

Behind the Breakthrough Podcast - University Health Network

Season 5 - Dr. Laurie Ailles

Transcript

BTB

Welcome to another episode of 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 Côté and with us on the podcast today, Dr. Laurie Ailles, award winning senior scientist at the Princess Margaret Cancer Center. Dr. Ailles' pioneering research revealed the origins of head and neck squamous cell carcinoma, a discovery that is now paving the way towards improved treatments and outcomes for patients with the disease. Dr. Laurie Ailles, welcome to Behind the Breakthrough.

DR. LAURIE AILLES

Thank you. Thank you for having me.

BTB

Let's start off with Laurie what is head and neck squamous cell carcinoma.

DR. LAURIE AILLES

So this is a cancer that arises in the squamous epithelial cells, which are the cells that make up the lining of your mouth and throat. So even though it's called head and neck, squamous carcinoma, it's actually really focused in these regions. So a squamous epithelial cell are cells that make up the layer that's kind of like your skin, but it's actually on the inside of your mouth and throat. So there's multiple layers of cells that make sort of a thicker layer, that's called the epithelium. And at the bottom of that layer of cells is the basal layer. And in that layer, there are cells that are considered to be stem cells, and those cells will proliferate and give rise to cells that kind of mature and move up to the surface. And at the surface, those cells are dying, and they're being sloughed continuously. So there's a continuous production of new cells all the time from those cells at the basal layer.

The cancers that we study, arise in cells of that layer, and we actually believe that they arise in cells of that basal layer where the stem cells reside. So once a cancer is initiated, they start growing into a tumor. And then those tumors once they progress can also spread. So initially, they will typically spread to the lymph nodes in the neck. And then beyond that, they can then metastasize to other parts of the body, which is when it gets really bad.

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And what causes this type of cancer?

DR. LAURIE AILLES

So there are two main causes. One is viral. So there's a virus known as HPV or human papilloma virus, that causes the ones that are further back in the throat, they can be in the tonsil, or the very base of the tongue that's at the very back of the throat, which is caused by an infection with this virus, or the ones that are more sort of in the oral cavity are more likely to be caused by smoking and heavy drinking. And they're very different cancers, they have different prognosis and different behaviors. The HPV related ones tend to happen in younger people, and things like that. So they're actually really almost two distinct diseases.

BTB

And talk to us then about the scope and scale of these diseases in Canada.

DR. LAURIE AILLES

So we have around probably seven to 8000 cases of this cancer in Canada every year. Worldwide, it's the six most common cancer so there are other cancers like breast cancer, prostate cancer, are more common, but head and neck is pretty high on the list.

BTB

And what's on offer in terms of treatment or cure?

DR. LAURIE AILLES

It depends a lot on which type you have. So the HPV positive ones have a higher cure rate, they respond very well to radiation. And if they're caught early, they're quite curable. One of the public faces of this disease is Michael Douglas, he had that type of had an HPV.

BTB

HPV.

DR. LAURIE AILLES

Yeah. The other type, which are more smoking related, is a little bit more challenging to treat. And if it's not caught early, the survival rate is around 50%.

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So that's where your groundbreaking research comes in. And I understand it was the goal you set for yourself, right after just completing your PhD, back in the 2000s. Your goal was to find the original cell, the stem cell that you referred to earlier of this particular carcinoma, that causes head and neck

squamous carcinoma, no one had ever done this before. So first of all, I'm curious what made you think you could do that straight out of completing your PhD?

DR. LAURIE AILLES

So my PhD was in the area of leukemia research. And so during my PhD, Dr. John Dick, who was here at the Princess Margaret, made the discovery that leukemias are driven by stem cells. This all kind of derives from the nature of the normal tissue where the cancer resides. So in the normal blood and bone marrow, you have stem cells that very similar to what I just told you about the squamous epithelium. You have a stem cell population, that's a rare cell, but it gives rise to all of the cells of the blood. And those blood cells are short lived, and they need to be continuously replaced. So there was a lot of research going on back then, in terms of identifying and understanding normal blood stem cells.

And then what John Dick did was he translated that idea to the cancers that arise in that tissue. So when you look at leukemias, it's like they remember a little bit what the normal tissue was that they came from. So they maintain that kind of structure where there's a stem cell population that gives rise to the tumor as a whole. So I really like to use an analogy for this, which is like a dandelion. So imagine you have a lawn where you have dandelions growing and you mow the lawn, the dandelions are gone. If that's your tumor, your dandelion is the tumor. But if you don't dig up the roots, the dandelions grow back. So the stem cell is like the roots. It's not what you see, when you're diagnosed with cancer, what you see is all of those cells that aren't stem cells, but the stem cells remain, and they grow back. So that's kind of the analogy I like to use.

So it started to become known that bone marrow wasn't the only tissue that had this stem cell type structure. Pretty much all the tissues in the body actually have this: the liver, the colon, the mammary gland, the prostate, there are stem cells, and all of these tissues that give rise to the mature tissues in the organ, but that have to continuously be replaced. So this kind of led to the idea, well, maybe we can apply the concept of the cancer stem cell that John Dick discovered in leukemia, to other tumor types. And so that was kind of the origin of that. And because I had been studying leukemia for my PhD, it was kind of a natural progression for me to think about, well, can we apply this idea to other cancers?

BTB

Okay, so then walk, could you walk us through then the mechanics of your study what you came up with, what did you do?

DR. LAURIE AILLES

Yeah, the way that we isolate cells. So if you think about a tumor as a mass of cells, we need to be able to kind of separate them. If there's different types of cells, like stem cells, or non stem cells, we need to be able to isolate them. So the way we do that is by using expression of proteins on the surface of those cells. So different cell types express different proteins on their surface. So it's kind of like, some of them are wearing a red jacket. Some of them are wearing a green jacket, like we kind of use them as markers to identify which ones are which.

So what we did for our head and neck tumors, so we got tissue from patients. So this is important that we obtained this tissue directly from patient tumors who were patients who were having surgery. And we dissociated those tumors into single cells. And then we stain them with antibodies to cell surface proteins. So antibodies are an incredibly useful tool in the lab. What each antibody does is it recognizes one specific protein. So the antibody will bind to that protein. So if the protein is there, the antibody will bind to it, and we can detect it. So what we did was we surveyed our head and neck cancers, for expression of a lot of different proteins on their surface. And we looked for ones where there was a subset of cells that had that protein. We didn't want ones that none of them had the protein. And we didn't want ones that all of them had the protein because we're looking for a stem cell, which is only a sub population of cells, once we found some that fit that criteria, and then we purified them, the positive ones and the negative ones for that protein. And we used an assay called a tumor initiating cell assay.

So it's a measure of whether a cell has the potential to regrow a whole tumor. So to do that, we have to inject these cells into mice. So we inject them under the skin of mice that have a compromised immune system. And this is necessary because they're human cells, and we're putting them into mice. So if they had a normal immune system, the cells would just be rejected immediately. We did these types of experiments, and we found that a particular protein on the surface of the cells called CD 44, when we purified them, the CD 44 positive cells grew tumors, and those tumors when we then re analyze them looks just like the parental tumor from the patient. The CD 44 negative cells no tumors grew, even if we injected 100 times more in terms of number of cells, no tumors grew. So what this told us was that the population of cells capable of propagating tumor growth was in that CD 44 Positive cell fraction.

BTB

That's the moment you knew you had isolated the origin.

DR. LAURIE AILLES

Yeah.

BTB

So stem cell that causes...

DR. LAURIE AILLES

Yeah,

BTB

... that leads to the growth of the cancer.

DR. LAURIE AILLES

That's right. It's kind of almost more of a fundamental conceptual illustration, that these tumors fall into that model, where you have a hierarchy. So you can have a small population of cells that gives rise to tumor growth, and a much larger population of cells that doesn't. Not only that, but that population of CD 44 positive cells could also give rise to all the CD 44 Negative cells, and we could re isolate them, re separate them, repeat the experiment, and the same thing would happen again. So also those CD 44 positive cells were propagating themselves, as well as giving rise to the non propagating population, which is sort of the definition of a stem cell. It needs to be able to grow all of the tumor back but also to renew itself.

BTB

When you are able to isolate this repeatedly, you're able to isolate this - what could this lead to?

DR. LAURIE AILLES

I should sort of temper it a little bit by saying the CD 44 positive fraction isn't really a pure population of stem cells. So it's highly enriched. So it shows that there's a smaller population that has this capability. But when we do experiments to say, well, what percentage of the cells can actually initiate the tumor is still not every single one. So then, you know, we have to go looking for more markers to purify it more and purify it more. And ideally, you get to a point where you can initiate a tumor with one cell. We haven't been able to do that yet. But what it does help us to do even with an enriched population is to compare the tumor propagating population with a non propagating population and look for things that are unique to the propagating population.

So by compare, I mean, looking at the genes that are expressed, the genes and proteins that are present in those cells. So what gives those cells that ability to do what they do? And once you identify that, that might help you to find ways to specifically target them with therapies. The real issue is that stem cells, even normal stem cells, as well as cancer stem cells are notoriously resistant to our treatments compared to the other cells.

BTB

Chemo, radiation.

DR. LAURIE AILLES

Chemo, radiation, yeah, they have special mechanisms to survive under stressful situations. And that's evolution, right? Because in the normal stem cells, you need that it's a survival thing for those cells to be resistant to stress. And that's what chemotherapy and radiation is, it's stress.

BTB

Can I ask you maybe to use your analogy earlier of the dandelions in terms of applying that to your discovery?

DR. LAURIE AILLES

Well, so if you could find a herbicide, for example, that specifically kills the roots, then you would be able to completely eliminate the dandelion. So that's kind of what we're looking for. We're not looking for drugs that kill the flower, we already can do that. In fact, a lot of therapies do that very, very well, that we already have. Patients are treated, and their tumors shrink away. And you can't even detect that there's anything left. But ultimately, many of them relapse. So it's the stem cell that's left behind that's responsible for that.

BTB

And this original paper, what was the reaction in the medical community after it published?

DR. LAURIE AILLES

It was really well received. It was great, I got invitations to give talks. And ultimately, it led to me moving to Toronto, to be honest, because it allowed me to get that recognition that I needed to move on from my postdoc to my faculty position.

BTB

I want to point out to our listeners, because you're being modest....so it was published in 2007. Correct?

DR. LAURIE AILLES

Yeah.

BTB

And it's been cited over 1600 times since then, what does that mean to you?

DR. LAURIE AILLES

Well, it's hugely gratifying. Citations are really the truest form of recognition, scientific community. So it's really great to have that recognition.

BTB

And so you've obviously continued this work. Where are you at today, like over a decade later?

DR. LAURIE AILLES

We tried for a long time to get to that goal of having the pure stem cell. But that's a very difficult goal to achieve. And I think the reason for that is because cancers are also quite genetically unstable. There's a genetic component to cancerous genetic mutations that have caused them to arise in the first place. And they tend to undergo mutation, additionally, over time as they progress. So there's some plasticity and the phenotype of those cells can change and evolve, and can be different from one patient to the next. So what we've pivoted to, is using what we call functional readouts of stemness. That ability, for example, to grow a tumor in a mouse, that's a reflection of the stemness characters of the tumor from which it was derived. There's huge variation from one patient to the next.

So for example, if we look at the proportion of CD 44 positive cells in one patient, it might be 1% of the cells. And another patient might be 30% of the cells, but they're still stem cells, or at least stem cell enriched. And when you look at those two patients, the one with the low frequency will typically do better and be more successful in their treatment than the one with the high frequency. So we can read these types of things out by looking at more simple readouts. So things like when we implant a patient's tumor into a mouse, first of all, is it successful at growing in that mouse? And second of all, how fast does it grow in that mouse? And what we found after implanting over 250 patient samples into these mice and tracking their growth is that we can actually have a very, very good indication of the patient's prognosis based on this one readout.

DR. LAURIE AILLES

So if a patient's tumor A if it grows versus doesn't grow, so about two thirds will grow about 1/3 will fail to grow. The patients that failed to grow, do extremely well. And it's almost like a 95% or more survival rate. Whereas the ones that grow are down in that kind of 50% range, so it's very, very different. And then when we look at how fast they grow, we can predict even more strongly the patient outcomes. So now we actually have a trial ongoing, what we call a prospective study, because we're not actually acting on it for clinical care, but we're doing a study to see if this assay could be a potential clinically useful assay.

BTB

Like a diagnostic tool.

DR. LAURIE AILLES

Or prognostic tool to predict which patients are going to do poorly, because it's not always easy to predict that when you have a patient come in with a tumor, you just see that patient as a snapshot in time, it's just one moment. And you know, when you take that tumor out, and that's what the clinicians

used to decide how to treat the patient, how big was the tumor, was there spread to the lymph nodes or not? Were there some other things you know, when you look through the microscope that might be indicative of whether this patient should have more strong or less strong treatment. But in some cases, we've had patients where the tumor is small, the lymph nodes are negative, we implant it into a mouse and it grows like crazy, it's really quick. And the patient does very poorly, even though you never would have guessed it just by looking at that patient at the moment that you got their tumor.

DR. LAURIE AILLES

So being able to predict this kind of thing would be really, really valuable for the clinicians to then be able to decide, well, actually, I should probably add radiation to this patient's treatment. Or I should probably add chemo to this patient's treatment.

BTB

Like how aggressive...

DR. LAURIE AILLES

How aggressive and how quickly to act exactly.

BTB

And do I have that right that also another spin off of your research in more recent years has been to identify markers that could become identifiers, unique to this particular carcinoma to again, I guess, aid early diagnosis?

DR. LAURIE AILLES

Yeah, not so much diagnosis, we mostly work on prognosis, as I just spoke about, but we are looking for markers. So we're using this growth rate in mice as a marker. But growing tumors in a mouse is not going to be an assay that can be adapted all over the world. So what we really need is a simple marker. So we've begun working with another scientist at Princess Margaret Thomas Kislinger, doing proteomics on these tumors.

BTB

And what is that?

DR. LAURIE AILLES

That's where you can take a tissue and look at all of the proteins that are expressed in that tissue. The proteins are really the mediators of what's happening in the cell, the genes decide which proteins are expressed, but the proteins themselves are the effectors, the ones that actually make things happen. And so knowing what proteins are expressed, for example, what we've been doing the ones that are really rapid growers in our mice versus the ones that fail to grow in our mice, so the two extremes, and

we profile all the proteins expressed in those and then find ones that are unique to the rapid growing, the ones that do very poorly.

And from there, then you have potentially a protein, which again, now we can come back with an antibody, which recognizes that protein, and that becomes a very easy biomarker for people to use. And it's accessible to labs all over the world, it's a very simple thing to just stain a tissue with an antibody and see, is it positive? Is it negative? Is it high? Or is it low? And from that potentially get your prognostic readout, which will be a heck of a lot easier than trying to grow a tumor in a mouse.

BTB

I understand another avenue of research for your lab is to try and figure out targets for head and neck squamous cell carcinoma for drug treatment. Can you talk to us about that?

DR. LAURIE AILLES

Yes, so the proteomics experiments that we're doing will not only provide us with biomarkers, but they'll also provide us with potential mechanisms. As I just said, the proteins are the things that are actually making things happen in the cell, what we call signaling networks, things that make the cells grow faster, or things that make the cells able to avoid radiation therapy and things like that. That's all mediated at the protein level. So in addition to finding biomarkers, if we can really get a detailed picture, at the protein level of what's going on in these cells, we can also potentially come up with what's the mechanism? Why are some tumors growing more aggressively, and some tumors not, and potentially be able to find ways to target that.

So that's my real passion is to be able to ultimately find a way to treat these patients whose tumors are growing really aggressively, because they're not responding well to the therapies that we're currently giving them. So they're the ones that need it the most. So that's where I would like to go. And then the other thing that I find quite exciting, is that because we have these tumors growing in mice, across literally a couple of 100 patients, we can test our hypotheses. So if we, for example, find a protein that we think might be important in the rapid growth of these tumors, we might be able to find a drug that will target that protein. And we can actually then grow these tumors in our mice and test the drug and see if it works.

BTB

So you've talked about like, you're well anchored in terms of animal models, a lot of the study and you're doing in your research lab, also prospective studies. Do you see a time - and I know it's hard to put a timeline on these sorts of questions - but in terms of when you can see this translating into the clinic?

DR. LAURIE AILLES

That's a difficult question. I mean, don't you, these things are very unpredictable, right? I mean, I think the biomarker goal is probably more achievable in the near future, we have actually some biomarkers that we found, and we're working on writing up a paper. And once the paper comes out, we might actually get that into a trial, which would be really, really exciting.

BTB

A Human trial.

DR. LAURIE AILLES

A human trial.

BTB

Amazing.

DR. LAURIE AILLES

Of seeing if this biomarker can actually predict outcomes in these patients. So that would be fantastic. And I hope to achieve that sometime in the next few years. The therapy is a much bigger ask and a much longer and more difficult challenge. Because once you've identified a target, there's still a very long path to developing a drug if necessary, if a drug already exists, that's great. And that's becoming more and more common that we're able to repurpose drugs for things like this. But if you have to develop a new drug, then the road becomes very long.

BTB

Do I have this right that there's also a lesson in your research over time in terms of the serendipity of science in that, as your head and neck squamous carcinoma cell research evolved, you discovered another avenue of research? Can you talk to us about what you found?

DR. LAURIE AILLES

Yeah. So one of the things we did once we found CD 44, as being a marker for the stem cell was, again, like I've mentioned already, we use the antibody to CD 44. And we went back to the original tumor tissue. I mentioned that, to find CD 44, we had to take the tissue and kind of mash it up and get it into single cells. But we went back to the intact tissues, just a piece of tissue and looked at sections on a slide that we stained with this antibody, so that we could see where are those CD 44 positive cells located. And this was one of the moments I remember still very clearly, when it happened, because I didn't expect it, I expected there to just be kind of a random distribution, CD 44 positive cells scattered around. And it wasn't random.

DR. LAURIE AILLES

There was very specific location of those cells. And that was located in what we call the basaloid portion of the tumor, which is very similar to that basal layer that I talked about at the beginning that's present in your normal squamous epithelium. And so this is really interesting because the basaloid layer is in close contact with what we call the tumor microenvironment, or the tumor stroma. So all tumors have not just cancer cells in them. They also have cells that are from the host, what we call the host or the patient, but they're not cancer cells. They're normal cells that the tumor recruits and uses to its own advantage. And one of these cells is a cell type called a fibroblast. So normally, fibroblasts are sort of a support cell, a structural cell, they make collagen, which gives your tissue affirm, you know, so you're not all squishy. And they're also very, very important in wound healing.

So mostly, they are kind of quiescent. But when you have a wound, fibroblasts kick into action, and they start secreting factors that then attract immune cells, for example. So if you have a wound, you might get infection, you want the immune cells to come on, they stimulate blood vessel formation, so that you can get tissue kind of having a good blood supply so that it can regenerate. They stimulate factors that induce other cells to proliferate, to kind of try and grow in and heal the wound. They also make collagen, which is scar tissue. So they do a lot of things when they're activated by a wound. When you look at a tumor, there are fibroblasts in there, but they are in a state that very much looks similar to a fibroblast when it's activated to heal a wound, but they're perpetually in that state.

DR. LAURIE AILLES

And this actually really helps the tumor cells, because you can imagine that having a proliferation signal, or having a survival signal, having a signal that recruits blood vessels, all of these things is actually very beneficial for tumor growth. And they also help tumor cells to migrate and to metastasize. So the fibroblast is a really important cell in a tumor. And when we saw that the CD 44 positive cells were kind of really close to the fibroblasts. This led us to think that the fibroblasts could be playing a really important role in helping those stem cells, for example, to survive chemo and to spread and migrate and metastasize and all of those things. So that kind of triggered our interest in fibroblasts. So I have a whole section of my lab now that's working on how do fibroblasts support cancer cells? What are the molecular crosstalk between those two populations? And can we find ways to disrupt that interaction?

BTB

What's fascinating to me, I guess, in terms of how science works and the way you've expanded your work from that one origin study back in the mid 2000s, it's proliferated into a number of different avenues of research for you that are all worthwhile.

DR. LAURIE AILLES

Absolutely. I mean, there are so many more things too, that are also interesting and worthwhile, but we have to rein ourselves in a little bit and focus on certain things.

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 on the podcast, we're joined by Dr. Laurie Ailles, senior scientist at the Princess Margaret Cancer Center. Dr. Ailles is a pioneer in the research of head and neck squamous carcinoma, and was the first scientist to discover the origin cell of the disease. Now Laurie, Behind the Breakthrough, we love exploring our scientists, 'aha' moment, their come-to-science moment, when they figure out that science is their calling, I understand for you the starting point, and from a very young age was biology. What's your sense of what it was with that subject matter that you connected with?

DR. LAURIE AILLES

That's a really hard question, because I can't really pinpoint any particular thing or any moment that really drove me in that direction. I just always really enjoyed the outdoors, nature, I was always picking up worms and looking for snakes and stuff like that I was that kind of a kid. And as I got a bit older, I always also really just was fascinated, for example, by documentaries on TV that talked about DNA, or talked about genes, or show time lapse videos of embryonic development or things like that. I always just really, really was fascinated by that.

BTB

And you were born in Windsor, Ontario.

DR. LAURIE AILLES

Yes.

BTB

But you didn't stay there long. You were just a year old. I understand. You and your family embarked on this long and winding journey that for the next 17 years takes you around the world, Nigeria, Australia, South Africa, Iran, the Caribbean and across Canada. Talk to us about the life I guess of a daughter of a CIDA employee?

DR. LAURIE AILLES

Well, it was never boring, I guess. You know, because it started at such a young age, I didn't really know any different. And I don't think it really bothered me until I was a teenager. Of course, then it started to get a bit more challenging. Because leaving your friends and having to make new friends every time you go somewhere else. It was tough sometimes to do that. But I never really resented it. I got to travel the world, I got to see so many things. And my parents were very, very supportive. I also had two siblings. So we did it all as a family. So I never really saw myself as having any problems from that. And if anything, I think it was actually really good experience overall.

BTB

Teaches you It's a big world out there.

DR. LAURIE AILLES

Yeah, exactly. Yeah.

BTB

And when you reflect on this, how does that experience do you think shape you today, as a medical researcher?

DR. LAURIE AILLES

There's a couple things I think, that are relevant. One of them being, as you said, you know, seeing the world as I did, including a lot of difficult places like Iran and Nigeria, really gives you an appreciation for what you have and for the opportunities that you have. For example, to go to university and to have the freedom to choose a career of your liking. I very much appreciate that. And I did even at a fairly young age, I think. But the other thing is, I think it really taught me flexibility, resilience, how to act in times when things are challenging and difficult and sort of be able to bounce back from that. I think that's a really important trait for a scientist to have.

BTB

Absolutely.

DR. LAURIE AILLES

Yeah.

BTB

In terms of your career journey. Talk to us about the role mentors have played for you in terms of say, compressing your learning that led to where you are today?

DR. LAURIE AILLES

One mentor that I had really early on, was during my undergraduate degree in Biology at Carleton University. So I actually volunteered in a lab, a molecular biology lab for a while. And then I did my fourth year project in that lab. And there was a graduate student in that lab who kind of took me under his wing, and taught me the basics. He taught me how to make solutions and how to do basic techniques. And I don't think I really appreciated it at the time but he was very kind and generous to donate his time to me and teach me these things. And he also had a great sense of humor and a great attitude. If I made a mistake, which I made money early on. He was just like, don't worry about it, just do it again, you'll be fine. No problem. And I think I really learned from him. That kind of important philosophy of, you can't expect things to work the first time you do them. It's no big deal. You just got to try again, you got to be persistent. And you got to enjoy yourself as you're doing it. So that was an important, I think, role model for me early on.

DR. LAURIE AILLES

My PhD supervisor was also a great mentor. So she was a clinician. So this is where I started working on leukemia. And where I transitioned from more sort of really basic science into more clinically related work. She was a clinician and so that helped me to kind of get that connection to having what we do actually potentially...

BTB

Translate.

DR. LAURIE AILLES

...translate it some day. But also, she really gave me freedom to develop my own hypotheses, design my own experiments, and actually follow things through right from the beginning to the end. And I think that was really important, because that's really what being a scientist is all about. And it's really important to learn how to do that. And she supported me through that, even though again, you know, mistakes are made along the way. But it's important to let students make those mistakes. And she did that. So I'm also very appreciative of that.

BTB

Do you have a mentorship style today with all the people in your lab?

DR. LAURIE AILLES

I think I do. I try to sort of follow that, where I allow my students to have some freedom, of course, they still need guidance, they still need to be able to talk about it with you, bounce ideas off of you. But I do like to give them that freedom to experiment and think about things. And quite often, they come up with amazing ideas that I never would have thought of, it's a total two way street. So that's one thing. The other thing is, I really try to impress upon them not to let failures get you down, because this is something I think a lot of young graduate students struggle with. And I try to tell them, it's not really failure, it's an experiment. You did the experiment, you had the outcome. And now you can adjust and try again. And then reassess, redo, reassess, redo, that's how science works. So I kind of try to have that mentorship style, I don't want to get upset with them or angry with them, when things don't go as expected, it needs to be a learning experience instead.

BTB

You're a pure scientist, and you work in the lab. I'm curious how you keep patients top of mind?

DR. LAURIE AILLES

I think, because we work so much with patient material. And we have these patient derived models growing in the lab, it's very easy to do that. Because we have a tumor growing in a mouse and it's growing quickly, the immediate connection that you make is to the patient, when you think oh, gosh, that patient's not going to do too well. So it's really easy because of the nature of our work. Even though we never meet the patients, we don't know their names, we have their tissue, and we're growing it and it's alive. So it's easy to keep that perspective. And then the other thing is at Princess Margaret, we have this incredible environment where the basic scientists interact with the clinicians a lot. There's a lot of cross pollination between the clinicians and the scientists. So lots of collaborations, lots of meetings, seminars, all kinds of things. So it's always really very much on the forefront of what we do.

BTB

Next question connected to that, then is how do you reconcile the fact that you have a sense of the urgency of need for patients for better treatments for cures? How do you reconcile that with the fact that science takes time?

DR. LAURIE AILLES

Yeah, that's a tough one. I mean...

BTB

Or do you ever reconcile?

DR. LAURIE AILLES

Not entirely, I kind of like to think of science as being a series of steps that we need to take towards that goal. And as long as we're making those steps, and we're successful at making progress, that's actually very satisfying, because you know, that even if I might not reach that goal, I might help somebody else who comes after me to reach that goal. So you still feel satisfied about what you're doing, and that you're actually making a contribution. So I think that's the way I think about it. Even though they're baby steps, even every baby step can take like six months or a year to achieve. So it's a goal in and of itself.

BTB

Do you ever feel pressure in your work?

DR. LAURIE AILLES

Oh, yeah. Yeah, there's a lot of pressure. I mean, it's just the nature of being a scientist, there's pressure to publish, there's pressure to get funding for your research, there's pressure, because you really want your students to do well. There's all kinds of pressure, you put pressure on yourself as well to just achieve what you want to achieve. So there's a lot of pressure, but it's not necessarily all bad. Sometimes pressure is a good thing, and it drives you to move forward.

BTB

Part of the exploration here in each episode is to try and from your perspective, pass on what it takes to be a successful scientist. I read once where Elizabeth Blackburn, who was a Nobel Prize winner. She was asked about the virtues of successful scientists, and she said resilience, persistence, which I'm sure you can identify with also being opportunistic and creative. Does that resonate with you?

DR. LAURIE AILLES

Yes, absolutely. 100%? Well, they're kind of one in the same in a way. It's being able to recognize when something happens that you didn't expect to be able to look at that and think, oh, this could be important. What does this really mean? And like with the fibroblast connection, where it's like, oh, this is not what I expected to see, but what does it mean and how can I move things forward based on this observation? So I think that's kind of what that's all about to be able to pivot and follow when you find something interesting. And that's actually happened to me multiple times in my life and led me to have to learn whole new fields sometimes.

DR. LAURIE AILLES

So as an example, in a different project that we haven't discussed, we found something related to the DNA damage and DNA repair field, which I really know very little about appears to be important in one of the cancers that we're studying. And so now I've had to learn that field and try to pursue our discoveries, because you don't just want to set it aside. It's like, oh, I don't know anything about that. So

I'm just gonna ignore it. You don't want to do that, right? So you need to keep learning all the time. And we're always learning new things all the time.

BTB

Curious what drew you to Toronto and the Princess Margaret Cancer Center in the first place?

DR. LAURIE AILLES

So I'm Canadian. And we were living in the United States for a long time. And we really wanted to come back to Canada. But most importantly, it was the opportunity here. I was in a conference in the United States, and I met with John Dick. And I had a conversation with him. I already had met with him before we kind of knew each other. But this particular meeting was important because I was at that point where I, we had published the head and neck cancer, CD 44 paper, and I was kind of thinking it's time for me to start looking for a faculty position. And I spoke with John and he was like, well, well, this is really great timing, because we have a position available that you should apply for. So I applied for it. And I was super excited, because it's like my dream position. It's in Toronto, it's with John Dick. It's a great Institute. And it all worked out. So I was really, really lucky.

BTB

I find increasingly these days for scientists, there's a, an added component to the job. And that is that there's an expectation of amplifying your work, not just within, say, your field in academic journals, and medical journals, but making it accessible to the general public. Do you have any guidance there for young scientists on navigating that world?

DR. LAURIE AILLES

It's really hard. All I can say is that I think it's important to jump at every opportunity that you get to do things, for example, like this podcast or, or other opportunities that are similar to try and get it out there that scientists are normal people like everybody else, and we're excited by what we do. And we're trying to do our best. And also to really make an effort to put your work into layman's terms, so that the general public can understand it. I really think the barrier to it is just having opportunities to do that. I think most scientists love doing it. I really enjoy talking to people who aren't scientists about my work, I always find that they find it interesting. They find it exciting, they ask great questions, and I really enjoy it.

BTB

There's a leadership author, Simon Sinek, who I love to quote he says people don't buy what you do, they buy why you do it. Why do you do what you do?

DR. LAURIE AILLES

Mainly because I really enjoy it. I love coming to the lab every day. My favorite times are when I meet with my students one on one, and they show me what they did that week. And here's what the experiment I did. Here's the results. And we talk about it. It's just so enjoyable, to see the progress and to know that you're working towards this new discoveries. We're always discovering new things all the time. And that's a huge privilege, actually to be able to do that as a career. So that's the main reason I do it. I really do enjoy the training part of it as well. I like seeing my trainees progress and develop into scientists on their own as well, which is very, very satisfying.

BTB

So what should we look for next from your lab in the coming months?

DR. LAURIE AILLES

Well, hopefully, we will have a biomarker prognostic biomarker coming down the pipeline pretty soon that we can get into a trial that would be amazing. And in the longer term, hopefully, we'll be able to actually start finding sort of more basic discoveries that could lead to new treatments, either targeting fibroblasts or targeting those aggressive head and neck cancers. That would be great, but it's hard to put a timeline on that.

BTB

Well, Dr. Laurie Ailles, senior scientist at the Princess Margaret Cancer Center, thank you for sharing your groundbreaking research with us and continued success.

DR. LAURIE AILLES

Thank you very much.

BTB

For more on Dr. Ailles work and the podcast go to uhn.ca or www.behindthebreakthrough.ca. And please let us know what you think we'd love to hear from you. That's it 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.

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