Behind the Breakthrough Podcast - University Health Network

Season 4 - Dr. Lorraine Kalia

Transcript

BTB

Welcome to 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, Christine Coté and today's guest, Dr. Lorraine Kalia, award winning clinician and scientist at UHN's Krembil Research Institute, Dr. Kalia is pioneering the investigation of Parkinson's disease in its early stages and testing drugs already on the market to see if they reverse movement difficulties, which are some of the earliest and most widely occurring problems faced by people with Parkinson's disease. Dr. Lorraine Kalia, welcome to Behind the Breakthrough.

DR. LORRAINE KALIA

Thanks so much for having me.

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Let's start big picture, what is Parkinson's disease? And how does it manifest?

DR. LORRAINE KALIA

So Parkinson's disease is what we call a neurodegenerative disease. It's a brain disease in which brain cells die faster than normal. Interestingly, all of us as adults are losing brain cells every day. But in Parkinson's disease, certain brain cells die faster than normal. And in particular, brain cells that make a brain chemical that we all use called dopamine, tend to be brain cells that are particularly affected. And they're really important for a variety of functions, but very much so involved in being able to move naturally and normally. And so when these brain cells die, people develop problems with movements and later on disease develop other symptoms as well. But this is really a disease of dying cells that in the best case scenario we really want to preserve and to be able to keep alive.

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And do we know why these particular cells die off?

DR. LORRAINE KALIA

We don't know why these cells die off. And as you can imagine, a very common question that people ask when they're diagnosed with Parkinson's diseases is Why me? And unfortunately, we don't have

any clear answers, we often will hand wave. And I mean, I think this is true that there are so many factors that are at play why one individual develops Parkinson's disease, whereas another doesn't, including genetics, exposures that people have had throughout their life, whether that be some viruses or toxins, and in a particular person that's combination of factors leads to them being the individual who has the disease.

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And what's the scope and scale of the disease in Canada today?

DR. LORRAINE KALIA

We don't have a perfect number for the number of people who have Parkinson's disease, it's estimated to be over 100,000. But what we do know very clearly is that neurological diseases are the primary contributor to disability worldwide. And we know that Parkinson's disease among brain diseases is the fastest growing and that's not just in Canada, that's across the world. And that's in part because we're living longer. And so in the past, when people would die from cardiac disease or cancer, they'd never live long enough to develop Parkinson's disease, but with treatments that are now keeping people alive longer, which is wonderful, people are now actually living later on into their life, because these tend to be this tends to be a disease of the elderly. And so once a person hits 60-70, they can develop this disease. And so it's a big issue. And some of my colleagues in the field, we talked about the COVID pandemic right now. But even before the COVID pandemic, many of my colleagues in the field were talking about the Parkinson's disease pandemic that we are facing and are going to continue to face.

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Is there a progression of the disease that we know of?

DR. LORRAINE KALIA

There is definitely a progression of the disease. I wish that when a person was diagnosed with Parkinson's disease, we could say, this is your condition. This is where it's going to stay for the rest of your life. But the major issue with Parkinson's disease is that it's chronic and progressive. And once a person is diagnosed with Parkinson's disease, it's a disease that they will have until death, and progresses to involve motor problems, which is often the early feature of Parkinson's disease, and those things can worsen. But more and more complicated are the other symptoms that people can develop so people can develop issues with their moods with their cognition, and Parkinson's disease. Actually, not many people think of it as a disease associated with dementia, but it's very commonly associated with dementia, whereas people tend to think of Alzheimer's disease as being the disease associated with dementia. But if an individual lives, decades with Parkinson's disease, it is very common that they will unfortunately have to face dementia at some point in their disease.

BTB

So you mentioned treatments. What do they involve?

DR. LORRAINE KALIA

So many decades ago, very smart people who discovered that the primary brain cells that were involved in Parkinson's disease made this brain chemical, Dopamine, of course, thought to themselves, well, why don't we just replace that dopamine? Those things are always easier said than done, and it took a fair amount of hurdles to get over but eventually treatments where we do replace dopamine in the brain, by giving pills that either have chemicals that the brain turns into dopamine or chemicals that mimic dopamine, or even chemicals that can boost our own dopamine levels. We use those as therapies right now. And we have a pretty nice toolbox of therapies. And they can really do great things for people with Parkinson's particularly early in their condition. The issue with dopamine replacement treatments that we use is that they're really just a band aid approach, because the brain cells are continuing to die as we give people dopamine. In addition, you can really develop some problematic complications taking these dopamine medications later in the disease.

DR. LORRAINE KALIA

So the medications can become a little bit more erratic, they're still helpful, but can become quite unpredictable in terms of their response. So an individual can be feeling great when they took their pills. But then after an hour, they can find that the pills were off, and then they're feeling their Parkinson's symptoms. And that's not so much an issue when they start on medication early in their disease, but later on in their disease, they start to have these ups and downs that as you can imagine, can be very troubling and disabling. People can also develop extra movements separate from their Parkinson's disease, which we call dyskinesia. And those in and of themselves can also be disabling. And then a very challenging situation can also be the development of psychotic features or psychosis. So hallucinations, delusions, and this is often a consequence of having to give people large amounts of dopamine to keep them moving well, but then they develop these side effects. And again, because the disease is progressing, and other parts of the brain are being affected, their brain becomes more susceptible to the side effects of dopamine.

BTB

And at this point, in my understanding, there is no cure for Parkinson's, correct?

DR. LORRAINE KALIA

No, there is no cure for Parkinson's. And when I talk about a cure, there's obviously nothing to stop people from getting Parkinson's disease, in part because we don't know what causes it if we knew that being exposed to this toxin and this toxin and this virus, were the causes of Parkinson's disease. And we were able to prevent people from ever having those exposures, we might be able to stop it or if they were the exact genes that we knew the combination where we could potentially, in time have genetic therapies that could prevent people from developing Parkinson's disease. But even what we call disease modifying therapies, which are ones that can slow the progression of the disease, best case

scenario, stop the progression in its tracks, we have none of those available therapies for people with Parkinson's disease. And in terms of million dollar questions in Parkinson's disease, this is another one what could be a disease modifying therapy?

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So let's move into the research front and your work. I understand. We have very little in the way of research models of early stage Parkinson's to work with and help us explore potential treatments and cures. What makes this disease so challenging on that front?

DR. LORRAINE KALIA

That's a great question. And I just wanted to touch on why it's important that we are looking at early models of Parkinson's disease. In the past, when we were looking for disease modifying therapies, we were excited when we found potential treatments that could be tested. And when we got to clinical trial, we would take people with Parkinson's disease often many, many years into Parkinson's disease, and try these therapies. And one after one they showed really no benefit and and failed in clinical trials. And I think rightly, so many in the field at the time, thought to themselves, well, perhaps we're just starting this too late. If we have a process that is slowly occurring, and you're losing brain cells over time, doesn't it make sense that we should be trying to find a time point early where we can preserve as many brain cells as possible. And also, maybe there's a time when the process that causes these brain cells to die might just not be reversible.

DR. LORRAINE KALIA

And so we've been continually in clinical trials looking to study earlier and earlier. And as a consequence, studying the disease in the lab, we've also been wanting to look earlier and earlier. So in a similar vein, many of the disease models that we've been using in the lab, really look at when the brain cells are gone. And one of the measures that we often use in some of the models is counting the number of remaining brain cells, in particular, the dopamine producing brain cells. And so these kinds of models are incredibly useful. They've taught us a ton about the disease and have led to important treatment strategies, but they're also using an endpoint where we don't want to be looking at necessarily recovering the disease when it's so far along. And so that's why early models to kind of partner with this concept of treating earlier in Parkinson's disease I think are important.

BTB

And to that end your research You landed on a really novel model of study, using the roundworm C. elegans, we will write that out in our behind the breakthrough page when we post your episode. But let's begin with what is a roundworm C. elegans?

DR. LORRAINE KALIA

So C. elegans is a worm, its people often are alarmed that we would even have such things in a lab. Sometimes they imagine that we have earthworms in the lab. And these worms themselves are not that type of worm. It's what we call a model organism, which has actually been used in laboratories for decades. It's an amazing organism in that it has many features that make it amenable to trying to understand biology. And since even as far back as the 1970s, amazing researchers have been using C. elegans in the early days to understand basic fundamental biological processes, like how cells die, how organs develop. And it has been an incredibly important organism when we started to understand genetics better, because one of the amazing things about the worm is that you can really manipulate its genetics and then be able to answer genetic questions, which clearly we can't easily do in humans, and wouldn't do so for studied but was also not easy to do in mammalian systems until many years after the development of the use of C. elegans in research.

DR. LORRAINE KALIA

And so in and of itself is a very small worm, it's about one millimeter in size, it lives for two to three weeks. So a very short lifespan. It has 40% of the same genes as humans do. So it's hard to imagine when you stand in the lab, you see a researcher at the microscope looking at this one millimeter worm under their scope, that's these two organisms share the same genetics, like 40% of their same genetics. And it has a nervous system. It has about 300 neurons, which obviously makes it a lot easier to study than a human which has billions of neurons. And it has a variety of simple functions. And one of the important functions is that it has to move around its environments. And it was that piece of the C. elegans model that I think is relatively novel and useful in the way that we've used it.

BTB

We're gonna drill down into this, but I have to ask, take us back to how you hit on the idea of using the roundworm C. elegans as a model?

DR. LORRAINE KALIA

So it was very serendipitous, was a very serendipitous experience that led me down this path, as is sometimes where the most fun and interesting science comes from. I was transitioning from doing work in cells and rodents for Parkinson's disease. And about to embark on some of my postdoctoral training. Just before starting my own lab, and Andres Lozano, at the time was mentor and suggested that I add some additional tools to my toolbox. I knew how to model Parkinson's disease and cells. I knew how to model Parkinson's disease in rodents, was there perhaps another tool that I could use and as it turned out, he had a relationship with Joe Culotti, at Mount Sinai Hospital at the Lunenfeld, who is a world renowned C. elegans researcher. And he suggested I might just have a chat with Joe, to see if there might be something that we could collaborate on.

DR. LORRAINE KALIA

And as it turned out, Andres didn't know this and I didn't know this. But Joe mentioned to me, actually, I have these worms in my freezer, because one of the great things about worms is that you can freeze

them, you know, make them, freeze them, use them at another time. And he had these worms in his freezer, that a prior postdoc had made that express this protein, alpha synuclein. And as it turned out, the previous research I'd done in my previous postdoctoral work was focusing on alpha synuclein. It's a very important protein in Parkinson's disease. When we talk about why brain cells die, we don't know exactly why they die. But we know that one feature of that is that this protein, alpha synuclein, starts to misbehave. And it starts to aggregate and make clumps and starts to not function properly. And that that's a key in the brain cell key driver in the brain cell that leads to cells dying and we in the lab had already developed models for alpha synuclein related cell death in cells and in rodents, and as it turned out, Joe had these alpha synuclein expressing worms.

DR. LORRAINE KALIA

And so I took them and started working on them. And the one thing that I noticed that others hadn't, because there are other worm models that express alpha synuclein, what I had noticed is that they moved funny. And I wondered if this might be a useful measure for the abnormalities in the dopamine cells of these animals, because as it turns out, C. elegans actually have dopamine cells. And what we found was that, and what's been known is that if you take alpha synuclein, and put that protein in neurons, it will call cause neurons to die. And if you take alpha synuclein, and put it in the dopamine neurons, of worm, it will cause those neurons to die. But what we found was that even before those neurons start to die, the animals start to move abnormally. And that I think, was the key in terms of what we were able to take advantage from with this model.

BTB

So thanks to this serendipitous connection, you happen upon a new animal model with which to work on early stage Parkinson's, were you having to trigger Parkinson's in the worm, or were they were already displaying the difficulties or movement difficulties of Parkinson's?

DR. LORRAINE KALIA

The way that we triggered Parkinson's in the worm is that we made them make alpha synuclein in their dopamine neurons. And that's really what initiated the abnormal movements and eventually, the loss of their own dopamine neurons.

BTB

Okay, so then the premise is, next phase is you would test drugs already on the market already approved and in production and safe to see if they might have an impact on the disease?

DR. LORRAINE KALIA

Exactly. So we took this repurposing approach or repositioning approach, which is an interesting approach that is being used in many, many areas of medicine. And I think one of the reasons that we want to do it, and perhaps we'll talk about this a little bit later, is about trying to expedite finding

treatments for Parkinson's disease. And so repurposing or repositioning drug approaches can help to do this, because these drugs are already approved, not for use for treatment of Parkinson's disease, but for treatment of other conditions. And because they have already have that stamp of approval to be used in humans, it can help to shorten the amount of time that's needed to actually get a drug into a clinical trial for Parkinson's disease. Whereas if we came up with a completely new chemical entity, it'd be a lot of initial work to just demonstrate that it's okay to even give the chemical to humans.

DR. LORRAINE KALIA

So we took this repurposing approach. And we did something actually slightly different as well is we used an AI screen. So an artificial intelligence screen as our very, very first step. So collaborating with IBM, we use their platform, Watson for drug discovery to first narrow down that list of drugs, and then tested them actually in our cell models in the lab first to narrow them down further and ended up on a shortlist that we then treated our worms with.

BTB

I understand that shortlist was six potential drug candidates, what happened when you administered them to the roundworm?

DR. LORRAINE KALIA

Five of them actually improved the mobility of the worms. And I think in part, that's because we use these extra steps up front to kind of shorten the list. And that was exactly what we were hoping would be the use for this movement abnormality. In the worms we had tested even before using the drugs on them, whether or not the abnormal movements of the worms was reversible. So taking things that we knew could save dopamine neurons, we had tested the worms to prove to ourselves that the abnormalities we saw in the worms could actually be reversible, because that's obviously an important piece to know, if you're going to use that as a measure for improvement. And so we found five of these drugs, were able to actually reduce the abnormal movements that these worms were experiencing.

BTB

I'm just curious, Lorraine, how many drugs did you have to sift through?

DR. LORRAINE KALIA

We started with a list of almost 700. And this was really more a proof of principle. Trial, one could imagine you could start with far more using an artificial intelligence screen. And actually we have a different project ongoing, where we start with a larger number. What we had started with, though, was limited to approximately 700 drugs because we were looking also for drugs that were funded and on a registry in Ontario so that we would be able to even look at drug registry information to pair with the data that we're getting from worm data.

BTB

So the five drugs that showed promise in the roundworm C. elegans were did you move those five drugs to?

DR. LORRAINE KALIA

So from there, we narrowed it down to one most attractive candidate, a drug called rifabutin. And what we haven't discussed earlier about the worm is one of the major advantages of it, is that it's relatively inexpensive. It's small. And so it doesn't take up a huge amount of space in a laboratory or a huge amount of space in a research facility. And the idea of testing drugs in mammalian models, such as a rodent model, you couldn't even imagine to think about testing a handful of drugs would be almost impossible. So we narrowed our selection down to one drug, and then moved it on to a rat model that we commonly use, which mimics aspects of Parkinson's disease, including the loss of dopamine neurons, some movement abnormalities as well. And we tested it in this rat model, and found it to do a lot of promising things. It improved the movement of the animals, it actually reduced the loss of dopamine neurons in the animals. And it reduced what we think are the bad forms of alpha synuclein, in the animals as well.

BTB

I'm curious, you published these results, I understand late 2021. What kind of reaction did you get?

DR. LORRAINE KALIA

We've actually had a very positive reaction. Clearly, this is not the last step for this work. And always the next step is going to granting agencies and saying this is the initial work that we've done. We have these ideas to take this idea further or advance this area of investigation, and look for funding. And we have a couple of projects based on this initial work one, looking more at rifabutin to try and understand why it does what it does. To get this drug also to be tested in humans, we would never rely on just the handful of models that we've used so far, we need to test them in still some more additional models. And in addition, we have used a different AI approach paired with our C elegans model, and have come up with different drugs that we are wanting to test now. And we have had a lot of enthusiasm. We have now funding, from Parkinson's Canada to do some of this work, from an agency called Cure Parkinson's in the UK. And we're also just in the process, we've been invited to submit a grant application to the Michael J. Fox Foundation based on some of this work. And so I think the reception has been great. And I mean, we're excited that we can get to continue to move this work forward and and push it where we really want to get it to is the clinic.

BTB

And this first drugs that you're talking about rifabutin used in the mouse model went from the C. elegans to the mouse model and published results in late 2021. Do you understand yet the mechanism of action?

DR. LORRAINE KALIA

So we don't. So rifabutin itself is an antibiotic that's used primarily for infection, a specific type of infection and usually an infection that happens in people who are immunocompromised, so that mechanism of action is clearly understood. But how it actually prevents brain cells from dying due to alpha synuclein in the brain cells that we don't know. And one of the arms of research that we have that is funded by Cure Parkinson's now is to understand that mechanism better. And in part that's, you know, important for us to understand the biology. But it's also important for us to understand what it does, because when we get this treatment to clinical trials, which is really where I hope it'll be, we're also going to need to measure that it's doing what we think it's doing in humans. And without knowing what the mechanism of action is, you can't find those kinds of biomarkers to tell us yes, the drug is doing what we think it's supposed to be doing. When we actually give it to people.

BTB

It's certainly an encouraging start. And the fact that you're testing other drugs in the market is very encouraging, as well. There's an important aspect that you indicated earlier that we should maybe dive a little deeper into and that's that you've been very strategic about the choices you make right from the get go. Talk to us about the rationale behind your approach with this particular research, Lorraine?

DR. LORRAINE KALIA

I guess the strategy and maybe it seems more strategic than it actually is.So the strategy here was trying to be economical, trying to get positive hits in a relatively quick and high yields type of way. So I think having the multiple steps that we have put in place, and we like to call it our preclinical pipeline, where we started with a list, did something that is relatively quick and inexpensive by just using artificial intelligence at a computer to try and reduce those numbers and then going on to testing things in cells, which is a pretty fast way to also test drugs, and then being able to test it in a full organism. So the nice thing about C. elegans is that it's not just cells in a dish, it's actually a moving, reproducing organism. And by having that step in there, I think it's allowed us, I have no proof for this. But I think it's allowed us to actually come up with a positive hit in a pretty fast way. And I am optimistic that we have, as I mentioned, we have another drug that is now going to be tested in our rodent model. And it'll be interesting to see if we have as positive results with this second drug because if so, then I'm going to feel even a little bit more strongly that this approach is saving us time and also money.

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You're listening to 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. In this episode, we're talking to Dr. Lorraine Kalia. Award winning clinician and scientists at UHNs Krembil Research Institute, Dr. Kalia is pioneering the investigation of Parkinson's disease in its early stages to find new treatments for the disease. Lorraine you were born and raised in Brampton, Ontario, both your parents are first generation immigrants both worked in the science field, and they encouraged you to do what you love. So you became a ballerina

rising to the Core to Ballet and the National Ballet of Portugal. What is the story behind your pivoting from world class ballerina to a career in medicine?

DR. LORRAINE KALIA

Seems like a strange story, doesn't it? So, yes, my parents were very supportive of me finding and doing what I love. And I guess as is not uncommon for little girls ballet was what I thought I wanted to do. And I did for many, many years, I actually went to the National Ballet School starting at the age of 10. And went through that school, graduated and went on to dance in Europe. Unfortunately, for me, which is the case for actually many dancers, is I was plagued by injury quite early. And with that, looking forward, wondered how much of a challenge it would be for me to continue on a career in dance. It also exposed me remarkably to the healthcare field, which is not a field that you know, I'm not I don't come from a family of doctors and healthcare was really only aspects that I'd see would be my own experience with them. So having had an injury allowed me to have to interact with physiotherapist very, very closely. I ended up having to have some knee surgery. So an orthopedic surgeon, actually at the Toronto Western Hospital was an early interaction that I had. And that turned me on to the idea of healthcare.

DR. LORRAINE KALIA

I thought that I wanted to be a physiotherapist. And it was actually the director of the National Ballet School, Mavis Staines, who was still the director of the National Ballet School told me to think about medicine, actual career as a physician, as she'd known me since I was the age of 10. And thought that I might be well suited for that. And so I explored that further, and went on to do undergraduate science as most people who are thinking about medicine do. And there was in that experience that I then got exposed to science itself research, which got me incredibly excited. And I tell this story often, I don't know if Don Weaver likes me telling this story too often. But I had in my first year of undergraduate science, taken a chemistry course, my dad is a chemist. And so I'd opted to take the Advanced Chemistry course, because I felt that chemistry was in my blood.

DR. LORRAINE KALIA

And in that course, they would have early speakers to try and inspire people as to why to go on in the field of chemistry. And one of the very early speakers that we had when I was at Queen's University was Don Weaver who was there at the time as a chemist. And he went and he himself as a clinician scientist. And that was actually my first exposure to the entity of a clinician, scientist, this person who sees patients, but also works in the laboratory and works to find better therapies. And I have to say it was at that point in time that I think I realized perhaps that really was my calling.

BTB

Amazing. I have to comment, like, what I find interesting in this pivot that you make is you essentially start over and you go on this marathon of education, like you mentioned, Queens, you get your biology degree and then you go on to a simultaneous MD and PhD in neurology at the University of Toronto

and then five years in a fellowship. What I want to know is this sticktoitiveness and motivation for all this what was driving you throughout that journey?

DR. LORRAINE KALIA

I think part of it is I love learning. And, you know, sometimes I call myself the perpetual person in training. And I think to do this kind of work, you have to love, progression of learning and acquiring and developing new skills. And definitely the MD PhD was that where every day was just building more knowledge and learning new things and exploring. And so that in part, I think, was an important driver, just loving the journey. I think if all I cared about was the endpoint, there would have been no point to actually doing this kind of training. But I think just loving the journey was in part, what really carried me through it. The idea of what that job would be at the end, was also a big driver, this idea of being able to eventually be a clinician and be a scientist, I often tell people that while I was going through it, and even in the early days of just starting independently, that I wasn't sure if I did make the right decision, because you never quite know what that job will be like until you have it. And now many years into the job, I know that I did make the right decision, because this is the best job that one could ever have, I think.

DR. LORRAINE KALIA

The other piece that I clearly had a lot of support from my family. And I think a really important factor, that I was incredibly lucky to have this just my life partner. So as it turned out, I met my husband during the MD Ph. D. Program at the University of Toronto. And we supported each other entirely through that program and continue to, as we both worked together on Parkinson's disease. And I think that was an also a very, very important piece to kind of getting through that incredibly long training period.

BTB

I'm curious Lorraine, did you find there were transferable skills from the rigors of being a world class ballerina to the benches of medical science research?

DR. LORRAINE KALIA

Most definitely, absolutely. Everything from being able to face rejection, having to have high expectations for yourself. And also, I think the creative piece as well. Clearly, being a scientist is not like being a dancer on stage. But there is a huge amount of creativity to being a scientist and thinking about things differently, or how to tackle a problem in a different way. And I think that Ballet has been an important part to me actually being who I am today.

BTB

And does luck or serendipity play a role in medical research?

DR. LORRAINE KALIA

Absolutely, too. I think luck is such a big factor that all of us know exists. In many ways sometimes wish it didn't, because it's that real element that is out of our control. Serendipitous piece, though I love it. Because when it happens, and when in hindsight, you realize just how serendipitous that experience was, it's a bit of a blessing. And just remind you how fun and keeps the work interesting, and that you have the surprises that sometimes you just don't expect. And so there have been so many serendipitous aspects of research that we do everything from having this worm model sitting in our lab right now to even just studying Parkinson's disease.

BTB

You mentioned failure. I'm curious how you navigate that aspect of medical research because not something we're taught in school?

DR. LORRAINE KALIA

Not at all. In fact, in school, we're often taught to not fail. And I think that one of many of the benefits of being a clinician and a scientist is that we have so many failures in the laboratory. And we need to have failures because you need to push the boundaries, you need to ask questions that aren't safe, necessarily. And so of course, having the failures can be difficult to manage. So one of the nice aspects of this job as a clinician and a scientist is that you can have all of the very frustrating aspects and the long timeframes that you have to manage in the laboratory, but then also have the amazingly rewarding experiences in the very, very short term with patients. And although we don't have cures for Parkinson's disease, there are a lot of wins that we have in the clinic that I see patients have on a daily basis, which I think counterbalance the challenges that one has in the lab.

BTB

The flip side of this is your clinician you see patients and as a scientist, you know you're in the lab every day, you know the urgency for a need for improved treatments. But how do you reconcile that urgency with the fact that science takes time?

DR. LORRAINE KALIA

Science does take time and always takes more time than I want it to take and I can tell you always takes far more time than patients want it to take. The great thing about seeing people with Parkinson's disease and being involved in part of their journey is that it is a continual reminder for me about the urgency? I can imagine without that, forgetting, in some ways, getting a little bit too focused on the details of aspects that are important in science and important and experiments. But getting a little too hung up on some of what might be minutiae in the grand scheme of things. And I think it allows me to have a big picture in mind all the time. So that I do know that there is a clock that is ticking for many people. And I have to say that patients are a major, major motivator for me.

BTB

So in turn, I'm wondering, do you feel pressure?

DR. LORRAINE KALIA

Definitely, I feel a need and an urgency. Sometimes it makes me maybe a little bit overly optimistic when I speak to people with Parkinson's disease, and they ask me, When are we going to have something new, I really feel a need to be able to have something to be able to provide to them. And so that's, I think, a major motivator. So yes, that's definitely a pressure and and I think it's a pressure that we should all have in the field of biomedical research, not to the point that we're doing sloppy science and not to the point that we're cutting corners. But just always knowing that, especially in contexts where we're trying to find new therapies, that if there are ways that we can actually shorten that course, that we should be thinking about that very strongly in the ways that we design the work that we do.

BTB

I'm curious Lorraine, about projecting your work beyond just the medical world, you've done a number of media interviews over the years, I'm curious about your take on the value or even the need for scientists to communicate their work to a mainstream audience?

DR. LORRAINE KALIA

I personally think it's incredibly important. I think without people knowing what you're doing, and you not being able to explain that to people, it's hard to understand how much impact you're going to be able to have. I again, have the benefit and the privilege of being able to see people with Parkinson's disease, and many patients will come to me with tons of research questions. The beauty of the internet, for many reasons are the access that people have to information, although some not accurate, but others incredibly informative, especially for people with a disease and being able to explain to people with Parkinson's disease or people who are interested in Parkinson's disease, what that disease is, what research we're doing to improve it, I think, is empowering for people who have Parkinson's disease, and just really our responsibility to the public, and the context of the work that we do in Canada.

DR. LORRAINE KALIA

And in research, we're using taxpayer money or philanthropic funds or monies that are raised by individuals and charitable organizations. And I really do think it's a responsibility for us to be able to explain to people what it is we're doing with those funds, and how we're trying to improve, that we should be held accountable to actually doing what it is that we were set out to do. Of course, understanding that science is unpredictable. And although you think you're going to be studying x, it may end up being y by the end of your project. But I think it's very important for us as scientists to be able to tell the public what we're doing and allow them to understand, science behind conditions such as Parkinson's disease.

BTB

There's a leadership author, I like to throw a quote from Simon Sinek at you. He says, People don't buy what you do. They buy why you do it. Why do you do what you do?

DR. LORRAINE KALIA

I'm hoping to make a difference. I'm hoping to actually have a long standing impact on this condition. I'm hoping that in 20 years time, people won't have to go to neurologists on a continual basis to get their dopamine therapies changed, that they can be started on therapy, and just continue on that for the rest of their life without any big changes in the symptoms that they're having. And that's really why I do what I do.

BTB

So when you reflect on that pivot you made from dance to medicine and medical research, when you reflect today, what do you make of that decision?

DR. LORRAINE KALIA

I would never change my early days in dance because it's really made me the adult that I am today and had a huge impact on my work ethic and the way I view the world in many ways. But I am thankful for actually being able to make that pivot at that point in my life. And I'm thankful to have, having had the experience to have been a dancer in the past. And yeah, it's funny that you asked that because in some ways, I will often talk about ballet as a past life. And although probably not entirely accurate, because it still influences me as a person but in some ways it is this kind of past life that I had that I can finally think back on and and be just happy to have known that I had it.

BTB

And your parents, you talked about them being first generation immigrants to Canada and they built a life for you and your sister to afford you opportunities. What do they think of your accomplishments?

DR. LORRAINE KALIA

My parents are incredibly proud. I think most parents are incredibly proud of anything their kids do and mine equally. So I think they would have been proud of whatever I did with my life. But I think that they're really proud of what I've done over the course of these many years. And I will often tell people, when I do any public speaking, that one of the reasons I do things such as this podcast is so my parents get to hear. It's funny when I was contemplating on some of these aspects when you kind of juxtapose dance to research, my parents don't get to see what I do really now, right? I mean, they don't sit in with me when I see patients, they don't sit beside me when I'm writing papers, or come to the scientific meetings, whereas dance is far more accessible. So they would get to see me on stage and actually get to see me dance. And so I think in part, I can tell you this podcast, I'm going to share with them so that they can listen to and I think that it'll make them proud.

BTB

Well, Dr. Lorraine Kalia, award winning clinician scientist at UHN’s Krembil Research Institute thanks so much for sharing your groundbreaking research with us and continued success.

DR. LORRAINE KALIA

Thanks so much for having me. This is great.

BTB

For more on Dr. Kalia’s work and the podcast, go to our website, www.behindthebreakthrough.ca and let us know what you think we crave feedback. And that's a wrap for this edition of Behind the Breakthrough, the podcast all about groundbreaking medical research and the people behind it at the University Health Network in Toronto, Canada's largest research and teaching hospital. I'm your host, Christian Coté. Thanks for listening.