



neuro
Montreal
Neurological
Institute



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the neuro

**DISCOVERY
INNOVATION
TRANSLATION
TREATMENT**

INTEGRATION IN ACTION

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executive summary ///

Brain disorders affect 1 in 3 Canadians. According to Health Canada, the economic burden of neurological and psychiatric diseases, disorders and injuries is conservatively estimated at 14% of the total burden of disease, or \$22.7 billion annually. As the population ages, these costs will increase dramatically. In Quebec, the population is aging faster than the rest of Canada and almost every Quebecer knows someone who has struggled with Alzheimer's or Parkinson's disease, or has seen the effects of a stroke or brain tumour in a friend or family member. In the next 20 years, neurological conditions will become the leading cause of death and disability, magnifying the burden of neurological diseases on patients, their families, our health care system, and society.

The Neuro – the Montreal Neurological Institute and Hospital of McGill University and the McGill University Health Centre – offers the highest standard of neurological and neurosurgical care to the Quebec population and provides access to research-driven innovative diagnostics and therapeutics options. Each year, there are more than 42,000 ambulatory visits to The Neuro, over 2,300 patients admitted, and more than 28,000 diagnostic and 1,800 surgical procedures performed. With the highest concentration of neurologists and neurosurgeons in Quebec and clinician scientists in Canada, The Neuro plays a crucial role in the Quebec health care network, delivering exceptional care to thousands of patients while functioning as a critical referral centre for the most difficult neurological pathologies and for patients lacking a definitive diagnosis. As the largest specialized neuroscience research and clinical centre in Canada, The Neuro is a central hub for neuroscience research, international projects, clinical and research training.

The Neuro is a resource for all and an institution that has brought international recognition to Quebec. Quebec is a leader in neuroscience research, and Montreal, with the highest concentration of neuroscientists in North America, is a major research, clinical and pharmaceutical hub. McGill is central to this international strength with more than 200 professors focusing on neuroscience. McGill ranked 15th in the world between 1997 and 2007 in terms of research citations in Neurosciences and Behavior, and The Neuro accounted for half of these. The Neuro is the main contributor to McGill's success in neurosciences and mental health funding, and the single largest recipient of CIHR funding in this field. The CIHR grant success rate of The Neuro's researchers is almost three times the Canadian average.

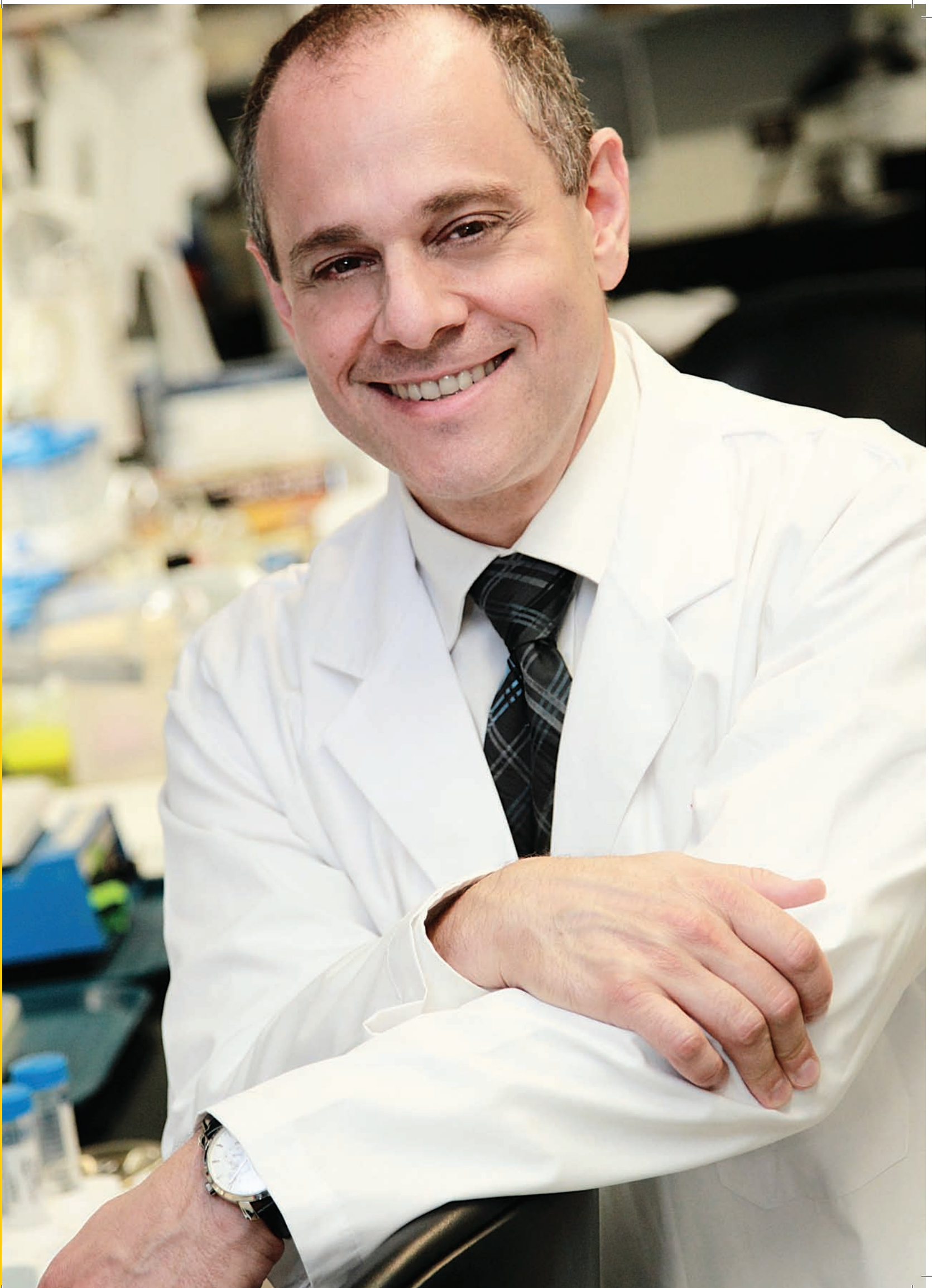
Recruiting, Training and Retaining Highly-Skilled Professionals. The Neuro's unique environment allows it to recruit exceptional faculty members from all over the world. These scientists and clinicians come to Quebec with advanced training that further strengthens the reputation of Quebec as a destination for highly skilled workers. In the past 20 years, The Neuro has recruited more than 40 outstanding researchers and clinicians. They have set up labs and clinical practices, trained new generations of scientists and physicians that have gone on to other academic institutions or industry. Together these recruits have brought in tens of millions of dollars in funding to Quebec and created vast networks of collaboration around the world. Since 1934, The Neuro has trained more than 1500 researchers, neurologists, neurosurgeons and neuroscience nurses.

An Economic Engine of Quebec. By fostering discoveries through direct support of innovative programs, in-house testing of breakthrough technologies to accelerate commercialization, and interactions with the pharmaceutical/biotechnology industry, The Neuro is a major contributor to the development of the Quebec economy. Fifteen companies have originated from The Neuro over the last 20 years. The economic impact of the R&D expenditures of these companies is estimated at more than \$46M annually and they have generated more than 450 highly skilled jobs for the benefit of Quebec.

The Neuro has facilitated the development of discoveries that diagnose and treat our patients and has had a major impact on Quebec's social and economic fabric. By combining the research strength of our scientists with our outstanding record of innovative compassionate clinical care, The Neuro will have a major impact on deciphering and treating the most serious nervous system disorders.



INTEGRATED



the integrated model the key to success

the neuro

An integrated neuroscience research and clinical centre that strives to advance our **knowledge** of the nervous system, discover new treatments and provide outstanding compassionate patient care.

values

Discovery, Innovation, Translation, Treatment

mission

To understand the nervous system, discover mechanisms of disease and develop and deliver effective treatments for neurological conditions including stroke, brain cancer, multiple sclerosis, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, and epilepsy.

To foster an outstanding research and clinical atmosphere by promoting interaction and collaboration.

To train and mentor new generations of scientists and skilled health care professionals and foster clinician scientists.

Previous page: Clinician scientist Dr. Edward Fon treats patients at The Neuro's Movement Disorder Clinic and is Director of the McGill Parkinson Program. In the laboratory, Dr. Fon's research focuses on the molecular events leading to the neuronal degeneration in Parkinson's disease.

neurological diseases and disorders: an increasing burden on society

One in three Canadians will be affected by a brain disease, disorder or injury at some point in their lives. For Quebec this translates to 2.6 million patients and their families. According to Health Canada, the economic burden of neurological and psychiatric diseases, disorders and injuries is conservatively estimated at 14% of the total burden of disease, or \$22.7 billion annually. When disability is included, the burden reaches 38% or more, and outweighs that of cancer and cardiovascular disease combined^{1,2}.

There are more than 1,000 diseases, disorders and injuries affecting the brain and spinal cord, including stroke, brain cancers, brain and spinal cord trauma, chronic pain, epilepsy and dementia. Currently, 5.5 million Canadians live with chronic neurological conditions. Many of which are progressive and degenerative, with no known cause or cure. Therapies exist for some, but in most cases, there is no way to slow progression of the disease.

With the aging population, the incidence of neurological and psychiatric-related conditions is forecasted to climb to one in two Canadians in the coming decades. Within 50 years, neurological conditions will become the leading cause of death and disability. Quebecers are aging faster than the rest of Canada and the impact of nervous system disorders on family, education, income, employment, housing and social participation will be profound and severe.

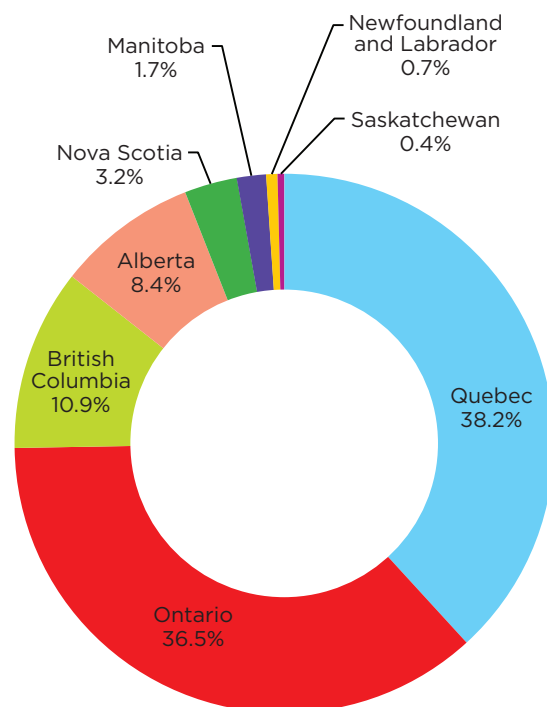
With such serious health, social and economic implications for individuals and society, managing neurological conditions has to be one of our highest health priorities. Integrating best standards of care with outstanding research is key both to unraveling the intricacies of the brain and nervous system and translating these discoveries in new effective therapies and cures. **The Neuro is uniquely positioned to have a significant impact on the understanding and treatment of nervous system disorders.**

neuroscience in Quebec: leading the world

Neuroscience and mental health research in Quebec constitute a strategic field of excellence recognized by the Quebec Science and Technology Council³. Quebec's national leadership in this field can be measured by Canadian Institutes of Health Research (CIHR) funding which directly reflects outstanding productivity and research excellence. Quebec has attracted 38% of CIHR funding for neurosciences and mental health research in the past three years, compared to 36% in Ontario, and 11% in British Columbia (Figure 1).

Figure 1: Distribution of CIHR funding for neurosciences, mental health and addiction over the last three years.

Source: CIHR, February 2012.



neuroscience at McGill: a legacy of strength and innovation

McGill is internationally recognized for its historical contributions to the field and for its high impact in contemporary disciplines that range from molecular and cellular biology to brain imaging and cognitive neuroscience. The breadth and depth of neuroscience at McGill is profound. There are more research papers published in neuroscience than in any other research domain

at McGill (Figure 2). McGill's strength in neuroscience is further illustrated by the high quality of its publications. This is reflected in both the number and H-index, a commonly use measure of publication significance (Figure 3). Using these measures, McGill ranks first in Canada and 15th in the world over the past decade.

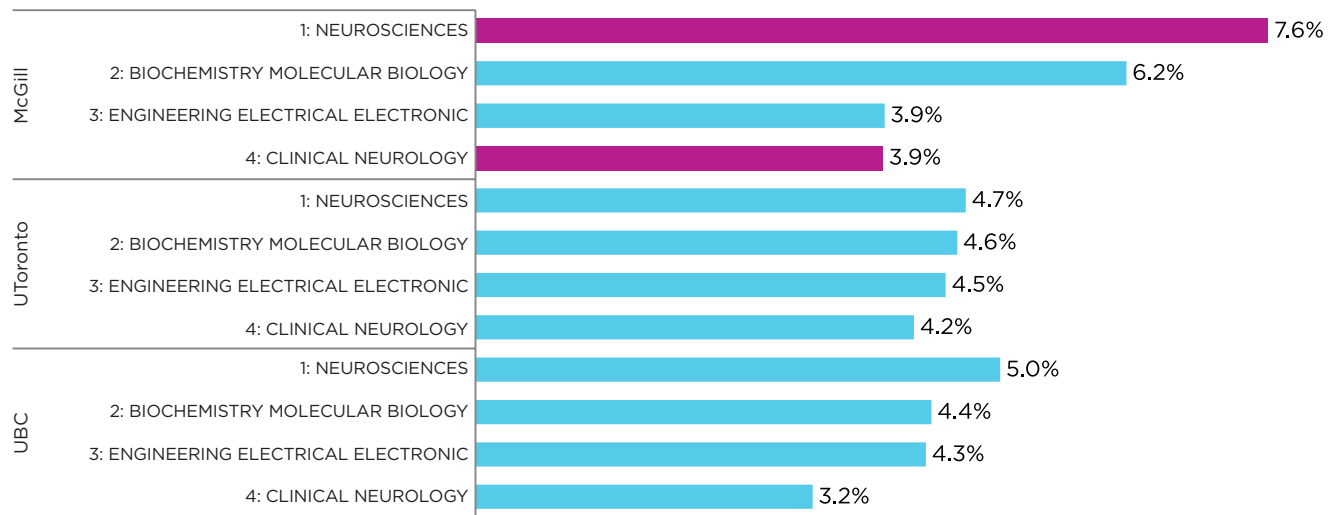


Figure 2: Percentage of total publications represented by the top four publication categories in three Canadian Universities. All research sectors are included. Source: ISI Web of Science, Thomson Reuters February 2012.

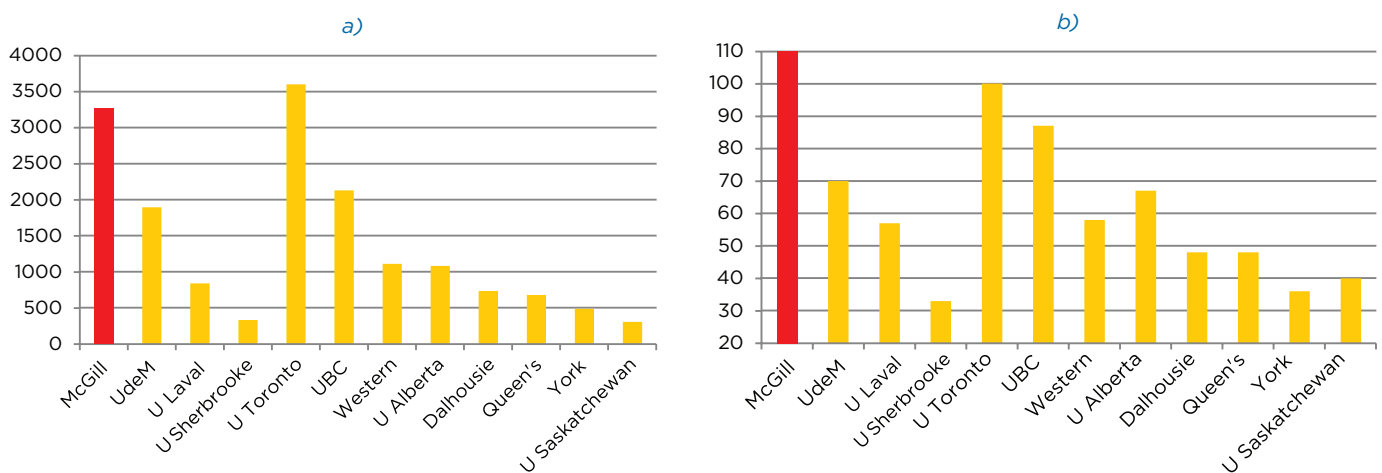


Figure 3: Analysis of publications in neurosciences for Quebec and Canadian Universities (McGill University, Université de Montréal, Université Laval, Université de Sherbrooke, University of Toronto, University of British Columbia, Western University, University of Alberta, Dalhousie University, Queen's University, York University and University of Saskatchewan) between 2002 and 2011.

a) Total number of publications (articles, reviews, proceeding papers, editorials, letters, discussions, book chapters).

b) H-index of these publications. The Hirsch index or H-index reflects both the number of publications and the number of citations per publication.⁴

Source: ISI Web of Science, Thomson Reuters February 2012.

the neuro: a unique research-driven medical centre dedicated to neuroscience

The Neuro – the Montreal Neurological Institute and Hospital – is the cornerstone of the neuroscience enterprise at McGill University. It is a research and teaching institute of McGill and forms the basis of the Neuroscience Mission of the McGill University Health Centre. The vision that clinical care improves when research advances basic biomedical knowledge was initiated by Dr. Wilder Penfield in 1934. Today, The Neuro is recognized internationally for integrating research, compassionate patient care and specialized training, all key to progress in science and medicine.

The Neuro offers the highest standard of neurological care and neurosurgery to the Quebec population and provides access to research driven-innovative diagnostics and therapeutics options. Each year, there are more than 42,000 ambulatory visits to The Neuro, over 2,300 patients admitted, and more than 28,000 diagnostic (angiograms, CT, EEG, EMG, MRI etc) and 1,800 surgical procedures performed. With the highest concentration of neurologists and neurosurgeons in Quebec and clinician scientists in Canada, The Neuro plays a crucial role in the Quebec health care network, delivering exceptional care to thousands of patients while functioning as a critical referral centre for the most difficult neurological pathologies and for patients lacking a definitive diagnosis. As the largest specialized neuroscience research and clinical centre in Canada, The Neuro is a hub for neuroscience research, international projects, clinical and research training.

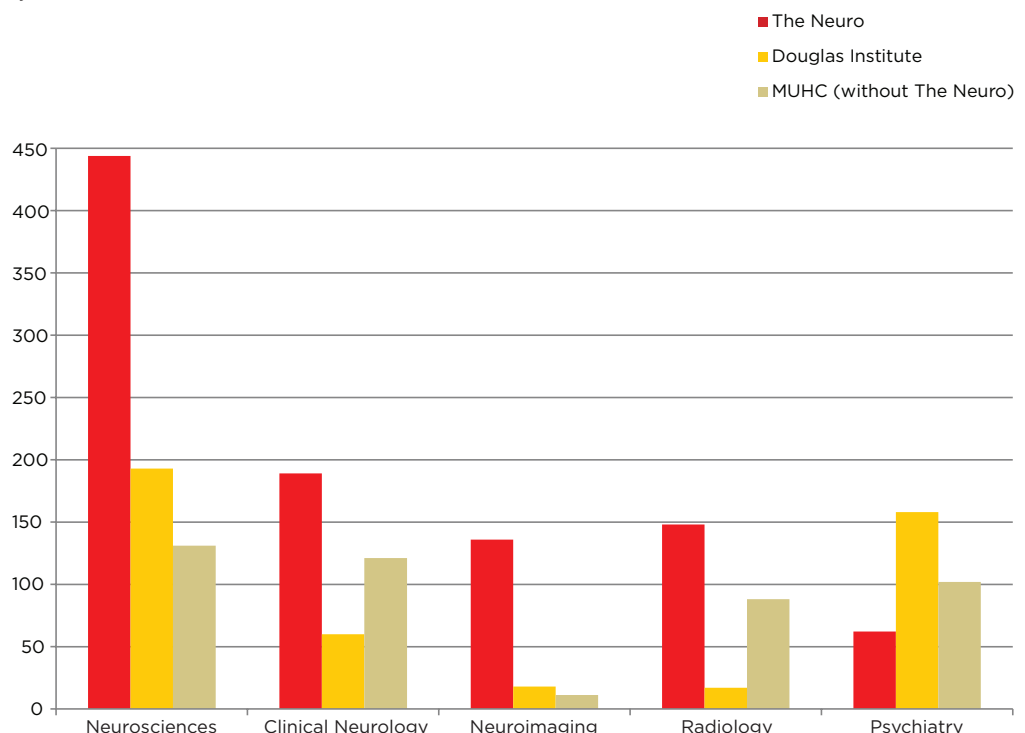
As a teaching and research institute, The Neuro is at the centre of McGill’s strategic plan in research and training in the neurosciences, is the cornerstone of the University’s largest graduate program, the Integrated Program in Neuroscience and a key site for McGill’s clinical training programs in Neurology and Neurosurgery.

Fifty-six faculty members lead international research teams that generate research and translational support from local, national and international agencies and private donors. The Neuro’s multidisciplinary teams, including an additional 220 academic staff, generate fundamental information that spans the full spectrum of neuroscience from cell and molecular biology to brain imaging and cognitive neuroscience. Over 300 graduate students and postdoctoral fellows from around the world pursue scientific training at The Neuro each year.

Neuro researchers are world leaders in cellular and molecular neuroscience, brain imaging, cognitive neuroscience and the study and treatment of epilepsy, multiple sclerosis and neuromuscular disorders. At The Neuro, bench meets bedside.

The Neuro has an impressive cumulative institutional H-index of 444, compared to 193 at the Douglas Institute or 131 at the MUHC, respectively 2nd and 3rd contributors to neuroscience in terms of publication number (Figure 4).

Figure 4:
Cumulative Institutional H-index. Comparison of the cumulative H-index for The Neuro, The Douglas Mental Health University Institute and the MUHC (without The Neuro), in 5 publication categories: neurosciences, clinical neurology, neuroimaging, radiology and psychiatry. The cumulative H-index is the addition of the H-index of each year for the last 10 years.⁴ Source: ISI Web of Science, Thomson Reuters February 2012.



the neuro: an engine of innovation that fuels the Quebec economy

RESEARCH FUNDING

The Neuro is the main contributor to McGill's and Quebec's neurosciences and mental health funding. Over the last five years, Neuro researchers have successfully competed for more than \$200 million in research operating and infrastructure support, all of which has been spent in Quebec. Of this amount, more than \$100 million was for research and much of this funding has come from outside of Quebec. All new faculty recruits to The Neuro are international leaders and have won support for lab equipment and highly specialized innovative platform through the Canada Foundation for Innovation (CFI), totaling \$46 million for the last fifteen years. The Neuro has 1% of Quebec's researchers, and yet it obtains

one tenth of Quebec's total National Institutes of Health (USA) funding. In 2007 The Neuro was recognized by the Federal Government as a world leader in neuroscience research and was awarded \$15 million as one of seven inaugural recipients of the Centre of Excellence in Commercialization and Research Award.

The Neuro's success rate for peer-reviewed operating grants with the CIHR, the main source of funding in Canada for biomedical research, is almost three times the national average (Figure 5).

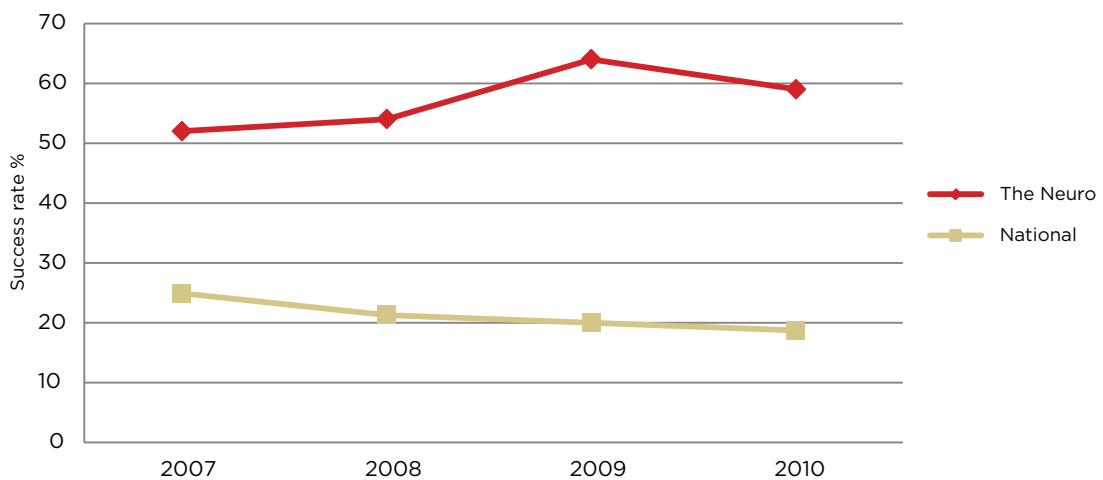


Figure 5: Success rate at The Neuro for CIHR open grant competitions between 2006 and 2010. The success rate is compared to the national success rate. Source: The Neuro and CIHR, February 2012.

INNOVATION AND COMMERCIALIZATION

By fostering discoveries through direct support of innovative programs, in-house testing of breakthrough technologies to accelerate commercialization, and interactions with the pharmaceutical/biotechnology industry, The Neuro is a major contributor to the development of the Quebec economy. Fifteen small to mid-sized biotechnology companies (listed below) have originated from The Neuro over the last 20 years. The economic impact of the R&D expenditures of these companies is estimated at more than \$46M annually and in the last five years, these companies have a cumulative GDP of more than \$200 million and they have created more than 450 private sector jobs for the benefit of Quebec. (Table 1).

Nine platforms and core facilities have been developed at The Neuro to support innovation. Investigators hold more than 50 patents and are engaged in active licensing deals to biotech pharmaceutical and medical device companies. This economic activity has resulted in \$1 million in royalties alone over the past ten years.

The Neuro is recognized as an outstanding research partner by a large number of corporations. Private companies turn to The Neuro researchers for contract research funding and as expert consultants. In the past three years The Neuro has signed 114 contracts for basic and clinical research worth \$29 million. These contracts included many clinical trials, which are essential to assess safety and efficacy of new pharmaceuticals therapies. This contract research at The Neuro contributes to the development of new diagnostic strategies and helps bring new drug therapies to the market.

COMPANIES FOUNDED BY NEURO FACULTY

- Aegera Therapeutics Inc.
- Painceptor Pharma Corp.
(Merger of Antalium and Neuroceptor)
- Thallion Pharmaceuticals
(Merger of Caprion Pharmaceuticals and Ecopia Biosciences)
- Stellate
- Biospective
- NeuroRx Research Inc.
- Advanced Bioconcept
(now part of PerkinElmer Inc.)
- True Positive Medical Devices
- Computerized Medical Imaging Inc.
- Neurovision Sciences Inc.
- Rogue Research Inc.
- Intelerad
- Hybex Surgical Specialties
- Scanwell Systems (NeuroShield)

RECRUITING, TRAINING AND RETAINING HIGHLY-SKILLED PROFESSIONALS

The Neuro's unique environment allows it to recruit exceptional faculty members from all over the world. These scientists and clinicians come to Quebec with advanced training that further strengthens the reputation of Quebec as a destination for highly skilled immigrants worldwide. In the past 20 years, The Neuro has recruited more than 40 outstanding faculty and clinicians. They have set up labs and clinical practices, trained new generations of scientists and physicians that have gone on to other academic institutions or industry. Together these recruits have brought in tens of millions of dollars in funding to Quebec and created vast networks of collaboration around the world. Over the last decade nearly 60% of Neuro publications were with international collaborators, for a total of 53 collaborating countries, compared to 33 to 46% for non-integrated institutions such as hospitals or university departments. Since 1934, The Neuro has trained more than 1500 researchers, neurologists, neurosurgeons and neuroscience nurses. Former fellows hold prominent positions in more than 60 countries around the globe.

Table 1

COMPANIES	CUMULATIVE ANNUAL ECONOMIC IMPACT LAST 5 YEARS
Aegera Therapeutics Inc.	GROSS OUTPUT: \$409 M GDP: \$237 M WAGES & SALARIES: \$143 M EMPLOYMENT: 1443
Painceptor Pharma corp.	
Thallion Pharmaceuticals	
Stellate	
Biospective	
NeuroRx Research Inc.	
Advanced Bioconcept	

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FACTS + FIGURES

the neuro: the highest calibre researchers, healthcare professionals and trainees

INSPIRING ACHIEVEMENT:

- 100 faculty members, 56 of which are principal investigators
- 19 clinician scientists – the highest concentration of clinician neuroscientists in Canada under one roof
- \$200 million in grant operation and infrastructure support over the past 5 years
- More than 1500 highly qualified medical and research trainees over the past 78 years
- More than 2500 papers have been published in international peer-reviewed journals in the past ten years
- One of the top two research centres in Quebec, measured by publication impact

Neuro faculty hold awards and grants from nearly 50 international funding agencies such as the Human Science Frontier Program, March of Dimes, and the National Parkinson Foundation.

FACULTY HONOURS:

- 3 Orders of Canada
- 1 Orders of Quebec
- 4 Canadian Medical Hall of Fame laureates
- 6 Royal Society of Canada fellows
- 2 Royal Society of London fellows
- 1 Gairdner Award winner
- 1 Balzan Prize winner
- 1 Foreign Associate of the National Academy of Sciences (USA)
- 2 American Academy of Arts and Science members
- 1 Killam Prize
- 13 Killam Scholars
- 2 Killam Professors
- 1 Killam Chair
- 9 Canada Research Chairs
- 8 James McGill Professors
- 1 William Dawson Scholar

clinical care



Clinician scientist Andrea Bernasconi and his team are giving new hope to untreated epilepsy patients. They are working on computer models that will automatically detect and delineate cortical dysplasia on an MRI scan and reproduce the biological character of the lesion.

The Neuro, the only Quebec centre specializing in neuroscience and neurological diseases, offers the highest standard of neurological care and neurosurgery to the Quebec population and provides access to research-driven innovative diagnostics and therapeutics options.

The hospital operates 80 beds including 14 in the highly specialized Intensive Care Unit, 4 operating rooms and 1 procedure room. Over 2,300 patients are admitted each year. More than 70% of these admissions are neurosurgical. 1,800 neurosurgical procedures are performed annually to treat patients with cancer, epilepsy, trigeminal neuralgia, intracerebral hemorrhage/stroke, cerebrovascular problems, peripheral nerve damage and patients requiring cervical or lumbar disc procedures (herniation repair or fusion), spine neuromodulation, shunts and brain neuromodulation.

We can count on 24 neurologists, 13 neurosurgeons – the highest concentration in Quebec, 3 neuroradiologists, 7 neuroanesthesiologists and 300 specialized nurses and health care professionals to offer their expertise to the Québec population.

clinical care

Divided in subspecialty programs and clinics including Multiple Sclerosis, Neuro-Oncology, Epilepsy, Chronic Pain and Neuromodulation, Spine, ALS, Neuromuscular, Movement Disorders, Functional Neurosurgery and Headache, The Neuro's ambulatory services see **42,000 patient visits** each year.

Furthermore, The Neuro's busy EEG CLINIC conducts almost **4,000 electroencephalograms** each year. The electromyography clinic performs more than 2,300 procedures annually. Each year, the neuroradiology department sees more than **17,400 patients** and conducts more than **28,000 interventional and diagnostic procedures and exams** such MRI, CT, fluoroscopy, ultrasound, angiography, stents, coils, etc. annually.

The Neuro's Preston Robb Day Centre welcomes patients requiring treatment for diseases such as multiple sclerosis, myasthenia gravis, and ALS. Their **5,300 annual visits** provide tertiary and quaternary care and prevent hospital admissions and emergency room visits.



Neuroradiologist Donatella Tampieri's department uses the most sophisticated equipment and technologies available to diagnose and treat more than 17,400 patients each year.

Statistics provided are based on activities in 2011-2012

S

STRENGTH

the strength of the integrated model

The government of Quebec recognizes that the most significant advances in patient outcome will emerge from centres that combine research and clinical care. To this end, it has designated University Hospital Centres⁵ as those that:

- offer outstanding care in highly specialized health domains
- play a leading role in teaching
- pursue research activities that keep Quebec medicine on the scientific cutting-edge
- evaluate new health technologies

The Neuro is world-class in each of these criteria and is a prime example of Quebec's vision for an integrated biomedical centre. The Neuro's intense focus on neuroscience and neurological diseases, combined with integrated research and clinical care, makes it unique in the world and recognized internationally for its expertise. Institutions around the world benchmark their programs against The Neuro. For example, the new \$400 million Tianjin Neurological Institute is modeled after The Neuro. An August 2010 Businessweek article quotes Rhode Island Hospital's Chief of Neurosurgery and Director of their new Neuroscience Institute as using The Neuro as their model. Max Cynader, Director of the Brain Research Centre at UBC, has stated that The Neuro is an ideal model for developing their neuroscience pavilion. In Europe, the new NIHR Cambridge Biomedical Research Centre in the UK and the new Brain and Spine Institute in France are attempting to replicate the integrated Neuro model. In Montreal, the new MUHC Research Institute and the Douglas Mental Health University Institute are modeling their current and future developments on the research and clinical integration pioneered at The Neuro.


Integration at The Neuro enables research and innovation that benefit society. Patients benefit from being treated in an institution with a combined research and clinical mission. Integration nurtures formal and informal interactions between researchers, clinicians, and patients. At The Neuro, science informs medicine and patients inform science. Our approach

has led to international recognition in the fields of epilepsy diagnosis and surgery, brain imaging, cognition, diagnostics of neurological diseases, human tissue electrophysiology, cellular neurobiology, Parkinson's disease and movement disorders, brain cancer, brain microvasculature, and Alzheimer's disease (biology and advanced diagnostics) and more. The Neuro's integrated approach has led to changes in clinical practice, defined the direction of research fields targeting disease, led to enabling diagnostic tools and propelled therapeutic development.

The Neuro's has more clinician scientists under one roof than any other neuroscience centre in Canada. These individuals are critical to The Neuro's mission. Their work spans the gamut from discovery to treatment to community and back. The added value of these interactions is acknowledged by researchers and clinicians, and importantly by patients who actively seek out experts at The Neuro and want to entrust their health to a research-driven environment. Neuro patients know they will have access to the latest approved treatments or procedures, and believe their involvement in research is valuable for themselves and for the community. In return, patients invaluablely enable and inform the research conducted at The Neuro, furthering our understanding of neurological conditions.

the neuro: using discovery-based research to propel changes in clinical care

at the interface: brain imaging research

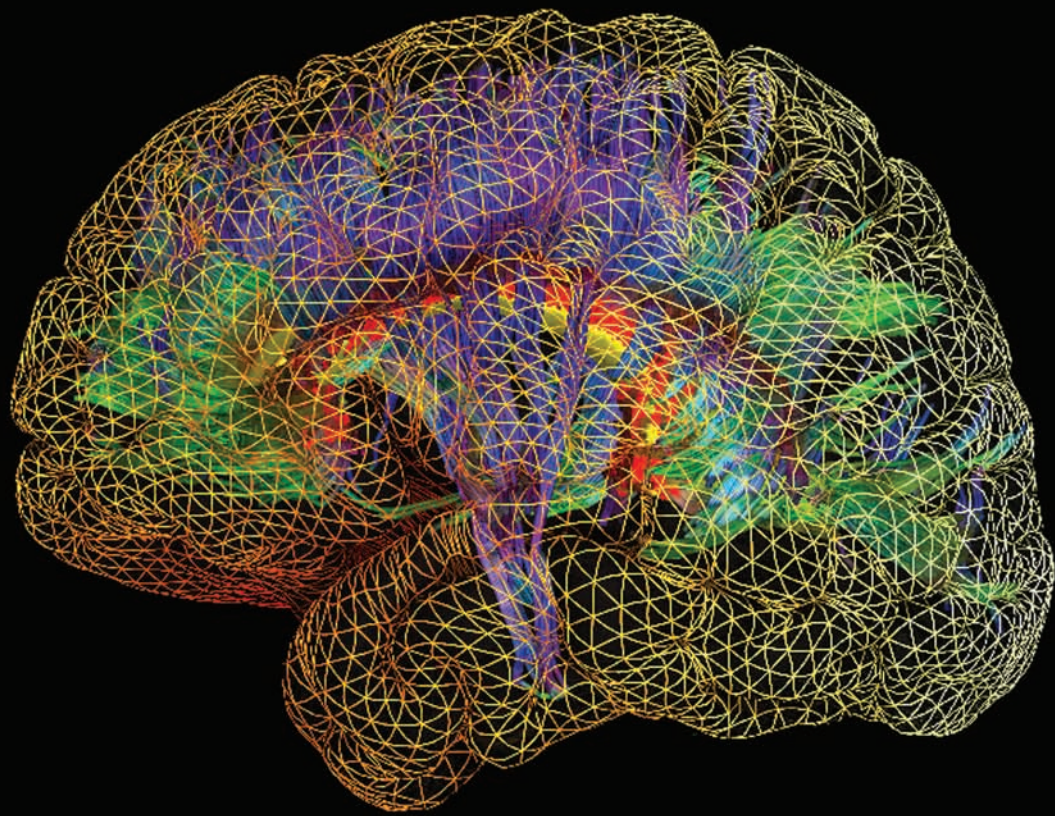
 Our neurosurgeons were the driving force in bringing new imaging technology (CT, PET, MRI) to Canada and in creating the group that would build the first PET scanner in Canada. Today, The Neuro's McConnell Brain Imaging Centre (BIC) is one of the top three brain imaging research groups in the world. The BIC is one of the most productive units of The Neuro and is the hub for neuroimaging in Quebec and Canada. It has a long history of developing new research methodologies

and translating them into routine clinical use. Fifteen faculty, 30 staff and nearly 100 graduate and postdoctoral students work at the BIC, and another 50 affiliated members collaborate with our team and use our imaging facilities. BIC scientists publish over 100 papers per year and these receive more than one third of the total citations for neuroimaging papers in Canada. Thus, The Neuro's BIC is a world leader in terms of publication number and impact.

KEY INNOVATIONS:

- Development of linac based stereotactic radio surgery – this was a breakthrough that revolutionized brain lesion treatment and radiosurgery in general.
- Development of MRI methods for imaging oxygen metabolism and cerebral blood flow.
- Functional MRI and Diffusion Tensor Imaging (DTI) for deep brain stimulation neurosurgery for Parkinson's disease and severe depression.
- Imaging nerve fibre demyelination and remyelination in patients with multiple sclerosis.
- Synthesis of novel radiotracers for use in PET analysis.
- Development of novel neuropsychological tests of frontal lobe function, language and memory, including specialized measures crucial in the pre-surgical assessment of epilepsy patients.
- Pre-operative functional imaging to guide the resection of tumors in brain regions involved in language and other critical functions.
- Novel clinical programs for image-guided neurosurgery.
- Development of multi-modal imaging technology.
- Pioneering work on deep brain stimulation for neuropsychiatric disorders.
- Development of MRI image acquisition and analysis protocols for longitudinal studies that assess child brain development (e.g. in autism) or disease progression in adults (e.g. in Alzheimer's disease). This expertise created the first online database on normal brain development – the Pediatric brain atlas.
- The Neuro's neuronavigation unit, recognized as Leading Practice in 2010 by Accreditation Canada, collaborates with neurosurgeons in planning all cranial procedures and helps patients and their families understand surgical procedures.
- Improvements to diagnostics and image guided surgery making surgical treatments possible for patients previously considered inoperable.

Opposite page: Nerve fibre tracks inside a three-dimensional representation of the brain's surface, produced from magnetic resonance images at The Neuro.



developing new tools to fight multiple sclerosis

Canada has one of the world's highest national rates of MS—about 1,100 new cases each year. Some 50,000 Canadians have MS. More than one in five patients are in Quebec. The Neuro's Multiple Sclerosis Clinic was the first to be established in Canada. In the 60 years since, it has remained a priority for clinical and research activities with a database of 5000 patients, 3000 of which are actively followed. Our MS team focuses on the full spectrum of MS: from brain imaging to

the basic biology of nerve cells and the immune response. This combined approach offers the best hope of translating research-based observations into clinical therapeutics, and relies on the existence of the integrated model. Our Clinical Research Unit conducts more clinical trials for MS than any other neurological indication and our MS team is engaged in a broad array of national and international collaborations.

KEY INNOVATIONS:

- Establishment of the Experimental Therapeutics Program for the collection and analysis of human biological samples, development of bioassays, and bioinformatics tools for new therapies.
- Pioneering basic research on the use of stem cell therapy for treatment of MS.
- New diagnostic imaging tools that identified new aspects of disease progression and improved treatment monitoring.
- Identified a new biochemical mechanism that helps to maintain myelin and potentially promote myelin repair.
- Discovery that babies with certain physiological characteristics could be at greater risk of acquiring MS. In a comparison study of control subjects, researchers concluded that the onset of childhood MS is associated with a smaller head size, smaller brain volume as well as a smaller volume of the brain's thalamus.
- Understanding that MS can strike children at a very young age and studies of risk of developing MS following after having acute demyelinating syndrome. This risk increases substantially if the child has the HLA-DRB1 gene, a discovery that could help physicians to distinguish between isolated episodes and pediatric-onset MS.
- Development of neuro-engineering to create an artificial synapse or nerve cell connection—which is a significant advance towards linking nerves to a microchip—and ultimately a solution for nerve cell repair. Further engineering could lead to the creation of an artificial axonal network to replace axons damaged by MS.
- Discovered new roles for B cells, components of the immune system, in MS patients. The study explained why patients whose B cells were therapeutically removed experienced substantially fewer new MS symptoms.
- In-house infusion treatment centre so that patients can be closely monitored for side-effects by an MS nurse and neurologists.

At 24, Alexander Normandin was an active third year medical student at McGill University when he was diagnosed with an aggressive form of MS and told he would be in a wheelchair within a few months. Unwilling to give up without a fight, he underwent an experimental treatment developed in collaboration with physicians and researchers at The Neuro. Today, Alex's MS has stabilized and he has successfully completed his medical studies.



decades of innovation in epilepsy diagnosis and treatment

Epilepsy affects 1 – 2% of Canadians and everyday another 40 people learn that they have epilepsy. One out of three patients cannot control seizures solely by using available medications. For these patients, surgical removal of the brain tissue causing seizures is the only known effective treatment for controlling seizures and improving quality of life.

The Neuro has maintained its reputation as an international referral centre for epilepsy diagnosis and treatment since 1934. A neurosurgical approach for epilepsy treatment

known as “The Montreal Procedure” which was developed at The Neuro is used worldwide thanks to the work of Dr. Penfield and colleagues like surgeon Theodore Rasmussen, and pioneer electroencephalographer Herbert Jasper. The ground-breaking work of neuropsychologist Brenda Milner and her colleagues, which linked cognitive functions to specific brain regions allowed for improvements in epilepsy surgical procedures that led to enhanced patient outcomes.



KEY INNOVATIONS:

- Stellate System, McGill's first spin off company, initially commercialized EEG analysis software developed at The Neuro to monitoring of epilepsy patients and has since developed many technical tools relevant to epilepsy treatment.
- The innovation continues with the adoption of new frameless stereotaxy for minimally invasive microsurgical interventions and development of novel brain mapping techniques that identify previously undetectable epilepsy foci.
- Scientists and clinicians at The Neuro pioneered the use of EEG to measure brain activity, and have developed new ways to diagnose and control epilepsy.
- Scientists at The Neuro study the genetic factors of epilepsy and epileptic syndromes, as well as treat psychiatric aspects of epilepsy.
- Brain imaging techniques developed at The Neuro have greatly contributed to the understanding of causes and consequences of epilepsy. These techniques have facilitated epilepsy surgery by unveiling brain lesions not seen by standard radiological methods.

Every day in Canada, another 40 people join the 430,000 diagnosed with epilepsy. In one-third, seizures cannot be controlled by medication or the side-effects are debilitating. Dr. Jean Gotman has spent almost 40 years investigating epilepsy, developing computerized EEG and trying to find ways to predict and prevent seizures.

discovering the mechanisms of neurodegenerative disease

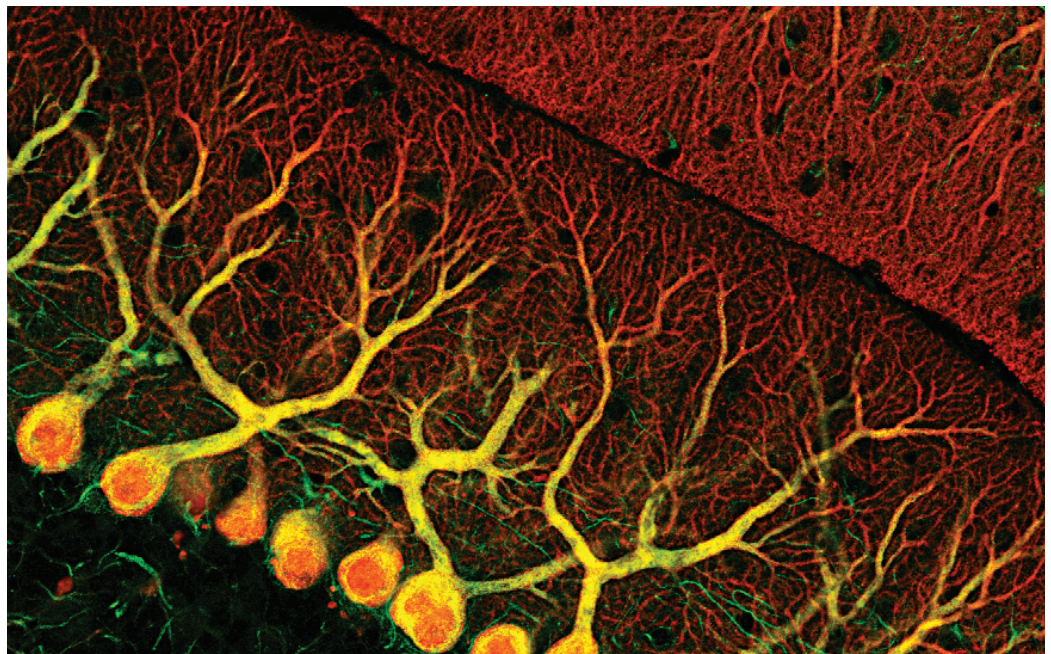
The Movement Disorders and Parkinson's disease Program draws on strengths in neurology, neurosurgery, neuropsychology, nursing, molecular biology and brain imaging to provide state-of-the-art interdisciplinary care for patients and to carry out cutting-edge research into the cause of disease. The Neuro is home to the largest Parkinson's disease surgery program in Quebec and participates in a number of clinical trials that are testing new Parkinson's disease treatments. Our program has received the highest rating of clinics in Canada for service delivery, support and access from the Parkinson Society Canada and

has been designated a Center of Excellence by National Parkinson Foundation for its seamless integration of research and clinical excellence.

In a recent commentary in the journal *Nature*, Richard Youle of the NIH (USA) referred to the landmark study on ARSACS performed at The Neuro, stating that it “demonstrates the importance of fostering interaction between the clinic and the lab. With further collaboration between clinicians and scientists, this understanding might translate into treatments for these devastating disorders in the not-too-distant future.”⁶

KEY INNOVATIONS:

- Identification of a cellular mechanism that is disrupted in one of the most common types of Parkinson's disease.
- The cellular pathology that causes ARSACS (autosomal recessive spastic ataxia of Charlevoix-Saguenay) identified and shown to be similar to that of other neurodegenerative diseases, such as Huntington's, Parkinson's, and Alzheimer's diseases.
- Development of a new surgical procedure for inserting deep brain stimulators to treat Parkinson's disease - this allows electrodes to be placed with greater accuracy with greatly reduced infection rates (zero in 2011-2012).
- Development of computerized tools and atlases that neurosurgeons use to plan and perform minimally invasive neurosurgical procedures. These techniques enable better visualization of the surgical target and permit more accurate placement of deep brain electrodes that are used to stimulate certain brain areas for customized treatment of the symptoms in Parkinson's disease.
- Cognitive and brain imaging studies of impulsive behaviour, learning, and attention span of Parkinson's patients to understand effects of medications used to treat the disease and improve the treatment of cognitive and mood problems that severely affect patients' quality of life.



*Altered neurons in the cerebellum of a mouse missing the ARSACS gene.
(Girard and Larivière et al, 2012. Mitochondrial dysfunction and Purkinje cell loss in autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS). PNAS 109 (5): 1661-1666.)*

finding answers and helping patients with neuromuscular disease

The Neuro is a leading centre for the diagnosis and treatment of neuromuscular diseases and metabolic disorders. The Neuro's group, initiated by Dr. George Karpati, covers a broad range of basic and clinical studies on neuromuscular and neurological disorders, utilizing a broad spectrum of technologies including clinical science, histology, cytochemistry, molecular biology and genetics.



KEY INNOVATIONS:

- Recognized the importance of dystrophin in Duchenne muscular dystrophy (DMD), and its absence in the muscles of those with the disease.
- Discovery of mutations in mitochondrial DNA that cause human disease.
- Developed the first animal models to investigate the transmission and segregation of mitochondrial DNA.
- Pioneered functional cloning methods to identify the genetic defects in individual patients with autosomal recessive mitochondrial disease.
- Development of molecular diagnostics for diagnosing neuromuscular disease.

Eric Shoubridge, International Research Scholar of the Howard Hughes Medical Research Institute, is renowned for his landmark research on the molecular genetics of human mitochondria.

giving hope to patients with brain cancer

The Neuro's Brain Tumour Program has introduced several surgical techniques, and developed new ways of providing holistic patient care in an environment that makes the emotional health of patients a priority. Neuro experts are launching innovative trials that will establish a new standard of care by using genomic/proteomic profiling to deliver the best in personalized medicine. In addition, new compounds are being tested at The Neuro through Phase III Clinical Trials carried out in co-operation with the Department of Oncology at McGill University and the MUHC's Department of Radiation Oncology. The success of the Brain Tumour Program has been recognized by the Quebec Ministry of Health's 'Lutte contre le cancer' program, which assesses interdisciplinary clinical practice, teaching and research. The Neuro's team is the only Quebec brain tumour program which has received this highest level of accreditation.

Neurosurgeon Kevin Petrecca specializes in treating patients with brain tumours and his laboratory is developing novel genetic-based techniques to control the spread of aggressive brain cancers.



KEY INNOVATIONS:

- Pre-operative biochemical characterization of common brain tumor types using magnetic resonance spectroscopy.
- Discovery of a novel cellular mechanism for brain cancer cell migration.
- Development of a robust clinical trials program. More than 60% of brain cancer patients at The Neuro are entered into clinical trials - this enrollment rate places us among the top 5 North American centres.



pioneering translational research

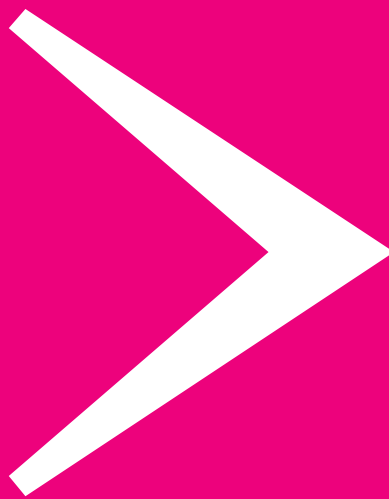
One of the very unique aspects of The Neuro is the integration of fundamental biological research with applied research in human physiology and mechanisms of human disease. The Neuro's Experimental Therapeutics Program (ETP) is designed as a complete 'bench to bedside and back' platform and expedites the translation of fundamental discoveries to the human disease context. Understanding the translational implications of novel fundamental discoveries is paramount. The ETP provides researchers at The Neuro with a bridge to technology that facilitates therapy development for use in humans.

The Neuro's Clinical Research Unit (CRU) evaluates the efficacy of new drugs and treatment regimens. Many patients come to because they want to have access to the newest medications and diagnostic procedures. Since 1992, 140 trials have been conducted within the CRU, giving over 1000 patients suffering from multiple sclerosis, epilepsy, stroke, ALS or brain cancer access to new treatments (see Table 2).

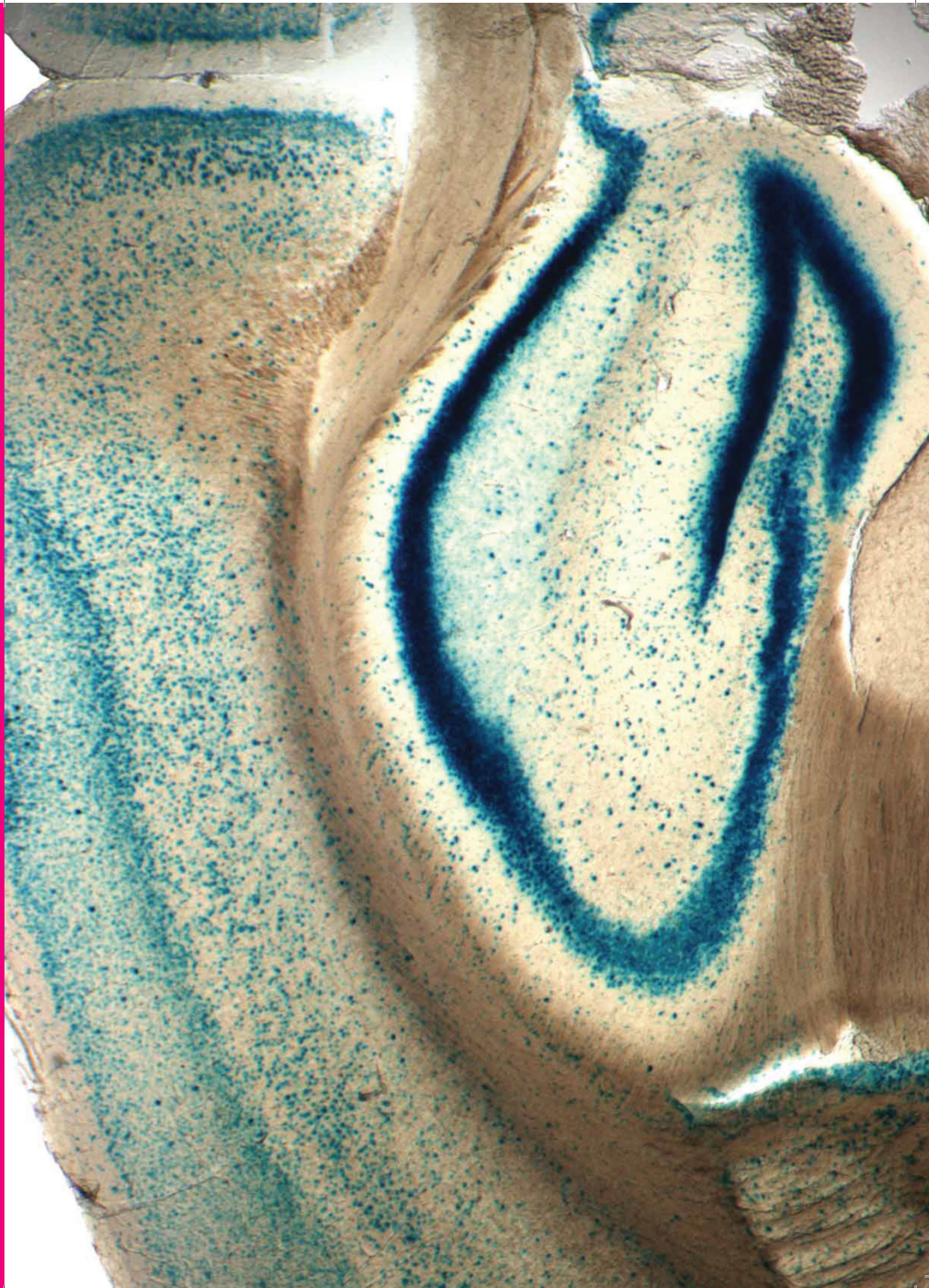
Table 2

CONDITION	NUMBER OF CLINICAL TRIALS SINCE 2008			
	COMPLETED	ON-GOING	FUTURE	TOTAL
Multiple Sclerosis	22	16	2	40
Epilepsy	3	4	2	9
Brain Tumour	4	3	1	8
ALS	4	2	1	7
Stroke	10	1	0	11
Pain	3	0	0	3
Migraine	2	1	0	3
Aneurism	0	2	1	3
Parkinson's disease	1	0	0	1
Myasthenia Gravis	0	0	1	1
TOTAL	49	29	8	86

Opposite page: Mrs. Grazia Anobile, recovering from back surgery at The Neuro, with nurse Annik Plamondon.



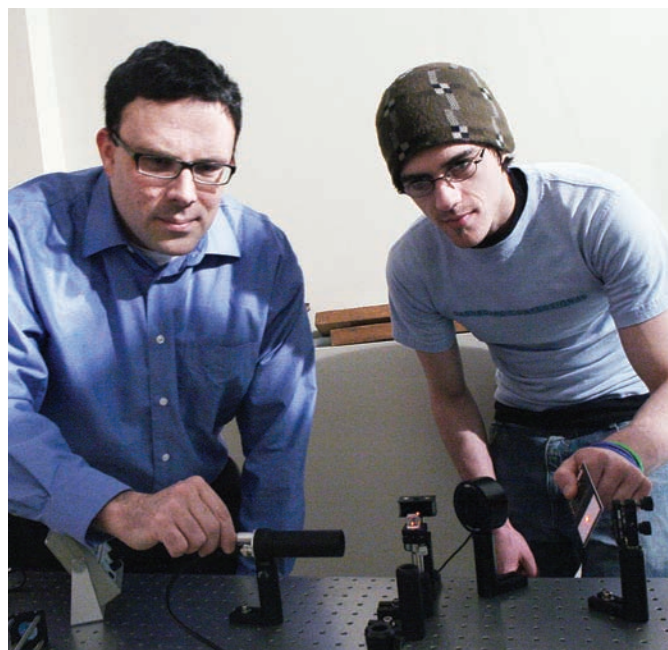
THE FUTURE



the neuro

leading the future of Quebec's health research

The Neuro is a pioneer in innovative approaches to understanding and treating neurological disorders. As we approach a veritable epidemic in neurological disease, the importance of The Neuro has never been clearer. The Neuro's scientists and clinicians are steadily expanding our knowledge of the nervous system and the conditions that afflict it. Indeed, it is our unique combination of clinical and research teams that will drive these advances and translate into innovative and effective treatments that are certain to have a major impact on health care in the 21st century.



OUR CORE PRIORITIES ARE:

> UNDERSTANDING THE NERVOUS SYSTEM

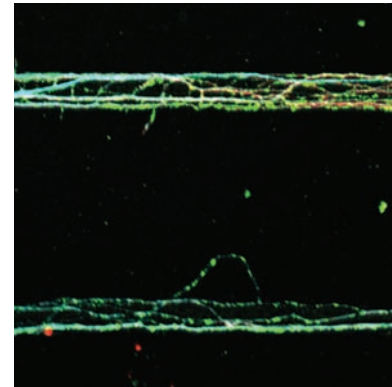
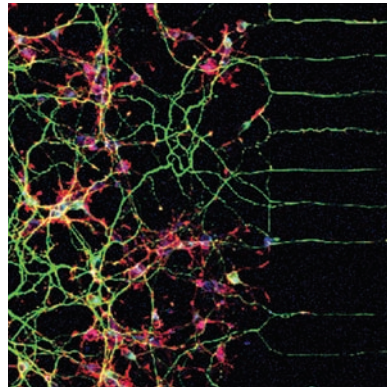
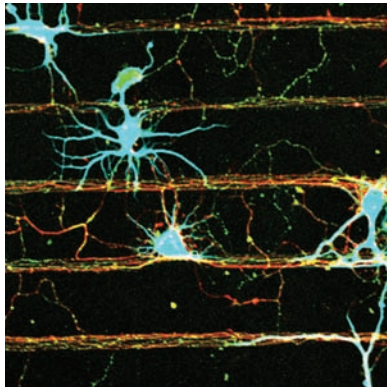
The Neuro's researchers and their colleagues are working toward a better understanding of the healthy brain and nervous system. They are making significant contributions to knowledge about the molecular biology of nerve cells, biochemical and electrical signaling in the nervous system, the functional relationships of different brain regions, and more. This work relates to the mechanisms controlling sleep, chronic pain, learning and memory, decision-making, addiction, and language processing to name a few.

> REPAIRING THE DAMAGED NERVOUS SYSTEM

The Neuro's researchers and their colleagues examine the effects of damage to the nervous system, such as head trauma or spinal cord injury, and study patients with neurological conditions such as stroke, Parkinson's disease, multiple sclerosis, epilepsy, depression, ALS (amyotrophic lateral sclerosis) and others. Our scientists are finding ways to minimize the damage caused by these conditions, reduce the consequences of nerve cell damage, and repair and restore the damaged nervous system. Our goal is to improve the functioning of the injured nervous system and enhance the lives of our patients.

Left: Canada Research Chair in Neural Circuit Development, Edward Ruthazer's work plays a critical role in our understanding of how the nervous system develops and forms the maps that are crucial for the functioning of the brain.

Previous page: A cross-section of a transgenic mouse brain that shows (in blue) activation of a cell signaling pathway implicated in a diverse range of brain functions, including learning and memory and response to infection and injury.



> **USING TECHNOLOGY TO EXTEND THE FUNCTION OF THE NERVOUS SYSTEM**

As materials, machines and software are developed to help the damaged nervous system function better, a new generation of devices will help patients with spinal cord injury, brain trauma, peripheral nerve injury, and the loss of limbs or senses. Ground breaking research in this area requires the marriage of neuroscience, physical sciences (chemistry and physics) and nanotechnology – a field where materials and tools are fabricated at sizes matching the scale of molecules in the body. Scientists at The Neuro are pioneering new approaches in this neuro-engineering domain.

> **INNOVATION AND LEADERSHIP IN IMAGING THE NERVOUS SYSTEM**

When The Neuro first opened its doors in 1934 much of the discovery in medical science was accomplished through post-mortem examination. Today, the most sophisticated pathologies are identified and studied in vivo through the extraordinary power of medical imaging and measuring equipment. The McConnell Brain Imaging Centre at The Neuro is a global leader in mapping the brain and tracking its functions. A new building, the North Wing Pavilion, will house state-of-the-art brain imaging facilities including Positron Emission Tomography (PET), Magnetic Resonance Imaging (MRI), functional MRI (fMRI), and a magneto-encephalograph (MEG). These cutting edge technologies will be supported by super-computer resources and advanced informatics facilities and will allow The Neuro to make global contributions to the study of the developing brain and to the understanding of a wide range of neurological diseases and disorders.

> **TAILORING TREATMENT FOR INDIVIDUAL PATIENTS AT THE NEURO**

When the Quebec government identified personalized health care as a strategic health priority, The Neuro was already a leader in this field. Our clinical research unit will have a major role to play in the orientation towards personalized health care as we increase The Neuro’s ability to run clinical trials and diagnostics that allow patient population stratification. This will help promote integration of innovative tools into clinical practice.

The Neuro’s allied health care professionals are deriving evidence-driven models of care that will improve treatment and outcomes at the bedside. Further, we are identifying key questions and concerns of patients and addressing them with individualized care plans through patient-centered interdisciplinary programs.

> **USING RESEARCH TO AID PATIENTS AND ALLOWING PATIENTS TO FACILITATE RESEARCH**

Patients coming to The Neuro are key contributors to the progress of research and the understanding of neurological diseases. Developing the infrastructure and resources to collect the wealth of information that our patients represent, provide each patient with a tailored treatment, and translating new therapeutics for the global community is a top priority.

Above: Researchers in the Neuroengineering Program grow nerve cells on micropatterned surfaces to mimic conditions in the brain. Cells grown in this manner can be used to study synapse formation, branching, growth cones and much more.

summary



The 2004 report of the “Commission d’analyse des projets d’implantation du CHUM et CUSM”, mandated by the Ministère de la Santé et des Services sociaux du Québec, stated that “there is international medical consensus that the close tie between the Montreal Neurological Hospital and the Montreal Neurological Institute spawned their development and that this characteristic must be preserved. [...] It is in the best interest of all Quebec residents to preserve the high quality of these (MNH and MNI) institutions and their international reputation”. This report and others recognize that the success of the integrated model relies not only on the close proximity of researchers and clinicians, but also the independence of the institution to identify and implement its strategic orientation and decisions.

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- 1 NeuroScience Canada. The Case for Increased Investment in Neuroscience Research. Ottawa, 2004.
 - 2 Canadian Institute for Health Information, The Burden of Neurological Diseases, Disorders and Injuries in Canada, (Ottawa: CIHI, 2007).
 - 3 Conseil de la science et de la technologie, Les neurosciences au Québec. Un créneau d’excellence au bénéfice de la société, Gouvernement du Québec, 2005.
 - 4 Hirsch, J.E. (November 15, 2005). «An index to quantify an individual’s scientific research output». PNAS 102 (46): 16569–16572.
The Hirsch index or H-index reflects both the number of publications and the number of citations per publication. A cumulative H-index is the addition of the H-index.
 - 5 Act on Health Services and Social Services and Ministerial Policies – R.S.Q., chapter S-4.2.
 - 6 Narendra, D.P. & Youle, R.J. (March 7, 2012) Trouble in the cell’s powerhouse. Nature News & Views. (483): 418–419.

The Neuro is a proud and leading participant in Quebec's innovative research, clinical, and education network.

It is a jewel in Quebec's crown that must be supported and nurtured.

discovery innovation translation treatment integration in action

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