After the Fact | From Lab to Life: What AI Tells Us About Long COVID

Originally aired August 9, 2024

Total runtime: 20:09

TRANSCRIPT

Dan LeDuc, host, The Pew Charitable Trusts: This is Dan LeDuc from The Pew Charitable Trusts. And I've got a question for you: What keeps you listening to our podcast? Tell us in our new survey at www.pewtrusts.org/podcastsurvey.

Once you do, we'll enter your name in a drawing to win a $100 gift card. The deadline is Sept. 15, so act soon.

Now, let's get into the next episode of our latest season, "From Lab to Life." We're hearing stories from scientists about how they got started in their fields and how their research is making the world a better place.

[Music transition]

Keyla Sá, postdoctoral fellow, immunobiology, Yale University School of Medicine: So I saw a group that was getting better, and I saw a group that was only getting worse and getting worse. I realized that something wrong was going on with those people, and I couldn't understand why.

[Music transition]

Emily Chow, senior producer, The Pew Charitable Trusts: You just heard from Keyla Sá. She's originally from Brazil. But right now, she's doing research at Yale School of Medicine. Our Dan LeDuc spoke to her about her latest research, which is about a health challenge that millions of Americans are dealing with.

Dan LeDuc: Hey, Emily. I had a fascinating conversation with Keyla. She's at work on long COVID, which is a disease, of course, that didn't even exist when she started her education as an undergrad. And here she is, a young researcher hard at work on this important subject.

Emily Chow: Right, Dan. When we were doing our own research for this episode, we found that 11% of Americans who have ever had COVID are currently dealing with the symptoms of long COVID. And that can last for three months or longer.

Dan LeDuc: And it's fatigue and all sorts of other really harsh symptoms. And it means millions of people. Keyla and her research are trying to do something about it.

[Music transition]

Dan LeDuc: So, Keyla, why don't you tell us where you're from and how you got interested in science?

Keyla Sá: I am from Brazil. I came from an area in the Amazon, the state of Pará. It's a very small city, Cametá. And I got very interested to work with science because the place that I came from, it's a very poor place. And we suffer about several seasonal diseases caused by virus.

So, for example, we have a lot of infections with dengue, Mayaro, chikungunya, Zika. And I remember that when I was in my undergrad, I think we had Zika spread through Brazil, and a lot of people were getting very sick, a lot of babies getting sick. And, seeing all of us, my people, me also, suffering and get infected by those virus every time was what make me start to think why this happens. How can that happen?

So, I got very interested about virus, because virus, they are protein, they are just a protein with genetic material like DNA or RNA, and they are not even considered alive. So, how can this lot of proteins and DNA together be able to cause so severe disease?

And so, I decided to pursue a scientific career to understand more about virus.

Dan LeDuc: When you first started talking, what came through was, you were motivated by people getting sick around you and wanting to do something about that. Has that been one of the guiding things for you as you've gone into your research?

Keyla Sá: Yes, yes, so mainly I like to do translational research so I can get in touch, get in contact with the patients and what are they suffering. And most of those disease or neglected disease, they don't have answer.

So, I want to go through that to give answers to how to understand how this disease is happening. And so, we can develop or we can think about better treatment strategies for those people that can really help them and not only give them palliative care.

Dan LeDuc: I want listeners to understand that you were in school and had made all of these decisions to study how viruses work. And you were motivated by a lot of different things.

But it was while you were in school this thing called COVID happened to the world. How did that change your outlook? How did it change how you've started pursuing your studies? Was this a big change for you as a researcher?

Keyla Sá: I think that was a big change for everyone, right? Yeah, for me too, at that time. So, I was working with a virus, doing my undergrad and my master's degree. When I went to my Ph.D., I started, I wanted to change, to expand my horizons and know different things, learn about different things. So, I started to work with Leishmania.

I went to the Universidade de São Paulo, and I started to work with Leishmaniasis; that's a neglected disease caused by a parasite. So, I was working in a very different field when the pandemic started in 2019, end of 2019. That which, it started in Brazil in the beginning of 2020. So, at that time, I remember that everything stopped, and we decided to, as a lab and the department also, we decided to work together to give answers to those people that were suffering, so on that time, I stopped my Ph.D. project with Leishmania, and I moved it completely to SARS-CoV-2. And I think that changed a lot of my life, because I was following a completely different path.

I mean, that was also in science, also doing research, and also answering those questions, but in a completely different pathway. Now, after the SARS-CoV-2, I moved to long COVID. And to the long COVID, I am an immunologist. So, for long COVID, because many of the symptoms, they are neurological symptoms, I had to move to neuroscience.

So, I am moving to a completely different field, because SARS-CoV-2 was moving me to the questions that came in, because the disease, because our research made me move even for not only, for example, parasites to virus, but also from a different field, immunology to neuroscience.

So, I think now I am an immunologist learning how to be a neuroscientist, but I think that was very impactful on my life and changed a lot of things.

[Music transition]

Emily Chow: Keyla's career path took some twists and turns. She started out as an immunologist and is now studying neuroscience.

Dan LeDuc: Well, you know, she's driven by curiosity, and hasn't that been a trait we've heard from all the scientists this season that we've been talking to? They're curious people, they come up with fascinating questions, and, as they learn more about things, their careers take them down different paths than maybe they expected.

Emily Chow: And even geographically, Dan, Keyla started out in a small town in Brazil, moved to a city, in São Paulo, and now she's in New Haven, Connecticut.

Dan LeDuc: And as a Pew Latin American fellow, she will do her postdoctoral studying here, and even go back to Brazil and create a lab there to continue her work. So, it's fascinating to see how the science, as you said, stretches across decades of knowledge and also geography.

[Music transition]

Dan LeDuc: Just as you're getting started in your career, so much happened to the world. And it just—did you feel like you were sort of riding a wave each day when you went into the lab to figure out what was going to happen next?

Keyla Sá: Oh, that's hard, right? I think none of us was expecting for a pandemic to happen, right? And we have to be very flexible with how the world is changing and what are the paths that we should choose now, so we can give to the people the proper answers, the answer that they want to hear or they are looking for.

Dan LeDuc: So, you're doing research, and COVID is happening in real time. When did you realize, or what was it like to realize, you and the other researchers, that there was this version of COVID that wasn't going away?

Keyla Sá: Yeah. So, doing my Ph.D., I was working with SARS-CoV-2. And I was following people that they have very severe disease. So, I had a group of people that I was following how they were developing through time. And I saw two groups, so I saw a group that was getting better, and I saw a group that was only getting worse and getting worse.

In the end, because all of them, they had very severe disease, all of them died, but I was seeing very clear: Even though those people that are getting worse, they were not infected by the virus anymore. That was like months passed after the initial infection, and they were getting worse and worse,

And at that time was when people started to talk about long COVID, that they were not recovering, that they were still feeling bad, even though after the acute phase of infection. So that was the moment when I was seeing that with my eyes following those people that we had something new going on over there.

That at that time we couldn't explain. Now we know that that's long COVID.

Dan LeDuc: And help people understand really what long COVID is.

Keyla Sá: Yes, so, long COVID is when you got infected by SARS-CoV-2, and after months you still feel symptoms. They don't have a very, very specific guideline nowadays, but usually if you were feeling the symptoms for more than one month, that's long COVID. So, most of the symptoms, they are fatigue, brain fog, headache, anosmia—that's loss of smell, or loss of taste.

And the symptoms, they can be very diverse. So, some people have, like, symptoms that are kind of rare, for example, tremors, change in appetite, cough.

Dan LeDuc: What do we know about why some people can get COVID and recover in a week or two, and why others suffer from long COVID, where they have these terrible ailments that continue for so long?

Keyla Sá: Nowadays, we don't know why those people, some people, they develop long COVID, and some people, they don't. What we know is that we have some groups of people that they have an increased risk to develop long COVID. And those groups, they are composed mainly by females, and we have been seeing association with hormonal levels.

For example, testosterone, estrogen, and cortisol are the main hormones that are associated with long COVID development. We also, we have several hypotheses about what is causing long COVID. One of the hypotheses is a virus reactivation or a virus reserve of SARS-CoV-2 that may be causing those symptoms, making those symptoms is staying for so long.

Another hypothesis—that's the hypothesis I have been working on—is autoimmunity. The third hypothesis is tissue damage. And the fourth hypothesis is an immune imbalance that may be causing long COVID.

[Music transition]

Dan LeDuc: Yeah. One of the things you're doing now is using artificial intelligence tools to research long COVID. What is the role of artificial intelligence in what you do?

Keyla Sá: Because long COVID is a so diverse disease, it's hard for us to differentiate this group of people based on what is causing they feel those symptoms. Because we believe that long COVID is a composite. We have these four hypotheses. So, we believe that long COVID is being maybe a mixture of these four hypotheses.

And we are working with very huge datasets, so we are collecting samples from patients and evaluating thousands of different markers. So, for we be able to identify

these patterns, we are using artificial intelligence to help us. So, we have several different symptoms between brain fog, headache, cough, dysautonomia. And those symptoms, they are very diverse. And not every patient has the same set of symptoms. So, we should be able to identify group of peoples, homogeneous group of peoples, so we can understand what is causing those disease on that subset of patients.

For each of that, we have been using AI. So, I am not an AI person, so I do collaborations, so the person that's helping me a lot with that is Julio Silva from our lab. And he's a machine learning expert, so we are developing these machine learning models where we can feed the computer with all this information for those patients, and the computer can see those patterns that we, at least I, with my human eyes, I cannot see.

So, we are able to identify those group of people and focus on them to identify what is causing the disease on them. And that have been helping us a lot.

Dan LeDuc: And so that helps you identify patterns in people's symptoms and in whatever chemical makeup is showing up in their virus. And are you at a stage in your research where we're still learning what long COVID is? Or are we at a point where you can start to try to think about a treatment?

Keyla Sá: I think we can definitely start to think about that. So, I think we are in this true stage. We are still trying to understand, and at the same time, we are progressing to the next stage to think about specific treatments.

So, I can talk a little bit about my research. So one of the hypotheses, like I was explaining, is autoimmunity. So, we believe that for some reason, a subset of people that got infected with SARS-CoV-2, they developed autoantibodies. So, an autoantibody is when our body—we have our immune system that's supposed to defend ourselves against an infection—so that means our immune system, for some reason, developed these autoantibodies, and it started to attack ourselves. So, our immune system, our bodies attacking ourselves, and that is one of the explanations that we have.

And what I saw, I got serum from those patients with long COVID, health controls, convalescent controls, that are people that were infected by SARS-CoV-2 and didn't develop long COVID. And I put five antibodies from those patients and evaluating that, using mice to study that, I saw that when I inject those antibodies in mice, those mice, they develop symptoms. The most important symptom that we saw was pain. So, the patients that have pain, when I purify the antibodies and inject the mice, the mice also develop pain.

So, that is a causative association. We were able to identify the cause of the disease, and, knowing the cause, we can definitely think about treatment for those people. So now, with my research and research from other people who also have been evaluating the same hypothesis, now we may be able to identify the subset of people that have those autoantibodies and treat them in a more specific way, that we are going to help them.

Dan LeDuc: And are the therapies that you described—you mentioned there's great pain relief, which is when someone is suffering, that's very important. But are you going at the actual source of the disease as well? Or are you simply affecting the symptom of pain?

Keyla Sá: So, we know that the source of this disease is those autoantibodies. We are working on that now. That's our research in progress. But we have some potential targets.

Dan LeDuc: So, what is your near-term plan for your research? Do you have some immediate goals and long-term goals?

Keyla Sá: Yes, so now my immediate goal is try to understand the mechanisms by how those antibodies, they are causing those symptoms. So, we have many different strategies that we are looking for now to understand how it's causing this inflammation and this nerve damage that maybe explain the feeling of pain, chronic pain, that these patients have. And, as an ultimate goal, I want to understand, how can a virus induce autoantibodies?

Dan LeDuc: So, you are a Pew Latin American fellow. That program has been around for a number of years now. And it brings promising young scholars like you to the United States for postdoctoral training. And then, most of you go back to your home countries. So you're eventually going to return to Brazil and start your own lab. So what are your goals and hopes for that lab?

Keyla Sá: For me, the most important is that I can come back to Brazil and open a scientific lab over there and help my country to develop it. So, I think knowledge is power, and I have this aim to be able to give that back to my society also.

My country, like I was saying, we have so many people suffering from so many different viruses. So, be able to study, develop models, understanding how those diseases are happening, and contributing to treatment strategies, treatment strategies that are going to be affordable for those people—that's the most important thing. I think I should try to give that back also to my country, to my people.

[Music]

Dan LeDuc: Oh, that's wonderful. Well, Keyla Sá, thank you so much for talking to us, and good luck with your continued research.

[Music transition]

Emily Chow: Long COVID is a newer health condition, but it's really transformed to be a chronic, persistent problem, and Keyla's research is really helping uncover some important and much-needed treatments.

Dan LeDuc: You know, so many of the scientists we've been talking to are doing just that. They're looking at these persistent problems. And in our next episode, we talk to Christie Towers, who is doing cancer research at the Salk Institute, and she's looking at why some cancer cells are just that. They're so persistent, they don't respond to treatment, and they seem to duplicate themselves. It's a really cool conversation.

Emily Chow: As always, for more information about this series, you can visit our website at www.pewtrusts.org/afterthefact.

Dan LeDuc: And, as always, if you have any ideas, questions, or feedback, write to us at podcasts@pewtrusts.org.

Emily Chow: For The Pew Charitable Trusts, I'm Emily Chow.

Dan LeDuc: And I'm Dan LeDuc. And this is "After the Fact."