**Fighting Blindness Canada Podcast
Season 1, Episode 1: Focus on Inherited Retinal Diseases Transcript**

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MI: Welcome to the Fighting Blindness Canada podcast. I’m your host, Morgan Ineson and I am excited to welcome you to our very first episode.

In this series we will be interviewing researchers & physicians who focus on the treatment and prevention of eye diseases. We’ll go behind the scenes to learn not just about their research, but also why they are passionate about what they do.

In every episode we will also pose a question to the vision loss community to learn first-hand about how living with vision loss affects them.

For today’s episode we are focused on inherited retinal disease research. An inherited retinal disease, or IRD, is a condition caused by a specific genetic mutation or combination of genetic mutations that lead to vision loss. There are over 20 known IRDs and researchers have found over 300 genes that can cause these conditions, with many still unknown. As science has advanced over the past decade, there has been a significant increase of research into how these conditions can be treated and managed.

Today we will be sharing an interview with clinician- scientist Dr. Elise Dr. Héon who has dedicated her career to the care of patients living with inherited retinal conditions. Then, we will hear from four individuals living with an IRD about their perspectives on vision research.

This is the Fighting Blindness Canada Podcast.

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MI: Dr. Elise Héon has been an ophthalmologist at SickKids since 1996. Her career focusses on inherited eye disorders, now mostly on inherited retinal diseases. She is the director of Ocular Genetics program providing comprehensive assessment, genetic testing and counseling of patients affected with inherited retinal disorders. She has trained numerous students of various academic levels from around the world. Dr. Heon joined us from SickKids to talk more about her experiences and the importance of communication.

Dr. Héon, thank you so much for joining me today for our first episode of The Fighting Blindness Canada podcast. You've had such an exciting career in vision science and your contributions to research, advocacy and patient care have meant so much to so many people. I'd love to start today by asking you about your inspirations. When did you decide you wanted to pursue a career in medicine? And were you always interested in ophthalmology and rare diseases?

EH: Thank you, Morgan, for your kind words. For me medicine was not calling and certainly not ophthalmology. I never thought I would get into medicine. And but I tried after I finished college, which is CEGEP in Quebec, and because I did my basic education in Quebec, and then I got in, so I was privileged to be part of, of that group. Ophthalmology, I sort of fell in love with a ophthalmology when I have a friend who's an optometrist, and she let me look at the slit lamp at her and, I saw the eye like so magnified. And it was, it was falling in love at first sight, it was just so beautiful. And so, I decided to try. I did rotations and then I applied and it's the only thing I wanted to do, and then never regretted it.

[03:27]

MI: That's wonderful. So you currently work at SickKids, and you're the director of the ocular genetics program there. This is a unique program in Canada, and I believe one of only a few in the world. Can you tell me more about this program, how it came to be and why it's so special?

EH: The program was created because of a care gap, and was the brainchild of Brenda Gallie, who was a pioneer in retinoblastoma which is a genetic disorder. And Maria Misrella, at the time, was struggling managing genetic disorders in a comprehensive way, like there was no support. And like it's, it's a patient population that has special needs, quote unquote, like it requires to do it well, a real interdisciplinary approach. And through the years Brenda's idea was to have a genetic counselor and coordinators specific for genetic eye diseases. And we started a database. And the program grew through the years, we now have two genetic counselors, a social worker, we have our own coordinator, we have an internal database that contains over 25,000 entries. And it's a great opportunity to be part of the team for the inherited eye diseases that are not cancerous. There's Dr. Vincent and myself as physicians. So, we're two physicians that are trained to deal with these diseases. We have the electrophysiology unit, the imaging equipment, the retinoblastoma program has grown on its own, and uses this the same resources, but the teams now function independently. So, it's a wonderful program that serves patients more on just the technical level, but the holistic level, we're involved with school, we're involved with their needs, guiding them through low vision, etc. And of course, we offer genetic testing to everyone. And we've been doing this since 1996. That started on the research base. And when the genetic testing became available on a clinical basis, we were just ready to continue to do that. And we always documented the data in our database, which is why we have so much information.

[06:06]

MI: It's such a great repository of information for the research that's going on, for sure. So, I want to talk a little bit more about the genetic testing. There currently is only one approved gene therapy for eye disease, which we can talk about in a bit. But why do you think it's so important for patients to get genetic testing and are there benefits to people even if there's not treatment available for them yet?

EH: That's a great question and you'll get different answers, but I feel very strongly about my opinion. And I think genetic testing is important for multiple reasons. The first one is that it confirms the diagnosis of a person and when you’re losing vision, or when you have lost vision, and you don't know why, I can't imagine how devastating that must be. And I'm always impressed at how patients are relieved, families are relieved, when we identify the genetic cause of their eye problem. So, confirming the diagnosis also plays an important role in confirming the inheritance, whether the risk of passing it on or whether the risk of having another affected child. And then through genetic subtypes of disease, there's some patterns that arise. And it can help us guide into what to expect, like some progress more than others. And in terms of our investigations. Then when we study groups of patients with mutation in a specific gene that allows us to better understand what the gene does, and that's what leads to treatments. And so there's only one treatment and there's not going to be a million treatment next year. But that doesn't mean that we're not furthering the knowledge of genetic eye disease exponentially every year. And I I'm a very strong proponent of genetic testing in general, I could talk an hour on this one.

[08.19]

MI: I know we've talked about genetic testing before. And I think what really sticks with me from our conversations is that genetic testing, it's not a judgment, it's about getting information. So, what you do with that information is up to you, but getting the most information you can to help with your health care.

EH: It's all about knowing, you know, it's all about like you say, it's, it's a piece of information that empowers you actually.

[08:52]

MI: Yeah, absolutely. So big item in the news in the last few weeks is that Luxturna, which is the gene therapy, that I mentioned before, that is available for patients who are affected by the RPE65 gene mutation recently been approved for public funding in Ontario and in several provinces across Canada now. And I know you've worked tirelessly over the past several years to make sure this treatment is made available and accessible to Canadian patients, and how are you feeling now that patients are actually accessing this treatment?

EH: Well, it's pretty wonderful. And I'm pretty tired, because it's a lot more work for me now. That it's, it's like a dream come true, to be able to offer a solution. And I'm really happy for the for the patients that they have access to this. We've done it for us, it took a long time in Ontario for the government to agree to reimburse the drug. So, it's only recently that we've been doing more cases that we've had the privilege of doing three cases where either the employer or benefits program paid for the treatment, which is a million dollars. And it's been a life altering experience for me, and for them. And even there was an older individual was the first case, even though by some perspective, the improvements were not big. But that change had a tremendous influence on his ability to function better, and to feel more autonomous and in charge. So, restoring some sensitivity to light, no matter what level, I think improves the quality of life of individuals.

That said, it's not a cure. We don't know how long it lasts. With we have a retrospective information on over 10 years of benefit. And so we know at least that. I think it's it's just it's a new avenue, but it's a surgical intervention. It's not without risk, and different people will benefit to different degree. And so it's very important to not generate hype over this. And it's only people with two variants in the RPE65 gene that are eligible. It will not work if you have mutations in another gene. And for some reason, we have a lot of patients here in Ontario, because we've been testing for this for a very, very long time. And now that the treatment is available, I've been advertising through networks and new cases are being identified. So we've, by the end of March, we'll have treated nine cases overall, in and we have a minimum of 17 to schedule, which is a big challenge, because each surgery is two eyes. And then we need to follow up. So it's not a trivial treatment. It's not just like taking aspirin. And it's not just like getting your hair cut. It's a serious intervention, that for which the risks are minimal, but do exist and it's an intervention that benefits only a specific group of people. But it's it's a wonderful change in our life. We'll be monitoring the outcome very carefully, through another study that's called Perceive that is sponsored by Novartis, which is a very important study that will monitor outcome over five years and adverse events. So it's important because you need to know, what could be the adverse events that come from this intervention?

[12:55]

MI: Absolutely, I think it's really interesting to you said that you already have 10 years of data such as shows how long this treatment is actually, even in clinical trials in the patient that we have 10 years of data. That's a long time.

EH: Yeah, yeah.

MI: Well, that's, that's great. And thank you for sharing all of that. And I know a little later in the episode, we'll be hearing from someone who has received a treatment already, which is very cool.

Have you had any personal experiences within the medical system that have influenced the way that you relate to patients and the way that you practice medicine?

EH: Oh, that's an interesting question. Because I do so I'm a survivor of breast cancer. And it was a, it was a horrible experience. I had to fight for my care and it made me realize how you're a number in the system, and how people don't value the importance of quality of life. People value a technical measure, and not the individual. And the individual is not asked, really what would be preferable, like, what do you need as a person. And so when I came back from my sick leave, of course, well, first I stopped working in cancer, because ocular genetics was just keeping me too busy to do it well. And, I listen more. And they think that's been underutilized because the patients know more than anyone what's happening. And if you listen to them, they'll you'll go give you a lot of information. And that led me to get interested in patient reported outcome measures. So we've been working with another group to develop patient outcome measures specific to inherited retinal diseases in the adolescent group, and we're working on developing one for the children. And so the bottom line, as much as I tell the patients and the trainees, the physicians we’re just people, like just a person. And we have good days and bad days, and some are more pleasant than others. And the patients are also people. They're not a number, and they have a family. And the impact of their condition is multifaceted. And we need to work together to figure out what can we do to help? And sometimes it's just listening. It's just being there. So the person's not not alone.

[15:27]

MI: What advice would you have for people who might be struggling to get the information they need in the medical system? Like you said, we're all people, What if they're, you know, dealing with a personality that is difficult, or just having a hard time navigating the system? What kind of advice would you give for them?

EH: So I get that question from especially the young patients, for some reason. And patients need to realize that in medicine, and especially ophthalmology. Ophthalmology is a field where you fix things, you have a problem, usually, I can fix it, either with drops, glasses or surgery, okay. So when people can't fix something, they're uncomfortable, okay. And if they're asked to fix something that they don't know much about, they're even more uncomfortable. And so, I equate to poor communication to discomfort, is that maybe you're not dealing with the right person. And so beating them up won't fix things, I think is reaching out to agencies like yours, who can guide them on which door to knock on. So luckily, there's more people being trained in the field, like in Ontario we're lucky, there's several more engaged in ocular genetics, but in the rest of the country, it has to improve, because the field of ocular genetics is just going to get bigger and bigger and bigger, as more opportunities become identified. And as patients and families realize the value of genetic testing.

[17:08]

MI: And what would you say is the most important thing that a patient or their family should know when they're first diagnosed with an eye disease?

EH: I ask them what they want to know. I ask them what they know. I ask them as them with the understand or with the previous person said, which is often they said Not much. And often the person may have said something but it doesn't register when you're like, you don't understand or it's a shock. And so I just go progressively, What do you want to know? And what are you afraid of? And most people are afraid of going blind. And then I would ask, well, what does that mean? Blind because blind means different things to different people. So I think it's I don't have a standard approach that works, it depends on the patient. Some patients, you can tell they can't handle the whole portrait of the condition that they carry. So then we give them some information and, and some recommendations and then we see them again and build a relationship. And then deliver more information. It's especially difficult with the children, you have to be careful with the children. And they tell the parents that the children that do best is when the parents are able to accept that there's a vision problem. And that it's not a disease, the child is not sick, the child can still have a normal life. But there's a vision problem. And we need to accept that, that it's part of the individual. And that goes for every age group.

[19:02]

MI: That's the perfect lead into my next question is is about kits. Because you see, obviously a lot of children both through having inherited retinal diseases diagnosed at a younger age, as well as working through sick kids. So how is the treatment of children different from adults? And even thinking about like clinical trials and developing these new treatments? What sort of special considerations do you need to think about when kids are involved?

EH: Well, that's a very important question, because clinical trials are designed for adults. And the outcome measures that are used to assess change and visual function are designed for adults. And those are very lengthy tests. And children have a short attention span. And some of those tests are difficult for them. And I think in the future, and I’ve lectured on this, it will be important. If we want to include more of the pediatric population well, it would be important to adapt the workup and the expectation of a performance on this specific test, to adapt that to children, like to have patient reported outcome measures adapted to children, but to have protocols also adapted to children to work on the experience, learn from the adults and the think back and say, okay, so what do we need to do? What's most useful? So for example, if we see a new child who's suspected of having a retinal degeneration, sometimes we'll start with the easiest test the OCT, that gives us a lot of information. And then we'll wait before doing the whole test. Again, it depends.

[20:50]

MI: So you've obviously been in the field for for a few years now. I just wondered how, how do you feel that the study of ophthalmology has changed since you began your career?

EH: Oh, it's incredible. I tell you, I have an anecdote we share. So when I started in in ocular genetics, we knew of two genes, okay. And I didn't know much about genetics. So I thought that was it. I was just like this is we could offer genetic testing. And we counsel patients. Next thing is a treatment five years, I'd say five years and five years, I can say five years. And since then, the imaging ability in the exploratory protocols have evolved, like so much like we are able to be such more precise, in our phenotyping of patients. It's marvelous. And then there's over 300 genes, like this two gene business is like, very yesterday, and those two genes, you know what, they don't have a treatment. Okay, so it's the newer genes that are being explored. And so it's totally different. And I used to say, when I started in ocular genetics, that's where cataract surgery was at its prime. And ocular genetics was not cool at all, like you were a nerd. But now, ocular genetics is pretty cool. And so I'm very proud of having seen an exponential change. Through the last late 26 years on staff. I started and I was a fellow in 1991. So that's like 30 years. It's just marvelous, is just marvelous to see the wealth of knowledge and And I mean, the internet has contributed immensely. And then the Human Genome Project, I could have never imagined that we do what we do today.

MI: I love that idea that it's ocular genetics time to shine here.

EH: Exactly, Prime Time!

MI: Exactly. Oh, that's great. Well, thank you so much for joining me. It's a pleasure to talk to you as always.

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JR: Fighting Blindness Canada is the largest charitable funder of vision research in Canada. To date, we have contributed over $40 million in funding for the development of sight-saving treatments for blinding eye diseases. With your support, we are advancing research to understand why vision loss occurs and how it can be slowed or restored. To learn more, visit us at: fightingblindness.ca.

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[23:39]

JM: Hi, my name is Jack McCormick and I live with a condition called Leber's congenital amaurosis. I was lucky enough to receive a treatment called Luxturna approximately a year ago to help prevent further vision loss in myself. My main hope for getting Luxturna was really to prevent my vision from getting worse. I was fortunate enough that it also did improve my vision.

MKF: My name is Mary Kate Fraser. I'm from Toronto, Canada and I live with retinitis Pigmentosa. I was diagnosed at age 20 and 10 years later I have about 20 degrees of central vision remaining.

CH: I'm Cathy Haverstock. And I live with an eye condition called retinitis pigmentosa an inherited eye disease that affected my mother, my aunt and my sister.

SML: My name is Stuart Matan Lithwick… I have been a person who has had retinitis Pigmentosa since the age of 22 so I've had quite a lot of time to sort of learn about what it's like to be visually impaired and to experience all the aspects of that.

MI: On February 28, 2023, the province of Ontario officially approved public coverage of the gene therapy Luxturna. Although this treatment was approved by Health Canada in 2020, it has been a long road to getting provincial coverage that would make this treatment accessible. Six provinces have announced a path to public payment for Luxturna and specialized teams across the country are now able to surgically deliver the drug.

This treatment slows and may even restore some vision loss due to inherited retinal diseases retinitis pigmentosa and Leber congenital amaurosis, caused by mutations in the RPE65 gene. This is the only gene therapy treatment currently available for an eye disease.

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MI: We reached out to members of our community to find out more about their reaction to the approval of this landmark therapy and their hopes for the future.

CH: The success of Luxturna in treating a specific retinal disease has been really very good news. And there's more good news hearing that successive provinces are now providing funding. It's encouraging to see that people with this rare disease will be treated through our medical system… the benefits for those who receive this once in a lifetime treatment are enormous, life changing.

SML: it's hard to believe actually because for a lot of years we talked about the idea that through research with very aggressive and patient work ultimately in the long run, we will actually get treatments for diseases that are really effective and safe and that can actually change people's lives and to think about that in the first place is something that sounds wonderful. It sounds like it would be incredible if it was possible. But it's hard to believe that it could actually happen and so to see something like Luxturnaactually come to pass and come to exist is, it's a miracle, it really is.

MKF: When I hear about clinical trials and treatment with Luxturna it makes me very hopeful that there will be a Treatment available for me one day. Although my particular genetic variant has not been identified it's very exciting to witness the first Gene therapies become available in a clinical setting. I was diagnosed 10 years ago and most of the new stories over the past decade have been about potential therapies or successes in the laboratory setting. So it feels like we're really at a turning point in the history of genetic disorders.

[27:03]

MI: There are only around 40-50 Canadians who are affected by the RPE65 mutation, a small percentage of the over 20,000 people living with different IRDs. However, the development and success of Luxturna has provided much hope that gene therapy treatments are possible and are coming. We asked our guests what hope looks like for them.

MKF: I am very hopeful that there will be a treatment available for me in the future. While gene therapy is a very exciting field there's still a lot of disease-causing genes that have not yet been identified, especially for retinitis pigmentosa. So it's encouraging to see research into gene agnostic therapies as well including drugs and stem cell therapy.

CH: I am hopeful that there will be successful treatments for inherited retinal diseases. Over the past few decades, science particularly genetics seems to have progressed so far. And scientific knowledge has a cumulative effect. Laboratory studies lead to animal studies that progress into human studies, and then into clinical trials, and then to specific treatments. But sometimes it seems to take so long. To be honest, I am not as hopeful for those in my age group at 74. Treatment to restore my vision seems an unlikely prospect. So, my hopes pass to those of the next generation, including my son. It's difficult to live with facial loss and the restrictions that brings particularly to an already aging body. One way to live better is to have the hope and the trust that others will be successfully treated, if not cured.

SML: When it comes to how I feel about the possibility of treatment for me in the future I'm definitely hopeful. I'm also realistic, and having been in research, I know that to do things right, to do it properly, it takes time. And so what actually brings me hope is both the prospect of treatment, but also the fact that they're doing it properly. You know when it comes to timing realistically, we're probably going to be talking 15, 20, 25 years before I see therapy for me.

There are many other things that I'm equally if not more hopeful about which is primarily the degree to which there are now efforts going on to promote and support the health and wellness of visually impaired people as they are living their lives, and as they are patiently awaiting the arrival of therapy for them.

For a long time in my life as I've been a person who's visually impaired there's been some stigmatization of being visually impaired you know people would sometimes give me weird looks when I'm walking down the street from my cane and there's so many efforts that are right now going on and are yielding results to make visual impairment not something that is to be stigmatized or be afraid of or to not recognize as being part of society, part of life and that change to the image and the view of visual impairment is having impacts in the lives of visually impaired people now, everyday.

CH: For me, supporting vision research is a way to stay hopeful and engaged. Those of us who are affected or have family members with vision loss know, the fear, the uncertainty and the challenges. We have the most at stake and the most to gain as treatments are discovered. We can't wait or depend on government funding, and there are hundreds of charities competing for public money. So we must continue to finance the scientists who collaborate worldwide on projects to halt vision loss.

MKF: I believe that it's important to support both basic and applied research. The treatments that are in clinical trials today are only possible because of the basic research done in past decades. I think it's very exciting and inspiring to hear scientists and medical doctors talk about a cure or restoring sight that has been lost. However, I'm interested in supporting a wide variety of treatment options including those that slow down the progression of vision loss. I think it's important to have a mindset of continuous Improvement and look at how treatments can become better and better in the future.

[31:15]

MI: For the few Canadians who are eligible for Luxturna, it holds the promise to slow or even reverse some vision loss. Jack McCormick was one of the first people in the country to receive Luxturna and we checked in with him to ask how he was feeling after receiving the treatment.

JM: I felt amazing after receiving Luxturna because of when I received the treatment it was really unknown how much of an impact it would have on my life. And so my main goal was for my vision to become stable for it not to continue to get worse after the procedure. And I was very fortunate in that I also received quite significant improvements for myself being able to see in dimmer lights being able to see more details being able to see color again.

The main thing I’d like to tell other people about Luxturna and sight saving treatment in general, is to not lose hope but continue living your life. You need to continue living your life because you don't know how long it's going to take to receive a treatment that could change your life. At the end of the day, it's entirely up to you in terms of what you're going to do with your life. But there is still changes in science. And more and more, science is becoming available every day to create treatments for people like me and you.

[32:48]

MI:Thank you for joining us for this debut episode of the Fighting Blindness Canada Podcast. I want to thank Dr. Elise Héon, Mary-Kate Fraser, Cathy Haverstock, Stuart Mattan Lithwick, and Jack McCormick for joining me and sharing their insights. Stay tuned for our next episode on age-related macular degeneration, coming soon. I’m Morgan Ineson. Thank you for listening.

JR: This podcast is brought to you by Fighting Blindness Canada.

If you have an idea for a future episode or have a story you would like to share, please contact us at education@fightingblindness.ca. For more information about us, visit us online at fightingblindess.ca/podcast

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