

Transcript: SickKids VS The Valley of Death

Cold Open

Hannah: Dr. Cynthia Hawkins has dedicated her life to fighting an aggressive and fatal cancer known as DIPG. DIPG, or diffuse intrinsic pontine glioma, is a fast-growing tumour. It develops in a part of the brain stem that helps control basic functions like a kid's heartbeat, breathing, and balance.

Cynthia: It obviously is an extremely challenging disease. I think, for me, it's motivating to try to take on a challenge that, you know, maybe not many other people have taken on.

Hannah: Surgical biopsies for patients with DIPG and most brain tumours have been critical for diagnosis and treatment. But they are risky, too.

Cynthia: Basically, it's sticking a needle into somebody's brain stem and taking out a piece of tissue. So, of course, there are potential risks associated with that. In the early days we would have taken a small piece of tissue and then looked under the microscope and said, 'Yes, this is cancer' or 'No, it's not.' And there were certainly some patients that suffered from the biopsy, you know, had long-term side effects from that or, in some cases, even died from that biopsy. So the community as a whole moved away from the idea of doing those biopsies. The diagnosis was made on the basis of imaging, and that was great—except for the fact that it really limited our ability to understand, you know, what is this cancer? How is this different from adult cancer? What are the things driving it, and how can we really treat it? So we went into this whole era where we were basically treating patients based on what we kind of knew about adult cancers that sort of looked the same, and none of that was very successful. And so we've gone back to, now, a renewed era of biopsy in these patients. Surgical techniques are better, so there's less chance of having side effects, but it's still a big procedure.

Hannah: That's why, in recent years, Cynthia and her team started developing a safer way to examine tumours—without the need for invasive brain surgery. The test is known as a liquid biopsy, and it's the world's first in paediatric care.

Cynthia: The idea with the liquid biopsy is that instead of having to sort of take out a piece of the skull and put a big needle down into the middle of your brain, you're now taking a little bit of the cerebral spinal fluid—so the fluid that coats the brain and goes down around the spinal cord—and look for little bits of the tumour DNA that are floating around in there and characterize that instead.

Hannah: But to get this test out of the lab and into the hands of healthcare workers around the world, Cynthia needed to analyze some liquid biopsy samples. And there was a huge hurdle standing in her way.

Cynthia: People talk about this as a major barrier that we sometimes see for developing new drugs. So you find something that works really well in your research lab, and now you want to get it into patients, and there's this huge chasm in between. You know, if I have something I want to bring from the research to the clinical side, it's *how do I get the money to do that?*

Hannah: You're listening to SickKids VS, where we take you to the frontlines in the fight for child health. I'm Hannah Bank, and this is SickKids VS The Valley of Death.

Act One

Hannah: Our story of how Cynthia hopes to get liquid biopsies out of her lab and into the hands of healthcare workers continues with an unexpected ally named Stacey Kline. Stacey is a corporate lawyer who started working with start-up ventures, both as a founder and investor. As a mother of four children living in Toronto, she's a big fan of SickKids.

Stacey Kline: Really, what sort of clicked for me in terms of how lucky we are to have access to SickKids—and the amazing access to healthcare that comes along with that—was when I had my first child 11 years ago and realized how lucky I am because of where we live. That we have unbelievable access to medical care that is not the same across the board. And that really kickstarted my interest in global child health and reached out at that time to see what opportunities there might be for me to get involved with SickKids.

Hannah: Stacey joined a donor program that engages the next generation of philanthropists through stories of courage, hope, and scientific breakthroughs at SickKids. She also helped deploy funding to the greatest areas of need at the hospital.

Stacey: As I left my career in law and moved into venture, one of the first places that I turned to for a conversation was SickKids. I moved into venture because of my interest in impact investing, which is investing in companies that are both looking to generate returns but also do really good things for people and the planet. Because of that time I spent getting to know SickKids, I knew that there was a ton of potentially commercializable research happening at the hospital that could have extremely significant positive impacts on not only child health but on health worldwide and really change the future for a lot of people. And so I reached out to my friends at the Foundation and said, you know, there must be a bunch of commercializable research that goes unfunded, and can I meet and talk to you about that?

You know, we often talk about this valley of death where projects have enough support just to sort of get off the ground but not enough support to get to where they need to be in order to get to that next set of funding, that next milestone.

Hannah You mentioned the valley of death. Can you give a brief explanation of what that is?

Stacey When we think about the lifecycle of a project from those initial stages in the lab, all the way to where we hope they'll be at the bedside, now that's a good 10 to 12 years before it reaches that point. And so when you think about all of the stages that that research has to go through to be validated and to really be brought to life, not only does that research have to be solid, but there has to be the right support for that research all the way through. As we know so well, even if the research is valid, you're competing for dollars—and there's only so much that, that goes around. So those projects just die.

Hannah: Around the same time Stacey was digging through research projects, she happened to meet another start-up founder and investor named Ben Gallacher, who started a company focused on concussion diagnostics.

Ben, can you remember your first encounter with Stacey? Where did you come into the picture?

Ben: We got connected through a mutual friend. And so, at the time, I had just been funding a VR project at the hospital. And I think that, you know, she had heard about that project and that just evolved to a discussion around what it might look like to formalize something in partnership with SickKids that was really focused on trying to commercialize lab-stage technology. So the conversation really, I think, just kicked off from we both fundamentally believe that making money and doing good can be related endeavours.

Hannah: Stacey and Ben stayed connected. And, together with support from SickKids, they collectively launched the Breakthrough Fund in 2020.

Ben: I think the Breakthrough Fund, in the simplest form, is a venture philanthropic fund that's focused on the early stages of commercialization from the lab and the ultimate goal of getting them to the bedside. I think how that manifests in actuality is there's a group of donors, we see a bunch of pitches from these entrepreneurs and scientists, and we decide where to place our bets. The goal is to place bets where we think we can have the largest impact to the healthcare sector as well as a large commercial outcome.

Stacey: And to the extent that these projects succeed and generate returns, those returns will be cycled back into the fund and, effectively, it will be evergreen so that there will be more capital available to fund future projects.

Hannah: As far as we know, there isn't another paediatric health fund set up this same way in Canada. But to understand what a lifeline funding like this means to scientists, let's go back to Cynthia.

Cynthia So it's very hard to get research funding to implement a clinical test. Our national funding agencies—and similarly, you know, in the U.S.—they're designed to fund new cutting-edge ideas that are going to find the cure for cancer or really understand how this cell works. But if that discovery has been made, but now I want to actually apply that to patients—that somehow doesn't seem as exciting. And so if you think about it from a practical perspective, it should be something that we're funding is how do we actually develop this into a tool that can really be used routinely in patients.

Hannah What did you think of the Breakthrough Fund when you first heard about it?

Cynthia This was this sort of an exciting new initiative that was trying to sort of marry philanthropy with enabling new, exciting ideas that were coming out of SickKids to actually get enough data and enough resources to move it to the next step. So it was built as almost like a—I would say like a Dragons' Den-type approach, where we had to pitch our business idea. And I think part of the idea was that you would be able to market this idea in the end. But I think maybe one of the differences with the Breakthrough Fund is that, you know, they are also quite interested in helping to develop things that would help patients. So if you could make money out of it, that would be great. But I think showing that you could help a large number of patients was also a critical piece of the successful applicants for this type of award, which is maybe slightly different than Dragons' Den.

Act Two

Hannah Here's Ben's take on how the Breakthrough Fund is unique from other investor groups.

Ben There's a team at SickKids that filters a lot of the initial applications and ultimately the team that the donors—the investors—at Breakthrough get a selection of anywhere between kind of like five and seven presentations from the scientists and entrepreneurs. And, ultimately, that selection is in the hands of what ends up being a majority. So there is an agency to where your dollars go, which I think really is something that people care about.

Once all the presentations have been cycled through, we have a chance to really circulate and have an open dialogue amongst peers to say, you know, why does somebody relate to something? What do they like about it? Ask questions amongst each other. And if there's anybody who has a specific expertise and has funded businesses in the similar sector in the past, we get to hear those individuals out. In the past, we've had multiple grants or investments that have been made in different entrepreneurs in the same year. And so it's really a variety, and I think this is an ever-evolving process that we're continuing to learn from.

Hannah Stacey says she and other investors are in this process for the long run.

Stacey The process is much more than a one-off pitch, so everyone in the room is equipped with information that they're given beforehand. The pitch in and of itself is really just sort of a final chance for the group to ask questions, to have a more in-depth conversation and, you know, really help to identify or solidify the thinking around which projects are going to be the ones that are supported.

Hannah: Over the past three years, winning projects have included new treatments for major respiratory diseases and lung infections as well as novel ways to treat brain tumours in kids. Back in 2020, during the Breakthrough Fund's inaugural pitch event, Cynthia made her case for liquid biopsies.

Can you tell us a little bit about what that experience was like? That sounds stressful.

Cynthia: Definitely stressful. Definitely, you know, not something that you have to do for a typical grant. Most of the time when you apply for a grant, you spend, you know, maybe months putting together all your data and you write it. And it's sort of ten pages of this is my background and rationale, and these are the ideas and what I'm planning to do. But you have sort of quite a lot of space, actually, to try to explain why it's important and what you're going to do.

This was literally five minutes of kind of go online, because of COVID. You were waiting in this, you know, the waiting room in Zoom and then you get pulled in. You've got all these other like pictures of faces in front of you. And it was just go. You were allowed a small number of slides, and you had this really small amount of time to make your case. And so it's a pretty compelling case. So at some level, from the patient perspective, I think it's pretty easy to sell the idea in terms of the need, right? I think the idea that you can make a diagnosis of a brain tumor without having to actually open up the brain and take a piece is an idea that's easy to sell. Maybe the harder part is convincing people that *you* can do it and why *you* should be the one that they should fund to actually carry that out.

Ben I have a ton of empathy for the scientists and the entrepreneurs. They've been working on this, in some cases, their entire career. They're trying to distill down everything that they've learned and everything that they're working towards in five minutes—sometimes maybe a little longer, sometimes maybe a little bit of less.

Hannah Cynthia had made her case. Now came the agonizing wait for the Breakthrough Fund's decision—which we'll share after this brief break.

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Act Three

Hannah In 2020, Cynthia's research on liquid biopsies won the Breakthrough Fund's inaugural pitch event, with an investment of around \$100,000.

Ben Ultimately, what it comes down to is the person. And when you get a chance to meet Dr. Hawkins, it's like without a shadow of a doubt that you would want to support this individual—really, no matter what she's working on. I think she's just very, very exceptional. And I think that that was something that definitely resonated with Stacey and I, and I think it's resonated with everyone that's been funded by the Breakthrough since. There's a common theme, which is you're really betting on the team at these early, early stages.

Stacey It was quite obvious just through what we were presented in terms of initial materials that the amount of funding that we would be able to support Cynthia's research with would really help to get her to that next milestone.

Hannah Since winning, Cynthia and her team have been granted approval to collect liquid biopsy samples from patients at SickKids and elsewhere in Canada. They've been streamlining how much DNA they need from a tumour. And they've conducted more than 100 tests while studying paediatric cancers and sharing results with patients and their families.

Cynthia Without the Breakthrough Fund, we would not have been able to run the samples we had. We would not be this close to being able to offer this in a real, day-to-day basis to patients. That money is essential for crossing that gap. You know it really has allowed us to get a lot more experience with the test and when it's going to work well, and when maybe it won't be as effective.

Hannah Now the team is preparing paperwork to obtain a license to sell their liquid biopsy test.

Cynthia So the idea would be that people will have MRI's, you know, whenever—every six months or a year, depending on their cancer—to see if there's any evidence that it's coming back. This, I think, could be another piece of that surveillance. So can we find evidence that it's coming back really early, which may be the best time to intervene, because that's the point when the cancer is the smallest and we have maybe the best chance of getting rid of it again. That's a potential very important use for this technique, in general, for everybody with cancer really.

Hannah For Cynthia, it's been helpful to stay connected with Stacey, Ben, and other investors from the Breakthrough Fund.

Cynthia: There was really this ongoing involvement where they would want to hear what was happening with the project and provide advice in terms of how are you going to make this work kind in a more businessy way and sort of really holding us to some of those numbers and, you know, how is this really going to work? Because obviously in the end, you can't just completely disregard what something costs. And part of—one of the things we try to think about when we do test development in general is: what's sort of the cheapest way of us doing this? I'm sure a lot of places will start doing this once it becomes more commercially available, maybe. I think at SickKids we really try to be at the forefront of technologies on multiple levels—and that includes in the lab and in diagnostics. And, you know for me, this is something that's going to be absolutely essential for patients.

Hannah: From SickKids Foundation, this is SickKids VS. Thanks for listening. If you want to support work like this, visit SickKidsFoundation.com/podcast to donate. And if you like this podcast, please subscribe and rate us on Spotify, Apple or Google Podcasts, or wherever you listen to SickKids VS.

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