Transcript of Lab 042 Pt 1: Understanding HIV

Titi: December 1st was World AIDS Day and December, the entire month, is HIV Awareness Month

Zakiya: And this December is particularly important because it's the 40th anniversary of the first five cases of HIV.

Titi: Wow, 40 years feels like not a long time, but so much has happened in those 40 years.

Zakiya: It's definitely not a long scientific time, you know? And you're right, so much has happened even thinking about what it meant to have HIV in the 80s and what it meant for your life compared to what it means now, thanks to advances in medicine and vaccine development, all kinds of things that are coming along for the treatment of HIV and AIDS.

Titi: Right. And our understanding, I think, of the virus has changed.

Zakiya: Yes.

Titi: And the way that we interact with people who have HIV has changed. Thankfully

Zakiya: You're right. I think there's so much to unpack, even though it was a short scientific time. There have been incredible developments.

Titi: Absolutely.

Zakiya: And I can't wait for us to learn all about it.

Titi: Welcome to Dope Labs, a weekly podcast that mixes hardcore science, pop culture and a healthy dose of friendship.

Zakiya: This week we're talking all about HIV. Now HIV has been around for a while and there's been all kinds of rumors like, Oh, they have a cure, and the government just doesn't want us to have it. But scientists have been working on an HIV vaccine for a pretty long time.

Titi: Yeah, there's a lot swirling around, but what's most important is what the science is telling us, and that's what we're going to get into today. I just saw this story in The Washington Post about an Argentinean woman who just became the second person on record whose body might have completely eliminated the HIV virus on its own. And when something like this happens, it's a huge deal for scientists who can study what happened in the patient's body and potentially use those findings to develop a cure.

Zakiya: Let's get into the recitation.

Titi: So what do we know?

Zakiya: Well, we know HIV stands for the human immunodeficiency virus and has been around for a long time. It's been about 40 years since the first case of HIV was diagnosed.

Titi: We also know that HIV is the virus that causes AIDS, so that's similar to how SARS-CoV-2 is the virus that can lead to COVID 19.

Zakiya: And HIV affects a lot of people, so about 37 million people worldwide have HIV, and about 1.2 million of those are Americans.

Titi: And we know that HIV is a virus that attacks the body's immune system, and if it goes untreated, it can lead to AIDS. So currently, there's no cure for HIV, but there are ways to control it through treatment that allow those living with HIV to have long, healthy lives.

Zakiya: So what do we want to know?

Titi: I think I want to know how is the vaccine development for HIV different from other types of vaccine development? We've talked about vaccine development in previous labs, and so I'm curious if it's the same. Is it different? And if it's different, how is it different?

Zakiya: And I think before we can even get to vaccine development, I need to know some basic biology about HIV. What's it looking like? How's it working? You know, I think we have to kind of understand those things before we know how we're going to stop it in its tracks. I also want to know the timeline to getting here. We didn't just start trying to make a vaccine. First there were medicines made available that now feel like super medicines compared to what may have seemed possible in the 80s. So there are things that can make HIV undetectable and thus non transmissible.

Titi: And why is this virus so different from other viruses that it's taken so long to develop a vaccine?

Zakiya: COVID got us wanting the vaccine in two years every time.

Titi: Yes, hyperspeed.

Zakiya: But this is a very good question, Titi.

Titi: Let's jump into the dissection.

Zakiya: Our guest for the next two labs is Dr. Christine Daniels.

Dr. Christine Daniels: My name is Christine Daniels, and I recently finished my postdoc at Duke University's Human Vaccine Institute.

Zakiya: Christine's work focuses on developing and testing novel or new vaccine candidates.

Titi: Christine is another one of me and Zakiya's actual friends in real life. We always tell you we know some very smart people. We all went to Duke at the same time, and so you might hear us call her Christine, but it is definitely Dr. Daniels. OK, so first things first, let's talk about the HIV virus and to understand what it is and how it works. We asked Dr. Daniels to explain it to us in the context of SARS-CoV-2, the virus that causes COVID 19.

Dr. Christine Daniels: So broadly speaking, HIV and SARS-CoV-2 are very similar.

Zakiya: Let's start with their structure. HIV and SARS-CoV-2 have a pretty similar structure.

Dr. Christine Daniels: They're both envelope viruses.

Titi: This means that the virus is surrounded by an outer shell.

Dr. Christine Daniels: They're both express their glycoproteins or their spike proteins per se on their surface.

Zakiya: So that an envelope or outer shell of the virus is covered in these little spikes or proteins. And those proteins have little sugars, that's the glyco-, attached to them. And those proteins allow the virus to bind or dock onto host cells, and that leads to infection.

Titi: And HIV and SARS-CoV-2 are also similar in terms of their genetic material.

Dr. Christine Daniels: They're both RNA viruses

Zakiya: And this means that they have single stranded RNA or ribonucleic acid as their genetic material instead of double stranded DNA like human cells have.

Titi: So in each HIV particle, you've got RNA inside surrounded by the envelope with a bunch of little spikes all over called glycoproteins.

Zakiya: And so when HIV enters the bloodstream, it makes contact with the cell. Those little spikes are attaching to the surface, and they begin to fuse with the host cell. This allows the center of the HIV particle that RNA to go right into the host cell and to get converted back into DNA. So now you've got viral DNA in your wholesale. So from there, the host cell is hijacked by HIV and begins to make more HIV particles inside the body.

Titi: But our body has an amazing natural defense when it comes to fighting off viruses, the immune system. And when our immune system senses that there is an intruder, it can unleash a swarm of targeted and general antibodies that will attack the virus, neutralizing it.

Zakiya: So remember those spikes we talked about covering the outside of the virus? Those glycoproteins are what specifically targeted by antibodies.

Titi: So SARS-CoV-2 and HIV viruses are structurally so similar. In fact, the decades that have gone into developing the HIV vaccine made it possible to develop the COVID vaccine so quickly.

Dr. Christine Daniels: Because they're so structurally similar. We're able to leverage the structure base a vaccine platform to design a vaccine for COVID 19.

Zakiya: So understanding what the virus looks like structurally, what happens when it gets into your body, how are vaccines disrupting this process? How do they work? Dr. Daniels gave us a great analogy. She thinks of a vaccine like a mug shot. The vaccine is going to tell your body, Hey, this is what you're looking for. This particle looks like this. It has this certain protein on it. When you see it, you know what to do. All systems go.

Titi: Now that we know generally how the HIV particle is structured and how vaccines work in general, how would an effective HIV vaccine work?

Dr. Christine Daniels: My lab specialized in protein design and expression, so we use what we know about how the natural virus is structured and its modes of infections in order to design synthetic versions of it that mimic the virus but aren't infectious. And using what we know, we're able to modify these synthetic versions of the virus to help increase the body's chances of recognizing them, basically, instead of trying to redesign a fake version of the entire virus you just take the piece of the virus that your body sees and develops an immune response against

Zakiya: And that piece of the HIV virus that your body sees. That's those spike proteins we talked about that are spread out all over the envelope of the virus, the glycoprotein.

Dr. Christine Daniels: So you have this big virus and you have these proteins spiking all over the surface. We just take one of those spike proteins and we just want to show that to the body so the body focuses on the right region.

Zakiya: The problem is, though, there's sometimes just one little piece isn't enough for the body to generate a strong immune response.

Dr. Christine Daniels: And so what you can do is you can attach that piece, so that spike that envelope protein, onto a nanoparticle and you can display multiple copies. So it's kind of like a mini virus. And also, the nanoparticle itself is composed of materials that will also activate your immune response. So you get a robust immune response because you're showing multiple copies of the right target and then you have something else that stimulating supporting cells to help enhance the immune response.

Titi: All of this is blowing my mind. So Dr. Daniels works on creating a copy of the envelope of an HIV particle covered in those glycoprotein spikes that your body will recognize and develop a defense against. And by the way, SARS-CoV-2 vaccines, you know, Moderna, Pfizer and Johnson and Johnson, they may have different strategies, but they all are working towards the same goal to help your body create a strong immune response against the coronavirus spike protein that surrounds the virus

Zakiya: And antibodies are one part of that immune response. Antibodies are tiny proteins that help your body recognize and clear foreign toxins, bacteria, and viral particles.

Titi: So they like the bouncers outside the club.

Zakiya: Yes, that's perfect. And Christine mentions neutralizing antibodies, and if you play on that bouncer metaphor, neutralizing antibodies are binding to the outside of a viral particle so that those spike proteins can't bind to any host cell. So it's like if the bouncers make a circle around you, right? A

Titi: I've seen it happen. Not to me but ive seen it.

Zakiya: It's like when I pick you up, when they hold the arms and legs and carry you out the club, that's a neutralizing antibodies are doing.

Titi: I've seen that happen to some people. It's pretty embarrassing.

Zakiya: They say your evening is over.

Titi: It's time to retire to the boudoir.

Zakiya: This is really amazing work. It feels like something we would do if we had a lab together. Yeah, biology with nanoparticles.

Titi: Oh yeah, we'd be all over it.

Zakiya: Man, This must be really challenging work, though.

Titi: Yes, I don't want to pretend like I know how to do everything with nanoparticles.

Zakiya: Same. Same same.

Titi: But it sounds I'm so cool. I would love this.

Zakiya: All right, we're going to take a break. But when we get back, we're going to talk to Dr. Daniels about the progress we've made so far towards an effective HIV vaccine and how far we have to go .

Titi: OK, we're back, and right before we went to break, we talked about non neutralizing antibodies, neutralizing antibodies and everything in between, but if you want to know more about that, make sure that you tune in to our episodes in the new year where we're talking all about the immune system. And before we get back to talking about the HIV vaccine, Zakiya, what's on tap next week?

Zakiya: Next week, we're continuing our conversation with Dr. Daniels around the development of an effective HIV vaccine. But we're going to shift the lens just a little bit from the science to the people.

Titi: Because we know science doesn't happen in a vacuum. So we'll be talking through the social context around HIV over the past 40 years and the people who are affected most. All right, let's get back to the show.

Zakiya: So here is what I want to know. We understand the similarities, and we understand that work on the HIV vaccine could have provided some scaffolding for process and distribution and other developments with the COVID 19 vaccine. But the COVID 19 vaccine got up and running pretty quickly. And we know, you know, a lot of people were working on it. A lot of resources were poured into it. What's been taking the HIV vaccine, which has been in development for many decades, what's been taking this so long?

Dr. Christine Daniels: So COVID was developed really quickly because it's an easier pathogen to design a vaccine against.

Titi: So even though HIV and SARS-CoV-2 are structurally similar and are both RNA viruses that use RNA as their primary genetic material, a major difference is that SARS-CoV-2 doesn't mutate as frequently as HIV.

Dr. Christine Daniels: HIV mutates incredibly quickly. It can incur about 10 mutations per replication cycle, and the replication cycle is less than 24 hours.

Zakiya: Scientists have estimated that one mutation of SARS-CoV-2 is established every 11 days or so. So now we're looking at HIV having a mutation rate that's four times that of SARS-CoV-2.

Dr. Christine Daniels: So developing a vaccine that's able to accommodate all of that variation. It's just really hard to do. So the way that we tried to do that is by designing vaccines that are based on the conserved portions of the HIV virus. And so even if the virus mutates, those are regions that don't mutate as frequently. And so if you get a response against those sites, then you

can likely be protected against a wide range of viruses. So that's the approach. And theoretically, you know, that should work.

Titi: The other challenge for developing an HIV vaccine is the length of time of infection. The infection window for SARS-CoV-2 is much shorter than HIV, and like we said before, once someone is infected, that person has HIV for life, with very few exceptions.

Dr. Christine Daniels: So an HIV infected individual can live with HIV and not experience any symptoms for a long time, even though they're infected with virus and it's infecting the body and not display symptoms until they're very sick.

Zakiya: That also means there's a much longer window for HIV to replicate inside your body.

Dr. Christine Daniels: So it can mutate, but it's less probable just based on that time window and amount of times it would have to replicate in a person within that time window.

Titi: And lastly, HIV is particularly elusive because it's able to essentially hide itself from the immune system until it's too late. HIV is covered with these sugars called glycans. The glycans can attach to the envelope that hard candy shell of the virus and effectively hide the spike proteins from any suspecting antibodies. So that's the challenge.

Dr. Christine Daniels: How do you generate a response that is able to learn to bind or evade those glycans to target the site?

Zakiya: That's really tricky because cells in our body naturally have glycans all over them. So your immune system isn't going to kick into gear when it sees glycans, because that would mean you're essentially attacking yourself.

Dr. Christine Daniels: So in order to generate an effective HIV vaccine, we need to figure out a way to generate antibodies that are able to bind to the glycans and to the protein at the same time. So that way they won't be auto reactive, and that's just hard to do.

Zakiya: I have a new appreciation for the challenges associated with vaccine design against HIV.

Titi: Right. Imagine trying to do a puzzle, and every time you go to put a piece down, all the pieces change their shape.

Zakiya: Or they're saying you basically got to put it down to pieces at a time glycan and protein.

Titi: Yeah, it's no wonder this vaccine is so hard to develop.

Zakiya: But you know, vaccines aren't the only line of defense. Prep, which is pre-exposure prophylaxis, is the medicine that people can take to prevent getting HIV. So when you take Prep as prescribed, it will reduce your risk of contracting HIV from sex by about 99 percent. That's a huge drop.

Titi: Prep works by setting up fortified walls around the cell that HIV is trying to infect. So those spike proteins can't bind and infect, and as a result of that, they can't replicate inside the host cell.

Dr. Christine Daniels: It's great because if people take it every day, then it reduces their exposure to infection. However, they have to take it every day. Simply stated, you can think about it like something such as birth control. Birth control, like if you're taking a pill, it's usually like 90 to 97 percent effective. If you take it according to the instructions, the instructions say that you have to take the pill at the exact same time every day in order for it to reach efficacy. For the people that use this type of contraceptive, how many times have you not taken it at 2:02 p.m. every day? How many times have you missed a day? If you think about vitamins, do you take your vitamins every day regularly? Do you go to the gym every day regularly? All of these behavioral things that we know will positively impact our health and the longevity, our quality of life.

Zakiya: Remember Titi's shoes?

Titi: Yeah. If you didn't hear the shoe story, go back and listen to the lab right before this one.

Zakiya: Where we talk about, you know, forgetfulness. Consistency. Taking a pill every day for the rest of your life can be costly, like a lot of people might not have access to the resources or insurance that allows them to get that medication consistently.

Dr. Christine Daniels: So we need a vaccine because a vaccine will go to healthy individuals before they have any potential for exposure and prevent them from being infected. You take the full regimen of the vaccine and you prevent it from ever getting the virus in the first place. So even if there's few instances, the breakthrough majority of the population will be protected, so they will never have to do that every day treatment or everyday preventative pill.

Zakiya: I'm really interested in where we are now as we learn with COVID. Getting the vaccine approved and on the market can be a very involved, expensive and time consuming process.

Titi: OK, so once a novel or new vaccine candidate is developed in a lab, it goes through a really rigorous evaluation process where it's tested for safety and effectiveness in humans before it's licensed for use. And this includes several different phases of clinical trials. You probably remember hearing about that with the COVID vaccines, too. So we wanted to know from Dr. Daniels, where are we at in terms of progress towards an effective HIV vaccine? Are we close?

Dr. Christine Daniels: Learning from my predecessors, I'm not going to say a timeline. What I will say is that we are having promising results from studies that suggest that we may be on the right path.

Zakiya: I'm sure it's hard to predict because historically the HIV vaccine has been pretty elusive.

Titi: In 1984, when HIV was first determined as the cause of AIDS. The United States Health and Human Services Secretary, Margaret Heckler, said that she believed a vaccine for HIV would be ready for testing in two years.

Zakiya: There have been multiple trials in different phases through the years. Most notably, VaxGen got FDA approval for the first large scale phase three clinical trial of an HIV vaccine in 1998. That vaccine was called Vax 004, but it ultimately failed. For a deep dove on that check out the June 2nd episode of Gimlet podcast Not Past It, which really breaks it down.

Titi: But there was a clinical trial in 2009 with positive results.

Dr. Christine Daniels: So to date, the only effective trial has been the RV144 trial that was done in humans, and it led to about 30 percent protection.

Titi: The RV 144 trial was a partnership between the United States and the royal Thai government from 2003 to 2006. Over 16000 people volunteered to receive a two vaccine combination, one prime and one boost. When the results were released in 2009 with a 32 percent efficacy rate for preventing HIV, it became the only trial that had any evidence of effectiveness and remains so to date. You need a much higher efficacy rate to get approval. But there were some really valuable learnings from this trial

Dr. Christine Daniels: That enabled us to learn a lot about what type of responses are necessary. That's kind of when we learned a lot of information about the fact that neutralizing and neutralizing antibodies contribute to the response.

Zakiya: And people have followed up on the things that were learned from that study

Dr. Christine Daniels: in terms of like more recently, the preliminary results from a lab from Scripps that showed that they were able to elicit precursor antibodies that may have that breadth and potency that we want to elicit from neutralizing antibodies and 97 percent of their participants. And so that's really promising. It's not a final result, you know, it's not elicited neutralizing antibodies, but something that has the potential to become a neutralizing antibody. And if that happens, that would jump to the front of the line as a candidate.

Zakiya: So this feels like we are trending in the right direction.

Titi: Yes, all of this information from Dr. Daniels has made me very excited about the possibilities

Zakiya: But I think if we've learned anything over the past two years, it is that we are not blank canvases for scientific advances. In that it is going to take a lot of understanding of social dynamics and just situating this research in the context of what's happened before and what's happening today.

Titi: Right. I think that is such a great point because with all that we knew before the pandemic hit, a lot of us thought that once the vaccine came out that everyone would be willing to take it,

and that wasn't the case. So when I think about the HIV vaccine, I wonder what pushback there might be from the general population.

Zakiya: Yes. And you know, even though it is a short history, it is a very complex history full of medical neglect and mismanagement in the early stages by research institutions. And so I think there is a lot to unpack and even just day to day general rumors that we kind of mentioned at the top of the episode. How will that affect how people receive new advances as it relates to HIV? So it's time for one thing, I want to know what's been on your mind or what you're loving this week, Titi.

Titi: For me around this time of year I think the feels are always the same. So my one thing this week is friendship. This time of year always feels difficult for a lot of people, for a lot of different reasons. Some people are far away from the people that they love. Some people have lost people that they love, and I think that friendship, family, framily, whatever you want to call it, your chosen family. I think that it's always super important to tap into those networks. And so that's what's been getting me through this week is my friends and my family. So that's my one thing.

Zakiya: I love it.

Titi: What's your one thing, Z?

Zakiya: The my one thing this week is kind of along those same lines. I've been doing a lot of reflection and having all the feels, and I've been using these prompts called Moon Lists. They're on Instagram, but you can also find them, I think, at MoonLists.com and they're just open ended prompts to help you think and reflect on how you're feeling. I think I talked about the Day one journaling app before, but it's just something to help you kind of start to think about what's going on on what you care about, how you're orienting in the World Day to day.

Titi: That sounds really cool. So Moonlists.com, I'm putting it into my search engine right now.

Zakiya: That's it for lab 042. What did you think? Call us at202-567-7028 and let us know

Titi: We'd also love to hear from you for an upcoming series we're working on for the New Year. We want to know about your New Year's resolutions for 2022. Are you making a list or did you skip the resolutions altogether? What are you focusing on? We want to hear from you. Call us at two zero two five six seven seven zero two eight and leave a message.

Zakiya: And don't forget, there's so much more for you to dig into on our website. There will be a cheat sheet for today's lab, additional links and resources in the show notes. Plus, you can sign up for our newsletter. Check it out at DopeLabspodcast.com!

Titi: Special thanks to today's guest expert, Dr. Christine Daniels.

Zakiya: You can find her on Twitter and Instagram @nAh_mino.

Titi: And you can find us on Twitter and Instagram @DopeLabspodcast

Zakiya: Titi is on Twitter @dr_tsho

Titi: and you can find Zakiya @zsaidso.

Titi: Dope Labs is a Spotify original production from Mega Ohm Media Group.

Zakiya: Our Producers are Jenny Radelet Mast and Lydia Smith of Wave Runner Studios

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Zakiya: and Zakiya Whatley**.**

Titi: That's great.

Zakiya: One take Jake... This time.