Bridging Science and Survival with Dr. Heather Hayenga Transcript

(Transcripts are generated by AI and may contain errors)

Podcast Introduction and Guest Overview

Welcome to the Doctors Making a Difference podcast, where we help physicians to be empowered with the tools they need to successful in medicine, in finance, and in life.

Join us as we highlight doctors and other professionals around the world who are making a difference. Today we have the privilege of having Heather Hayenga.

Heather has a unique story and is a unit person. I'm really thankful that she was able to come on the podcast today and talk about her story. She is PhD researcher at the University of Texas and has an interesting connection with my story, and with so many other folks who have cancer and research cancer.

And so we'll go through that. Think you'll be really interested to hear Heather's story And I appreciate you coming on. Telling the audience about yourself, introduce yourself a little bit.

Sure. Yeah. So I am an associate professor of bioengineering at the University of Texas at Dallas, and I'm a boy mom and my research focuses on cardiovascular modeling as well as cancer for the last five years.

Cause I unfortunately developed a rare cancer, a solitary fibrous tumor that originated in my brain. back in 2013. That's a brief introduction to a very complicated long story.

Tell us a little bit about when you were thinking about what kind of work you wanted to do in college. How did you decide on medical research and specifically cardiovascular research?

That is where your initial focus was. Yeah, like we were talking before, I am really driven by hardships. I guess I think hardships drive motivation. And so unfortunately, my father, we were playing basketball and he passed away of a heart attack and I couldn't bring him back.

Heather's Background and Cardiovascular Research

That was devastating to me. The next week I joined an immunology lab and wanted to start working on cardiovascular research. It's a disease that has been the number one cause of death for over a hundred years and we haven't come up with a cure.

It still the most prevalent disease. And I just thought we have to change that. That's how I got into cardiovascular research. Then I went on to graduate school.

I was very intentional and said, I want to work on cardiovascular researching. My advisor at Texas A&M, he said that's not something we do in the lab, but I have some discretionary funds.

if you have a clear idea. And I was like, yeah, I do. Well, that would be great. I got to use sort of modeling techniques and grow mice with plaques and see how mechanics affects plaque rupture and stability.

Now my graduate student just graduated, my fourth graduate He's going to create a company that can go into the clinic and it's gonna be a cardiovascular tool that predict plaque rupture, as well as what treatment would be best to treat atherosclerotic plaques in people.

So I'm really excited that he's bringing that to fruition. All of those 15 years of work, yeah. Oh, yeah. How old was your dad when he passed away? It would have an impact on anybody, but having passed way so suddenly while you were playing basketball would've been just devastating.

Yeah, I think I was 24 some of the time and he was 52. So he still had a long life ahead of him. He was, my brother was still in high school and after he graduated in High School, he would blame me on traveling.

And I just, Yeah. Oh yeah, 52 is really young, especially by today's standard. The average age that people live in the United States is well into your 80s.

For most folks, a lot of people, maybe sometimes late 70s, but to suddenly be gone at 52, it's crazy. I have a lotta cardiovascular disease in my family as well.

It is crazy! So I can see why you were motivated to do that. And it sounds like you spent your graduate school years focusing really a ton on that side of research.

It sounds it was, and you've had people that have done that and it's been a successful journey, but you pivoted and I want to hear, unfortunately, like, you shared at the beginning, solitary fibrous tumor is a disease that you and both unfortunately have.

Obviously that affected your life. So do you mind describing that process of pivoting from cardiovascular research to oncology research? Yeah. So as an engineer, I like to find solutions, right?

And when I found out that I had this cancer, and I did a lot of research and, uh, found that the oncogenic driver of this is a fusion between two genes on chromosome 12. so basically that NAB2, which kind of suppresses proliferation, things like that.

And STAT6, Which augments proliferations. They work together. So one is a negative feedback and one it's positive feedback. But in this cancer, unfortunately, they fuse together and so that repression never happens.

And so it just, the feedback loop stays on. I thought, okay, if this is genetic mutation or fusion, aberration, let's just use CRISPR. Let's reverse it.

gene in there or something like this. And there we go, problem solved. It will be very specific to, like, the CRISPR will find the Neptune-Statsix fusion and it will only edit the DNA of the cancer cells.

Pivot to Solitary Fibrous Tumor Research

So UT Dallas is a very collaborative environment. We had a genetic engineering professor from across the Bay. I told him about my diagnosis and I have been very, I don't know, display that I have this cancer very often, but I told him about it and I said, what do you think?

Can we use CRISPR? He said I don't know, I'm willing to find out. We started in the petri dish and unfortunately we didn't have any of these rare cancer cells because I had brain surgery and they fixed all the tissue and it's so rare that we couldn't get the cells.

So first we had to engineer the cell. First we put the gene fusion in cells and that took about six months because it was pretty hard to do, transfect parasites and the cell type of thought to be the type that this cancer is derived from.

So we put the gene fusion in there and then we designed a CRISPR enzyme to targeted and edited, and it was pretty successful. It reduced the proliferation rate significantly by 60 to 80%. So we're like, great.

And then we were teaming up with other people for drug delivery approaches. But unfortunately, CRISPR has not really been used readily in the body systemically.

That is because for delivery to solid tumors, the efficiency is so low. So if you can imagine that even if he put it in the IV, it has to go to the tumor cells, the CRISPR enzyme, and then pass the membrane, then past the nuclear membrane and they go into the DNA and edit it.

And we in a lab, we can use transfection agents and things like this to help put a high concentration right on the cells. You can't do that in body. So that was our roadblock of that original idea.

It was a kind of a delivery system or the ability to deliver that CRISPR gene into the actual affected cells deep within a tumor was lot harder in vivo than it was in vitro because you're dealing with all those layers of cellularity and just membranes and a lot of things.

So that sounds like that was brilliant idea. And I'm assuming since then you've been able to shift and try other things, what else have you been to try in your lab?

Yeah, so we're still working on adenoviruses and other nanoparticles to package the CRISPR enzymes. But then we thought, okay, what if we don't edit it at the DNA level, but more at RNA level?

Then it has to just cross one membrane. So we designed a CRISP-Cas13 to target the RNA-level, still the deliverability was a bit challenging. So then we pivoted to antisense oligonucleotides, which are mRNA, sequence of mRNA.

And they bind, like one of the COVID therapies were mRNA as well, but mRNA basically binds to the gene fusion, the neptustatic gene diffusion, and will block it from being translated into a protein.

So that showed pretty good promise as And so we're still working with this in California to develop ASOs. And we did an animal study with the ASO and it slowed the proliferation in SFT tumors in mice, but didn't exactly kill them.

So it's not, it will just slow the growth, that it didn' kill. them so the gene editing, the ESOs, and then we tried immunotherapies. A lot of cancers are driven by a few or a limited amount of gene aberrations or mutations.

And so because this cancer is really only driven one mutation, we thought that this one can be translated into a protein that can chopped up in little bits of peptides expressed on the MHC class complex.

And then T cells will come and recognize that peptide, if we develop antibodies and modify the T-cells, and then we can use an immunotherapy approach and have T cell targets these SFT cells specifically and eliminate them.

So first we have to see if there is a little peptid, unique peptides on the MHC complex And so we ran mass spec on the SFT cells that we had in the lab.

At this point, we have some donor samples. We have three patient drive cell lines now, in addition to our engineered cell line. But the mass-spec wasn't sensitive enough to detect the peptides.

So we're in a process of looking for more sensitive mass speck in Germany, and teaming with them to develop a more mass sensitive protection method of these unique new antigens or peptides.

So immunotherapy is our third therapeutic approach. And then the other one that was funded by R01 just last year is repurposing of drugs.

CRISPR, RNA Therapies, and Drug Repurposing

We have all of this cancer drugs, right? And 2,600 FDA approved drugs were specifically screened on these patient-derived cells and engineered cells to see if any of them selectively would kill the cancer cells, but not the normal cells.

And so we had about, I don't know, 20 hits or so. So we're looking at the most promising ones right now, which is nephropressin and some other ones that may be able to be repurposed to have a better chance at treating this cancer.

I just want to thank you for what you're doing. Like, it obviously impacts you and your life and you family, but all of

us that have solitary fibrous tumor are very thankful for you, and for your ability to understand it, you are right in the middle of it.

It's interesting, I think people are placed where they need to be for a reason, that's quite interesting. I would never wish solitary fibres tumor on anybody.

But isn't it interesting that a PhD researcher who knows how to run clinical trials and do all this stuff has this diagnosis and it's not just an abstract interest.

You're very interested in it because it affects your life and your family. And so I wanted to ask you about that. How has that experience been to be diagnosed with solitary fibrous tumor?

You shared with me that you have children at home and you're in that phase of life where things are so busy and then to still be working and living the patient life, but at the same time having to go and research it and try to research your own disease.

Right. We all juggle being a full-time doctor, full time professor, as well as mom, and as patient. So the department has been super supportive. And so I think that's really helped, I guess, changing my research in my lab to also look at SFT cures allows me to look out treatments for myself and do research for that while still publishing papers and getting grants and things like this.

So I just found a way to merge the two together, doing research that's impactful. while also helping pave the way for treatments for myself and understanding the treatments.

Because I have not taken the conventional approach, the standard of care approach. I know a lot of doctors like to take the protocol treatment off the shelf, which is chemo and systemics.

But some doctors are willing to just think outside of the box and be open when take this journey with me. And so I'm working on my third case study with my liver ablation doctor.

He said, I've treated 119 tumors in your liver. That's a world record. No one in the world has had that many tumors treated by ablation. This has happened over five years and he was willing to take the journey and just treat six tumors every six months or so.

And the liver is fortunately the only organ that I know of that can grow and regenerate. And so we've just been slowly combating these tumors. So he's going to write a case study to show that maybe going straight to drugs is not not necessarily the only approach.

Another oncologist at MD Anderson, he wanted me to go on drugs in 2019. And I said, the overall survival is two years, and I don't like that. I mean, okay, you can try a different approach, so I tried this sort of local approach through surgery and radiation and ablation.

Two years later, I came back in 2021, you don't have any side effects, you have no pain, and he was just so impressive. If you were to go on Systemix and look this good, I would be so happy.

I wouldn't be celebrating right now. And I'd be saying, good job. You did something good. So I don' have Systemics to recommend to you right know because whatever you're doing is working.

and so I think you need to be brave and courageous. I've had good mentors in my life and really had surgeons and good doctors and yeah, we've taken the sort of unbeaten path.

Oh yeah. What about, you told me just before we hit record about histiotripsy and that's a little bit more recently published. I mean, I've noticed that some cancer centers can do it, some can't, but do you mind telling, not everybody on the podcast will know what histiotripsy is because it's little newer.

Do you want to walk us through what that is and how you've used that for tissue ablation? Yeah, so I was developed at the University of Michigan and then I went to Europe and clinical trials there and had very good rate of success.

And so I was the third patient in the US to try it when it came for clinical trial here. It's basically using ultrasound waves to cause these micro bubbles at the tumor location, at tumor site.

This rapid increase and decrease in micro-bubbles causes mechanical deformation and it ruptures physically the cell membrane and the cells.

Living as a Patient-Researcher

And so they're thinking that there could be some immune global effect because all the cancer bits are released and immune cells can target that and potentially target other cancer in the body.

I didn't have any immune response, but the three lesions that were treated in trial two years ago have been disappeared and gone. Hystotripsy, you don't have to make any incisions.

You just put a water bath, essentially, on your stomach or wherever you're treating, and then put the transducers on that. And the interventional radiologist determines all the physics and things like this to modify the traducers.

I wake up from general feeling like nothing happened. It has very little side effects. I think it's promising technology. And Histosonics, which is the company name, just got bought out by a whole corporation of people.

So it is moving forward. It's really developing and getting better. Dr. Hinshaw, the ablation doctor at UW, he said eventually it will be used for more things than just the liver.

They could treat cancers within 14 or so centimeters of the surface of skin in the brain in other places. I'm staying in tune with that technology. Oh yeah.

So right now it's just approved or studied mostly in liver, but has a potential to help with many different tissue types. It's, I am sure it is dependent on the ability of tissue to carry sound waves because of, because the nature of treatment because I know I inquired about it a little bit on lung metastases and that's one of the tricky things because there's so much air within the alveoli and the lung tissue it would be a bit harder I think to get really reliable results but I don't know it's interesting to see how far that technology can come and how much it could change the way we treat some of these relatively rare or slower growing type of cancers.

Yeah the one in fact they had to because it was deep in my liver and more towards the top of the liver so they actually did have to go through the lung and so, they weren't successful the last time a couple weeks ago in actually treating the cancer itself because of a sound wave going through, the ribs, bone, muscle, lung area, you could just imagine each one of those is a different material and so sound waves travel differently and it's really hard to get them to meet up at the tumor site exactly.

It's better with homogenous material types. Oh yeah. Well, so Heather, you're a cancer warrior. Not only do you have this and are treating it as a patient, but you are out there fighting the fight for all of us that have cancer.

I think people listening to this, there might not be too many people that has solitary fibrous tumor. But how about somebody listening this either has it or has a patients that it has as physicians.

Like I know about sarcomas, But as far as solitary Fibrus tumor, if I had ever read about it, I didn't remember it was such a rare cancer That was another question I was gonna ask you.

On these super rare cancers where you're talking about one in a million patients and the sample size on most of the studies are super low, where do you see that going?

What do think would make the biggest difference for us as physicians or researchers when we're taking about these rare cancer types? Because in some ways it feels hopeless because there's so little information and yet you've outlined a whole series of things with the right tweaking and funding and adjustment.

Could really work and go from the world of systemic therapy to a lot more focused Immunotherapy and things of that nature that could really move the needle on this and I'm curious what your thoughts are on rare cancer research in general Yeah, yeah and this you said it solitary fibrous tumor is point six in a million I think I heard seven thousand rare cancers or diseases or something like that the in the warm foundation is working on and ultra rare ASO treatments for ultra-rare cancers and diseases.

So I think it's important, even though it just affects a small population, of course, funding and the government and stuff like this, you have to make these decisions.

Are you going to treat cardiovascular disease that affects pretty much a lot of people or treat or work on SFT, provide funding for Sft research that only treats a handful of people.

So what I find is that we can establish a technique or an approach. And cancer in general is driven by oncogenic mutations or alterations in the DNA. A lot of our therapy approaches are focusing on understanding these mutations at the genetic level.

If we could develop a treatment that combats that mutation or whatnot, then theoretically it could be applied more broadly to other cancers.

Histiotripsy and Local Tumor Ablation

And that's my hope, is that if we find something then not only will it affect a small group of SFT patients, which alone is important, but can also affect more probably other people by applying the same approach.

And as we understand the molecular biology and the understanding of what signaling mechanisms and what DNA mutations are involved, I mean, there's a lot of hope because what you mentioned, CRISPR technology and messenger RNA technology allow you to get right down to that signaling level, like you say, either in the nucleus or out in cytoplasm with the messenger rna to determine instead of just broadly hitting all cancers or like stopping all vascular growth like we do with Avastin, try to get a little bit more specific, whether it be immune therapy that we're delivering through messenger RNA or, like you say, if you can express some of those peptides or some those antigens on the outside of a cell and trigger your own immune system to go and fight the cancer.

Those things are fairly broadly applicable, not just to solitary fibrous tumor, but you could see those same principles being applied, almost like a tailor-made approach for an individual with cancer.

If you say, this is your cancer, your DNA, not just that you have breast cancer colon cancer or whatever it may be, but you this specific thing. And that level of specificity, I think that from everything I've read, that day is coming.

But for those of us that have cancer I want that data to be here now. Yeah, in one patient-specific treatment, and I that is where we are headed as well.

That is going to And that's what my cardiovascular work, too. It's patient-specific modeling, because cardiologists have to make these hard decisions on how to treat someone's cardiovascular disease.

Is this plaque going to rupture? Do I need to put in a bypass? do I put it in the stent? And one cardiologist told me that insurance typically doesn't fight or give us any grief if the plaque blocks the artery by 70%. And then we can just go put a stint.

But if you look at autopsy studies, a lot of times the larger plaques, like the 70% plaque, are more stable and they don't cause any damage. It's those sort of new plaqs that are developing that aren't stable, and those rupture more often.

Our modeling technique can put all the imaging data into a machine algorithm and finite element analysis and hemodynamic analysis really create a patient specific model that tells them the vulnerabilities within that plaque, atherosclerotic plaque.

So yeah, I think that's what I want to see is. individualized treatments and care. Cause we're not all the same. No, we try to think of diseases. I'm a primary care doctor.

And so the training is to. You have diabetes or you have cardiovascular disease or whatever. But I think diabetes is another good example of there's so many different types.

We don't break it down into subtypes, but I can think. Hundreds and hundreds of patients I've treated with diabetes. And they react so different to the medications, the progression of the disease, and the speed at which they respond.

The type of medications that they use, what diet they need. And it's really all individualism. I do hope for a day where most medicine is individualized at that level right down to the cellular level so we understand what the person needs and so it's a day that I hope for and pray for especially in the cancer world and on behalf of my patients but also for myself and my family and you and your family Heather I want that so bad.

Another question for you, what would you tell folks who like to tell other doctors, say you find someone with solitary fibrous tumor, or you'd find some with an ultra rare disease.

I think as doctors you're like, boy, I've never even heard of this. So I'll send you to an oncologist, but a lot of oncologists have fairly limited experience with this particular one, just because it's so rare and other rare cancers find themselves in that same boat.

What would your advice physicians to do when they find. Someone with. An ultra-rare cancer diagnosis. Yeah, I would say listen to the patient because I am unique in that I have the background to understand the science and I've done a lot of research, but I feel like a lotta people with rare diseases, they do a wanna research.

Rare Cancer Research and Personalized Medicine

They look up all this information and so if you just start by listening to what the patients knows about the disease, then that can maybe trigger some ideas and some therapies that aren't standard, because there typically isn't a straightforward answer.

And I know I do that with a lot of the SFT patients online, on the Facebook forums and whatnot. A lot them come to me and they're like, I have this new disease in this place, what should I, how should treat it?

And so I just tell them what I think and I that's all that patients are trying to do is just find answers and alternative approaches so they don't end up with a statistic.

And some, I know that this personally, some physicians could be a little bit not really intimidated, but they just, they see the patients as arrogant or potentially like coming across like they know something when they haven't gone through all that training in the eight years or whatnot.

But I think some of the most experienced and best treatments I've received are from doctors that just take the journey with me and they're willing to try.

In addition to my liver being treated more times than anyone, he said that, as he knows have ever been treated in the world, in my brain I have had 140 lesions, SFT lesion, treated by gamma knife radiation.

And again, when they are small… Your story has been wild. Wow. Yeah, he took that journey with me, the radiation oncologist, like we get him on that three millimeters.

And radiation these days has developed so focused and precise that you can treat a lesion and it goes away. It completely just, if you look at my brain scan, it looks like a fairly normal brain, a brain skin, no lesions or anything in there.

He also Dr. Warnock at UT Southwestern. We have never treated this many lesions in the brain before in our clinic. He's willing to take the journey. I'm willing take journey and so far we've been fairly successful.

And I know at some point I am hopefully going to develop a cure, but until then this approach has been a game changer. Yeah. No, I like that. Just thinking about what you said.

I think it's much more meaningful for me as a patient sounds like for you as patient when the physician is ready to go on a journey and doesn't have to predetermine the thing that we are going to do no matter what, especially on rare stuff like this like I.

There's a lot of things that you research and understand and know, and your physician may or may not. They understand a lots about cancer, but they may know much about this particular cancer.

So that joint decision making and advocacy on behalf of a patient, I think that makes a huge difference when you know you're heard and listened to. and you've been blessed with physicians who have done that for you and that's quite a gift to find people who are willing to do that and also to take the time because it takes more time to listen and go on these journeys rather than just to prescribe whatever is kind of the quick standard of care because, it's never quick but it is a more thoughtful journey if you have to go and explore and advocate and then if don't live by a place that does some of these more advanced or more, I guess, just cutting edge type things.

You may have to send people to travel to those places or contact colleagues in those locations. And it sounds like you've been blessed with doctors who have been willing and able to do that.

Yeah. I'm only here because of the doctors. They say, yeah, they're behaving a new way, but if the doctor's wouldn't agree with it and treat, see some merit in it.

suggest ideas and things like this, then yeah, I don't think I would be here. Wow. It's a miracle, Heather. I just hope it keeps being successful and that we keep finding more and more answers.

The more people that look into it, the more awareness that comes, and the people who research it. We can do things collectively as a group when we put our minds to it and it takes research money, it take resources.

But like you said before, I don't think that's money poorly spent. Those things are broadly applied to many different cancers. undergraduate I had a degree in microbiology with lots of molecular biology and at that time there was a lot known but since that Time CRISPR technology came out and there's just so much more like messenger RNA being able to modify that and deliver therapeutics that involve that technology.

I just feel like it's exponentially grown even in the time since I was in my undergraduate degree and so I think it I think it's fascinating, but also has very real world applications.

It's neat that you've been able to mix the two of those things. Yeah, yeah. And I had core biopsies in a calf muscle, SFT, and I told the physician, I was like, if one of my grad students comes up and we got the IRB stuff approval and everything, could we get some sample?

And she was, like I'm going to cryo-ablate this tumor. Do you want to do research or do you wanna get treatment? And I was like, both. Core biopsies and then give them to my grad student who drove five hours back to the lab and started trying to start a patient drive cell line.

And then she finished off the cryoablation to rest of the tumor. Yeah, just doctors that are open too. furthering science, but also providing patient care and yeah, it's really great.

Yeah. So what would you tell someone who is a medical student right now? Maybe they're an MD, PhD student, and they are thinking about getting involved.

You've been able to stay in this despite serious health challenges. And I think a lot of people would have just left a career at that point or tried to live on whatever disability insurance they might have had.

But you've stayed engaged and focused, which I thing is amazing and miraculous.

Advice for Physicians and Aspiring Researchers

I guess I want to know what you would tell somebody who is an aspiring researcher, a clinician, especially those that are pursuing that MD-PhD path, or they're a PhD candidate looking for opportunities to do clinical research.

What advice would you give them as you look back over time? Yeah, it's really a personal choice. One kind of research PhD side of things. I have a lot of friends who have done an MD PhD and their decision after they get their degrees is do I want to go to practice or do want be a researcher?

Because if I wanna be researcher, that's a lotta work. You have to apply for grants, you have get funding, and then if you wanna do clinic, thats really demanding too, patient care.

And so it's really hard to do both fully and successfully So my advice would just be to find a way to merge the two where you're seeing patients of a certain type of disease that is motivation for you.

You have a personal connection or some kind of drive to solve that. And then if your hospital's fortunate enough to have the clinical lab, then you can get patient samples and do research in the lab and really kind to do both efficiently and effectively.

and how to make those two merge together. It will keep you from the burnout that you talk about and just trying to juggle multiple things and not having time.

Well, I don't think you would still be doing what you're doing, number one, if you didn't have good clinical care, but number two, you wouldn't keep doing it if weren't passionate and driven to solve this for yourself and for others.

So just in the deepest, most sincere way I can say thank you, Heather, for what your doing on my behalf and on behalf of so many patients who have this disease and others I love the passion and the drive that you've exhibited and I think that's really good advice for those who are coming on board.

If you find something that you love and you're passionate about, find a way to strike that balance so it doesn't overwhelm your life, you can find such a successful career.

And anyway, I've loved this discussion so much, Heather, just in total admiration of what you are doing and just appreciate it so. Do you have any other final words or advice you'd want to share with our audience?

I just want say thank you Peter for being the voice and letting different physicians I've been listening to them for since I met you. And yeah, it's so amazing what doctors can do with not only their skills and their experiences, but also just as a good human being, going out into the world and just helping people and developing things and seeing needs and solutions.

Yeah. and the support that we get from helping each other. So it's really inspiring. And thank you, Peter, for facilitating all this. Thank you so much.

Heather, keep in touch. I'll be very interested to hear your story and your journey.

Closing Remarks and Podcast Outro

Of course, I'm very interesting in your research as well. We'll also be in-touch and I appreciate it so, much thank-you very much! Thank-You! Thanks for tuning into the Doctors Making a Difference podcast.

And thank you for what you do to help your patients and your community. Your work truly helps so many people. We produce this content to have the tools you need to stay in medicine and to highlight the amazing work being done by physicians around the world.

Please note that while I am a physician and many of the guests on this program are also physicians or other professionals, the discussions on the podcast do not represent my employer or any professional organizations to which I belong.

This podcast is for your information and entertainment only, and should not be taken as professional advice. You should seek appropriate professional advise pertaining to your own situation.

Please check out more of our content on our website, doctorsmakingadifference.com. Also, please follow, like, or subscribe on your podcast player or YouTube channel, and give us a five-star rating.

It really helps to spread the message. Finally, if you'd like to be a guest on the podcast, Or if we'd to nominate someone else to the guest, Please visit the website or email admin at doctors making a difference dot com.

See you next time.