Your Complex Brain - Season 3 Episode 3 – 25 Years of Momentum in Spinal Cord Injury Research

Dr. Laureen Hachem 00:01
[Your Complex Brain theme music] What's been shown is that there's this pool of cells in the centre of the spinal cord that has stem cell-like properties, so they have the potential, under the right conditions, to replace other cells. And, what we see is that, after spinal cord injury, they become activated. So, they're normally quiet and then, after an injury state, they become activated to become other cells. And so, that's kind of like the body's own way of trying to protect the cord or have a positive response to that injury.

Heather 00:32
[music continues] This is Your Complex Brain, a podcast all about the brain, the diseases that impact it, and the path to finding cures. I'm your host, Heather Sherman, and I have the great pleasure of working alongside the team at the Krembil Brain Institute in Toronto, Canada, a leader in brain research and patient care. In each episode, we'll take you behind the scenes into our clinics and research labs to meet the game-changers of the future. We'll empower you with the latest research to help you take charge of your own health. You'll also hear from people who are living with brain disease, as well as their loved ones and the care teams who support them. Join us on a journey to unravel the mystery of your complex brain. [theme music continues then fades out]

[superhero theme music plays] The year is 1995. Actor, Christopher Reeve, is injured in a horseback-riding accident, leaving him quadriplegic, paralyzed from the shoulders down. He became a tireless advocate and a passionate supporter of research. Christopher's dream was for those living with spinal cord injuries to have a better quality of life and, one day, to walk again. [electronic music plays] More than 25 years later, thanks to advances in surgical approaches, neuroprotective drugs and gene therapy using stem cells, that dream is becoming closer to reality. And, that is welcome news for the more than 86,000 Canadians who are currently living with some form of spinal cord injury, including John Ruffalo. Here is his story.

John Ruffalo 02:19
[light, bubbly, electronic music] I'm John Ruffalo, founder and managing partner of an investment firm called Maverix Private Equity, and I have been a longtime investor in both venture capital and private equity. September of 2020, on the day of the accident, I'm actually gearing up for the first close of my new growth private equity fund, and on a gorgeous day, like I'd done many other days, went from my house and went for a nice solo cycling ride. I went solo because it was during COVID and it was a 100-kilometre ride from my house in Toronto to north of Toronto in kind of a loop to Stouffville.

About 5 kilometres away from my midpoint of the destination, I heard a very loud truck—I suspected it was an 18-wheeler—right on the tail of my back tire, which is very troubling and a fear of many cyclists. Just before I could react, the truck had hit me. He was going about 80/90 kilometres an hour, hit my back, obliterated my vertebrae, and sent me flying for a secondary impact quite far away from the first impact. In the benefit of hindsight, I didn't know, but I had about an hour to get to the hospital or I would pass away.

[music continues] The ambulance was there very quickly and I was awake during the whole ride in an ambulance, and they got me to hospital in about 25 minutes, and then I was immediately induced into a coma and spent the next six days or so in a coma. I didn't have any surgery for the first 36 hours. There was a big fear that the trauma of the surgery would be a third impact on my body and my body may not

be able to have absorbed that impact. By the time it hit the 36-hour mark, then they made the decision to perform two surgeries. They did my pelvic surgery first; my pelvis was split into six pieces. All of my ribs were broken in multiple places on one side of my body, damaged organs, you name it, but the pelvis was the complicated surgery, so I first did that surgery and then they rotated me and then did the surgery on my back. And, the combined surgery was about 15 hours.

I've had some serious cycling crashes before, but I'd been able to bounce right back up. On this one here, I immediately knew I was paralyzed from the waist down, and there's this feeling of nothingness. I could wiggle my fingers, I could move my head, but I couldn't do anything below my waist, so I already knew.

After I had gotten out of the coma, after about the sixth day and the intubation was removed, I did ask the nurse what was the prognosis, and I was diagnosed with the worst grading of spinal cord injury. It's called an ASIA A, which basically means you are a complete spinal cord victim and you'll never, ever have use of your legs again, which obviously is a shock to anyone to hear that. [music fades out]

[gentle, glitchy electronic music] After a few weeks of being in hospital—so I was at hospital at Sunnybrook—I then had a meeting with Dr Fehlings and they had me do some initial tests, you know, MRI, etc., and Dr Fehlings concluded that, in order to maximize my functional recovery, he thought that I should get my spinal cord decompressed. He said it's a very, very complicated surgery. There is a lot of risk with that surgery. Very few people know how to do it because of the sensitivity, and I said, "What are the odds of success?" and he said, "Odds have been around 50/50," and I told him, "I am a venture capitalist. I'm in the 1% odds game. 50/50 is ginormous for me," and he's like, "Do you want to think about it?" and my wife and I both said, "No. Let's do it." And, three weeks later, we removed the pins and the rods in my back and another seven-hour surgery. He removed all of the fragments and rebuilt my vertebrae with the bone fragments that were remaining and then reinserted the rods and the screws.

[gentle, uplifting electronic music] And, the surgery was a success and my spine was decompressed. So, for the first two months, I'm really in still the acute care, so first at Sunnybrook and then at Toronto Western. Then, you go into a rehab stage and I went to Toronto Lyndhurst, and there, you're really just recuperating. My body just needed lots of time to heal and, at the same time, I really started needing to commence physio.

[music continues] My body started recalling the memory in my spinal cord of certain movements in my body and the funny thing is my body started to recall the movements of cycling before it did on walking. I am still officially designated as a complete ASIA A, and yet I cycle and walk daily – now, not unaided, but I'm walking and peddling. If you were to ask Dr Fehlings and some of the other doctors, they are shocked at the amount of recovery that I've experienced, and one of the factors is I believe in—so does Dr Fehlings believe—the decompression has enabled me to increase my chances for a recovery, but I also have, on top of that, undergone a massive amount of physical therapy, which is really, today, the only known treatment to at least improve your situation – not to necessarily solve it, but to give you a life that could become bearable. [music fades out]

[light electronic music] What I had been told was, "You will see your recovery in the first 6 to 12 months, but by the end of 12 months or thereabouts, your recovery period is over and you're not going to really experience any improvements in terms of your functionality." Well, I discovered that's not true. It takes a lot of time and money. It's unfortunate on the post-acute care – there's not a lot of significant

resources available to you. So, one of the things that I have been fortunate is that, four months after my accident, I did go back to work. My physio routine is seven days a week, about 18 to 20 hours a week without stopping, and I am still improving and I am getting stronger both on my pedalling; my walking is getting stronger and more independent, but it's still not fully independent.

And, the reason why I think people underestimate the power of physio and your neuroplasticity is that you have to be extremely stubborn or stupid—or both—to want to continue to go through the pain and the discipline that I need to go through to continue doing this. [music fades out]

[upbeat, gentle electronic music] After 6 to 12 months of constant physio, you really want to get on with your life, and I think I made physio a part of my daily life. When the accident occurred, I was querying whether a solution would be available in my lifetime, and a year goes by and the amount of research and knowledge is growing at a logarithmic pace. And, what's interesting is part of the challenge is not necessarily the technology, per se, but it's rather the communication amongst the global community of projects that others are doing and people not being aware of the project.

I think we are between a 5- and 10-year time frame, possibly, to actually both partially, for sure, and perhaps wholly solving spinal cord injury. And, that's where I am mostly focused in on. My message is one of hope and never to take away the hope. [music fades out] [light, bubbly electronic music] I understand now—I didn't before—how easily it could get you into a dark place, the moment you lose hope. It was my message to the hospitals, as well, and I said to them, "Hey, just a little bit of piece of advice, and I know that you have to manage expectations, but there's a fine line on managing expectations and removing hope. Do not cross the line of removing hope." My message to folks is I believe that something very significant will occur within the next 10 years, but every year I've been cutting the estimate by half and I hope to be saying, a year from now, "Boy, was I wrong. It's going to be within the next five years."

The one thing that you can do is get physio right now and get your body moving and allow your body to feel the movements again, and hopefully have technology to give you that extra boost to get some more functionality. [music fades out]

Heather 13:01
[Your Complex Brain sub-theme music] My guests today are on the forefront of truly pivotal and pioneering research in spinal cord injury. Dr Laureen Hachem is a neurosurgery resident and PhD candidate at UHN's Krembil Brain Institute and the University of Toronto. She's joined by her supervisor, Dr Michael Fehlings, a senior scientist at the Krembil Brain Institute and a professor of Neurosurgery at U of T. Dr Fehlings also holds the Campeau/Tator Chair in Brain and Spinal Cord Research. [music continues then ends]

Welcome and thank you both for joining me today on the podcast.

Dr Michael Fehlings 13:41
It's a pleasure to be here.

Dr Laureen Hachem 13:42
Thank you so much for having us.

Heather 13:43

We heard earlier from the patient, John Ruffalo, who is living with a spinal cord injury, and I know you're both familiar with John's story. What does it feel like to hear a story like John's, firsthand, and truly understand what some of the biggest challenges are for patients living with spinal cord injury? Dr Hachem?

Dr Laureen Hachem 14:01
Yeah, I really think stories like John's-- I think he's a remarkable individual and kind of his persistence and perseverance on his road to recovery is really an inspiration to both us, as care providers, and other patients. And, I think that, really, it is the heart of what we do, both from a clinical standpoint and, research-wise, we're trying to find cures for patients that sustain these injuries, and I think it really is a driving force as to why we're all here doing the work.

Dr Michael Fehlings 14:26
I would echo Laureen's comments and maybe add a few of my own. John is certainly one of the most determined, remarkable individuals that I've ever met and, you know, I really take inspiration from the people I've taken care of with spinal cord injury, and John is an exceptional individual. He's had a remarkable drive to push his recovery, and he and I have gone on a journey together in terms of undertaking decompressive surgery, which has helped Mr Ruffalo in terms of his recovery. But, John also, his story really tells us the limits of what we can do with surgery and the tremendous need to pursue improved treatments through regenerative neuroscience.

Heather 15:14
And that's exactly what we're going to be talking about today. So, in terms of the momentum that we've seen in spinal cord injury research and care in the last 25 years, 30 years, can you set the stage for us, Dr Fehlings? Since you first entered this field, what are some of the biggest advances and what are some of the most promising advances?

Dr Michael Fehlings 15:30
Probably 90% of what we now know, related to spinal cord injury and regenerative neuroscience, has been learned in the last two to three decades. So, we now have a better understanding of the mechanisms that cause cell death after a traumatic spinal cord injury, the concept that the primary mechanical trauma in sites—what's referred to as a secondary injury, which is provoked by damage to the blood vessels and ischemia and cellular toxic events—and we've been able to develop surgical strategies to decompress the spinal cord that have had a dramatic impact on people's outcomes, and there also have been efforts to develop so-called neuroprotective strategies to attenuate the extent of cell injury.

When I was a student, it was said that the central nervous system cannot regenerate and that, when someone has an injury such as a severe traumatic spinal cord injury, that's it. We now have a much better understanding, and what's emerged over the last several decades is a new area of science referred to as regenerative neuroscience where we have learned to overcome inhibitory factors in the central nervous system to induce regeneration, and we've also been learning how to activate endogenous stem cells, as well as to have improved techniques to deliver exogenous stem cells.

Heather 17:05
Can you expand on that, Dr Hachem, because I know that's a big focus of your work?

Dr Laureen Hachem 17:09

Yeah. So, some of the work that I've been doing in the lab has been focusing on this endogenous pool of neural stem cells. And, essentially, a stem cell is the type of cell that's not yet committed to a mature cell, like a neuron that we know is critical for signalling, or glial cells that support the neurons to do their job. And so, what's been shown is that there's this pool of cells in the centre of the spinal cord that has stem cell-like properties—so they have the potential under the right conditions to replace other cells—and what we see is that, after spinal cord injury, they become activated. So, they're normally quiescent or quiet, and then after an injury state, they become activated to become other cells. And so, that's kind of like the body's own way of trying to protect the cord or have a positive response to that injury.

[gentle electronic music] What we see though is their numbers are not sufficient, and this is largely restricted to a very early time point, post-injury. So, some of the work we've been looking at is how can we understand those early mechanisms of their activation so that we can now either prolong their activation state or start to modulate them or change them in subacute or chronic—so months out from the injury—and get maybe another reactivation to help with regeneration or cellular replacement.

So, a lot of the work I've been doing in the lab has been looking at what are those early mechanisms, and interestingly, we found kind of a discovery earlier in my work, was that some of the toxic chemicals that are released after injury, the ones that kill off the neurons and other cells, are potentially the ones that might be activating these cells. So, we kind of termed that the "glutamate paradox", glutamate being one of those chemicals. And so, now we're looking at how we can use those mechanisms. I'm looking at a drug that kind of modulates glutamate receptors, specifically AMPA receptors, and how we can now translate that understanding of the mechanism into a therapy that's clinically relevant – so, a pharmacological agent that we've been studying and we can now apply that in subacute or chronic injury to try to reactivate these cells. [music ends]

Dr Michael Fehlings 19:09
It's really an exciting time and, really, the era of regenerative neuroscience has emerged, and what we have learned is that the centre of the spinal cord is the key to the regenerative response, and the centre of the spinal cord is where stem cells reside in people's spinal cords. The challenge right now, though, is that the number of so-called endogenous stem cells is quite limited and, while stimulating people's own regenerative response is very exciting and at the cutting edge of research, from a more practical perspective, we are looking at the concept of transplits of so-called neural stem cells. And, neural stem cells are the developmental building block of the whole central nervous system, and we now have techniques where we can engineer a neural stem cell that's customized for the person, themselves. We could take any cell from their body, for example a skin cell, and using a technique called induced pluripotent stem cell engineering, turn that cell—called a somatic cell—into a customized neural stem cell.

And then, we can now go even beyond that where we can use a technique called CRISPR Cas9 genetic engineering to put in molecules into those neural stem cells to modify the environment in a customized fashion, so, for example, to break down the scar tissue that forms in a chronic injury. So, these are very, very exciting developments that are occurring in regenerative neuroscience.

Heather 20:55
Amazing. And, are there certain subsets of patients, Dr Hachem, that would benefit the most from regenerative therapy or gene therapy?

Dr Laureen Hachem 21:05

Yeah, that's a really good question. I think, at this stage, from a research stage, it's relatively early to know which therapy will target or benefit which subset of patients, but that does really open the door to the whole concept of, there's a lot of heterogeneity in patients, and so we're seeing this from a clinical perspective, both traumatic spinal cord injury and degenerative-related or arthritis-related injuries at the spine. We're seeing different trajectories or paths that patients take. Some have more recovery, some have less recovery, and it may not necessarily just be an injury-related response. There could be some underlying factors in the patient, so I think this kind of opens the whole research world to understanding, you know, what genetic or molecular predispositions are there to someone's response to an injury, and I think understanding that, from a very mechanistic or biological perspective, will help us understand that clinical heterogeneity and then target those treatment strategies.

I think, from a regenerative standpoint, we do see most patients in a subacute or chronic setting, so obviously that's the time period we want to help regenerate those axons or those neuron-signalling mechanisms.

Heather 22:09
So, how does that work? I mean, you're on call, Dr Fehlings, and a patient comes in with a spinal cord injury. Take us through the process a little bit about how you determine the extent of their injury and what they might be a candidate for, in terms of therapy or treatment.

Dr Michael Fehlings 22:22
[gentle electronic music] Yes. So, from our work at the Krembil Brain Institute in Toronto, has emerged the concept that has now been universally adopted, which is "time is spine", in that the timing of intervention is critical. So, individuals who sustain a spinal cord injury will be transferred to a centre such as the Toronto Western Hospital that specializes in the care of these individuals. They'll undergo a diagnostic examination using standardized neurological testing, and then there'll be advanced imaging, including CT and MRI to document the extent of the injury.

Most people with spinal cord injury sustain a fracture and there's pressure on the spinal cord, and so we recommend that surgery be undertaken in individuals and, optimally, as soon as possible, where the spinal cord is decompressed and stabilized. And, at the same time, individuals with a spinal cord injury are cared for in the intensive care unit by a multidisciplinary team, and one of the critical factors in the management is to augment the blood pressure artificially—and this is done often through drugs called inotropes. [music fades out]

After the first week to two, most patients are ready to go to a rehabilitation facility such as Lyndhurst, which is one of the largest spinal cord injury facilities in the world—and is part of UHN—and, there, individuals will undergo targeted rehabilitation to try to enhance their underlying recovery, and also learn approaches to regain some degree of independence, and this will vary depending on the severity of the injury.

At around two to three months after an injury, we have a very good idea what the trajectory of outcome will be. Individuals with a spinal cord injury in 2024 have a dramatically different trajectory of outcome than they may have had two or three decades ago, so many, many more patients such as Mr Ruffalo are having substantial recovery. But, as John's case has also exemplified, despite the fact that substantial recovery occurs, many individuals are left with significant residual neurologic deficits. So, this might involve loss of motor function, so challenges with walking and with transferring. Often, people can have

quite significant pain, related to injury in the nervous system, and there can be impairments also in the control of the bowel and bladder function.

And so, at around two to three months after injury, if one has the sense that individuals are going to be left with substantial residual impairment, this is where you start considering the options of regenerative treatments, and individuals at around three to six months after injury are probably in the optimal time frame to receive regenerative technologies, although these are still now in evolution. And then, after six months, the injury becomes chronic, largely because of the deposition of scar tissue, and through some major breakthroughs in our laboratory and a few others around the world, we're learning ways to overcome the barrier of the scar tissue, and we can essentially convert a chronic injury back into a subacute injury where there is sufficient endogenous plasticity to allow some of these regenerative techniques to be effective.

Heather 25:54
And so, some of these patients may have progressed to a point where, as you're saying, it may be a chronic injury or disability at that point, but you're actually able to reverse that, in a way, to bring them back to a point where they may be a candidate for some of these more innovative therapies?

Dr Michael Fehlings 26:08
Yes. And, that's been one of the big breakthroughs that has occurred in our laboratory is the ability to overcome the scarring in the spinal cord. And so, this essentially converts a chronic injury back into a subacute injury where there's a much greater potential for regenerative techniques to be effective.

Heather 26:32
On the surgical front, Dr Fehlings, we talked a little bit about early decompression surgery, also known as microsurgery, that was really pioneered here in Toronto at the Krembil Brain Institute at University Health Network. Can you just tell us a little bit more about it, and just really how revolutionary it is for treating patients with spinal cord injury?

Dr Michael Fehlings 26:49
When I was a resident in training, individuals with a spinal cord injury would be told that their paralysis was permanent, nothing could be done, and often these individuals were put on bed rest or in traction for weeks to months. That has now changed. With significant advances in imaging, surgery, anaesthesia, and intensive care, we now have the techniques where we can surgically take the pressure off the spinal cord—it's called a decompression—and then, we can stabilize the injured spinal column with implants. And, studies, pioneered by our unit, in particular the STASCIS study, published about a decade ago, showed that individuals who had surgery within 24 hours had dramatically improved outcomes. And, this has now been adopted around the world with guidelines that will now be emerging.

Heather 27:41
[light, bubbly electronic music] We're hearing a lot in the news about a lot of different brain-powered implants and biomedical devices. We're hearing about Elon Musk's Neuralink and a Swiss pilot study looking at different implants for patients, so I really wanted to throw it out to both of you to help us kind of separate fact from fiction – or science fiction, really. I mean, what is real, and what is really going to help patients in the years to come? Dr Fehlings?

Dr Michael Fehlings 28:04

We're in a remarkable era, and the science underlying electrical stimulation of the nervous system to evoke movement, the use of brain computer interfaces, the science is there and it is real. The reality, however, is that these devices are still investigational and there is further research that needs to be done. So, these devices do not represent a standard of care. This is not something that can be easily done and applied on a universal basis in all patients.

But, having said that, I do envision, over the next 5 to 10 years, that we will learn which patient will benefit the most from these devices and there will be advances in the implementation of these implants, and we envision that the Toronto Western Hospital UHN will be at the forefront of these innovations. And, one of the young researchers in our community, Dr Newton Cho, who did his initial work in my laboratory and then subsequently went to Switzerland to work with Dr Grégoire Courtine, has now brought these technologies back to Toronto and we're very hopeful that Dr Cho and other colleagues around the world will be able to advance this science from the level of early investigation to the clinical application in patients. [music fades out]

Heather 29:35
Dr Hachem, are you equally optimistic?

Dr Laureen Hachem 29:38
Yeah, I definitely agree. I think things are still early in the investigational pipeline, but there is promise, I think, particularly with the stimulation therapies, in terms of seeing an effect. I think, ultimately, a lot of this will very likely be a synergistic kind of effect, so stimulation, potentially with pharmacological or drug therapy, or rehab and other types of, you know, harnessing endogenous mechanisms, as well. So, time will tell which kind of strategy and which combinations may have the most effect, but it is likely that not just one single treatment would be the way.

Dr Michael Fehlings 30:12
And I would echo that concept of what we have referred to as "combinatorial treatments", and this is where the art of medicine will link with the science of medicine, so knowing which combination of treatments to apply in an individual patient.

Heather 30:32
And, that brings us to the term that comes up often in our world and often in a lot of our episodes, which is "personalized medicine". I mean, would you ever have equated thinking about spinal cord injury in the context of being able to provide personalized medicine to patients?

Dr Michael Fehlings 30:45
Three decades ago, we had very few treatments that could be applied in spinal cord injury and, when you don't have a lot of treatments, it's hard to personalize treatments when they don't really exist. But now, as treatments are starting to emerge, we have the ability to now customize the approaches that are correct for each individual, and I think, where we are now in 2024, we are in the era of where personalized medicine approaches can be applied to individuals with a spinal cord injury.

Heather 31:20
Dr Hachem, you're part of the new generation of neurosurgeons that's going to be able to capitalize on all of these advances. How do you feel about that? How excited are you about the next 25 to 30 years of research?

Dr Laureen Hachem 31:31
I think it is a really exciting time. I mean, I started actually in the lab with Dr Tator in 2009, and then now with Dr Tator and Dr Fehlings so, even within that period of time, it's really exciting to see how far the field has progressed. You know, and also with the advancements of different technologies, a lot of which I've started to incorporate my research so, you know, I'm collaborating with other teams. We've talked on this kind of podcast about, you know, the molecular, the biology, but then now opening up to kind of circuit-level research, electrophysiological research, the whole transcriptomic side, so I've been fortunate in the lab to be able to integrate and work with and collaborate with other labs doing those, so I think it really opens the doors and ultimately will hopefully facilitate us finding a treatment for patients with spinal cord injury.

Heather 32:16
We're talking about big advances but, Dr Fehlings, you and I have talked before about, you know, even some of the small wins when it comes to spinal cord injuries and giving people quality of life back are important, as well. So, tell us a little bit about that in the context of these advances.

Dr Michael Fehlings 32:28
[upbeat electronic music] Yes, indeed, Heather, and you're absolutely right, and one of the things that I have learned from individuals with lived experience, such as John Ruffalo and others, is that what might appear, to you and I, as a small effect can actually be a big deal. So, for example, in an individual, say, with an injury of the cervical spinal cord where these people lose the ability to control their hands, recovery of hand function, even if people can't recover the ability to walk, can be a game changer. And so, to you or I, this might appear to be a relatively small improvement, but to such an individual, it's a big improvement.

[music continues] And, another example might be the ability to have better control of one's bowel and bladder. You know, this is something that most people just take for granted. It just sort of happens. But, when you lose that function, it can have a big impact on your life. And so, again, this is an area where it might, at first blush, appear to be relatively minor, but to people with a spinal cord injury, this is a pretty big deal. And so, that's one of the big lessons that I have learned from listening to people with spinal cord injuries – to pay attention to some of these details and to focus on these, as well. [music fades out]

And, you don't necessarily have to have the big, home-run cure to be able to have an impact on people with spinal cord injury, and I think, sometimes, you know, with difficult problems, it's more realistic and pragmatic to take a step-by-step approach and, you know, to try to advance improvements incrementally.

Heather 34:14
I've heard patients like John talk about the whole idea of hope and how important it is to always give patients hope. So, can you tell us about that as a clinician and a scientist? How do you talk to patients about not losing hope, despite the circumstances?

Dr Michael Fehlings 34:28
One of the most important things that I have learned from my patients, from people with lived experience who've had a spinal cord injury, is how important it is to have a sense of hopefulness. Hope is so important. And, one thing that I've learned not to say to patients is that, “There cannot be any recovery.” And, the art is to provide a sense of hope to people who have sustained a severe injury such as a spinal cord injury, and the art is to retain honesty, but to present the facts in a hopeful way. And,

the reality is that, sometimes, people can show much greater recovery than you might be able to consider, and in Mr Ruffalo's case, I believe he may have been told that his injury was permanent and complete, and there was not a hope for recovery, and this is when I met him and I gave him the option of having decompressive surgery because I felt that there was the potential to have a recovery and, fortunately, in Mr Ruffalo's case, there has been substantial, albeit incomplete, recovery. But, you know, there certainly has been improvement. And, I think that John's case exemplifies the idea that, even when you're, you know, conveying the facts of an injury or a serious disorder, that the clinician should always bear in mind how important it is for people to retain hope.

Heather 36:04
[light electronic music] Dr Hachem, what inspired you to get into this field in the first place? And, I'm curious what motivates you to continue every day?

Dr Laureen Hachem 36:11
I think really seeing, you know, the patients, frontline, is really the driving factor. As Dr Fehlings mentioned, you know, we do surgery, there are rehabilitation strategies, but we're still really looking for that treatment that could maybe reverse the injury and really allow significant regenerations. I think seeing that, day-to-day on the front lines in the clinic, is really the motivation for all the work that I'm doing.

[music continues] I first started out actually [chuckles lightly] in grade 12 in the lab with Dr Tator as a co-op student. What I was fascinated about was this concept of the body's own potential ability to regenerate the spinal cord, and we see that in other, you know, species, that is these endogenous stem cells are one of the critical players that allow them to do that. But, I think, still at this point, we haven't yet found a way to really harness that, and so that's where I, you know, starting off in the lab, really wanted to focus my work. So, throughout the PhD, we've been looking at these mechanisms. How can we really harness the body's own endogenous stem cells and synergistically use those cells with other treatments to try to regenerate, you know, lost circuitry? [music fades out]

Heather 37:14
I know one individual who had an impact on you, personally, who you knew well, was Christopher Reeve. Right, Dr Fehlings? So, you had a chance to meet him and to get to know him. And, I just wonder, based on everything we've talked about today, had Christopher had his injury today, and science and research has progressed to a point that we're at currently, would he potentially have been able to walk again one day?

Dr Michael Fehlings 37:38
It's hard to say. Well, Chris was a big inspiration to me and he was a great friend of the Toronto Western Hospital. You know, so would Christopher Reeve's outcome have been different? That's hard to say. He sustained a very severe injury and he underwent, you know, what, at the time, was very good treatment, but it's possible that, perhaps, with modern surgical care, modern advances in intensive care, targeted rehabilitation, it's possible that Chris may have had a somewhat better outcome and perhaps he might even still be with us now.

[Your Complex Brain sub-theme music] And, what Chris's case also illustrates is that, for people with particularly a cervical spinal cord injury, it can unfortunately shorten people's lives. And so, advances in medical surgical care are not only important in terms of restoring quality of life and independence, but in a very realistic way, are lifesaving, in that they will help to prolong people's lives.

Heather 38:44
[subtheme music continues] Thank you both for joining me today. It's been a great conversation, and I hope you'll come back and tell us when there are updates.

Dr Michael Fehlings 38:50
Thank you for the opportunity.

Dr Laureen Hachem 38:52
Thank you so much. It's been a pleasure chatting.

Heather 38:57
[Your Complex Brain theme music] Thanks so much to John Ruffalo for sharing his incredible story. Thanks also to Dr Michael Fehlings and Dr Laureen Hachem for joining me on the podcast today. If you'd like to hear more about John's journey, head to our website, uhn.ca/krembil, and click on the show notes for today's episode.

[music continues] This episode of Your Complex Brain was produced by Jessica Schmidt. Dr. Amy Ma is our executive producer. Thanks also to Kim Perry, Meagan Anderi, Sara Yuan, Liz Chapman, and Lorna Gilfedder for their production assistance.

[music continues] If you enjoyed this episode of Your Complex Brain, please tell your family and friends, and don't forget to leave a rating and review on your favourite podcast listening app. We'll be back in two weeks with another exciting episode. Have a great day. [music continues then ends]