

Behind the Breakthrough Podcast – University Health Network

Season 1 – Episode 4 – Dr. Milos Popovic Transcript

CHRISTIAN COTÉ

This is behind the breakthrough, the podcast all about groundbreaking medical research and the people behind it at Toronto's University Health Network, Canada's largest research and teaching hospital. I'm your host Christian Coté. Today's guest on the podcast is Dr. Milos Popovic senior scientist and director at a UHN's Toronto Rehab research arm called KITE short for Knowledge Innovation Talent Everywhere. Dr. Popovic is an award-winning rehab pioneer who invented a medical device that restores upper limb mobility to people with paralysis caused by spinal cord injury and stroke. He joins us in a minute. But first, here's the backstory on Dr. Milos Popovic.

One of his early memories growing up in Belgrade Yugoslavia is at age 7, a natural lefty, young Milos was told he must learn to be right-handed. Not wanting to stick out he complied. A conversion he believes affected his spelling and memory. At the same time making all the more challenging another demand, learning a second language English. For university he was drawn to medicine and physiology, but because of his memory issues Milos chose engineering where he excelled in a world of numbers, equations and spatial thinking. Then in 1991 came another challenge. While looking at PhD programs ethnic tensions are on the rise. Yugoslavia was on the brink of a brutal civil war. The military was looking for conscripts. Milos vividly remembers soldiers banging on doors in his parents apartment building. But as they approached his door, one of the soldiers said will come back. The next day he received a call from a professor at the University of Toronto asking if he'd like to come to study in Canada. Milos leapt at the chance and no sooner was on a plane to Toronto with nothing more than a student visa and relentless ambition.

Today, he's called a game-changing leader in the world of rehabilitation therapy helping to restore function to stroke and spinal cord injured patients. Dr. Milos Popovic, senior scientist and director of Toronto Rehab's KITE research arm. Welcome to Behind the breakthrough.

DR. MILOS POPOVIC

Thank you.

CHRISTIAN COTÉ

Let's start with people who survive spinal cord injury or stroke. What's the outlook typically for them in terms of movement and quality of life?

DR. MILOS POPOVIC

These are two very different pathologies. So in the case of spinal cord injury there are two major groups in sense of either they have full body paralysis both upper limbs and lower limbs and the other group actually has primarily lower limbs which are affected. There are about 50:50 percent is the distribution. The population is very small, you're looking at about one thousand people in Canada annually. However, the fact that they're not able to do a lot of things themselves and they need to attend them care and things of that nature puts them in a situation that they have long recovery periods, they have complicated rehabilitation programs intensive rehabilitation programs. In many of these patients that you do not recover independence in activities of their living.

CHRISTIAN COTÉ

So for those patients with upper limb paralysis, what's been on offer previously to help them regain function and movement?

DR. MILOS POPOVIC

There are conventional therapies that we have applied to the patient's physiotherapy occupational therapy. Then there is also tools how to substitute missing function. So it's not really restoring the function but it's substituting if you cannot do it this way what kind of trick or what kind of tool can you use so that you can carry out the task on your own with the limited function that you have in your arms. So that was the dominant approach. In last couple of, last 10 or 20 plus years, a couple of things emerge robotics technology I've seen it on TV. People are trying to use robotics as a way to deal with that. And the other technology which evolved was electrical stimulation but not as a therapy rather as a way to substitute the function. So if the person is paralyzed you could electrically activate the muscles in the arm and generate artificially reaching and grasping movement. That technology has been out there for about 30 years by that. So, I'm a late comer to the game.

CHRISTIAN COTÉ

So, this has been started in the 60s?

DR. MILOS POPOVIC

In 60s. They've been using it but they use it as an orthosis, which means like a substitute for the movement that came to the idea to use it as a therapeutic tool to retrain the brain that was new.

CHRISTIAN COTÉ

So that previous paradigm in terms of treatment of substituting the ability to move, my understanding is, we're going back to the 90s now, that didn't sit well with you and you wanted to change that paradigm?

DR. MILOS POPOVIC

That's correct. So, one thing which is important fortunately and unfortunately I have not been trained in the art of therapy in physiology, I came from totally different space. I come from robotics and aerospace engineering and electrical engineer

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CHRISTIAN COTÉ

When are we talking about here? Where was this?

DR. MILOS POPOVIC

We are talking here about 1996 or 1997. In Zurich. That's actually at Swiss Institute of Technology, that is ETH, this is one of the premier engineering schools in the world, like European M.I.T. They actually commissioned me to move to the hospital, which is Balgrist, it's part of a university health system in Zurich to work on this technology and these patients. So what happened was I was I was listening to the colleagues so you know when you're in Rome you do what the Romans do, so let's build this electrical stimulation to substitute the function.

CHRISTIAN COTÉ

So in the mid late 90s when you're developing this machine, what's it look like when it's hooked up to a patient?

DR. MILOS POPOVIC

At that time it was like a box, about half of a shoe box size, it had four cables coming out of four pairs of cables and each side of the cable has little self-adhesive electrode which is kind of like a sticker. You know when you go to ECG recordings cardiologists when they put this little electrodes on your chest something like that. Where you provide very specific low energy electrical pulses to the muscles, actually the nerves which are going to muscles, and by doing that you get muscles to contract. What we do is we go and target very specific muscles which are responsible for example for you touching your nose. So, there's a whole slew of eight to 16 muscles which are involved in that task. So, we fired them all in a coordinated fashion that your arm which is paralyzed will be able to touch your nose without you being able to control the process.

CHRISTIAN COTÉ

How did you know where to put the electrical stimulation?

DR. MILOS POPOVIC

That's like cooking right? You know which muscles you want to activate to get a task.

CHRISTIAN COTÉ

Yeah.

DR. MILOS POPOVIC

And then you put the electrodes on them, you fire them and you know sometimes the arm doesn't go to your nose it pokes you in the eye, but then you slowly adjusted and fight to it until you get it. So, there's a knowledge physiology obviously, but there's a little bit of that kind of master chef moment in which you need to add a little bit of your skills to make it work. Now as we were doing that, I essentially prescribed a physiotherapist to work with this assistive device with the patient for 40 plus hours, 40 to 60 hours, and you know a therapist takes that device starts working with

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the patient and they often go and do their thing with a patient and I go and I do my thing. And then 40 to 60 days later the patient comes and says You know I don't need this anymore.

CHRISTIAN COTÉ

They have function?

DR. MILOS POPOVIC

And usually in assisted devices, patients when I tell you they don't need it it's because they don't like the color, the nurse doesn't want to put it on, it's not doing the function they want. And actually, the gentleman came and said no no look at my fingers I'm doing fine, I actually don't need it anymore. And remember I know nothing. I'm just you know the guy who built the airplane just six months ago. So I come and I said 'OK. That's interesting.' So, I take the patient to the neurologist and I said so what's going on. And the neurologist said, 'Oh no, you were just lucky. He has a spontaneous recovery.' Going back to the fact that I have no previous experiences, I said 'OK, that's a legitimate answer.' I thought. Neurologist tells you it's a spontaneous recovery, it's a legitimate answer. But, after 34 spontaneous recoveries I thought you should not listen to what he's saying. Something is happening here. The challenge with this is there is little kind of personality traits that I have, right? I'm very reverent to authorities. I don't listen to that stuff. I don't believe people. I want to see if it's real or not. So, I had a lot of conflicts in my high school and university that I would correct my professors what is wrong. Right? So for me this is not the first time that I would go against the grain. Right?

CHRISTIAN COTÉ

So you're a disruptor?

DR. MILOS POPOVIC

Yeah. So when I saw that that I apply common sense. OK. Let's look. Then I worked with a therapist, with my engineers, and we will try to see what's going on, always making always an assumption that we are wrong in what we are judging or thinking is going on, and having that skepticism that we are wrong and maybe they're wrong as well, let's see what's going on. And you know like a proper scientist let's do an experiment and see what will happen, and when you have three experiments which end up being positive and they're against what you read in neurological books then you start thinking that the books that you're talking about recovery in spinal cord injury patients are probably wrong. And that's how all that started? So we changed the paradigm. So instead of using this electrical stimulation which activates the muscles artificial and gets them to contract instead of using it as a permanent or toxic device substitute we tried to use it as a therapy to see how much of the change can you elicit in the patient. So in '97, '98, '99, we were doing this people ridiculing that, which is fine the results not the idea the approach I say OK OK. Results they thought it was just an outlier, it just happened, right. And the other thing which was also relevant at the time is that people didn't believe in this right. They didn't believe that neuroplasticity exists. Neuroplasticity was not in vocabulary in '97.

CHRISTIAN COTÉ

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You should probably explain what you mean by these concepts?

DR. MILOS POPOVIC

Neuroplasticity is the concept in which the brain changes itself dynamically all the time and the external inputs can change the way how the brain is wired, right. So somebody who for example has a paralysis by intensive training and activating all the elements of the system which are responsible for the movement, you can actually reprogram the healthy part of the brain, which before was not used to perform this task. For example opening closing a hand is performed with one part of the brain, and you can actually train the brain in the latter part of the brain which is not affected will relearn how to do that task and substitute the part of the brain that was damaged due to stroke or spinal cord injury.

CHRISTIAN COTÉ

And so is the concept of neuroplasticity a case where after 20, 30, 40 treatments you're able to do this on your own without the electrical stimulation?

DR. MILOS POPOVIC

That's correct. So you slowly start gaining the ability to voluntary move some of the muscles and at the end you're able to move all of them on your own without the help of otherwise. By that time because we had all these different testing in Zurich, we actually knew that patients are improving and at that time UofT offered me the job. So you know I took those boxes, about 30 something boxes that we manufactured, and I put them in a container together with my chairs and furniture and pots and pans and whatever and moved it to Toronto where I became assistant professor in 2001 and then I start using those devices on Toronto Rehab patients, UHN patients, in clinical trials. It is very unusual for engineer to run randomized controlled trials. Even the biomedical engineers. So I had to learn how to do that. I had to partner with excellent clinicians like Dr. Craven, who is with us, and Dr. Colleen McGillivray who is at Toronto Rehab, and they were my door into the system. And also *inaudible* who was with stroke patients, so they opened the doors to access to stroke patients, spinal cord injury patients and I worked with the. And we were fortunate to convince a couple of granting agencies to put serious money behind that even at the time that this was not obvious it will work. And with these clinicians and that funding, and my team we managed to start getting very exciting and really dramatic results in random mass control trials which nobody else could match neither in this technology or any other competing technology.

CHRISTIAN COTÉ

So others were trying?

DR. MILOS POPOVIC

Others were trying to do it with robotics, others were trying to do it with electrical stimulation, others were trying to do it with brain implants, and nobody came even close to the numbers that we have.

CHRISTIAN COTÉ

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So what were the outcome of your trials?

DR. MILOS POPOVIC

So for example I will take a patient who is fully paralyzed, so he has no movement in the arm, upper limbs so shoulder, elbow, wrist and fingers and we'll take them from that, to them picking up a pen and writing their name after 40 to 60 hours.

CHRISTIAN COTÉ

So, Milos what kind of reaction were you getting from the healthcare industry to the results of your trials?

DR. MILOS POPOVIC

It took quite a bit of time for the community to understand that this is real. I had actually no names, but I had the person fly in specially to check the technology, to check the videos, to check how we measured data, and how all this was done. Another scientist who was in the field and he thought that it's impossible to get these results because he was competing with us in that space and he could not come even close. So when he came and reviewed that then he asked me for the slides and he became one of our strongest advocates. So he start telling other people this is real you need to look at this.

CHRISTIAN COTÉ

Is part of the skepticism the fact that it seems really simple?

DR. MILOS POPOVIC

The part of the skepticism is, I think it's human nature. How can this strange looking man with the funny KGB accent do that? Who is trained in some strange university and I who had been trained in Harvard can't do it, it's impossible right? So that's what it is. See, when our scientists usually fail is they're trying to follow the path with everybody else does. We start flying not because we followed the path of French and German scientists who tried to fly, we needed Wright brothers who were bike makers to go and build the first airplane. We were all on the wrong track. These two people who were not in aerospace, who were not flying, who decided one day we're going to do it change tools change the approach and took us to flight? So you need somebody who is going to come in and be sufficiently disruptive. And it is not one person, it's not that I came and I changed the universe right? But I was one of the many voices in cacophony saying you know people we should look To this potential aspect of the technology. And I spent a lot of time and energy to voice that and to promote it and to do trials and to get things done. But I'm not the only one and I'm not the only person who has done this. So I was just one of the contributors.

CHRISTIAN COTÉ

Where am I going to find a rehab clinic in Canada that offers functional electrical stimulation?

DR. MILOS POPOVIC

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You will go to companies web page which is 'MindTech' and you will have a list of all the private clinics who are offering that. Even the clinics at UHN, at Toronto Rehab, which are offering this are private clinics.

CHRISTIAN COTÉ

And how widespread is this in Canada?

DR. MILOS POPOVIC

I believe we have 18 clinics in Canada which are delivering that. Most of them are Ontario.

CHRISTIAN COTÉ

Is this a health procedure or a treatment that's covered by provincial?

DR. MILOS POPOVIC

Is not covered by provincial government.

CHRISTIAN COTÉ

You're shelling out of your own pocket?

DR. MILOS POPOVIC

That's correct. Which is actually bizarre, and I'll tell you why this is bizarre and I've been talking about it all the time. So provincial government and federal government, through various grants, have enabled me, UHN and our team to develop this technology. They probably have spent order of magnitude 10 to 15 million dollars... 10 million dollars to get this done.

CHRISTIAN COTÉ

Helping you prove that it works.

DR. MILOS POPOVIC

Exactly. Then they helped my company in a startup to create the product. The product saves tremendous amounts of money per patient. For example, if you're a spinal cord injury patient and you cannot use your upper limbs hands you caused the system 5.5 million dollars.

CHRISTIAN COTÉ

How so?

DR. MILOS POPOVIC

Because you need attendant care, you need somebody to feed you, to help you transition to the toilet, help you transition to bed, out of the bed, dress you. All these things. If you get your hand function back the expenses go to 2.5, 2.7 million dollars over the lifespan of a patient. So 40 hours of therapy for a spinal cord injury patient which costs maybe a couple of thousand dollars will save the system 2.5 million dollars to 3 million dollars in a single sitting. Why is this not the best practice?

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CHRISTIAN COTÉ

Yeah so I'm guessing.

DR. MILOS POPOVIC

Why is this not paid by OHIP? OHIP prefers to pay 5.5 million dollars then to pay 2.5 million hours plus three thousand dollars.

CHRISTIAN COTÉ

I'm guessing you're working on convincing them otherwise?

DR. MILOS POPOVIC

Yeah this is this is an opportunity as well right. I mean they need to hear this. I do it in every conference. We do it through company we do it through every possible venue same as stroke patients. We have talked to LHINs when they existed and they knew that if they will apply this technology in their system they would save between a quarter of a million to half a million dollars per stroke patient. We have fifty thousand stroke patients in Canada every year. You can do the math.

CHRISTIAN COTÉ

What are the implications Milos for this technology in terms of other kinds of treatment for people who've lost the ability to move?

DR. MILOS POPOVIC

So, now have launched the hand and arm program first because that was the biggest item in my opinion on the menu for people with disabilities right. The next one is locomotion - walking because we have protocols for walking, building protocols for standing to help people learn how to stand up stand and balance. Also for sitting and now we're moving this technology in the space of treating different pathologies like depression and other things.

CHRISTIAN COTÉ

And these are trials you're working on right now?

DR. MILOS POPOVIC

We are working on trials right now. We are working on depression right now. We just had the pilot trial with 10 patients who used electrical stimulation of the face to treat major depressive disorder. We have excellent results. We're writing a grant to do first randomized controlled trial to demonstrate that it works.

CHRISTIAN COTÉ

What's it mean to you to play a role in like transforming a patient's outlook?

DR. MILOS POPOVIC

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That's what made me leave the aerospace industry in the first place. I can build airplanes it's exciting, but you don't have the impact on the customer. Right. This is tremendous. You changed the life of the patient. You changed the life of their family changed the life of their kids. It's transformation. And how often can you have such an impact.

CHRISTIAN COTÉ

You're listening to behind the breakthrough, a podcast about groundbreaking medical research and the people behind it at the University Health Network in Toronto, Canada's largest teaching and research hospital. I'm your host Christian Coté and we're speaking today with Dr. Milos Popovic, Director of Toronto Rehab's research arm called KITE an inventor of a device that helps restore mobility in patients suffering from upper limb paralysis.

CHRISTIAN COTÉ

I'm guessing as an inventor you've dealt with some failures along the way? What do you learn from failure?

DR. MILOS POPOVIC

Failure is my staple of diet. I fail 99 percent of time. I think the failure is essential element. If you have no hesitation to fail you can get somewhere if you hesitate to fail you're not going to get anywhere. So, I fail every day regularly couple of times and I don't have any problems with that.

CHRISTIAN COTÉ

It doesn't sound like you sit around sulking for very long.

DR. MILOS POPOVIC

No. Not at all. I tried to teach my students, try to get things done and you will fail many many times along the way. And don't worry about it. But if you fail without learning out of that that's a disaster. But if you fail and you learn something and you move to the next phase and fail again and move the next phase and eventually after fifty five thousand failures you hit the jackpot. That's what we're looking for.

CHRISTIAN COTÉ

What keeps you going?

DR. MILOS POPOVIC

You know a number of things which I had the privilege to work with in my life have been transformational, like this particular therapy has been transformational. And that is an exciting thing to do. So, I take pride in doing things exceptionally well and in a different way that hasn't been done before. And these are the type of projects these are the type of things I enjoy doing.

CHRISTIAN COTÉ

I've seen names attached to you in stories in the media and that sort of thing. Game changer. Rock star. Is that an added pressure to live up to for you?

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DR. MILOS POPOVIC

You know I just ignore that. I just do my thing.

CHRISTIAN COTÉ

You could probably write your ticket anywhere in the world it seems in terms of medical research. What keeps you here in Toronto?

DR. MILOS POPOVIC

Toronto is a very unique place. People don't really understand that a couple of elements about Toronto. First of all when you look at University of Toronto UHN, it's an outstanding group of scientists and people. The students who come to University of Toronto, this is the pipeline that flows into my research are probably one of the best in the world. So, they're absolutely outstanding students. Every single student I had in last 20 years that I've been here. Each one of them has been outstanding. Period. So, now here's the situation you have an outstanding partners outstanding collaborators 8 million talent with all kind of different healthcare pathologies in urology. And you have this outstanding students. So, my job is to put this together, enable them to do their thing and get out of their way. And I enjoy being in that environment and people are easy to work with. The politics is not as nasty as in some other places that I had privileged to work. People get things done and there's a healthy competition in the environment. And when you look I just finished annual review for our scientist and when I look at how our scientists are performing they're outstanding. They're not good. They're number one in the world period. There's no discussion about and you can look at it there's data in front of you. Look at the date that you know that your center is the number one.

CHRISTIAN COTÉ

I get this feeling from talking to you your enthusiasm must be infectious with people, I'm curious how you mentor your students?

DR. MILOS POPOVIC

I always felt that my end product of what I'm doing is not the papers is not mine. Move therapy it's not that I always build the my end product is this outstanding people who will be the next generation to run rehabilitation and neuroscience? So, my effort is always put to train them to be the best that they can be. Of course I select the best I can select and then I drill them like a military sergeant for four or five years like I always promised them that I will drill them really hard and my objective is for them to be exceptional scientists that totally independent they write papers without me necessary in the loop to contribute. The present really well they'll be full package as a person package as individual as a scientist as a contributor and they could find a job anywhere in the world in 15 minutes. So, all my students got jobs before they graduate. Every single one of them. They didn't have a situation I go to unless they insisted on that thing they want to take a time off, couple of months, but all of them would have job offers before they would leave my lab and I take pride in that over the period of whatever 20 years I have trained probably between 12 and 14 people who are now professors worldwide. That's what I'm very proud of. What's your advice then to a young

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aspiring scientist. Think Different. Yes you read all these journal papers that tells you what other people have been doing. Check everything yourself. Every single thing which is out there you must validate it yourself. Make sure that you are absolutely certain that this is correct. And then you publish everything has to be impeccable. Anybody in the world should be able to repeat what you have done which means that it's authentic it's real and then you can build on that even if the move the changes are small or may not be time you build on this and then you build your reputation you build a quality all these good things. I actually teach them to watch for quality. That's my focus.

CHRISTIAN COTÉ

Going back to the beginning of the podcast, we talked about your backstory, of how you came to Canada from Yugoslavia when your homeland was descending into civil war. You land in Toronto really with just a suitcase and your visa. When you reflect back now what do you think of the young man in his 20s who made that decision?

DR. MILOS POPOVIC

It's a crazy thing to do. It forms you as a person. You moved in. There's no way back you know you walk the plank, you go to the other side and then you throw the plank into the water. So, you cannot go back. So, you're in a new space you have to make it work and that sets you in a different way.

DR. MILOS POPOVIC

And Zurich was the same thing right. When I moved to Zoya I have to learn the language? I had to learn the physiology. I had to learn how to treat patients. How do you communicate with patients? I had to learn older so, decision was. I'm going to do that and I think being ready to start things completely new in a new environment and being able to do that is very important. That kind of makes you fearless. But you know puts you in a situation that doesn't faze me. I can do that. I think that was one of the best things I have done for myself.

CHRISTIAN COTÉ

Well.

DR. MILOS POPOVIC

It was brutal, I'm not suggesting that this is gentle and it's easy. It was absolutely brutal.

CHRISTIAN COTÉ

Well you literally had Yugoslav military circling your apartment you likely would have been pressed into military service. What did you think when you got that phone call from Toronto?

DR. MILOS POPOVIC

I was very excited. I was great. I mean that was a life changing event. I mean Andrew Goldenberg who was my mentor, I don't know what possessed him to give me a call because you know some person calls from Yugoslavia which is you know 90 percent of people do not know Yugoslav and will not be able to point it out on a map or particular North America. Fortunately he knew because he his background is Romanian she actually knew where this is on the map and for some reason he

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thought I would be a good candidate. And he was very kind to offer me to come and to provide the funding for me to come. And during my tenure with him I have tried to do my best that not at any point in time. He has a second thought that he made an error in judgment that puts additional pressure on you. But I'm very grateful to Andrew Goldenberg and I will not be who I am if it was not for him. And my mentorship style, I actually learned from him. His style, well here's your problem, go solve it. That's it. That's the mentorship to solve the problem. Of course he would come in and say I don't like that I don't like this but he will not tell you how to solve it. And then you become self dependent. You learn things on your own. You figure it out. And that was the best lesson in life I got.

CHRISTIAN COTÉ

I'm curious if you have ever allowed yourself to think about what might have been had you not got that call from Dr. Goldenberg in Toronto?

DR. MILOS POPOVIC

I usually don't reflect on that? You make your choice, you decide where you're going and you try to make most out of it. And if that path turns out not to be the right path you shift and do something else. But I don't spend time looking I mean definitely will not be what what has happened and I will not be here? And will not have this conversation.

CHRISTIAN COTÉ

You go home still, right?

DR. MILOS POPOVIC

Still I do go home and I my parents are still living in Belgrade. Now this is Serbia right. So, they're living in Belgrade. Then I go visit them once or twice a year depending on how much time I have.

CHRISTIAN COTÉ

And what did they think of their son?

DR. MILOS POPOVIC

My parents were because I have done all this on my own. They were just watching all that and they were fascinated by the fact that I've done all these jumps and and did all this so, my parents are extremely proud. But they also know what what were the cost of that. If I didn't have parents who were supportive and who provided me with proper guidance and within their means right I would not be here? And same applies for my wife. Right I have a wife which tolerates a crazy person. So, having somebody who is there for you and make sure that you are on the right track and you don't get insane, these same processes it's a major asset. Not many people have that and that is something that I cherish.

CHRISTIAN COTÉ

What should we look for next from Dr. Milos Popovic?

DR. MILOS POPOVIC

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A couple of things I'm now the director of the Institute the KITE Institute right. I think we will see dramatic growth in that enterprise and they're working on it very hard. They have an extraordinary team of scientists and management who is really doing their utmost to make this stand out and work exceptionally effective. And I am very proud of that team. And the second thing I have a new generation of students and we are diving into using electrical stimulation stem cells. I'm very proud of that. That's very exciting.

CHRISTIAN COTÉ

Dr. Miller Popovic senior scientist and director at Toronto Rehab's KITE Research Institute. Thanks for speaking with us and continued success.

DR. MILOS POPOVIC

Thank you so much.

CHRISTIAN COTÉ

For more on the podcast go to our Web site [www dot behind the breakthrough dot c a](http://www.behindthebreakthrough.ca) and please let us know what you think. That's a wrap for this episode of Behind the break through the podcast all about groundbreaking medical research and the people behind it at University Health Network in Toronto, Canada's largest teaching and research hospital. I'm your host Christian Coté, thanks for listening!