

# Behind the Breakthrough Podcast - University Health Network

## Season 4 - Dr. Eleanor Fish

### Transcript

#### **BTB**

Hello and 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 Côté and joining us on the podcast today Dr. Eleanor Fish, recipient of the Order of Canada and award winning scientist emeritus at the Toronto General Hospital Research Institute. Dr. Fish is a world leading immunology researcher, her groundbreaking work is focused on fighting viruses by harnessing a naturally occurring antiviral protein in our body called interferons. Dr. Eleanor Fish. Welcome to Behind the Breakthrough.

#### **DR. ELEANOR FISH**

Thank you very much delighted to participate.

#### **BTB**

I want to let's start with this family of antiviral proteins in our bodies, interferons, you've called them our first line of defense when it comes to fighting off a virus. How many are there and how do they work?

#### **DR. ELEANOR FISH**

There are 14 different interferon alphas there is one interferon beta. And there are a number of interferon Landers. So they're a whole family of proteins. And the ones we're going to focus on in terms of my research, are what we call the type one interferons, interferon, alphas and beta, which we have known for decades, are very effective in blocking any and all virus infections and what you will appreciate that viruses come in through all different routes to infect us. Right now, we're absolutely focused on respiratory viruses that come in through the respiratory tract. And you also know as well as the corona viruses that are influenza viruses. We have viruses that affect the liver, like hepatitis, viruses that affect the heart, the kidney come in through the skin like West Nile virus. So what's unique about interferons that they're not what we call pathogen specific, doesn't matter what the virus is. And that's why they're absolutely critical for our first line of defense, regardless of the virus.

#### **BTB**

How do they work?

## **DR. ELEANOR FISH**

They work by invoking many different effects. And again, that's why they're our first line of defense because viruses have co evolved, because interferons are so important to encode in their genomes factors that will block the interferon response. But that response is so widespread it targets for example, the ability of viruses to get into cells. Interferons will target the viral genome, they induce factors that will chop up the virus's genome, hasn't got a genome can't replicate, they will prevent viruses from uncoating. A number of viruses have an envelope. So interferons induce factors in cells that will block that uncoating can't uncoat, can't expose the machinery to replicate, no replication, they will also prevent proteins coming together to form that virus. So multiple direct targets to inhibit viruses. At the same time. And this is what really is important. Interferons will induce and activate different immune cells to come to the site of infection and to clear the virus. So there's direct inhibition. And we've heard of that drug Paxlovid, which is being used. It's a direct inhibitor, but it has no impact on the immune system. Interferons directly inhibit viruses, and at the same time, muster an immune response. So multiple targets, there's no way viruses can evade all of that.

## **BTB**

Before we dive into your work, what led you to investigate interferons in the first place?

## **DR. ELEANOR FISH**

That's an interesting question. So my graduate studies that I started out in the UK, were looking at some of the effects of interferon in those days, interferon was purified from blood. So there's very little bit of around and there's very little you could actually do. I moved to Canada, and was working as a research associate in a lab. And my former graduate supervisor in the UK, contacted me he was now at a company called Genentech, which probably your listeners have heard of. It's was at the time the largest biotech company, and they had cloned this was the first protein that was ever cloned. They had cloned interferon, and they started scratching their heads because it wasn't one interferon. It was multiple interferons. And he contacted me and he said, Eleanor, would you be interested in studying these? And that's where it all started.

## **BTB**

So what was your take then in terms of its potential as a therapeutic agent against viruses?

## **DR. ELEANOR FISH**

It was very obvious very early on that this is their primary role, primary role actually in protecting cells from becoming infected. So once a cell is infected, that cell is done and dusted, there's little you can do to salvage that cell. The beauty of interferons is that that virus in that cell triggers interferon production, that will then protect all the neighboring cells. So this is a way of protecting cells. And that was intriguing to me. So that's why I realized, hey, we're looking at something that is actually protective, as well as killing the virus. And that's pretty much been lost in all the noise that's gone on around

interferons. And hopefully, we'll talk a little later in the interview. And I'll tell you why that is really critical with pandemics.

## **BTB**

Well let's start to build on the results of your research beginning. I think I have this right and going back to 2003. Your first real world tests of the therapeutic benefit of interferon, you are addressing a Severe Acute Respiratory Syndrome virus outbreak called SARS, it spread to 26 countries and hit Toronto quite hard with over 40 deaths, set the scene for us. Take us back to the onset of SARS and your advocacy to try interferon as an antiviral?

## **DR. ELEANOR FISH**

So as I said, remember, this is a broad spectrum antiviral doesn't matter what the virus was. And we at the time of the outbreak in my research group, we'd already done some studies looking at oh I don't 40 or 50 different viruses. And amongst them were Corona viruses. And I was fortunate to have a colleague in the States who had an isolate of the SARS virus that was causing this outbreak around the world. And I sent him some interferon and said, Please test it in lung cells with your isolate. And compare it with what at that time was the standard of care, something called Ribavirin. It was very obvious from the results that he sent me the next couple of days later, that whereas Ribavirin was essentially totally ineffective in blocking the infection in cells. Interferon completely eliminated the virus, interferons were already approved at that time for the treatment of hepatitis C so and we'd had years and years of experience. So we knew the safety profile, we had a guesstimate of what the dosing should be. And it was FDA approved, approved in Canada and approved around the world.

## **DR. ELEANOR FISH**

So we were using an approved drug, but repurposing it for another virus. So then I approached colleagues in Toronto, and then at the outset, there was honestly little appetite at all for using this drug. And as I said, it became clear that the standard of care was actually causing more harm than good. They were using corticosteroids because this was an inflammatory disease, and they wanted to shut down the inflammation in the lungs. But that just made me very scared. Because if you shut down inflammation, that's one of the ways to clear viruses, cut to the chase, after there were a considerable number of deaths, and there were also incredible anxiety and burnout in hospitals. A colleague said, Eleanor, I'm in, what do we need to do? So we very rapidly approached Health Canada got approval, we were able to set a very rapid protocol, consent patients in one of the hospitals in Toronto, and my colleagues in the States who had the interferon alpha I was interested in, were incredible.

## **DR. ELEANOR FISH**

They literally flew it in person to Canada. I met them at the airport, picked up the interferon, took it to the hospital. And UHN was also remarkable because we had an opportunity not just to treat patients, but also to collect samples from these patients to analyze them, to then afterwards and during the study

to ask the question, if it's effective, why is it effective? What are we targeting, and UHN set up a lab within 48 hours for me, obviously, it had to be a very contained lab. They provided me with the resources immediately to go out and purchase equipment. Some of the equipment companies, again, were amazing. They gave me incredible prices. It was a team of people who came together during an outbreak under pressure. We did the study and what was remarkable was within 12 hours I had my phone with me at that time was a pager and I got a call within 12 hours saying this is remarkable. Our patients are no longer crashing. We've turned the corner here. And again it was a guesstimate of the dose, it was, I don't know how many doses it was all, just based on prior discovery research, then we went that route. But then we got good results, the WHO invited me to Geneva to share my data and the protocol, which was then adopted by other countries.

**BTB**

Talk to us, then Eleanor, but the scope of the application to help arrest the spread of SARS?

**DR. ELEANOR FISH**

Well, the problem was that, as I said, it took a very long time to convince my medical colleagues that this was a strategy they should seriously consider. So we actually only introduced interferon as an intervention therapy, really at the end of the outbreak. So what the protocol was set aside, as I said, by the WHO to be used in subsequent SARS outbreaks. So yes, across Ontario, there was a use of the drug, it was adopted in the US and few other countries in a handful of cases and was very effective in all those cases. So what we effectively did was we accelerated improvement of the lungs, you know, by about four days versus 11 days, or by about seven days. And we reduced some of those blood biomarkers, which indicated heavy inflammation. So it was adopted, but it was very late in the day, pity it wasn't adopted sooner.

**BTB**

In terms of then the timing of it's being adopted. Do you think your advocacy to try interferon saved lives in Toronto during SARS in 2003?

**DR. ELEANOR FISH**

Well, we certainly had no fatalities. So yes, I think we absolutely did. And that was the reason I think at that point, the incidence of fatalities was such that, you know, anything was being considered. So we weren't the first thought, but we were on the list. And I think, having demonstrated during the SARS outbreak, that we have an effective tool. I was confident, perhaps with the benefit of hindsight, I don't know why. But I was confident that this would be a game changer. In terms of considering interferon for future viral outbreaks.

**BTB**

Let's continue then in terms of testing the therapeutic value of interferon against viral infection in the mid 2000s. There was the H5N1 virus. You also used interferon to treat patients during an Ebola outbreak. Talk to us about the experience and the results you had there.

**DR. ELEANOR FISH**

I was invited by the WHO to participate on an expert panel to look at potential therapeutic interventions. And we had this huge meeting in Geneva, where health ministers senior politicians, folks involved in looking at the Ebola outbreak in West Africa, were invited to Geneva as well as this expert panel to look at what might be used again, this was a virus for which there was no approved therapy, and for which there was no vaccine, we should appreciate that was the same with SARS. So here we were, again, in a situation where there was no approved treatment. And our panel was inundated with well over 100 potential therapeutic interventions. And we were invited to evaluate these therapeutic interventions and discuss with the West African delegates, our thoughts on these. It became very obvious that we were comparing apples and pears. Different laboratory models were being used, different small animal models were being used. And it was very difficult to compare the outcome in one model system to the outcome in another model system.

**DR. ELEANOR FISH**

So very rapidly, again, at the UHN, I was fortunate to find colleagues and we very rapidly set up a system, which allowed us to actually test different potential antivirals, in what we call a level two facility. So you have to appreciate that Ebola is level three, very few facilities around the world, none in West Africa, very few around the world that had the capacity to work with Ebola, and very few of those facilities around the world even had the viral isolates. So what we did was we took the virus, we chopped it up a little bit, so we got rid of all the bad parts. And we added a little fluorescent tag to the virus that we generated the virus particle, so that when we infected the cell, the cell fluoresced, if we had a good therapeutic, it blunted that fluorescence. We tested all kinds of antivirals that were being considered. And I was delighted that interferon beta, at that point, turned out to be the most potent. So armed with this information. I was at the Geneva conference. And we were instructed that we were not allowed to rank any of the therapeutic interventions, we were only to present them.

**DR. ELEANOR FISH**

And as I was sitting in the audience while my colleague was presenting the data I could hear behind me, this was Guinea, they speak French. Fortunately, I do as well, I could hear them, commenting on their frustration, what was the use of this, we need advice on what we should be treating with not presenting us with data. So during the refreshment break, I went over to the Guinean delegation and mentioned to them that I'd be happy to go through the data with them, talk about it, explain. And also, I would be very interested in conducting a clinical study in Guinea. Again, cut to the chase. That's exactly what happened. We found a treatment center in Guinea called Koya. We got all the health approvals. The company, Biogen that manufactured the drug, made it available, not only did they make it available, they put it in prefilled syringes, they provided incredible support, expedited its delivery. And we were able to undertake a clinical study in Guinea.

**DR. ELEANOR FISH**

And at that time, the fatalities were very high. And we were able to reduce the fatalities from at that point in time when we did the study from 67% to 19%. And we eliminated many of the symptoms. So again, this was a great study showed us that we had a potential drug there and what I had made the decision to again with the benefit of hindsight, I don't think I'll change my decision, but impacted the ability to introduce interferon. As I said, the fatality rate was very high. At the start of the outbreak, it was over 90%. By the time we started testing interferon, it was about 70%. And I felt given all the information that we had, it was unethical to do a trial where we randomize people to no treatment, in other words, randomize them to a high likelihood of death. The Guinean colleagues there and the health ministry also, were not interested in a what we call double blind, placebo controlled two arm study, they wanted a single arm study. So we only treated every individual who consented to be treated, and compared the outcome with historical age match individuals that isn't sufficient for approval of a drug in this day and age. So once again, we had very promising data, but didn't meet the gold standard of a randomized, placebo controlled trial.

**BTB**

In some ways, it's like a victim of your own success.

**DR. ELEANOR FISH**

Yeah, and you know what, I still wouldn't have changed it. Treat people to save lives.

**BTB**

Let's move into 2019 then. We're getting the first notifications about a Coronavirus late in the year. And by March of 2020, the COVID 19 pandemic is declared I'm curious, going into this pandemic in January, February. Did you believe we were prepared?

**DR. ELEANOR FISH**

My family will say yes, yes. She believed she told us to stop worrying. I absolutely did believe because after SARS, there was an incredible effort across Canada with all the public health agencies and various experts who weighed in that this should never happen again, that we should have surveillance systems, we should have systems set up which designated hospitals, individuals, that we'll be well prepared. I guess the footprint of this pandemic was so huge that No we weren't prepared. So yes, in 2019, when things started happening, I thought, don't worry, don't worry, we're well prepared in Canada. People have looked to us around the world to follow what we have done. So we're in good shape. There you go.

**BTB**

Okay, so when the pandemic hits, I'm guessing you got right back into the interferon designing research trials. Let's begin with the one in Wuhan. How did you frame the application of interferon in that case?

**DR. ELEANOR FISH**

This was actually before even things were happening in Canada. So at the time, I heard of the Wuhan outbreak. I have a good colleague who's the head of the CDC in China, and I approached him, George Gao, Dr. George Gaoy, and I said, Okay, here we go again, because he knows about my interest in Interferons. And I said, this is an opportunity. And I would welcome if you could put me in contact with MD's in Wuhan. And we can design a trial and get on with it. He was incredible. did just that. Got a hold of a senior woman in one of the Union hospitals in Wuhan. We sorted out what the trial should be. And at that time, the standard care was a drug called arbidol. So they were not about to drop out of it all. So it was going to be arbidol or arbidol plus interferon.

**DR. ELEANOR FISH**

And what you must appreciate also that at that time, everyone who was identified as PCR positive, didn't go home, they automatically went to a hospital. And there were different hospitals for those that had severe disease, those that had mild disease. Some of them were makeshift hospitals and those which had moderate disease. So we had, very quickly, a nice cohort of patients. And we designed the trial and this time rather than using an injectable interferon, which is what I'd used in SARS, and what I'd used in Ebola. Because this is a respiratory infection, we use an inhaled interferon alpha. And again, this was a pilot study. So this was not intended as a randomized control trial. So we looked at those individuals who had arbidol alone, and those who had arbidol plus interferon.

**DR. ELEANOR FISH**

And once again, the data were very compelling. We accelerated viral clearance, these are all hospitalized patients with moderate disease, so they weren't in the ICU. We accelerated their viral clearance, they got out of hospital much sooner. They had reduced symptoms. And we never saw the spikes in some of those inflammatory markers, which are very indicative of progression to severe disease. So that pilot study, we published very quickly, because we wanted to get the information out there. And that led to subsequent engagement with interferon and other trials.

**BTB**

Right. Talk to us about the second trial in Chile. How was that trial conducted?

**DR. ELEANOR FISH**

Before that, I was consulting and advising the NIH, in their trials that involved interferon. And the way they wrote their protocol, it was a template protocol. And they just kept testing different antivirals. And the issue with that was that these were hospitalized individuals who already had disease progression.

And I didn't think at that stage interferon was going to be effective. So you'll recall, the very beginning of this interview, I mentioned to you that one of the key advantages of interferon is that it protects cells from being infected. So if you early on treat, it will certainly kill the virus in infected cells, but it will also protect neighboring cells, the utility there is that you want to catch the virus infection early on, before people are in hospital. So that led me to the Chilean trial, where, at this point in the pandemic, we had a vaccine. So we knew and we know now that we're able to limit severity of disease. But the biggest issue now is preventing transmission.

#### **DR. ELEANOR FISH**

And we will never get rid of this pandemic. It may turn out to be a seasonal virus, but we will never eliminate this pandemic until we can find a mechanism to prevent transmission. We have very effective vaccines, and we have an antiviral, we have monoclonal but how do you actually prevent transmission? So this was the basis of the Chilean trial. So the intent was to find from their registry, those individuals who tested PCR positive, so like we do here in Canada, you go get a PCR test, and it's recorded somewhere. We went to the central registry, and we identified individuals that were PCR positive, we then telephoned them and said, Would you be interested in participating in a trial, where you will be treated with interferon. And all those individuals in your household who've been exposed to you but not infected we'll also treat with interferon to see if we can prevent transmission.

#### **DR. ELEANOR FISH**

Now there are eligible household contacts between again the ages of 18 and 80. So they all got treated in that household. But there are also ineligible those who are too young, infants, toddlers under the age of 18, pregnant women, and very elderly over the age of 80. We also wanted to see whether treating the eligible household contacts and the index case would protect them. Initially, we approached over 5000 index cases, we ended up with about 1200 that were quote eligible because we caught them early enough that we could enroll them in the trial. We had close to 350 households. I'm just crunching all the data and have been doing. And it looks as if there's a 95% probability of reducing household transmission across the board eligible and ineligible. We've had good results. And this is using an injectable interferon, just giving three doses, over 16 days, we see the most effect during those 16 days doesn't protect later on necessarily all the impact is while they're being treated. And again, that's fine, because you're only shedding virus for a short space of time.

#### **DR. ELEANOR FISH**

And the importance is this, we're not going to give interferon to every single person in the world. But the plan is that you would actually give interferon to those uninfected cases at greatest risk. Healthcare workers in the ICU, paramedics, long term care facility workers, you could identify who should be taking interferon. And again, if there's an outbreak, you can hopefully squelch it. I'm giving this a ring prophylaxis, it's what it's called a Ring of Protection. And the next trial is to move away from the injectable one, to use just a nasal spray. So if you are at risk of getting infected, you would go to your pharmacy and just take a nasal spray.



**BTB**

I'm curious, then, Eleanor, given the results you've had during SARS, Ebola, and through the COVID 19 pandemic, what's it going to take to make interferon a standard of care, rather than just a research experimental drug?

**DR. ELEANOR FISH**

Well, I think part of it is that, you know, with vaccines, they have incredible utility because they prevent severity of disease. So what I'd like to suggest that interferons have utility, in select cases. a select niche, you know, so you have a very severe disease early on. Yes, there's the potential of fatal disease. If you want to prevent an outbreak, there's a utility there right now, the pharmaceutical companies that are making interferon cost is very high. And because the interferons that were being used, were being used for hepatitis, and now there is a cure for hepatitis, the production and manufacturing capacity has literally dwindled down to virtually nothing. We used interferon beta, because it's being used in multiple sclerosis. So there's lots of it. What I want to do is find an interferon alpha. And that, as I said, we can use as a nasal spray, a relatively cheap, generic form. But again, we're going to have to test it before anybody is going to approve it. I think what I hope is that the cumulative data, and certainly, in the context of COVID, the importance of the interferon response has been proclaimed loudly in the literature. If you have in any way, a compromised interference system, you have much worse COVID.

**DR. ELEANOR FISH**

This is clearly been demonstrated. So overriding that compromised system by coming here with interferon has demonstrated the utility. Hopefully, once we publish the data that we have right now, there will be an increased appreciation.

**BTB**

So help me understand and help our audience understand where the bottleneck here is. Is it the scaling up in terms of production? Is it the acceptance of it as a treatment? It's certainly not safety or tolerability?

**DR. ELEANOR FISH**

I think one is, if there was a Pfizer or a Moderna, or a Gilead that was interested in interferon, the story would be different. I'm not an MD, I'm a PhD, venturing into clinical trials. I think I'm accepted for my knowledge of interferons and I'm asked all the time to talk about it. But I think that leap of faith where interferon wasn't the magic bullet for cancer hasn't cured hepatitis. So this is an old drug, that it's hard to break down those barriers of resistance. Fortunately, I'm not dead yet. So I'll keep plugging away. And as I said, I hope that we can find a formulation that will be relatively cheap. I mean, the vast majority of the world have no access to vaccines, what I would like, you know, the approach the Gates Foundation, but they're not falling over themselves. I'd like to, as I said, find a formulation, whether it's

nasal drops and nasal spray, that we can actually use in those countries where there's no vaccines, make it cheaply available.

**DR. ELEANOR FISH**

So my pitch to the pharmaceutical companies and this is why it doesn't resonate too well, is they would have exclusive rights to all the first world countries. And I would retain the rights for resource poor jurisdictions that could get the drug at cost. So my next pitch in the next few weeks is going to be to Gilead, wish me luck.

**BTB**

I'm curious, what keeps you up at night when it comes to outbreaks and future viruses and pandemics?

**DR. ELEANOR FISH**

The resistance to be more proactive and be more accepting of what I think is really a really important therapy. We make this ourselves viruses block it at every stage when they encode factors to block it. I mean, if nothing else, this should tell us this is a really important therapeutic that's been approved for a worldwide use. I just get, you know, again, with this monkey pox outbreaks, we could have just prevented transmission so quickly. If somebody would have taken a leap of faith and said, you know, what? Isn't interferon effective? Why don't we just treat with interferon in those outbreak settings. But no we have to go through all the trials for every single virus. It's frustrating, we need a pan approval. And I don't know which jurisdiction around the world is prepared to do that. We need to rethink the approval of something that's been around for over 30 years, which we know is safe in MS patients and cancer patients. Trials, the interferons have shown it's safe. If you've got a highly infectious, fatal virus, why are we not going there first. So that's what keeps me up at night.

**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. Eleanor Fish recipient of the Order of Canada, an award winning scientist emeritus at the Toronto General Hospital Research Institute, and a world leading immunology researcher. Now Eleanor, you were born and raised in London, England, I understand your early passion started with music and fine art, until you realize that you can be creative and take risks in the world of science. Take us back though, through your thought process, when you started to decide on pivoting from the study of art to science?

**DR. ELEANOR FISH**

Okay, well, that was an interesting decision I had to make. So in the UK, in high school, you have to make a decision at a certain age, whether you're going to take those courses, which move you towards science or towards arts, and I was pretty mediocre. In all my subjects. I got decent grades, but none of them jumped out as well. You should be taking English literature or you should be taking physics. And I

remember thinking, Well, what am I going to do? How am I going to make the decision here when a chemistry teacher turned around to me and said, If you go into the arts, you will never be able to go back into the sciences, the amount of training you'll have to do to play catch up is going to be huge. If you go into the sciences, you can always continue with the arts. And you'll have a wonderfully balanced life. And that was the turning point that made that decision. And I'm forever grateful to him.

**BTB**

How old were you then?

**DR. ELEANOR FISH**

I was about 15?

**BTB**

I'm curious then over time, was there sort of an aha moment for you when it came to connecting to the world specifically of immunology? Or was this an incremental journey for you in terms of being drawn to this research?

**DR. ELEANOR FISH**

Well, I've always been interested in what's called translational biomedical research. And discovery research is incredible. And it's very focused. But for me, the interest has always been well, I'd like to be able to translate that into some sort of clinical utility. I'd seen with family members who'd struggled with various autoimmune diseases or cancers. There were certainly some tools available, some therapeutic interventions, but not that many. And yet we understood a lot about these diseases. So targeted interventions. I was fortunate in my first graduate degree, to be recruited to a pharmaceutical company that wanted me to do my graduate studies while I was conducting research, and they had a very focused approach. What you do is going to end up with a pharmaceutical product. And then when I moved as I said to Canada, while doing the discovery research I was doing Genentech approached me and their goal was to have drugs that could be used in the clinic.

**DR. ELEANOR FISH**

Then Amgen approached me. Their goal was to use drugs that could be used in the clinic. So there was always those collaborators, who reinforced my notion that the potential to take basic discovery research into the clinic, in a fairly short timewise framework, was possible. And that's what pushed me in that direction.

**BTB**

And I'm curious about the qualities, you know that you need to pursue a career like this. There's a famous scientist, Nobel Prize winner, Elizabeth Blackburn, who was asked about the virtues of

successful scientists. And she said, resilience, persistence, as well as being opportunistic and creative. Does that resonate with you?

**DR. ELEANOR FISH**

Absolutely. opportunistic. and creative. Yes. resilience, persistence? Well, you've just heard my story with interferon. So if that's not persistence, I don't know what it is And taking risks and being creative. So because I've had the opportunity to work with pharmaceutical companies, that often gave me funding with no strings attached, they wanted my expertise. And I said, Okay, well, then give me the funds, I'll certainly support and help you and consult on what you're interested in. But I want some money just to play with, because our funding agencies globally, will not fund you for at risk projects, you have to demonstrate that you've accrued sufficient data that you already know what the outcome of your research is going to be. If you want to do a risky project, there's no way you'll ever get funding. So you have to be creative. I've been fortunate because I've worked with pharmaceutical companies and biotech companies for many decades, I've always been able to put money aside for my at risk projects.

**DR. ELEANOR FISH**

And that's allowed me to do some research projects, which would never have been funded, which some of them have worked out really well. And some of them haven't. And taking risks in scientific research, from my perspective is an absolute necessity.

**BTB**

I'm curious, how do you keep patients the urgency of their needs top of Mind? Because as we know, and you know, better than anyone science takes time.

**DR. ELEANOR FISH**

Yeah, well, I think working in a place like the University Health Network, where there are patients all around you, being aware of, as I said, with this pandemic, the tremendous impact it's had on the world, in people's lives and their mental health, and their physical health, their families, their economic health. There's an urgency to make change to elicit change. And I'm fortunate that I can at least attempt to do that. I have over the decades built up contacts, friendships, colleagues, who are like minded, and will work with me to that effect. This isn't a solo effort. It's having all those individuals who appreciate what we want to do, having that contact in Wuhan having those contacts so you know, now the WHO, across Canada, having graduate students during SARS, who were working hours and hours and hours, supporting me dropping their graduate student projects and saying this is important. We're prepared to work what can we do Eleanor? So having individuals who are prepared to sacrifice and and go the extra mile is huge.

**BTB**

Do you ever feel pressure?

**DR. ELEANOR FISH**

Do I ever feel pressure? The only pressure is the pressure that it's not moving quickly enough? That acceptance isn't there? That's the only pressure.

**BTB**

When you come up against challenges or roadblocks failure? How do you learn to navigate those challenges, because it's not something we're taught in school?

**DR. ELEANOR FISH**

The first failure, you're desolate by it, you have many failures, you learn to pick yourself up, you know, have a song I sing with my grandkids, you know, to pick yourself up, dust yourself down, start all over again. I think that's the reality. If you just look at granting applications, if every time a grant was rejected, I would have walked away. One of my first grants I ever did not related to interferon was related to HIV, where I found that there was a receptor, which interacted with those immune cells called T cells and something on the surface of cells that touched those immune cells that were very important in HIV. And I thought, well, wow, why don't we just make a target to block that receptor? And I remember submitting that grant, and it got the lowest score I have ever received and was the bottom of the pile? You know and I kept that rejection. Well guess what, how do they now treat HIV, they target those disorders. So you know what, if you take rejection and failure to heart too much you'd stop.

**BTB**

I know, mentorship is very important to talk to us about the genesis of your beyond Sciences Initiative?

**DR. ELEANOR FISH**

So this is an initiative where I'm looking to the next generation of scientists. And what we've done a small group of us, you know, I founded it in 2013, and it's completely student run, there are no faculty, I'm the only one. And our intent is to engage young scholars, scientists, trainees around the globe, provide them a platform to engage in scientific discussion, provide them a platform, which gives them unrestricted access to knowledge. So in many places, people don't have access to the kinds of online libraries that we have, make that widely available. I've been in the business long enough that I have colleagues who are internationally recognized for their expertise. And I've recorded lectures that they've given to be posted, so that, again, universally accessible.

**DR. ELEANOR FISH**

And in addition to making that network of young people who professionally hopefully, we'll stay connected, because as I mentioned, having those colleagues has enabled me to do what I've done over the years. So create a professional network. And at the same time, highlight how privileged these young people are. Even if you're an MD, trainee, in Kenya, you're amongst the creme de la creme at the top of the list. There are many who never get to that position. So look to your community, see what

else you can do in your community to support it. So we have these trainees around the globe, who are working in refugee camps, who are working with street kids who are working with HIV kids, who are doing all kinds of different things within their communities, to give them an appreciation of their community, to let them realize how fortunate they are, and hopefully will drive them even more to be serious about their scientific careers.

## **BTB**

The COVID 19 pandemic has certainly put medical research in the spotlight, giving it to me, it seems an unprecedented public profile. In some ways, it feels like a once in a lifetime opportunity to show the value of medical research is an essential service and that it's intertwined with health care. My question to you is as the pandemic fades, will medical research fade in prominence?

## **DR. ELEANOR FISH**

I hope not. It's incumbent upon us as scientists to continue that communication to reinforce the value of scientific research and many different disciplines. How it improves, enhances the value it adds to our lives. We haven't done that very well, principally because a lot of scientists, they're really good scientists and perhaps lousy communicators. So engaging politicians engaging those policy makers in discussions, we can't let that fail. There's something called research Canada, which is very proactive in that area. And through the media, all different levels. It's really important. We continue that engagement with the general public.

## **BTB**

Well, you have the word Emeritus, your title, many in your position would have put the finishing touches on their career and be in retirement, what keeps you going?

## **DR. ELEANOR FISH**

First of all, I love it. It's stimulating. It allows me to engage with people of so many different disciplines. Case in point is during COVID. I've been invited to participate on expert panels in Canada that report to politicians, you know, make recommendations on vaccines and therapeutics. And we brought together individuals who I would never have interacted with normally, public health folks, modelers, behavioral scientists, I mean, remarkable group of people. In Canada, we have this unbelievable expertise. If I'd have walked away, I'd never had the opportunity to interact with them to learn from them. I also think because of my background, and the knowledge I've accumulated over the years, I've got stuff to offer. I don't necessarily need to have a wet lab and graduate students or ongoing wet lab research. But now I've made that transition to be more involved in international Clinical Studies. The OSI is prominent I want to support those young people, I can connect them, arrange exchanges, I can be a mentor. Don't ask me how many graduate students, I'm on supervisory committees around the globe. There's an expertise that if I would just shut shop, I think that would be unfortunate. And I love it. As I said, it's something that helps me to wake up every day.

**BTB**

Have you thought at all about your legacy?

**DR. ELEANOR FISH**

Maybe my paintings? No, I don't really.

**BTB**

You have not stopped fighting and advocating on behalf of the benefit of interferon. That's got to be part of your legacy.

**DR. ELEANOR FISH**

Well, I hope that I've made a dent in understanding the utility of interferons and how they should be considered, certainly the last three years, it's very obvious that this is the case with COVID. And I think maybe, if I keep at it a little bit longer, those walls will begin to crumble a little bit more and there'll be more individuals who say, You know what, maybe she's got something here. We should consider it.

**BTB**

Well, Dr. Eleanor Fish award winning scientist emeritus at the Toronto General Hospital Research Institute, and a world leading immunology researcher, thank you so much for sharing your groundbreaking research with us and continued success.

**DR. ELEANOR FISH**

Thank you.

**BTB**

For more on Dr. Fish's work and the podcast, go to our website, [www.behindthebreakthrough.ca](http://www.behindthebreakthrough.ca). And let us know what you think we crave feedback. 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