After the Fact | From Lab to Life: Why Cancer Resists Treatment

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TRANSCRIPT

Emily Chow, senior producer, The Pew Charitable Trusts: Hi, I'm Emily Chow. As a producer for “After the Fact,” I'm usually behind the scenes researching the stories and guests, but today I'm on air to ask you: What keeps you listening to our podcast? And what would you like to hear about in the future?

Tell us in the short survey at pewtrusts.org/podcastsurvey. When you do, we'll enter your name to win a $100 gift card. The survey deadline is Sept. 15. So, fill it out soon for your chance to win.

Emily Chow: Welcome back to “After the Fact.” For The Pew Charitable Trusts, I'm Emily Chow, a senior producer on the podcast, and we're wrapping up our latest installment of our series, “From Lab to Life.” And our host, Dan LeDuc, is here to tell us about the final guest we have for the series.

Dan LeDuc, host, The Pew Charitable Trusts: Hey, Emily. In the final episode, we're talking to Christie Towers. She's a researcher at the Salk Institute doing important work to improve treatments for cancer. She's also the first Black scientist at Salk and has some really interesting things to say about the role of diversity and how important it is in scientific research.

Emily Chow: I'm really interested in hearing more about her success and the milestones that she's achieved in increasing diversity in science, Dan.

But let's start with her research. We've made great strides, for example, with people who are diagnosed with breast cancer; the survival rate after five years is at 90%. And it's a little bit tougher for people that are diagnosed with pancreatic cancer. That's at 13%.

Dan LeDuc: Right. And Christie's research is trying to address some of that discrepancy. It's like, why are some cancer cells more resistant to treatment than others? She's going to tell us a lot more about that. And she's also got a great personal story.

[Music transition]

Dan LeDuc: We are joined by Christina Towers from the famed Salk Institute. Everyone calls you Christie, so we will too. Thank you.

Let's talk about what got you started in science.

Christina (Christie) Towers, Ph.D., assistant professor, Molecular and Cell Biology Laboratory, Salk Institute for Biological Studies: I fell in love with science in the second grade, and it was a project where we had to use the alphabet and draw a picture of every animal that starts with that letter. And we each had a habitat that we were assigned, and I was assigned the ocean. And I, honestly, I just fell in love with the ocean.

And from that moment on, I wanted to be a marine biologist. I wanted to study all the animals in it. I did all the research of like, what college should I go to to do this? And, you know, what are the careers that I can have with this?

And that was really my insight of like, I want science to be part of my life. And, I did go to college to be a marine biologist. I went to the University of Miami in Florida, which is right on the coast.

I took my first intro to marine biology course, and actually in the first week of that course, I decided that this is not for me. And I realized a sort of tangible fact that was really important, which is that I get extremely seasick, and a career where I would have to be on a boat for like extreme amounts of time was just not going to work for me.

But I still loved science, and honestly, I'd had like 15 years of my life geared at being a marine biologist. I was like, what do I do now? I think I still love science.

Dan LeDuc: Well, is that hard? Wait a minute. So, I mean, wait a second. There's a— timeout, you know, from second grade on, this is what you wanted to do. You get to college and you know—listeners take note, hang in there. We're going to tell you what she's doing right now because it's really cool—but, but the getting there is kind of cool, too.

Christie Towers: Oh my gosh. It was a rude awakening because as a child, you don't think about these like small details of like what you actually do in that career, right? You just think about the glory parts of it. And it was definitely a rude awakening for me.

Dan LeDuc: So you're getting seasick and thinking, this isn't the right science for me. What was next? Because it wasn't what you're doing now yet.

Christie Towers: No, exactly. So next, you know, honestly, it was my parents who were like, well, you know, you love science. You should just be a physician. That's what you do if you love science, you should go into medicine. And I was like, OK, well, I guess that makes sense, right? So I, started volunteering a lot in inner-city hospitals around the area and especially in emergency rooms.

And in Miami, a lot of the patients coming in are either uninsured or vastly underinsured, and they're really using the emergency room as their primary means of care. And I will never forget a woman that walked into the emergency room, and she had breast cancer, and it was like her first or second time being seen.

And she was going to die of a nearly curable disease at this point, really just because she didn't have access to care. And it was, it was absolutely heartbreaking for me. And I just realized that in that moment that I just didn't have the heart to see patients in that capacity. But I still, I still loved science and I just felt like I was like crossing off this list of like, OK, well, I can't be a physician. So, so now what?

And, I went to my biology professor, and I told him about my experience and how much I still love science, but I just didn't know what to do with it. And he was like, oh, well, you should try research. And I was like, research? What does that mean? And he really took a chance on me, and he was like, let me just put you in this lab, just see if you like it. And he got me involved in this lab in Miami that studied B cells and aging and B cells, which are a type of immune cell.

And I just fell in love with it. And, sorry, teaser, I don't study B cells now, I don't study immunology now, but I fell in love with the pursuit of knowledge. I fell in love with research at its core, and I never left the lab.

I changed my entire schedule in college, I rearranged all of my classes so that I can be in lab as much as possible, and until this day, I just fell in love with research.

[Brief music transition]

Dan LeDuc: And tell us what you do now at Salk.

Christie Towers: Yeah, so now I study cancer cell metabolism. And cancer cells are such a unique cell in our body because they are, they are self. They are cells that arise from your own cells, but they have figured out a unique way to survive and to persevere and to continue to divide and grow and survive. And one of the ways that they do that is they have a unique way of metabolizing.

And so metabolism in itself is breaking things down and building things up. That's all of what metabolism is. And cancer cells have a unique way of doing it. And in particular, my lab studies how cells recycle things. How do they take things that are already built, break it down, and re-use that same material?

And it's a process that's called autophagy, which I know is a funny word, but in the Greek it breaks down to auto, which means self, and phagy, which means eat. So we study how cancer cells break down the material they already have and recycle it in order to build new material, but cancer cells can hijack this process to be able to recycle their own nutrients and divide and grow faster, which means that if they're in a limited nutrient environment, they have an advantage.

[Brief music transition]

Emily Chow: Dan, this is a really fascinating time in cancer research.

Dan LeDuc: Yeah, as Christie was telling us, you know, for the past decade, the human genome project has been offering a lot of insights into cancer research, and now Christie's moving sort of in a different direction and looking at how cells actually metabolize.

[Brief music transition]

Christie Towers: In the cancer field, about, you know, 10 years ago, it was this idea the human genome project is underway. We can cost-effectively sequence, and this idea that if we can sequence every tumor, we will know the exact genetic driver of that tumor and that will be the cure if we know it, then we can treat it, and that's all we need. And I think we're there now, we can sequence, most people's tumors, we can sequence them. But I think the sort of crude awakening in that was that that's not the answer, that genetics is not the answer, and that there's so much more beneath that, and things that are happening below the gene level, and realizing that, that cell metabolism is important, and that's below the gene level, right?

And to me, it's an example of where, in science even, we think, oh, we know what the answer will be, right? We know the formula to get to the answer. We don't have the answer, but we know how to get there. And then, we spend a decade and we do the formula, we work our way through it, we get to the fact where we can sequence every tumor, and then we realize, you know what, that wasn't the answer.

And we've just opened up 10 more questions, 10 more avenues of how do we really get to the point of understanding every person's tumors. Just an example of science just ever evolving.

Dan LeDuc: So you mentioned that it's natural, that our cells react this way and our bodies do this naturally, but do cancer cells also have this ability naturally, or is it just the result of when they're trying to resist treatment?

Christie Towers: Such a great question. It's really both actually. So we think that in order for a cancer cell to not be cancer and to stay normal, it needs to get rid of

damaged material in the cell. And so it uses actually autophagy to break down damaged material.

So autophagy is a really good thing. It protects our cells. It keeps them healthy by getting rid of damaged material.

And then, once a cell actually becomes cancer though, now a cancer cell will use autophagy as, for its own gains, right? It will use autophagy to just make material that we'll just use over and over to grow faster.

And then the third aspect, which you just brought up, is what happens when we treat cancers? Well, autophagy can actually protect cells from these damaging chemotherapies.

So chemotherapy is, all that that means is it's a therapy that just induces cell death. It targets very fast dividing cells, and it's just a toxic material to the cell, and there's different flavors, different ways that you can do this.

But if a cell can get rid of that toxic material quickly, if it can create more material that can sort of swamp out that toxic material, that allows a cell to become resistant to those drugs. And so, autophagy can get upregulated, can be increased in response to different drugs. And so this has actually led to a lot of the things that my lab is studying now, which is how can we block autophagy in cancer cells to prevent them from becoming cancer in the first place.

But then once they are a cancer cell, how can we prevent them from growing? And how can we make them actually respond to the chemotherapies or the treatments we already have? All of those things are, are a reason why we want to block autophagy.

Dan LeDuc: So they're taking this sort of natural process and twisting it, you know, for their evil ways, because no one likes cancer, and actually using that to resist treatment. That's fascinating.

Well, can you tell me more about how your work fits into all of this? What is your lab looking at?

Christie Towers: What we're really studying is, even if you don't treat the cancer cells, and you just look at the cancer themselves, are doing more autophagy. And if you block autophagy on its own, that will kill a lot of cancer cells, but what we discovered is that cancer cells can actually get around the autophagy inhibition.

And so they can actually acquire resistance to blocking autophagy itself. And the way I like to think about it is that is if you think about a highway system in any city, if

there's an accident on that highway, it like gums up all of the traffic, like horrible traffic, nobody to work on time. Everybody's just sitting there mad on the highway.

And so you think about that as just like targeting a core pathway in a cancer cell. Like autophagy, it's a central pathway that will block a lot of the cancer cells' metabolism, and those cells will die.

But if we go back to our analogy, right, and you really think about if you are actually sitting stuck in traffic and you're mad and you're trying to get to your meeting, what are you actually going to do? What you're going to do is you're going to pull out your phone, and you're going to ask it to reroute you to find another way to get to work. And it works quite well, right?

Well, we have discovered that cancer cells are just as cunning. And they can also rewire their metabolism. And so even if you block this central pathway, the cells will find another route to get the same thing done.

And the question that my lab's really trying to understand is not just the one pathway, not just the one highway, but what are all of the other alternative streets, right? What are the off ramps to these highways? What are the different ways that cells get back on these highways? And if we can understand those pathways, then we cannot just block one, we can block different pathways simultaneously. And that's, that's my lab's goal.

Dan LeDuc: And what's the end result of success for you? I mean, is it specific knowledge about how stuff works, or is it knowledge that your lab could actually turn then into treatment?

Christie Towers: Yeah, it's, again, it's really both. And I really think of my lab as split into two halves. And half of my lab studies fundamental cell biology. We want to know how autophagy works. We want to know what all these other pathways are that connect to it. And the goal there is to understand the pathway. What pathways link to what? And just deep diving into each of these pathways.

But then the second half of my lab is really focused on translating that knowledge into new therapeutic strategies for cancer patients. And so there, the end goal is really identifying drug targets that will allow us to treat cancer better.

And importantly, not just what are the targets, but what drug combinations work the best. And it's not just about randomly trying different drugs and just seeing what works best together. But it's leveraging the first half of the lab. It's leveraging that fundamental knowledge of these different pathways to strategically design ideal combination drugs.

And we really study the fundamental process, but then we collaborate with the chemists to design the drugs. We collaborate with the clinical trial people at different hospitals to build the clinical trials and then actually implement these different strategies. And it's really a collaborative process from start to finish with different physicians and different scientists.

Dan LeDuc: Is there something about the way science is practiced that maybe is difficult to translate to people? I mean, you, you have experiments and sometimes they don't work or sometimes your hypothesis is wrong. And sometimes people accept things and move six steps down and then suddenly realize, no, this isn't right.

Christie Towers: Absolutely. First of all, it, it really saddens me, in general, that there is this mistrust in the scientific community.

And I will say I do think some of the onus is on us, as scientists. I don't think historically we've done a great job in connecting with the community and making sure they understand how science works. How do we derive a hypothesis? How do we test that hypothesis? How do we disprove our own hypothesis and then move on to a next and better hypothesis?

And I, in my own lab, am really prioritizing having chats with people in the lay public and really trying to make sure they understand how we do science. And importantly, the trainees that I bring up in my lab, I make it a priority that they know how to have communications with, with the broader public and make sure people understand what we do and why we do it.

Science should provide the best information it has at the time. It should relay that information. We should not hide that information. But then as soon as we have new updated information, as soon as we realize, OK, you need this type of mask, that should be relayed immediately to the public. I really think it's important for the public to understand that we don't have all the answers right now. And the idea is to test the hypothesis, get an answer, and then generate a new hypothesis to test again, right?

And I want to go back to the process of science, because again, one of the best things about how science is created is, it's all about science standing up to the test of time. So when someone makes a discovery, they publish that. Then the next group around the world is going to take that discovery and say, oh, I want to test the next question.

And as part of testing that next question, they're going to repeat the exact experiments that somebody else already did. And then they're going to say, oh, actually, I think this person maybe got it wrong because the conditions were a little different or they didn't notice this one thing. Or actually, yes, this is right, we can prove it over and over again and now we're moving on to the next thing.

And so it's not just one person's one discovery that that's the answer, it's that one person's discovery that then 10 people are going to try again and again.

Dan LeDuc: We were talking about the process of science that includes scientists. You are the first Black faculty member at Salk. Why does diversity in science matter? Why does it matter who's looking through the microscope?

Christie Towers: So it's been shown, scientifically shown, that having more diverse perspectives in any room allows innovative thought.

And especially in a field like science you need people to think, that think a little bit differently.

And if everybody comes from the same background, from the same university, from the same region of the nation, from the same part of the world, you don't think differently.

It's having chemists and bioengineers and biologists in the same space. It's having people from different regions of the nation, of the world, who think a little differently, who maybe think, well, actually, I come from a more humid part of the nation, and so have we ever thought about actually changing the air temperature or changing the oxygen levels, right? Maybe that affects the biology, and it does. But maybe if you come from a different part of the nation, you would never even think to manipulate that variable, right?

But then it's also having people that come from different aspects that think about things like access to care, right? What if we're coming up with a drug that we think could really work, but we don't think about the fact that this drug is five times more expensive. And so people in this part of the nation that maybe don't have as much money won't even have access, even if it works amazingly, will never have access.

So maybe the question is not which drug, but it's how do we make this drug more affordable? How do we make this drug more accessible? And maybe we need to be thinking about that question at the very beginning when we're doing the basic science like that happens in my lab, right? And so it's having these diverse perspectives at all levels that really, really matter.

And so at Salk, yes, I am the first Black faculty at Salk, and my mantra is that I am honored to be the first, but I refuse to be the only. And so now I am building programs and pipeline programs that help not only diversify our trainees and our staff and our faculty at the Salk Institute, but that help build a more diverse and trained pool of scientists for the entire nation.

Dan LeDuc: Talk about some of the challenges you've had to face yourself.

Christie Towers: Yeah, I think they really fall into two different buckets. I've had challenges for me as a scientist, how do I become a successful scientist, and then there's been challenges in the science itself.

So, in the first bucket, you know, it's always challenging to be the only, and then growing up and through all of my science courses, I have always been one of the only underrepresented scientists, and I have really relied and benefited on fantastic mentorship and on pipeline programs.

It's also been a challenge to be a mom in science. And I, I have two small kids, which I had as a graduate student and really balancing, having children and having a family and also being a scientist. And again, I have relied on fantastic mentors and women ahead of me to get advice and really benefited from them.

So then the second bucket of challenges is, you know, the science itself. What, what's been the most challenging scientifically? And I think it's really been building models that allow us to study fundamental biology in a way where we can manipulate things. How do we change this gene? How do we manipulate this pathway?

But how do we make sure we're in a system that's still, so that those discoveries are relevant to people. And so being at the Salk Institute, it's been a phenomenal place to do that kind of science, and I have taken advantage of amazing collaborations with people here.

Dan LeDuc: Well, during your time in academia, have you seen things start to change when it comes to diversity in science?

Christie Towers: Yes, absolutely. And I would definitely say that I have seen change for the better in the last decade. And I would argue that I only sit in this chair right now because I sort of stand on the shoulders of those who have come before me and who have fought harder battles to fight to get to this place for underrepresented scientists across the nation.

But I am definitely optimistic about the place that we are in right now. And there is a much larger push. For science to be for everyone. And there are many different ways that that's happening. The NIH itself, the National Institutes of Health, is creating grants and opportunities that help diversify the pipeline, making sure that there's equal access to training.

Making sure that the models that we use, right, are these mouse models of cancer, are those representative of all populations, of all types of cancer, of all races that have different types of cancer, right?

And so really getting at sort of the equity and health disparities research, there's a lot of money that's going into that as well.

[Music transition]

Emily Chow: There's been a lot of effort to increase diversity in the scientific community. And that includes people, researchers from different racial backgrounds, geographic locations, and also increasing diversity of the types of people participating in clinical trials.

What we've learned this season, of course, from all the scientists that we spoke to, is that what really motivates them is their natural curiosity.

[Music transition]

Christie Towers: Really what gets me out of bed in the morning is just the sheer curiosity. And I'll say it again, I absolutely love the fact that we answer one question to generate 10 more.

And the truth about what I do, specifically, about studying fundamental cell biology, is I might not get a drug into a patient's arm tomorrow, right? Our discoveries are going to take really years and years before they really translate into a therapeutic strategy that's beneficial to a patient.

So, what motivates me can't always be just saving the next life. That can't always be your number one motivation in science. I really think it has to be the sheer curiosity. You have to just want to know the answer.

Because when you do an experiment, you will get an answer to that question, but sometimes the answer is no. Sometimes the answer is no, that hypothesis is wrong. It's not that drug. It's not that pathway. It's not that molecule. So that can't destroy you, right? That answer has to be enough to drive you to be like, oh, but that means it has to be the next question, right?

And so that's really what drives me. And that's what I'm looking for when I'm building my team is people that are driven by that sheer curiosity of the next question.

Dan LeDuc: One last question after a great conversation that this has been, Christie, is, you've talked about curiosity, you've talked about patience and all of that's what it could lead to, but like in your heart of hearts, what is your hope for your work?

Christie Towers: In my heart of hearts, the hope for my work, I would say, is probably threefold. The hope for my work is, ultimately, I really do hope that the

fundamental knowledge that we uncover will lead to therapeutic strategies that will extend the lifespan of our cancer patients.

And then the second thing, I really hope that we advance science. I hope that we come up with new discoveries that make people realize what is autophagy? What is it doing? Where is it happening? What parts of cells, what kinds of cells are doing it? Really building that fundamental knowledge of, of this process.

But the third thing that I really hope that at the end of my career I would count as an immense success is that I have trained a generation of scientists that are diverse and that are curious and that go on to make more discoveries beyond what I could ever imagine. And my trainees, they are my legacy, and I really invest a lot in mentorship, and in fostering really the next generation of scientists.

[Music transition]

Emily Chow: Christie Towers wraps up our five-part series, “From Lab to Life.”

Dan LeDuc: We've had a lot of fascinating conversations with some really interesting researchers. And if you've missed any of them, you can check them out wherever you listen to your podcasts. And you can always find out more information from us at pewtrusts.org/afterthefact.

Emily Chow: And we're working on more new episodes now.

Dan LeDuc: And if you have questions or feedback that you'd like to share, let us know what you want to hear about. You can write us at podcasts@pewtrusts.org. For The Pew Charitable Trusts, I’m Dan LeDuc.

Emily Chow: And I'm Emily Chow. And this is “After the Fact.”