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MUHC
MCGILL UNIVERSITY HEALTH CENTRE
HEALTH PERSPECTIVES

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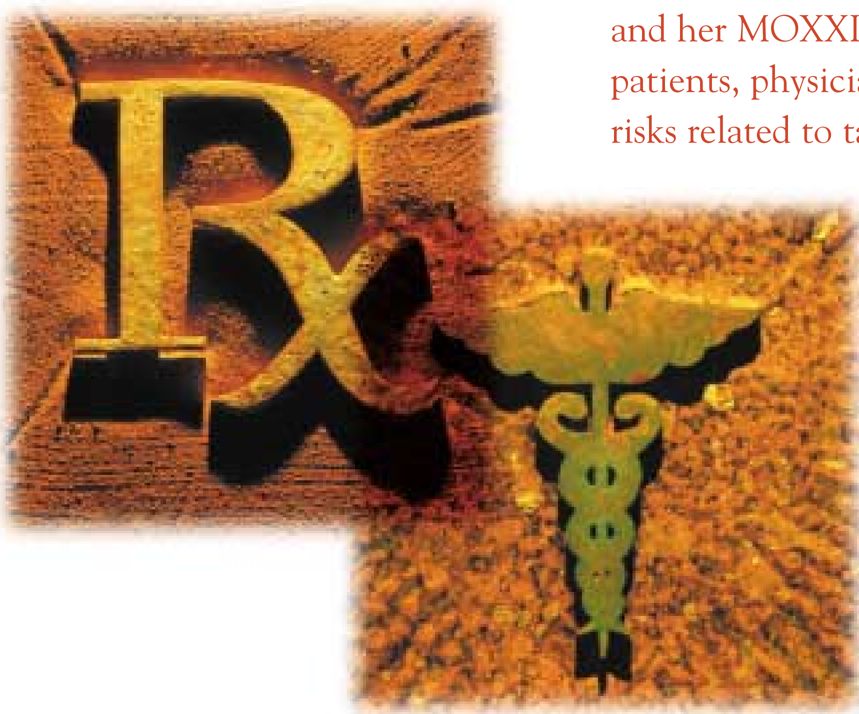
Moxie enough to go round

Canadians can thank Robyn Tamblyn's determination and energy — and her MOXXI project — for an electronic system that allows patients, physicians and pharmacists to work together to reduce the risks related to taking prescription drugs.



From her base in a renovated brownstone tucked in beside McGill's McIntyre Medical Building, Robyn Tamblyn, an epidemiologist at the McGill University Health Centre (MUHC), is developing the third phase of a program that has the potential to significantly reduce the risks associated with taking prescription drugs. Even better it could contribute to improving the efficiency of health care across the country.

The program is known as MOXXI (pronounced moxie), an acronym of sorts for Medical Offices of the Twenty First Century, and it has been around in various stages since Tamblyn made a simple observation more than a decade ago.

What the McGill University graduate observed was that senior citizens accounted for a large number of hospital admissions due to drug-related events. In a study conducted between 1991 and 1993, Tamblyn discovered an unsettling statistic: half of all senior citizens in Quebec were at risk of being prescribed a potentially harmful drug combination, with the result possibly landing them in hospital or even killing them.

The sicker the patient, it seemed, the greater the risk, and Tamblyn wanted to do something about it. "We realized there was a communication breakdown

(continued on page 2)

(**Moxie** *continued from page 1*)
between patients, physicians and pharmacists," she explains, "and there's still a breakdown." The reason is simple: sick patients tend to see a variety of specialists who sometimes prescribe medications without knowing the full range of the patient's health conditions or what other medications he or she may be taking. "When you throw in the fact that many patients remember their drugs only by size and colour and not by name and dosage, it's not surprising that they sometimes wind up in emergency rooms."

Good intentions notwithstanding, it took Tamblyn and her team of four research coordinators two years, until 1996, to find the funding to set up the first phase of the program. MOXXI's primary goal was to determine if providing physicians with rapid electronic access to their patients' prescription profiles would result in fewer prescription errors. To this end, the team enlisted the help of more than 100 primary care physicians in Greater Montreal who approached 14,000 of their elderly patients, those who were publicly insured, to see if they would be willing to participate. "Almost all of them consented once they understood that their privacy would be protected," says Tamblyn.

The next step was to put a computer in each doctor's office and connect it to a provincial database that profiled prescription information for all publicly insured patients in Quebec. Managed by the Régie de l'assurance maladie du Québec (RAMQ), the database uses a software to link with pharmacies throughout the province so they can register every prescription the public system pays for. Tamblyn thought it was a system she could build on. "After getting approval from the Quebec College of Physicians, we worked with software developers and with the RAMQ to create an interface for doctors," she says. The first phase of MOXXI ended in 1998.

"Let's face it, if you're taking ten different medications, chances are you won't remember the names and dosages of all of them when you visit a new specialist who might not have your chart. Then you could wind up in the emergency room in a coma because two of the ten drugs weren't meant to be taken together. Even worse, the attending staff in the ER wouldn't be able to do everything they could because they wouldn't have quick access to your prescription information. MOXXI is addressing these problems."

The conclusion it came to wasn't surprising: informed physicians make better decisions. In fact, problems arising from prescribing patients new drugs were reduced by 20 percent in the test group, as was the incidence of doctors making duplicate prescriptions. "The doctors discovered, to their utter horror, that they weren't aware of 40 percent of the drugs their patients were taking," Tamblyn says. "This was because the drugs had been prescribed by other doctors."

It was time to see whether the benefits of the MOXXI program could be extended to other patient populations. Studies from across North America and Europe had shown, and continue to show, that the prescription drug problem is a serious concern not only for the elderly, but also for patients with chronic conditions such as diabetes, hypertension, and asthma. These patients also tend to see multiple physicians and take several different medications.

MOXXI II, as the second phase of the program came to be known, would build on the results of the first phase to include chronically sick patients. It would also expand to test whether patients would receive better care if doctors were provided rapid access to electronic medical records for their patients along with computerized alerts and reminders for preventive care.

Once again funds were required, and these arrived in 1999 in the form of $1.25 million in grants from Health Canada's Health Infostructure Support Program and its Health Transition Fund. This time around 20 primary care physicians and 8,000 consenting patients were recruited. An electronic medical record for each patient was compiled and included a graphic representation of drugs prescribed (from information given by the RAMQ) and dates of emergency room visits and hospitalizations in the preceding 12 months. The records were made available on computers in the doctors' clinics so they could be accessed during patient visits and updated on a regular basis. Alerts and reminders were made available at the same time.

In the end, the team found that MOXXI II was an invaluable learning experience for the online transmission of medical information in terms of managing the various aspects of the computer hardware as well as the electronic records.

While MOXXI II was still in full swing in early 2001, Tamblyn and her team began preparing for the third and current phase. "From our experience, we knew that the MOXXI program could address the prescription problem on a greater scale than it had before, so we decided to concentrate MOXXII III on this area," says Project Manager Mélodie Faucher. "We realized that by building on the link created by the RAMQ, we could create a system for sending and receiving prescriptions electronically that would include privately insured patients."

In practical terms, MOXXI III needed to expand from 8,000 to 28,000 the number of patients being tracked. It also had to increase the number of participating primary care physicians to 40. Equally important to the program's success was that pharmacists had to be brought into the picture because the medications taken by these patients weren't registered at the RAMQ but were recorded at the pharmacy where they were purchased. The final piece of the puzzle was to create

Clarification

The Cedars Breast Clinic of the MUHC is remarkable in that it strives to provide accurate examination, testing and diagnosis all on the same day or evening, even on the weekend. The generosity of the Cedars Cancer Institute in bringing this clinic to the MUHC is widely appreciated and should have been highlighted in the article "Signalling Progress," *Health Perspectives* #3.

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a database for managing electronic prescriptions.

The green light came with a $2,300,000 grant from the Canadian Health Infostructure Partnerships Program, after which the MOXXI team moved to secure the collaboration of the AQPP (l'Association québécoise des pharmaciens propriétaires), the ABCPQ (l'Association des bannières et chaînes de pharmacie du Québec), and the Quebec Order of Pharmacists.

"The pharmacists were unanimous in wanting to play a greater role in advising patients on the correct use of medication," says Tamblyn, although as independent businesses they had different concerns from those of the public institutions involved with the project. "We also found that illegible hand-written prescriptions were a huge headache for them."

If addressing these details weren't enough, Tamblyn faced an enormous undertaking: designing an interface between participating doctors and pharmacists. This meant creating a system similar to the one run by the RAMQ, but one that could include publicly and privately insured patients. To execute this task, Tamblyn brought in medical professionals from the MUHC and specialists in pharmacology, pharmacy, business and economics from McGill University, Concordia University, and l'Université de Montréal, as well as five different software developers.

In the end, a MOXXI database was created and housed at the MUHC behind a secure firewall. It could track and profile all medications, whether they were paid for publicly or privately. At the same time the team produced a software that would allow the pharmacists to connect to the database and another that would do the same for the physicians.

> "The doctors discovered, to their utter horror, that they weren't aware of 40 percent of the drugs their patients were taking," Tamblyn says. "This was because the drugs had been prescribed by other doctors."

To protect the privacy of the patients, access to patient medical records was restricted to the physicians and Tamblyn.

The team also built in an automated system that would suggest to doctors optimal treatments for approximately 50 chronic conditions, for which hundreds of variables must be taken into account when prescribing medication. These had been identified by physicians from across the country.

Finally, a handheld portable digital office assistant, called the ipaq, was customized for use in MOXXI III. This piece of equipment lets doctors connect wirelessly to the database from any location in order to check their patients' prescription profiles and recent medical interventions. The doctors also use it to send prescriptions electronically along with medical indications to explain their reason for prescribing. When patients go to pick up their medication, the pharmacists connect to the database to retrieve the prescription.

Today, 28 primary care physicians in the West Island of Montreal have signed on to MOXXI III, as have 30 pharmacies in the same area, including chains and independently managed establishments. In December 2002, seven of the 28 doctors received ipaqs and began their training. Faucher explains, "We're still recruiting physicians and patients, and we're also looking for enough funding to make the project permanent." An important selling point is that the potential exists to use aggregate data from MOXXI III, which will run through December 2003, to determine if doctors' prescribing patterns are within the norm of other practitioners. If they aren't, MOXXI will send them a red flag. In this way, the program could become an educational tool for health-care professionals.

The ipaq is a handheld portable digital office assistant that a physician uses to wirelessly consult a patient's medical profile and prescription history when prescribing new medications. In this way, potentially harmful drug interactions are caught before the patient leaves the doctor's office.

Everything learned in the MOXXI project is being made use of in a much larger research project called IRIS Quebec (Infostructure de recherche intégrée en santé du Québec). Launched last year, IRIS has the goal of optimizing the use of electronic medical records to make the entire health-care system safer and more efficient. "We'll be able to alert physicians as soon as an excessive rate of adverse events occur with certain drugs, not ten years down the line after 500 people have died," says Tamblyn, who is heading up the project. Funded by two grants totalling $33 million from the Canada Foundation for Innovation and Valorisation-Recherche Québec, IRIS will build prototypes like MOXXI across Quebec by 2005 and may expand to other provinces as well. Tamblyn says, "The hope is that these prototypes will make prescription drugs safer for all patients across the country." ❊

Equipping Excellence

Radiotherapy is one of the treatments available to cancer patients. Its main goal is to destroy cancer cells while causing minimal injury to surrounding normal cells. Of the two forms of radiotherapy — external beam and brachytherapy — external beam is the more commonly known and involves a machine called a linear accelerator, which delivers high-energy x-rays directly to the tumour.

Linear accelerators (also known as linacs) were developed for cancer treatment in the 1950s by a research group at Stanford University. They have two major components: a moveable treatment couch on which a patient lies, and a rotating unit surrounding the couch, called a gantry, from which an intense x-ray beam is released. The beam matches the size and shape of the patient's tumour, and depending on its energy level, can penetrate deep into the body without causing surface damage. It is possible to deliver radiation to the tumour from any angle by rotating the gantry and moving the couch.

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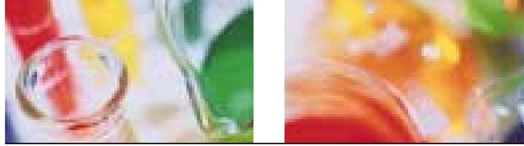
For radiotherapy to be successful, it is crucial that the patient be consistently positioned from one treatment session to the next, which often takes time to achieve. Typically, the radiation beam is turned on for about one minute and the patient's tumour is irradiated from two or more angles. During the treatment, the patient does not feel anything, but can hear a buzzing noise.

A representative price for a linear accelerator equipped with all modern accessories, such as multileaf collimators and portal imaging, is approximately $3,200,000, although prices vary depending on the manufacturer and product features.

If you want to learn about the equipment used by MUHC professionals, or if you want to test your knowledge in this area, visit the MUHC Foundation's web site at **www.muhcfoundation.com** and take the "How Much Does It Cost?" challenge in the News and Publications section. ❊

This series is intended to be informative; the McGill University Health Centre Foundation does not endorse any particular manufacturer or model of the equipment shown and described here.



Finding the Keys to Acceptance

Jean Tchervenkov doesn't take rejection lightly. In fact, he has spent the last 12 years at the Royal Victoria Hospital site of the McGill University Health Centre (MUHC) diligently fostering acceptance. But it isn't personal acceptance that Tchervenkov is after. Rather, the MUHC's gregarious Surgical Director for Transplantation is dedicated to finding ways to help transplant patients avoid rejecting donor organs.

It was Tchervenkov's interest in immunology, a key component in suppressing organ rejection, that steered him in the direction of transplantation in the early 1980s. "When I was starting my career, my initial fascination was with re-implanting toes and fingers to make people functional again after an accident," he says, "but then I learned about immunosuppression research. At that time it was just taking off, and I realized that we might actually be able to overcome the problem of donor organ rejection, which until then had kept most transplants from succeeding."

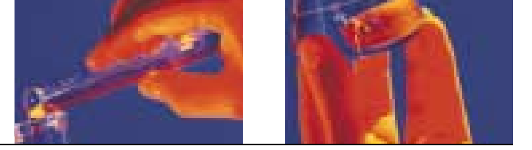
The discovery of new drugs, such as cyclosporine in 1989, helped clinicians put a stop to the attack response that is triggered in the immune system when a donor organ is implanted. According to Tchervenkov, "These drugs marked a turning point in transplantation. They meant we could be consistently successful in giving our patients a new lease on life."

That is just what Tchervenkov has been doing since he was recruited in 1990 by Dr. Jonathan Meakins, former surgeon-in-chief, to launch the liver transplant program. "I had butterflies in my stomach when I did my first solo transplant that year," he recalls, "but my patient is still doing great. She's shown me photos of all the grandkids she's lived to see, which is uplifting. A lot of my patients have stayed in touch over the years. I love that. We share a special connection because for most of them, the transplant was lifesaving."

> "The liver has an astonishing capacity to regenerate itself rapidly, so that if half of your liver is removed, within six weeks the remaining half will grow back to its previous size. We've been able to use this to help our patients. By splitting a donor liver in two and transplanting the pieces into different recipients, we can save two lives with one liver. We've already done this successfully six times."

Tchervenkov now oversees all liver, pancreas and kidney transplants carried out at the MUHC, and 85 percent of the patients under his watch live past the critical first year, when the majority of donor organ rejections occur. This survival rate is one of the best in the country and has helped give the MUHC a reputation for excellence in solid organ transplantation. Tchervenkov was instrumental in building this reputation. His first solo transplant was also the first successful liver transplant at the Royal Victoria. Since then, he has performed and assisted with over 800 successful transplants.

Teaching is also important to Tchervenkov: he is associate professor of surgery at McGill University, his alma mater, where he instructs medical students in the basics of transplantation and the latest surgical techniques. He has lectured at medical faculties throughout the eastern seaboard and has supervised over a dozen graduate and medical student research projects on transplantation. Currently, he is participating in several research projects that look at various aspects of donor organ rejection and tolerance.



One of these projects focuses on hepatitis. In 1997, it led to the discovery of how livers can be transplanted in patients with hepatitis B (HBV), an incurable disease that causes cirrhosis and cancer of the liver. Five years ago, people with HBV weren't candidates for liver transplants because the virus invariably returned to damage the new liver. However, Tchervenkov and his colleagues made international headlines when they implanted a liver into an HBV patient who was subsequently able to avoid post-surgical recurrence of the virus. They accomplished this by administering an autoimmune-boosting drug, Intron A®, before the transplant to reduce the patient's viral load, and then HBIg, a drug commonly used to control HIV, after surgery. It worked. Today, transplantation programs follow a similar protocol. Now Tchervenkov is trying to find a way to offer the same possibility for a successful transplant to hepatitis C patients. Altogether, people with hepatitis B and C make up more than half of MUHC liver transplant patients.

Tchervenkov is quick to point out that he doesn't work alone. "Transplantation is far too complex for one specialist to tackle. You really need a multifaceted approach because the human body has many interacting components. If you fix one problem, such as a damaged liver, without looking at other parts of the puzzle, such as how immunosuppression drugs may cause kidney failure with long-term use, you don't save more lives," he explains. "Thankfully, I'm blessed with a talented team of transplant experts who work together across the MUHC's sites."

The team was formed shortly after the MUHC was created in 1997, and Tchervenkov was chosen to lead it partly because of his proven ability to forge strong collaborative ties. Prior to 1998, he had regularly assisted with complicated transplants at the Montreal Children's and the Montreal General. "Today, we're all part of the same organization, and by pooling our strengths we can do more for our patients than if we operated independently," he says. "For example, we've been able to address the common problem of kidney failure after a heart or liver transplant." In fact, the MUHC boasts a 1 to 2 percent renal failure rate following the transplant of a major organ, the lowest in North America.

Laparoscopic living donor kidney transplantation is another example of the benefits of collaboration. Living donor kidney transplants, which have been performed at the MUHC's Royal Victoria site since the 1950s, involve the patient receiving a kidney that is donated by a relative. This saves the patient from waiting a long time, in some cases years, for a compatible kidney to be found. The drawback is that in the traditional procedure, the nephrectomy, or removal of the kidney, requires a 15-centimetre-long incision, and the donor faces a painful, week-long recovery. However, recent advances in laparoscopy, or minimally invasive surgery (MIS), have made it possible to remove a donor kidney through a four-centimetre-long incision, which allows the donor to return home only two days after surgery with much less pain (for more information, see *Health Perspectives* Volume 1, Issue 1).

Doctors at the Montreal General had been developing a proficiency in MIS abdominal techniques since 1989. With the formation of the MUHC, Tchervenkov and his teammates realized that patients could significantly benefit from combining the General's MIS expertise with the Royal Vic's strength in performing transplants. They adopted a system whereby the laparoscopic nephrectomy takes place at the General and then the kidney is sent to the Vic for transplantation. To date, 35 laparoscopic living donor kidney transplants have been carried out, making up a quarter of all kidney transplants done at the MUHC.

"I'm happy we can offer this to our patients, but it's still not ideal because the donor has to recuperate at the General, away from his or her loved one, who is recovering at the Vic. We're the only centre in North America that does this procedure on two sites. When we all move to one site at the Glen hospital, this won't be a problem," he explains.

In the meantime, one of Tchervenkov's goals is to apply the living donor transplant program to liver transplantation at the MUHC. "Because of the liver's ability to regenerate, it's actually possible to take part of a living donor's liver and implant it in someone else. The two halves will then grow to normal size in both the donor and the recipient," he says. "We're studying how other people are doing this and we hope to get a program up and running by this summer."

Tchervenkov's optimism and drive are contagious. Not only are his colleagues excited by the prospects of improving on the care they deliver, so are many of his former patients. Some volunteer at fundraising events that support research and patient needs, while others contribute financially to help ensure that the MUHC has the equipment and resources to allow Tchervenkov and his team to meet their objectives.

Recently, Ernest and Marilyn Avrith made a generous gift to set up an endowment to establish the MUHC Liver Transplant and Liver Diseases Program. It will provide funds for research into the contributing factors in liver transplant rejection. Gifts like this make Tchervenkov happy. "Support of this kind helps make it possible for us to look for answers so that one day in the future, patients won't even have to worry about donor organ rejection." ❇

Portraits in Time

Thousands of individuals have helped advance the development of the McGill University Health Centre, and in every issue of *MUHC Health Perspectives*, we feature one or more of these significant contributors.

ISOBEL BLACK-MACLEOD

In 1953, Isobel Black-Macleod was named Director of Nursing at the Montreal General Hospital (MGH). She was the first non-graduate of the hospital to hold the position, and the first to have a master's degree, which she earned at Columbia University. Twenty-two years later, she retired with a reputation as one of the most inspired and inspiring nursing leaders to ever have served at the MGH.

Drawing on the broad perspective in community nursing she learned while working with the Victorian Order of Nurses, Black-Macleod focused the Division of Nursing on a "patient and family" approach to care. She also forged strong links with the community, developing a home-care-liaison nurse role in the hospital to facilitate the transfer of patients back to their families.

In 1969, in the face of a nursing shortage, Black-Macleod supported Project 16, a research study that helped liberate nurses from administrative functions while providing them with a greater bedside role. A firm believer in ongoing professional development, she established an in-service education department and raised funds to provide bursaries for nurses seeking to enrol in post-graduate studies.

Named to the MGH Board of Management in 1969 and to the Medical Advisory Committee in 1971, Black-Macleod was able to provide nurses with a voice in decision-making. In 1972, she received an honorary doctorate from McGill University, and three years later an annual conference was initiated in her name by the MGH. In 1994, Black-Macleod received the General's Award of Merit for distinguished service. ❇

The Gene Hunter

Like all scientific explorers, Guy Rouleau is unremittingly curious, a necessary quality in someone who is determined to uncover the genetic causes of hereditary neurological diseases. Admittedly, curiosity comes naturally to the 45-year-old neurologist-geneticist, but when asked if he thinks it is hereditary, Rouleau shrugs his shoulders and smiles. “Certainly, there’s a genetic component to novelty-seeking, but is there a gene responsible for human curiosity? Well, let’s just say that with an estimated 35,000 genes in the human body, anything is possible.”

When it comes to uncovering the genesis of a particular hereditary disease, identifying the “anything” is Rouleau’s ideal challenge. For a lesser man, it would be a daunting one. Gene identification includes sifting through massive amounts of genetic code from different people and comparing the findings in an effort to uncover similarities that might indicate which gene, when mutated, could be linked to the disease. This can take months and sometimes years. Considering the time and variables involved, the chances of successfully pinpointing the offending gene seem astronomically slim. But that is exactly what the McGill- and Harvard-trained Rouleau has done — several times over — in his 22 years at the Montreal General Hospital site of the McGill University Health Centre (MUHC).

To date, Rouleau and his colleagues, who work out of his neurogenetics laboratory at the MUHC’s Research Institute, have identified the genes responsible for more than ten neurological diseases. They include: two forms of amyotrophic lateral sclerosis (ALS or Lou Gehrig’s disease); neurofibromatosis type II; oculopharyngeal muscular dystrophy (OPMD), the most prevalent type of muscular dystrophy in Quebec; certain forms of ataxia; and several forms of epilepsy.

What facilitated their research was something called the founder effect. “This refers to the genetic similarities that arise among members of what is called a founding group, or a group of people that has been isolated for several generations,” he explains. Some well-known founding groups are populations in Newfoundland, Iceland and Quebec. The members’ genetic similarity means that sometimes several of them will develop the same disease for the same genetic reason. When this happens, it offers a gold mine of information for genetic researchers because it is easier for them to mark and track the genes from similar genetic profiles.

“If you’re looking at a disease that runs in a family, you follow it through the branches of the family tree,” Rouleau explains. “To do that we use linkage analysis, which is when you track a distinctive segment of DNA — for one gene or one chromosome, or sometimes one piece of a chromosome — that acts as a landmark, called a marker. If the marker follows the disease through the family tree, you have a clear indication that you’re getting physically close to the gene that causes the disease. Without linkage analysis, identifying the gene associated with a disease would be like looking for a needle in a haystack.”

Last spring Rouleau made a splash in international genetic research circles with the discovery of a gene that is linked to juvenile myoclonic epilepsy (JME), a type of epilepsy that accounts for 25 percent of all generalized cases worldwide. Rouleau and his colleagues found that having a mutated alpha 1 sub unit of the GABAA receptor gene, which plays a crucial role in controlling the electrical activity in the brain, predisposes individuals to JME. To find the mutated gene, they used linkage analysis to study a Quebec family in which eight of its 14 members had JME. Of the eight, all had the mutated GABAA gene, and the six without JME didn’t, confirming the mutated gene’s role in this form of the disease.

Rouleau’s findings represented a breakthrough and as a result are sure to have clinical implications. For example, many currently prescribed epilepsy medications aren’t universally effective in controlling patients’ seizures and can lead to unwanted side effects such as nausea, headache and blurred vision. “My hope is that with the new understanding of the genetics behind JME, other researchers will be able to develop better treatments for it that will be easier on the patient.”

Rouleau spends about 70 percent of his time doing research and the other 30 percent as a neurologist, caring for people with hereditary neurological diseases. “My interactions with the patients inspire me to push harder in my research,” he says. “You never know if the next discovery will lead to a medication or therapy that will improve life for the patients.” His research success has won him considerable recognition, including the title Scientist of the Year, bestowed by Radio-Canada in 1993. In 1999, he received the Prix Léo Parizeau from ACFAS (Association francophone pour le savoir), and one year later the Canadian Institute for Health Research honoured him with the Michael Smith Award. Rouleau attracts close to $2 million in research grants a year for a total so far of nearly $20 million.

Despite his success in locating the causes of a handful of relatively rare hereditary neurological diseases, Rouleau is always looking for new challenges. To this end, he has expanded his lab’s focus to include more prevalent diseases, such as Tourette’s syndrome, autism and schizophrenia, which are treated in both neurology and psychiatry. “These are hugely challenging diseases because they can’t be traced to one gene. For example, nobody would say that you’ve got the gene for schizophrenia, because it’s probably caused by the interactions of many genes as well as environmental factors,” he explains. “But just like with founding groups, patients with these diseases share similarities.”

To find these similarities, Rouleau is teaming up with other MUHC experts such as Dr. Chawki Benkelfat and Dr. Yves Dion at the Allen Memorial, Dr. Eric Fombonne at the Children’s, and Dr. Phil Barker at the Neurological Hospital site. “We hope that by putting our heads together, we’ll eventually find answers that will lead to new treatments in these areas. You know, genetic research moves forward incrementally. You’ve got to be curious, but persistence is really what pays off!” ❊

> “Genetic research is slow work and advances are made incrementally. Despite all the hype, we’re still far from having a clear understanding of anything in the neurosciences. I’m happy that we’ve made a lot of discoveries in my lab, but really, we’re just beginning to scratch the surface.”