# Behind the Breakthrough Podcast - University Health Network

# Season 5 - Dr. Cristina Nostro

# Transcript

**BTB**

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. On today's episode, Dr. Cristina Nostro, award winning senior scientist at UHNs McEwen Stem Cell Institute. Dr. Nostro is a pioneer in the field of regenerative medicine. Her focus is harnessing the promise of stem cells to cure type one diabetes. Dr. Cristina Nostro, welcome to Behind the Breakthrough.

**DR. CRISTINA NOSTRO**

Thank you, Christian. And thank you for having me and for the very kind introduction.

**BTB**

Our pleasure. So if you don't mind, Cristina, I to understand your research, I think it would be useful if we get a short primer about type one diabetes. It's an autoimmune disease that, for some unexplained reason, attacks the beta cells in the pancreas, and those beta cells are the hormones that produce insulin. Now we'll circle back to those beta cells and how fundamental they are to your work in a moment. But first talk to us about the role of insulin and the consequences. If it's not being produced in our bodies?

**DR. CRISTINA NOSTRO**

You're absolutely correct Christian, type one is an autoimmune disease and beta cells to produce insulin, those cells are found in the islets of Langerhans in the pancreas are destroyed. And they produce this hormone that essentially is fundamental to maintain the normal sugar level in the bloodstream. It signals through other cells in the body to uptake this sugar, which is necessary for maintaining our normal function. So in the absence of insulin, our body has no way to take up this sugar from the bloodstream. And we risk severe consequences.

**BTB**

So hence, the need for that relentless schedule that people living with type one diabetes exams are very familiar. And this is their entire lives, right? It means taking their blood several times a day to monitor their blood sugar levels, it means insulin injections or pump to regulate those levels. What's the scale of type one diabetes in Canada?

**DR. CRISTINA NOSTRO**

In Canada, approximately, I think 300,000 people live with type one diabetes. And as you said, it's something that is affecting the daily life. You can't forget about this disease, we don't have a way to prevent it, and we don't have a way to cure it. So it's typically diagnosed in children even though recently there's been an increase in the number of adults diagnosed with type one diabetes. And you have to think about it as a disease that affects not only the person living with type one diabetes, but his entire family and close friends.

**BTB**

And since the discovery of insulin by Banting, and Best at the University of Toronto, back in the early 1920s. There's really only been limited progress, when it comes to treatments, there's pancreas transplant, but that's quite limited because it relies on a very limited supply from deceased donors. And there's islet transplantation which emerged as a treatment option I understand back in the 1990s. Talk to us about this particular treatment and the scope of its use in Canada today?

**DR. CRISTINA NOSTRO**

So islet transplantation has been really uptaken in the world in Canada in particular, in 2000, thanks to the Edmonton protocol, which is a new way of harvesting the islet from disease donors, and also to infuse them back in a patient with type one diabetes. But it is not a cure. It certainly improves the life of people living with type one diabetes. But in some cases, this patient will still need to be on insulin. Having said that, if you ask anyone who received an islet transplant, if they are happy with the treatment, they are 100% happy. They don't have severe hypoglycemic events anymore. They are not risking their life anymore. So it's definitely changing their lifestyle. It's wonderful, but it comes at a cost because for any type of transplantation, you need immune suppressive drugs, they dampen your immune system, and they could potentially also lead to tumor formation.

**DR. CRISTINA NOSTRO**

So obviously, you're not going to offer this type of treatment to young adults or children. It's only offered to people who have severe hypoglycemic events and can't control their sugar level just with insulin administration. It's true that we haven't had major breakthroughs. But the technological aspect of treating type one diabetes has advanced the way we treat patients, or people living with type one diabetes, because now with what we call an artificial pancreas, it's a pump connected to a continuous glucose monitor. We have a semi automated way of delivering insulin to people living with type one diabetes, so you don't need to constantly prick your finger to check your blood sugar and you can do less and less of that and the time that you maintain your normal sugar level in the bloodstream has increased thanks to this technological advances. So clearly, it is better. But it's certainly we can do better.

**BTB**

So for most people living with diabetes, where treatments such as islet transplantation, or pancreas transplant are not available. What's the typical trajectory of their disease and lifespan?

**DR. CRISTINA NOSTRO**

There are studies it has been estimated that the lifespan can be decreased approximately by 10 years. So not only you're constantly thinking about the disease, so you know, mentally it's draining for you and the people living with you. But it's also has effects long term, and there are severe complication that can occur if the diabetes is not managed properly.

**BTB**

Okay, so let's dive into your research. You've been pursuing a whole other treatment option or approach, trying to leverage the promise of stem cells. In this case, and you correct me if I've got this wrong, you take an immature or unformed stem cell, which can then go on to be anything in the body could be a muscle and organ, a limb. And you figured out how to coax this unformed cell into becoming something very specific. Those all important insulin producing beta cells. If you could walk us through the first phase of your lab work after you joined UHN in 2007, walk us through that first phase?

**DR. CRISTINA NOSTRO**

Yeah, this is actually very exciting work. And if we can really harness the power of stem cells, as you said, these stem cells have the potential to become any cells in the body, then we have a way of creating cells or tissue to regenerate the missing cells. And for type one diabetes, this is almost like a no brainer. We know that islet transplantation works. So we know that if we put islets back into a patient, this can actually normalize the sugar level in the bloodstream. If we can make these cells from stem cells, then we have a way to create lots and lots of the cells. And one day we can actually protect them from the immune system. So eliminate immune suppression and then deliver a cure that could be used for everybody, not just adults with severe hypoglycemic events, but potentially even children and young adults.

**DR. CRISTINA NOSTRO**

I joined UHN in 2007. At that time, I was a postdoc under Gordon Keller, who's the now director of the McEwen Stem Cell Institute. He's a leader in the stem cell field. And when I joined here in Toronto, we had this idea that we could take the stem cells and generate insulin producing cells. Those were early days, you know, we were just trying to…

**BTB**

It was just an idea at the time.

**DR. CRISTINA NOSTRO**

Yes and I remember I could see some cells that were expressing insulin, they were making insulin in the tissue culture dish under the microscope. But those were few and far between. We didn't know if they were the right cells, it turned out they weren't proper insulin producing beta cells. But it was the start. It's something that resembles an islet. An islet is a group of cells that contain the insulin producing beta light cells.

**BTB**

So let's eight years of my understanding, to get to that first step, right 2015. And you publish. These are groundbreaking results after testing these insulin producing beta stem cells. What happened? What did you discover?

**DR. CRISTINA NOSTRO**

In 2015, we published this paper in stem cell reports where we actually reported the protocol that allowed us to generate a pancreatic progenitor. So this is a cell that has the ability to give rise not just the beta cells, the insulin producing cells, but all the cells in the pancreas. So the pancreas is an organ that is composed by the hormone producing cells, the insulin producing cells, glucagon producing cells, and so forth. But also other cell types like the acinar cells that are important to produce enzymes to digest food, and ductal cells that deliver these enzymes to the intestine. So what we showed at that time was a way to efficiently generate these pancreatic progenitors. And it was amazing because when we transplanted these cells into diabetic models, we could see that they were forming pancreatic structures with all the necessary cells that you would expect in the human pancreas. So it was very exciting. I still remember the day that I saw the cells under the microscope, we used a specific reporter to show that we were making the right cell population. I could see that reporter, which was green at the time. And I couldn't believe my eyes, you know, so I talked to the people that I was working with, we repeated the experiment, and that moment was beautiful.

**BTB**

What was the reaction then of the research community, I'm curious?

**DR. CRISTINA NOSTRO**

It was great actually, the paper has been cited many times, many people have been able to reproduce what we did, which is what you want, right? You want to be able to have something solid and other people being able to generate the same results. So that was great. And on top of that, this year, our publication was chosen as one of the top 10 picks of the last 10 years from stem cell reports,so.

**BTB**

Congratulations.

**DR. CRISTINA NOSTRO**

It was great. Yeah, to see that.

**BTB**

You have the ability to use stem cells to create insulin producing beta cells, very promising. But then you run into a roadblock. What happened?

**DR. CRISTINA NOSTRO**

We realized that why we were making these pancreatic progenitors, we were not as efficient as we thought we were. So sometimes if the differentiation protocol is not perfect, additional cell type can contaminate your pancreatic progenitors. And because these are coming from pluripotent stem cells, they still have the capacity to give rise to other cell types. So you may see structure that could resemble intestinal cells within the pancreatic organoids, or other cell types. And so this is a problem, of course, because if you're trying to generate something that could be used in the clinic, you want to be 100% sure that the cells that you are going to one day transplant into patients are safe. So we realize that these contaminants could be a big problem for translation to the clinic. And we started to collaborate with scientists at Princess Margaret Cancer Research Center, particularly Thomas Kislinger, who's an expert in mass spectrometry to identify markers that could help us identify the off target population. And we did that actually, we figured out that there was one specific marker that could target just the pancreatic progenitors.

**BTB**

I just want to go back for a second, then if you just tell me, what would be the risk, or what did you identify as the risk with these contaminants?

**DR. CRISTINA NOSTRO**

The risk is that if you transplant an off target population, that this off target population can grow and potentially form a tumor, if you transplant under the skin of the patient. So you have to eliminate that tumor. And by eliminating the tumor, you eliminate the entire graft also containing the insulin producing cells, so you risk that. On top of that, we don't know for sure there is no evidence for that at the moment. But if the tumor can migrate, it could have severe consequences. So the promise of regenerative medicine is huge. But we also need to pay close attention to safety.

**BTB**

You faced a roadblock. But you didn't stop. You pivoted. As you mentioned, I'm just curious. This is really the essence of science. How did you think about this problem and how to go about pivoting?

**DR. CRISTINA NOSTRO**

As a scientist, you're searching for answers to do things better. And it's also your environment, how you can use what you have at your disposition to make things better. And so being here at UHN, we're surrounded by tremendous skill sets and clever people and technological state of the art techniques. And so that was a beautiful collaboration that we had with Thomas, because he was able to bring in a technique that we had no expertise about, proteomics. And so he was able to analyze all the proteins that were expressed on the surface of our pancreatic cells, and identify specific markers of this population. This was, you know, something very new at the time, nobody had applied this level of technique to stem cell derived products. And it was great teamwork.

**BTB**

This is around 2017, I understand you reached out to Dr. Kislinger. And just so I have this right, essentially, what you're trying to do with his collaboration is see if you could intercept these bad cells before they ever start growing, with some sort of a purifying process before transplantation. So walk us through then…

**DR. CRISTINA NOSTRO**

What happened?

**BTB**

…what the two of you as a team did together?

**DR. CRISTINA NOSTRO**

After discovering this marker, we wanted to make sure that this was something real, that it wasn't just an artifact of the culture that we were generating in vitro. And so we set up another fantastic collaboration with a group at Vanderbilt University in the USA, to make sure that the markers that we were seeing was actually identified in human tissue developing pancreas, and this collaboration with Marcela Brissova and Al Powers, demonstrated that indeed, the protein that we were studying existed also during normal development. So with that in mind, we said, Okay, this is something real, can we actually purify these pancreatic progenitors using this marker and maintain the potential to give rise to beta cells? That was the experiment number one, right? If you remove these cells from all the other cells that you're generating? Are they still able to make it to a beta cells? Because we didn't know at the time whether the other cells could actually be important for the development of beta cells. So we needed to demonstrate that alone, they could do it. And so the first step was okay, we were able to demonstrate that they were making beta cells in vitro. And then that took us to the next step, which was can we actually do it in an animal model?

**BTB**

Right? Okay, so this process that you eventually were able to achieve was to essentially allow you to purify the beta cells, remove those bad cells?

**DR. CRISTINA NOSTRO**

Correct.

**BTB**

So now you have a way to generate safe, reliable insulin producing beta cells that are clean, so to speak. So in 2022, you publish your findings. What did you publish?

**DR. CRISTINA NOSTRO**

2022, was the time that with postdoc, Y Aghazadeh and Farida Sarangi, my lab manager has been with me, you know, since the beginning of time pretty much. We were able to demonstrate that if we purify the pancreatic progenitors and then transplant in animal models, these cells actually give rise to islet like cells in vivo. This is the demonstration that this is applicable to the treatment of people living with type one diabetes,

**BTB**

And no more bad cells contaminated?

**DR. CRISTINA NOSTRO**

And no more bad cells, we eliminated the tumor forming cells.

**BTB**

So what was the reaction of the medical community after that paper?

**DR. CRISTINA NOSTRO**

It was great. Yes, the paper was published again in stem cell reports. And it's something that other people are using, the protein that we're discussing is called GP2 Glycoprotein 2. And again, similar to other studies, I've noticed that other people have started to use this protein to monitor the development of pancreatic progenitors in vitro to sort for the cells. But nothing is perfect. As you know, there is a catch with sorting cells, because we lose a lot of cells it’s a very inefficient process.

**BTB**

That's what I was gonna ask you about, because this is like another challenge that you're presented with, because of the process of purifying or filtering out the bad cells, you reduce the volume of what

you're producing, that affects the therapeutic efficacy, I imagine. So how do you now go about boosting volume, so to speak?

**DR. CRISTINA NOSTRO**

So we are attempting to understand how we can expand this pancreatic progenitors. This is something that is ongoing in the lab. And by all means, we are not the only one working on this, because if you can expand this population, it will be of tremendous help in manufacturing. The other areas that we're working is it's actually trying to bypass this step and push the pancreatic progenitors to make islet like cells in vitro. And by keep differentiating the cells longer in vitro, we eliminate the tumor formation. So right now, the idea would be not to transplant the pancreatic progenitors, but to actually transplant something that is more closely resembling the islets. And by generating those islets, I can't say 100% sure, but it's like it would be an extremely rare event to have tumor formation cells at the end stage. So the goal is now to go next and generate islet producing cells.

**BTB**

What would then be the clinical application, if you got to that stage of the volume that you needed, there's no bad cells, contaminating them, et cetera, et cetera?

**DR. CRISTINA NOSTRO**

These type of approaches are already in clinical trials. So both stem cell derived pancreatic progenitors and stem cell derived islets are in clinical trials being tested for safety at the moment. And so we live in a very extraordinary moment. The results from these trials, especially the trial using stem cell derived islets are extremely positive, UHN is one of the sites where these trials are ongoing, and two of the patients transplanted are off insulin, which is remarkable. We are hoping that our differentiation protocols will improve these islet producing cells even more, and deliver something that is going to be better and more equitable for people because if you think about it, if more people work on this, we will always improve, and we will deliver something that will be a little bit more affordable in the future. By creating competitiveness in the field.

**DR. CRISTINA NOSTRO**

The product that we have at our hands right now we call it islet like cells, because they look like islets. But they're not exactly behaving like adult islets. So they're still a little bit immature. So we like many in the field are working towards the generation of something that is more mature, and the generation of something that contains only pancreatic endocrine cells or cells of the islet, because we're still occasionally making other hormone producing cells in this islet. And we want to make sure that those are eliminated.

**BTB**

So what should we look for next from you and your team?

**DR. CRISTINA NOSTRO**

Okay, I love this question, because we have so many things going on at the moment. One of the biggest problem I told you about islet transplantation and stem cell islet transplantation would be the use of immunosuppression. If you need to use immunosuppression, we're now back to the islet transplant, we need to eliminate this. And so there are two ways to think about this. Either, you're going to physically protect the cells with a barrier with a physical barrier, whether it's a device or encapsulation system, or you modify the cells genetically modify the cells to make them invisible to the immune system. And we have a beautiful collaboration with Dr. Dave Russell from the University of Washington in Seattle, where he generated cells, stem cells are invisible. So what we have done now is to differentiate these invisible cells into islet like cells. And we have data suggesting that they can be indeed invisible to the immune system. So this is actually gonna be revolutionary, I think, for the field. And again, we're not the only one doing this, many people are working on this, companies are working on this, and I think the future looks, you know, really promising.

**DR. CRISTINA NOSTRO**

The other thing that we're working on, which we just published in a Bio Archive publication, is the core transplantation of stem cell derived islet with accessory cells. And in particularly, we're using immune cells. Macrophages are like fascinating cells. They've been described as having different facets, like they can be killer if they are attacked and destroy pathogens, but they can also be builders, they can help with tissue remodeling and promotion of angiogenesis. And we think the macrophages that we're using are actually the builders. So by using them together with stem cell derived islets, we can improve the survival and engraftment of these islets in vivo. So we're very excited about this work. It’s the work led by a fantastic postdoc in the lab, Adriana Migliorini, and it's in collaboration with the director of the Institute, Gordon Keller, because he's the one that can generate stem cell derived macrophages. So lots of exciting things. We're also have ways to improve the formation of the islets. So things are looking good.

**BTB**

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. And today we're speaking with Dr. Cristina Nostro, award winning senior scientist at UHNs McEwen Stem Cell Institute. Dr. Nostro is a pioneer in the field of regenerative medicine, harnessing the promise of stem cells to one day cure type one diabetes.

**BTB**

Cristina, you were born in Florence, Italy, your dad was an architect, your mom worked in a legal firm and you once wrote, you found high school biology fascinating. But it wasn't really until years later, after your bachelor's degree in biology while working on your PhD, that you embark on an exchange trip to the University of Manchester in the UK and something about medical research clicked for you there. Talk to us about that?

**DR. CRISTINA NOSTRO**

Oh, my God, those were amazing times because it really was during my undergraduate degree in Italy. And I had the fortune to go into this Erasmus program and go to the University of Manchester. And while I was there taking exams, I was lucky enough to work in a lab for the first time in my life. I was working in the lab of Chris Potts, and he was stem cell biologists in fact. He was a leader in the field of intestinal stem cell biologists and skin stem cells. And I was working together with a postdoc doing experiment. First time, you know, I had no idea how to pipettes, I had no idea how to look cells under the microscope. It was like really early days. But I learned about what it takes to do research. And I was impressed by the power of stem cells, in particular, the stem cell testing that continuously replenished the intestinal epithelium. And I learned about stem cells and apoptosis. And I decided that I wanted to do a PhD.

**BTB**

So I'm curious, when you reflect today, do you have any sense of what it was that you connected with internally that made you go this is my vocation?

**DR. CRISTINA NOSTRO**

I think it was the discovery parts. You know, we were testing drugs that could be used to prevent or decrease colon cancer at the time. And I remember clearly, the curiosity when I was looking at those slides and counting the cells under the microscope to see whether the drug that was used to treat that particular animal had an effect. The findings, you know, the discovery of something new and being able to see that for the first time was exhilarating, I think, yeah.

**BTB**

That's amazing. Okay, so after your PhD, you end up in a postdoctoral position. You mentioned earlier at Mount Sinai School of Medicine in New York in the lab of really a giant in the field of stem cell research, Dr. Gordon Keller, who is today the director, as you mentioned, of UHNs McEwen Stem Cell Institute? It's like you stepped right into the big leagues. How did you go about landing that position, I'm sure younger scientists would be curious to know how you did that?

**DR. CRISTINA NOSTRO**

You know, it was not easy. Not easy because I first heard Gordon Keller speak at a conference in Manchester. It was a stem cell conference organized by the Christie hospital there. And Gordon was one of the few working on embryonic stem cells, it was very new all the time. And he was leading the field. And I had to really, you know, it took all the courage in the world to go and talk to him, try to meet the guy. And eventually, when it was time for me to look for a postdoctoral position, I asked my supervisor if he could reach out to him. Eventually, I got an interview in New York, and well, it was my first time in the States, first time in New York as well. So I think I was overwhelmed by the city. And I was overwhelmed by what was happening in his lab he had at the time, probably, I would say, you

know, 12, postdoc in his lab working on different aspects of embryonic stem cell differentiation. And everybody was so excited to be there. And that excitement, you know, was contagious. I really wanted the job. I asked him, on the day of the interview, did I get the job?

**BTB**

That's great.

**DR. CRISTINA NOSTRO**

I was so naive. And he didn't answer me for some time. But eventually, he offered me a position and I think I interviewed in September of 2003. And in May of 2004, I moved to New York.

**BTB**

I want to go back to when you were a PhD student, because something about your journey in that moment fascinates me because that you're in Manchester, you're studying blood stem cells. And then a few years later, you move to New York, for your postdoc work with Dr. Keller. What I marvel at here is, English was not your first language at this point. You're tackling complex scientific subject matter, while at the same time you're learning a new language on the fly. How did you do that?

**DR. CRISTINA NOSTRO**

Well, it started when I was an Erasmus student in Manchester. That was the hardest part. My first month, I was ready to go back to Italy, like every other day, you know, I was sharing a room with a Scottish girl, Elsa MacDonald. And my English was really bad, really poor. And her English was Scottish. And I'm telling you, I could not understand the words he was saying. But luckily, like everything in life, you go through, you, you meet people in the same position. And I think that's key, you know, you're sharing your experience with somebody else. And you learn that it's not just you that you're not the only person that is struggling with this. And somehow sharing that pain lets you go through.

**DR. CRISTINA NOSTRO**

And little by little you learn, you learn English, you learn how to communicate with others. And that was such an eye opening experience, because all of the sudden, I'm able to communicate with people coming from all over the world, Manchester is a university that is really international. So it really gave me this amazing opportunity to realize, you know, I'm coming from Italy, everybody knows Italy, but it's just a small country, in the world if you think about it, and there's so much more to learn. So that was a fantastic experience. When I wrote my PhD thesis, I wanted to cry every time because the correction for my supervisor were enormous, but I learned how to write scientifically, it's a skill.

**BTB**

Dr. Keller has been a part of helping guide you along the way. In general, I'm curious what role for you has mentorship played in shaping your medical research success?

**DR. CRISTINA NOSTRO**

It was huge. Gordon was very inspiring. But I think maybe like many people, I've always worked with people that were really passionate about their work. And it wasn't just direct supervisor, also collaborators and friends in the field, who really enjoyed what they were doing. It's not at the end of the day, I think many people will tell you it is not work. If you are really enjoying what you're doing doesn't feel like a duty or, you know, you want to come to the lab to talk to the people you know, working on a project and see the progress and you want to read about other groups investigating similar aspects and trying to create ideas and experience that.

**BTB**

I'm curious then, Christina, what's your advice to young researchers about what it takes to be a medical research scientist?

**DR. CRISTINA NOSTRO**

Well, you have to have passion, you have to really like what you're doing. So if you're searching for a mentor, I would say the first thing is you need to know what they're doing. You need to be familiar with the type of research and the question that they're trying to ask. That work has to excite you because if it doesn't excite you It's not going to work for you, I would say, make sure that the person, the supervisor that you're working with is dedicated to your success. And you can try to find this through talking to the people working in the lab. And I was very lucky, because I always had very candid conversation with everybody in the lab when I joined. And I think it's useful. But most of all, you have to have that drive.

**BTB**

Does luck or serendipity play a part of medical research?

**DR. CRISTINA NOSTRO**

It's probably number one, you know, I can’t tell how many times we started with an hypothesis and things didn't turn out the way we wanted. And so you look at the data, and you have to be objective, it's not telling you what you expected. And you have to start thinking about it objectively and say, okay, that this is the data, what does it mean? And maybe it means that you need to start reading on another topic altogether, and learn, and I think that's the most beautiful aspect of science, that you're constantly learning, and discovering new things. And it's the part that I think is really fulfilling.

**BTB**

Your work is rooted in basic science, your time is in the lab 100%, which is really the lifeblood of medical research. Yet we live in a time where there's so much focus on the translation of medical research to the clinic and results. I'm curious, is there a pressure you feel in trying to yield a return on your work?

**DR. CRISTINA NOSTRO**

You know, it's definitely what we're doing is very competitive. But it's also the nice aspects. I mean, we do basic research, but we have that closeness to people living with type one diabetes. And because some groups are already testing this in clinical trial, it feels really like what we're doing can have a huge impact. So yes, sometimes it's hard because you feel like, how can you contribute a little bit more, but I think every little aspect helps. And so every little discovery done in the lab can improve the final output, it might not be tomorrow, but it might be in 10 years, that we have a better way to generate the cells, whether it's like these are you know, cells that can engraft more successfully or produce more insulin or be resilient to the harsh environment of a person living with type one. Everything will matter.

**BTB**

You've just pointed out sometimes the length that science takes, I'm wondering how do you wrestle with internally or reconcile the urgency of patient need, with the fact that science takes time?

**DR. CRISTINA NOSTRO**

Yes, it takes time. And sometimes it's hard, right, because people will ask you, is this ready? And most of the time, the answer is no, we're not ready. But we're making strides. It is hard, especially when you're talking to people, even with type one diabetes. I wish we were faster. But honestly, if I think about it, I think what we've done in the last 20 years is remarkable. 20 years ago, we didn't even know how to take the stem cells and generate the very first step in embryonic development is whether the cells give rise to one of the germ layer that eventually will form the entire gastrointestinal tissue. So we didn’t know that and in 20 years, we've learned how to make that first step and understand how to pattern this. We call it a tube. It's like the gastrointestinal tube, we've learned how to pattern this to become pancreas to become liver to become intestine to become lung. So what we've achieved, and in particular for the pancreas, not only pancreas, but beta cells, and we are in clinical trials, 20 years, I think it's fast, you might not feel fast for a patient, but we are getting there.

**BTB**

Compared to previous generations of scientists, it seems your generation has an added demand on you. And that's to amplify your work, not just within the industry, you know, with academic journals, etc. But to make it accessible to the public. What's your attitude towards this trend?

**DR. CRISTINA NOSTRO**

Yes, you know, I have to say, we're very thankful to people like you, who allow us to speak to a large audience. And it's definitely something that I had to learn. I'm not a natural in front of a microphone or in front of a camera. But I've learned that being able to describe what you do to everybody, not just your colleagues is very rewarding at the end of the day. So it's taken time, but I'm actually enjoying it now. And it's the same as teaching. You know, we work in a research institute. So the majority of our time is dedicated to research. But at the same time, we're teaching the students in the lab, we're discussing things with postdoc and occasionally we teach at the University of Toronto. And that aspect is also extremely important.

**BTB**

I think in essence, you know, you're communicating the value of medical research to taxpayers, who can help make decisions in terms of where medical research funding should go, and how intertwined it is, with advancing patient care. What would be your advice to young scientists entering the field, on embracing this responsibility?

**DR. CRISTINA NOSTRO**

They're probably communicating a lot better than we used to. They're learning from us, you know, they see us more on social networks and on podcasts and YouTube videos. So they're probably better, I don't know if I can actually give them advice. I see it already in my students, you know, the presentation that they provide, during our regular lab meeting, are really well done. Their ability to use technology to generate creative content is definitely superior to what mine was. So I think they're doing great. It's something that they need to do to be able to communicate their science, for sure.

**BTB**

And over the years, how have you navigated failure? Because it's not like we're taught this in school or university?

**DR. CRISTINA NOSTRO**

You know, it's hard, right? For everybody. And probably the hardest part is, I mean, it's not failure. But it's when you you write a grant proposal, or you write an article, and you submit it, and the reviewers come back, and maybe you didn't get the grant, or maybe your paper was rejected, that first reading those words are really hard because you put your heart into this project. But I've learned that with time, you have to grow out of this, you know, you learn from those comments, you try to remove the personal aspect, and see it with fresh eyes and say, okay, you know, maybe they have a point, maybe there's something here where I can improve and do better. And the other thing is like failure, sometimes you might think you're failing in the sense that your hypothesis, as I said before, is not correct. But then you you learn something new. And maybe you can make lemonade out of lemons.

**BTB**

There's a leadership author named Simon Sinek, who I love to quote, and I wanted to ask you your reaction to this. He says, People don't buy what you do, they buy why you do it. Why do you do what you do?

**DR. CRISTINA NOSTRO**

I think, because I enjoy it. I enjoy the research aspects, and I enjoy discovering something new. I also love what I'm doing, because I can see that there is a potential clinical opportunity here. I can see how it can change people's life. I see in particular the power of regenerative medicine, how it can shape a new way of treating not just type one diabetes, but many other diseases. So I do it because I enjoy it. But I also do it because I see it has so much potential.

**BTB**

But what I have to believe is there was obviously within you a drive and a belief in yourself.

**DR. CRISTINA NOSTRO**

Absolutely. I think that's something that I have to thank my parents for. I never doubted myself. I knew I could do everything. And this is my lesson to all people out there and all the women out there.

**BTB**

Dr. Cristina Nostro, award winning senior scientist at UHNs McEwen Stem Cell Institute. Thank you for sharing your groundbreaking research and continued success.

**DR. CRISTINA NOSTRO**

Thank you so much, Cristian.

**BTB**

For more on Dr. Nostro’s work and the podcast, go to our website, www.behindthebreakthrough.ca. And let us know what you think we'd love to hear what you think. 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 Christine Coté. Thanks for listening.