The brain sends information via the nerves to tell our bodies how and when to move, and in turn, receives sensory information – such as sight, smell, or touch – from the nerves. The brain also enables us to think, feel emotions, have a personality, form memories, and learn new skills. In other words, our brains play a role in all of the things that make us human.

The problem of brain disease

Because the brain has so many important jobs, when something goes wrong in the form of disease or injury, there can be devastating consequences. In Canada, brain disorders are among the leading causes of disability. Approximately one in three Canadians will be affected by a brain disease, disorder, or injury at some point in their lifetime. This includes Alzheimer’s disease, autism spectrum disorder, schizophrenia, depression, and concussion.

Dr. Guy Rouleau is both a neuroscientist (a scientist who studies the brain) and a neurologist (a doctor who treats brain disorders) who has worked for over three decades to find solutions for diseases that affect the brain and nervous system. As the director of the Montreal Neurological Institute-Hospital (The Neuro), Rouleau knows just how challenging this can be. “The problem with neuroscience is that it’s very complicated,” says Rouleau. Unfortunately, the complexity that makes the brain so interesting is also what makes it so dif-
Back to the basics: genetics

So how do scientists solve a problem as complex as human brain disease? For Rouleau, the solution was clear: look at the building blocks of human biology – our genes. “A lot of treatments help a bit or may even help a lot, but they’re not targeting the disease,” says Rouleau, “but if you find the gene that caused the disease, and if you understand the biology of the disease, you can design treatments that will work.”

Rouleau and his team have identified more than 20 genetic risk factors and disease-causing genes for both degenerative and developmental brain disorders – including schizophrenia, autism spectrum disorder, stroke, and epilepsy. To find these troublesome genes, Rouleau looks at the whole genome.

Genomes are similar to instruction manuals. Every living organism has their own genome, which contains all of the unique genetic instructions that make them who they are. Within each genome are many different genes, which act like sentences and paragraphs within the manual, each containing their own specific set of instructions. Genes are composed of a chemical code known as DNA. If we think of genes as sentences, then DNA provides the letters of the code. When these letters combine to form words, they provide the genetic instructions that tell the cells in our bodies what to look like and how to function.

Sometimes, there is a mutation or change in the DNA code of a gene. If we continue to think of DNA as letters, then a mutation can be as simple as a misspelling of a word by a single letter, or as large as a duplication or deletion of whole words or sentences. While not every mutation is bad – some simply have no effect, and some may even be beneficial – some mutations can have very serious consequences.

To find these problematic mutations, Rouleau uses tools such as single-stranded conformational polymorphism (SSCP) analysis to locate single-point mutations and the newer technique of whole genome sequencing. Whole genome sequencing literally means getting the entire DNA code sequence of an entire genome.

This can be very powerful, as you can compare the different code sequences of different genomes (say between diseased and non-diseased individuals), and look for differences. In turn, these differences may provide clues to the underlying causes of the disease. “With whole genome sequencing you can find all the variants […] all the insertions and deletions, and rearrangements,” Rouleau explains. But once a difference, or a mutation has been identified, how does this help people living with brain disorders?

From gene to medicine: a success story

A powerful example of the success of Rouleau’s genetic approach is his work on amyotrophic lateral sclerosis (ALS). ALS, also known as Lou Gehrig’s Disease, is a fatal disease where the neurons that control movement begin to die. Over time, this causes the brain to lose its ability to communicate with the muscles of the body, resulting in paralysis.

Rouleau has been researching ALS since 1986. “I was involved in the identification of many of the major genes and have done a lot of work trying to
understand what these genes do and how they lead to ALS,” says Rouleau. Eventually, all of his hard work paid off.

In 1993, Rouleau and his team used SSCP analysis to identify mutations in a gene called SOD1 in a subset of patients with familial ALS. Approximately 5-10% of ALS cases are familial, meaning the disease is passed on from a parent to their child. The SOD1 gene is important because it provides the instructions for making the SOD1 protein, a protein which is involved in breaking down toxic molecules. When the SOD1 gene is mutated, this protein does not work properly.

Rouleau explains that by understanding the mutation in the gene, you can reverse or stop the effects of the mutation. This goes beyond simply addressing the symptoms of the disease, to actually finding the root mechanism of why the disease occurred. “If you don’t understand the mechanism, it’s just a shot in the dark”, Rouleau explains, “[When] you understand the mechanism, you can do specific, targeted treatments.”

Open Science: the way of the future

So how do we ensure more success stories for brain disease? Rouleau strongly believes the way forward should involve the practice of open science. Open science is a new approach for conducting scientific research that promotes the sharing of resources, methods, and data between scientists and labs. In Canada, Rouleau has pioneered the practice of open science, and in 2016 he turned The Neuro into the first open science research institute in the world.

While science has always aimed to be a collaborative endeavour, there are several barriers at the systemic or institutional level that can prevent scientists from sharing their resources and data. This includes complicated legal contracts such as patents and material transfer agreements that limit resource sharing, as well as journal paywalls that prevent scientific papers from being freely accessible.

Open science is effective because it removes these obstacles and creates a system where scientists can quickly share their work – both with the public and with other labs. “By sharing freely and sharing quickly, you eliminate barriers to collaboration,” says Rouleau. Collaboration is what makes The Neuro such a powerful research institute. When many scientists can work together towards a com-
mon goal, it accelerates scientific discovery.

The hunt for a vaccine for COVID-19 is an example of how effective open science can be. “The [genetic] sequence was available within days, and you have 10,000 scientists studying COVID-19 right now, maybe more,” says Rouleau, “And they can only do that because a lot of the data was freely available […] Instead of taking 10 years to make a vaccine, it might take less than a year.”

As Rouleau points out, if open science has been so helpful in the case of COVID-19, neuroscientists should adopt the same method of information sharing for brain disease research. “If sharing is accelerating things, why don’t we do the same thing in the rest of medicine?” Rouleau asks. With many scientists tackling the same problem from different perspectives, new treatments and medicine would be available faster.

As Rouleau champions open science – especially as it applies to brain disease – he reminds scientists of the importance of sharing discoveries, “We share freely because [science] should be for the greater good.”