# Bridging Science and Survival with Dr. Heather Hayenga | Living with Metastatic Cancer Series Transcript

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## Introduction to Heather Hager

Welcome to the Doctor's Making a Difference podcast, where we help physicians to be empowered with the tools they need to be 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 Hager.

Heather has a unique story and is a unique person. I'm really thankful that she was able to come on the podcast today and talk about her story. She is a 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. I think you'll be really interested to hear Heather's story, and I appreciate you coming on. Heather, would you mind 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, my mom. And my research focuses on cardiovascular modeling as well as cancer for the last five years, because I unfortunately developed a rare cancer, solitary fibrous tumor that originated in my brain.

But 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's where your initial focus was. Yeah, like we were talking before.

Like I am really driven by hardships. I guess. I think hardships drive motivation.

## Early Motivation and Cardiovascular Research

And so unfortunately, my father, we were playing basketball in he passed away on horseback and I couldn't bring him back. And so that was devastating to me.

And the next week I joined an immunology lab, and I wanted to start working on cardiovascular research. And it's a disease that has been the number one cause of death for over 100 years.

And we haven't come up with a cure. It's still the most prevalent disease. And I just thought we have to change that. That's how I got into cardiovascular research.

And then I went down to graduate school, and it was very intentional that I want to work on cardiovascular research. And 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, that would be great. And I go to use modeling techniques and grow my flax and see how mechanics affects like rupture and stability.

Now my graduate student just graduated, my fourth graduate student. He's going to create a company that can go into the clinic, and it's going to be a cardiovascular tool that can predict plaque rupture, as well as what treatment would be best to treat that there's going to be flexing 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, but have an impact on anybody?

But having passed away so suddenly while you were playing basketball would have been just devastating. Yeah, I think I was 24, so at 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 high school, he was going home traveling and we just.

Yeah. And 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 is crazy. I have a lot of cardiovascular disease in my family as well, and it's 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 like 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 I both unfortunately have.

Obviously that affected your life. And 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. When I found out that I had this cancer, we did a lot of research and I found out that the oncogenic driver of this cancer is a fusion between two gene on chromosome 12.

So basically now two, which kind of presses liveries and things like that. And step six which augments liberation. They work together. So one is a negative feedback. And one is positive feedback.

But in this cancer unfortunately the fuzed together and so that repression never happens. And so just the feedback loop stays on. And so I thought okay this is a genetic mutation or a fusion aberration.

Let's just use Crispr. Let's reverse it. Let's put a like a kill gene in there or something like this. And the real problem solved. And it will be very specific to like the Crispr will find the Neptunes Stat6 fusion, and it will only edit the DNA of the cancer cells.

So you did all this is very collaborative environment. And so we had a genetic engineering professor across the earth, and I told him about my diagnosis.

And I have been very I don't know, I don't 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?

We I don't know, but I'm willing to find out.

## Cancer Diagnosis and CRISPR Research Pivot

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 I couldn't get cells. So first we had to engineer the cells. So first we had to put the gene fusion in cells. And that took about six months because it was pretty hard to do to inspect parasites in the cell type of blood, to be the cell 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 edit it. And it was pretty successful. It reduced the proliferation rate significantly by 60 to 80%.

So really great. And then we were teaming up with other people for drug delivery approaches. But unfortunately, Crispr has not really been used broadly in the body systemically and and that is because food delivery to solid tumors, the efficiency is so low.

I'm sorry if you can imagine that even if you put it in the I. V., it has to go to the tumor cells. The Crispr, the enzyme, and then pass the membrane and then pass the nuclear membrane and then go into the DNA and edit it.

And we in the lab, we can use transfection agents and things like this to help put a high concentration rate on the cells. You can't do that in the body.

So that was a roadblock of an original idea in recent work. So 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 a lot harder in vivo than it was in vitro, because you're dealing with all those layers of secularity and just membranes and a lot of the things that.

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

And your lab. Yeah. So we're still working on adenoviruses and nanoparticles to package and the Crispr enzymes. But then we thought, okay, if we don't edit it at the DNA level, but more of the RNA level than it has to just gross one membrane.

And so we designed the Crispr CAS 13 to target the RNA level. But still the deliverability was a bit challenging. So then we pivoted to antisense like a nucleotides, which are in the RNA sequencing of mRNA.

And they bind like what are the Covid therapies for Imani as well. But the mRNA basically binds to the gene fusion the next year as a confusion and will block it from being translated into a protein.

And so that showed pretty good promise as well. And so we're still working with this in California to develop cells. And then when we did a animal study with the Aso and it slowed the proliferation in tumors in mice, but didn't exactly kill them. So it's not now just world growth.

And they didn't kill them. So the gene editing the answers and then we tried immunotherapies. And 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 by one mutation, we thought that this one mutation can be translated into a protein that can be chopped up.

And little bits of peptides expressed on the MHC class one complex. And then T-cells will come and recognize that peptide. If we develop the antibodies and modify the T-cells.

And then we can use an immunotherapy approach. And and T-cells targets these as a T-cells. Specifically and eliminate them. And so first we have to see if there is a little peptide unique peptide on the NHC complex.

And so we ran magic on the cells that we had in the lab. At this point we had some donor samples. We have three patient groups of right now in addition to our engineered to link.

But the mass spec wasn't sensitive enough to detect the peptides. And so we're in the process of looking for more sensitive mats back in Germany. And teaming with them to develop a more sensitive detection method of these unique new antigens are peptides.

So immunotherapies are third therapeutic approach. And then the other one that was funded by or one just last year is repurposing of drugs. So we have all of these cancer drugs, right.

In 2600 FDA approved drugs were specifically screened on these patient cells in engineered cells to see if any of them selectively would kill the cancer cells, but not the normal cells.

And so we had about 20 hits or so. And so we're looking at the most promising ones right now, which is never aggressive. And, 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, it impacts you and your life and your family, but all of us that have a solitary, fibrous tumor are very thankful for you and your ability to understand it.

And you're right in the middle of it. It's interesting. I think people are placed where they need to be for a reason, and I think that's quite interesting.

And I would never wish solitary fibrous 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?

## RNA Therapies, Immunotherapy, and Drug Repurposing

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 and full time professor, as well as mom as well as patient. So the department has been super supportive and I think that's really helped.

I guess changing my research in my lab to also look at, as of teachers that allowed me to look at 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, you know, a lot of doctors like to take the protocol treatment off the shelf, which is chemo and systemic, but some doctors are willing to just think outside of the box in the open when I take this journey with me.

And so we've I'm working on my third case study with my liver ablation doctor. And he said, I've treated 119 tumors in your liver. That's a world record and is no one in the world has had that many tumors treated, I believe shouldn't. Wow, this has happened over five years, and he was willing to take the journey with me 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. And so he's going to write a case study to show that maybe going straight to drugs is not necessarily the only approach.

Another oncologist and in the Anderson, he wanted me to go on drugs in 2019, and I like the rules of silence two years and I don't like them anymore. Okay. You can try a different approach.

And so I try this sort of local approach. And through surgery and radiation and ablation, you and two years later, I came back in 2021 and he's wow. You don't have any side effects.

Do you have any pain. And he was just soon pressing. He were to go on system exam. That's good. I would be so happy. I would be celebrating right now.

I would be saying good job, I did something good. And so I don't have any systems to recommend to you right now because whatever you're doing is working.

And so I think it has you have to be brave and courageous and I don't know what I'm doing, but like, I've had good mentors in my life and, and really good surgeons and good doctors and, and yeah, it's we've taken a sort of on beaten path.

Oh, yeah. What about you, Tony? Just before we hit record about History of Trips and that's a little bit more recently published. I mean, there's, 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 a history of trips is because it's a little bit newer. Do you mind walking us through what that is and how you've used that for tissue ablation?

Yeah, so I was stopped at the University of Michigan, and then I went to Europe and clinical trials there and had very good renal success until I was very patient in the US to train when it came through clinical trials here.

And it's basically using ultrasound waves to causes microbubbles at the tumor location at the tumor site. And this rapid increase and decrease in the microbubbles causes mechanical deformation.

And it ruptures physically, the cell membrane in the cells. And so they were thinking that there could be some immune bubble effect, because all the cancer rates are released and immune cells can target that potentially target other cancer in the body.

I didn't have any immune response, but the three lesions that were treated in the trial two years ago have been disappeared. And it's really nice because history trips the 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. And the interventional reorders determines all the physics and things like this to, to to modify the transducers.

And I hear we got from general feeling like nothing happened. But there's very little side effects. So I think it's promising and technology and history.

So next, which is the company name, just got bought out by of Corporation of People. And so it's moving forward. It's really developing and getting better and and well Doctor Henshaw the ablation person doctor at UW he said eventually leads for more things than just the liver.

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

So right now it's just approved or studied mostly in the liver, but it has a potential to help with many different tissue types. That's it. I'm sure it's dependent on the ability of the tissue to carry the sound waves because of it, because of the nature of the 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 would be a little bit harder, I think, to get really reliable results.

But I don't know it 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 in 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 when couple of weeks ago. And actually treating the cancer itself because of the sound wave going through the ribs, the bone, muscle, the lung, air, you could just imagine each one of those is a different material and you can travel differently.

And so it's really hard to get them to meet up with the tumors. Right. Exactly. It's better with homogenous material types. Oh yeah. So you're a cancer warrior.

## Living as a Researcher and Patient

Not only do you have this and are treating it as a patient, but you're out there fighting the fight for all of us that have cancer. And I think people listening to this are there might not be too many people that have solitary fibrous tumor, but I'll bet somebody listening to this either has it or has a patient that has it as physicians like I know about sarcomas, but as far as solitary fibrous tumor I had, I don't if I had ever read about it, I didn't remember.

It was such a rare cancer. That was another question I was going to ask you on these super rare cancers, where you're talking about 1 in 1,000,000 patients and the sample size on most of the studies are super low.

Where do you see that going? What do you think would make the biggest difference for us as physicians or researchers when we're talking about these are 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 that, 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 as you said, it's solitary fibrous tumors. When 60 million I think I heard 7000 rare cancers for diseases or something like that.

The Enorme Foundation is working on ultra rare. And so treatments for ultra rare cancers and diseases. So I think it's important even though just it affects the small population of funding and the government and stuff like this.

You have to make these decisions. Are you going to treat cardiovascular disease? It affects pretty much what are people who are right here. We're going t provide funding for city research that we treat even people.

So when 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. And so a lot of our therapy approaches, we're focusing on understanding these mutations at the genetic level.

And so if we could develop and treatment that combats that mutation or not, then the radically it could be applied to. But more broadly to other cancers.

And that's my hope, is that if we find something, then not only will it affect this small because there's a T patient which alone is important, they can also affect more broadly 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 the cytoplasm with the messenger RNA to determine, you know, 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 of 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 fibers tumor, but you could see those same principles being applied and 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, whatever it may be, but you have this specific thing and that level of specificity.

I think of that from everything I've read. I think that day is coming. But for those of us that have cancer, I want that day to be here now. Yeah. In a one patient specific in treatment, I think that is where we are headed as well.

That is going to be the future. And that's with my cardiovascular work too. It's patient specific modeling because cardiologists have to make these hard decisions on how do you treat someone's cardiovascular disease.

Is this plaque and rupture? Do I need to put in a bypass? Do I need to put an instant? And when 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 could just go up an instant.

But if you look at our studies, a lot of times the larger plaques, like the 70% plaques, are more stable and they don't cause any damage. And there's no sort of new plaques that are in all being that are in stable.

And those rupture more often in our modeling technique to input all the imaging data into a machine algorithm and finite element analysis and hemodynamic analysis, and really create a patient specific model that tells them the vulnerabilities within that plaque, others going back.

So yeah, I think that's what I want to see is individualized treatment and care because we're not all the same. No we're not. We try to think of diseases.

## History of Trips and Local Ablation Treatments

I'm a primary care doctor. And so the training is to think of you have diabetes or you have cardiovascular disease or you have whatever. But I'm thinking diabetes is another good example of there's so many different types.

We don't break it down to subtypes, but I can think of hundreds and hundreds of patients that are treated with diabetes, and they react so different to the medications, the progression of the disease, the speed at which they respond, the type of medications that they respond, the diet that they need.

And it's really all individualism. And 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. You know, another question for you. What would you tell folks who tell other doctors? Say you find someone with solitary fibrous tumor, or you find someone 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 are find themselves in that same boat. What would you advise a 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 this means, and I've done a lot of research, but I feel like a lot of people with rare diseases, they do a lot of research, they look up all this information.

And so if you just start by listening to what the patient knows about the disease, and that can maybe trigger some ideas and some therapies that aren't standard because they're typically isn't the straightforward answer.

And I know I do that with a lot of this of patients on line on the Facebook forums and whatnot. One of them come to me and they're like, yeah, this new disease and this new, please, what should I do?

How should we treat it? And until I just tell them what I think, and I think 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 some way.

I know that this personally. I know that some physicians can be a little bit really intimidated, but they just we see the

patients as Eric potentially like coming across like they know something and they haven't gone through all that training in the years or whatnot. But I think some of the most experienced in best treatments I received here from doctors, I just take the journey with me and I'm willing to try.

In addition to my liver being treated more times than anyone, he's having his. He knows I've ever been treated in the world. In my brain. I've had 140 lesions and 50 lesions treated by gamma radiation.

And get it when there's no telling your story has been wild. Wow. Yeah. He took that journey with me. The radiation oncologist. I think we get him on that three millimeters in radiation these days has developed.

So focused and precise you can treat the lesion and it goes away. It completely does give you look in my brain scan it looks like a fairly normal brain.

Think a brain scan like no no lesions or anything in there. And so it's just it. And he also Doctor Warnock it is a Western. He's we've never treated this many lesions in the brain before you know clinic with he's willing to take the journey.

I'm willing to take the journey. And so far we've been fairly successful. And I know at some point and hopefully going to develop a cure. But until then, this approach has been.

The game changer in. Yeah, no, I like that. Just thinking about what you said. I think it's much more meaningful for me as a patient. It sounds like for you as a 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 lot about cancer, but they may not know much about this particular cancer.

## Rare Cancer Research and Personalized Medicine

So that that joint decision making and advocacy on behalf of a patient, I think that makes a huge difference when you know your heard and listened to and you've been blessed with physicians who have done that for you, and that 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's kind of the the quick standard of care, because it's never quick, but it's a more thoughtful journey if you have to go and explore and advocate.

And then if you 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, yeah, I'm. I'm. I'm only here because of the doctors I saved, paving a new way that if the doctors wouldn't agree with it and treat you some merit in it and suggest ideas and things like that.

Yeah, I don't think I would be here. Well, for 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. The more people that research it, the more we'll learn. We can do things collectively as a group when we put our minds to it.

And it takes research money, it takes resources. But like you said before, I don't think that's money probably spent on those things that are broadly applied to many different cancers.

The more we learn about it, the more useful it becomes. I'm thinking back to my undergraduate. I had a degree in microbiology, 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.

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

And it's neat that you've been able to mix the two of those things. Yeah. Yeah. And, you know, you had core biopsies in the calf muscle safety. And I told the physician it was like one of my grad students comes up and we got the entire beast of approval and everything.

Could we get some sample? And she was like, I'm gonna cry horribly. This tumor. And so do you want to do research or do you want to get treatment? I was like, oh, no, in Seattle for biopsies and then give them to my grad student who drove five hours back to the lab and started, I'm trying to start a patient line.

And then she finished off the cry ablation to the rest of the tumor. Yeah, just doctors that are open to furthering science and but also providing patient care.

Yeah. This is really great. Yeah. So what would you tell someone who is a medical student write down right now. Maybe they're MD PhD student and they're 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 try to live on whatever disability insurance they might have had.

But you've stayed engaged and focused, which I think is amazing and miraculous. And I guess I want to know, what would you tell someone 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 we look back over time? Yeah, it's really a personal choice. What kind of research? PhDs. I have things. I have a lot of friends who have done it and PhD in their decision after they get their degrees.

Do I want to go to practice or do I want to be a researcher? Because if you want to be a researcher, that's what it work. You have to apply for grant funding.

You have to write me to it. And then if you want to do a clinic, that's really demeaning to 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 a clinical lab, then you can get patient samples and do research in the lab and really kind of do both efficiently and effectively.

So to start thinking about that and how to make those to work together, you will keep you from the burnout that you talk about and just trying to juggle multiple things and not having time.

Yeah, but 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, I don't think you would keep doing it if you 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 you're 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. I just in total admiration of what you're doing and just appreciate it so much.

## Advice for Physicians, Trainees, and Closing Remarks

Do you have any final words or advice you'd want to share with our audience? I just want to say thank you, Peter, for being the voice in many different positions.

I've been listening to them through, and since I've met you. And yeah, it's so amazing where 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 and.

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. And of course, I'm very interested in your research as well. So we'll be in touch and I appreciate it so much.

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