and a multidisciplinary team of researchers at McGill University are developing tiny sensors that can quickly and accurately pick up the subtle signs of disease.

Dr. Grutter and his colleagues are working on a microcantilever sensor – a tiny silicon structure similar to the microchips found in computers. The cantilevers can be coated with a substance that will bind with a biological molecule so that they move when the sensor is exposed to a particular biological signal. This microscopic movement, detected by lasers, will instantly signal the presence of a potential health problem. For instance, high levels of exhaled acetone are an early indicator of congestive heart failure. Doctors could use the tiny sensors to measure the amount of acetone on a patient's breath and begin necessary treatment.

Other potential applications of the microcantilever sensor include measuring blood glucose in people with diabetes, detecting viruses and bacteria, and screening people for genes that increase their risk of developing a disease. While this technology is at least a few years away from widespread application, it could become a faster, cheaper and more sensitive disease detection method.



Dr. Peter Grutter
McGill University

Excellence in Research

Electrifying nerve growth

Nerve cells, the delicate communication lines that keep the human body operating, are difficult to re-grow. Peripheral nerve cells, located outside of the brain and spinal cord, do have the ability to rebuild, but regeneration is slow and often incomplete. Dr. Douglas Zochodne of the University of Calgary is helping to change that, bringing new hope to people with nerve damage.

Researchers have known for some time that electrical fields can promote and guide the growth of nerve cells. Dr. Zochodne and his team are trying to develop an implantable nerve regeneration “tube” – an artificial structure covered in electrodes that could be implanted at a nerve injury site. The tube would then electrically stimulate the neighbouring damaged nerve cells to grow towards each other and re-form connections.

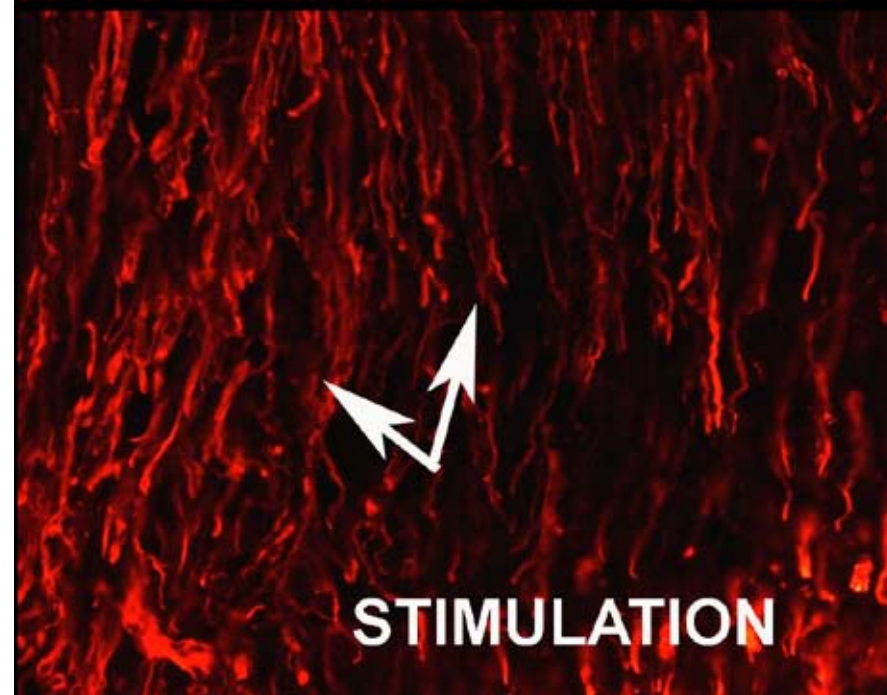
While it’s not known exactly how electrical fields guide nerve cell growth, Dr. Zochodne and his colleagues are investigating several possibilities. For example, the electrical fields could be stimulating the production of a growth factor known as BDNF, which may be an important key to making nerve cells grow. The researchers have also designed a microchip that can electrically stimulate isolated nerve cells. This microchip and the BDNF research are important steps towards creating an implantable regeneration tube to heal damaged nerves.



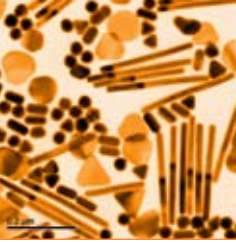
Dr. Douglas Zochodne
University of Calgary



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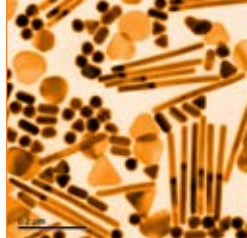


STIMULATION



Images of outgrowing axons from an injured mouse peripheral nerve, growing (from top to bottom) without (control group) or with a local electrical stimulation protocol. Note the more extensive outgrowth after stimulation. Photo courtesy of Dr. Douglas Zochodne, University of Calgary.

Looking to the Future

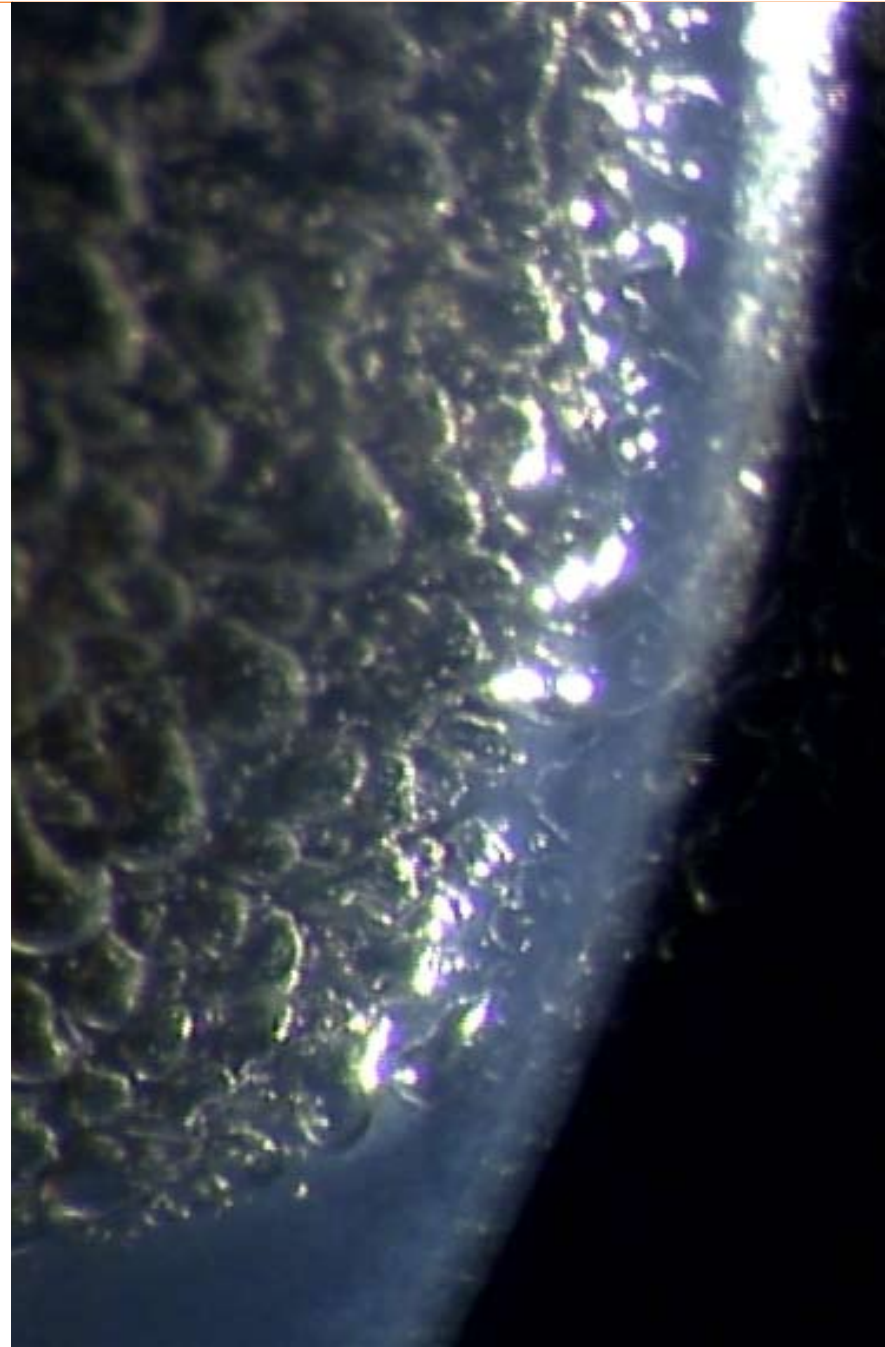


With its broad focus on research needs across the many domains of regenerative medicine and nanomedicine research, RMNI is well placed to take advantage of local, regional, national and international research initiatives. This integrative approach is unique in the world and reflects CIHR's mandate to bridge all themes of health research.

CIHR and its partners are moving forward with RMNI, and are committed to helping researchers see their projects reach fruition. By working together and rewarding excellence, we will be able to translate advances in regenerative medicine and nanomedicine into improved health for all Canadians.

"Canada is in a truly unique position. By combining regenerative medicine and nanomedicine in a single large initiative, CIHR has fostered collaborations not only between all types of health researchers and physical science experts but also with sociologists, philosophers, ethicists and regulators for approval of novel products. But to fully benefit from their leadership, Canada must now invest even more significantly in large teams that aim to solve important health problems by harnessing the unique opportunities offered by regenerative medicine and nanomedicine. Are we all up to the challenge?"

Dr. Rémi Quirion
Inaugural Scientific Director, CIHR's Institute of Neurosciences, Mental Health and Addiction



Microcavitation bubbles generated by femtosecond laser ablation in human cornea. Photo courtesy of Dr. Isabelle Brunette, Maisonneuve-Rosemont Hospital.



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