‹ All episodes

The UMB Pulse Podcast

An Inside Look at COVID-19 With Coronavirus Researcher Dr. Matthew Frieman

September 02, 2022 Professor Matthew B Frieman, PhD Season 2 Episode 9

The UMB Pulse Podcast
An Inside Look at COVID-19 With Coronavirus Researcher Dr. Matthew Frieman
Audio Player

00:00 | 54:25

Rewind Speed Chapters
Chapters

The UMB Pulse Podcast
An Inside Look at COVID-19 With Coronavirus Researcher Dr. Matthew Frieman
Sep 02, 2022 Season 2 Episode 9
Professor Matthew B Frieman, PhD

What is it like researching COVID-19 — the disease that has changed the world? And where do we go from here? University of Maryland School of Medicine Professor of Microbiology and Immunology Matthew Frieman, PhD, takes us on his journey in this supersized episode to researching coronaviruses (2:41), the future of therapeutic medications battling COVID-19 (20:38), and what we should expect this fall (49:09). We also hope we didn't jinx Dr. Frieman about COVID-19 (16:42), and ask him what keeps him up at night: variants, new viruses, or a return of an old virus (39:01).

What is it like researching COVID-19 — the disease that has changed the world? And where do we go from here? University of Maryland School of Medicine Professor of Microbiology and Immunology Matthew Frieman, PhD, takes us on his journey in this supersized episode to researching coronaviruses (2:41), the future of therapeutic medications battling COVID-19 (20:38), and what we should expect this fall (49:09). We also hope we didn't jinx Dr. Frieman about COVID-19 (16:42), and ask him what keeps him up at night: variants, new viruses, or a return of an old virus (39:01).

Matthew Frieman: 0:04

You're listening to the heartbeat of the University of Maryland, Baltimore, the UMB Pulse

Charles Schelle: 0:16

Welcome to the UMB pulse. I'm Charles Schelle. Jena Frick is on vacation, but we do have Danna Rampolla

Dana Rampolla: 0:22

Hi, Charles. I'm here.

Charles Schelle: 0:24

Hi, Dana. Thanks for joining me, because I need all of your brain power for this heady episode. So we're going to be talking to Dr. Matthew Frieman. And we're going to be really diving into what is it like being a researcher on a virus that has reshaped how we go about our lives. And where do we go from here to treat COVID-19? Dr. Matthew Frieman is an internationally recognized biologist and microbiologist here at the University of Maryland, Baltimore, which is Maryland's public health law and Human Services University. He spends time teaching Microbiology and Immunology, as well as dedicating a great deal of time, energy and expertise working in Coronavirus research.

Dana Rampolla: 1:01

Frieman is one of the nation's leading researchers on highly pathogenic coronaviruses having published dozens of research studies over nearly two decades on the inner workings of these viruses, and how certain viral strains led to outbreaks of SARS and MERS. Recently, his research is focused exclusively on developing vaccines and treatments like monoclonal antibodies for COVID-19, which is caused by the SARS-CoV-2 coronavirus. To name just a few as of his accolades Dr. Frieman was awarded the UNC Chapel Hill postdoctoral award for research excellence. And a few years back, he was named The Daily Record Innovator of the Year and multiple times he has earned the teaching commendation for Host Defenses and Infectious Diseases here at UMB. We're going to talk and a little bit about how Dr. Frieman's life journey led him to be in the right place at the right time in 2020, when the world shut down, and we're also going to delve into a discussion about what the last couple of years have been like since the onset of the COVID 19 pandemic for him specifically. And then later, we'll learn what Dr. Frieman anticipates lying ahead for our country and the world at large in terms of Coronavirus and its variants. So Dr. Frieman, welcome. Thank you very much. Did you have to take off your lab coat and run down the street to get here?

Matthew Frieman: 2:15

It was it were a little across the street, but it was all good. No problem at all.

Dana Rampolla: 2:19

Good. Good. Well, we are super excited to have you here. And I'm hoping that you're going to help us understand the nuts and bolts of coronaviruses. But before we get to that the University of Maryland School of Medicine, which we should explain is just one of the six professional schools and the Interdisciplinary Graduate School that make up the University of Maryland, Baltimore, or as we like to casually call it UMB. So Dr. Frieman, how long have you been at UMB? And tell us your journey? What, what led you to ultimately study coronaviruses? Did you, did you just as a little boy love science and that brought you to this this end?

Matthew Frieman: 2:54

So I've been here at University of Maryland, Baltimore for since 2009 where I started my lab here as assistant professor. I grew up in Baltimore actually I grew up in Owings Mills. I was kid. And then I went to, I really started my science journey in high school. So I was always a math and science kind of kid. My parents always wanted me to be a doctor and I didn't really like sick people. So I did not want to be an MD. But I really had a really longtime interest in genetics and something along those lines. I didn't really know what that meant when I was in high school. And then before my before I went to college, I spent a summer at Brown in a summer genetic engineering program for three weeks and I was hooked. So it was I got to be in a lab and use a pipette. One of these little dropper things we use to move things around the lab liquids around. We played with plasmids and bacteria, and it was just great. And so when I was applying to college, I went to Washington University in St. Louis, which is essentially as far away as I was allowed to go. And I worked in a lab there all four years. So I got into a summer program and I was there before freshman year. It was not in a virus lab. It was in a plant biology lab. And I had a fantastic mentor. A guy named Craig Picard who was just a great lab to be in it was

small, worked on plants in a great kind of very diverse biology department right at undergrad. And it was it was wonderful just to be in that place where they really enjoyed science enjoy doing it. I learned how to you know the hard parts about science, the fun parts about science, and was very clear. That's what I really wanted to do for the rest of my life.

Charles Schelle: 4:26

So how do you go from plants to coronavirus?

Matthew Frieman: 4:29

So that was the next step. So -err- two steps. So after undergrad I was applying to schools. And I ended up back at Hopkins. So back in Baltimore. So I applied to a bunch of graduate programs and ended up working at Johns Hopkins University in the School of Medicine in there in a lab by a guy named Brendan Cormack. It was a yeast lab so not to viruses yet. And it was a very basic cell biology use lab. It was great again, wonderful PI. It was his first grad student. And I could kind of have all these really cool questions to ask that had to do with the yeast question working on, which is basically how one of the kinds of proteins in the yeast get to the outside of the cell. And from there, well, so when I was an undergrad, I met my current wife, Jill Ann Fahrner, who is now a assistant professor at Hopkins, in the Clinical Genetics department. And she was doing her MD, PhD. After undergrad, she went to UNC Chapel Hill, and I went to Baltimore to Hopkins. We stayed together, amazingly enough, and she was able to do her PhD at Hopkins. So I was still there. And we were still together. We got married in Baltimore, actually, we got engaged in Baltimore. She's from St. Louis. We got married back at WashU on campus, and when we were both graduated with our PhDs, we were going back to to North Carolina for her to finish her MD, the third and fourth year for MD from MD PhD. And I interviewed a bunch of labs. Some there was one yeast lab in immunology lab, but really basic biochemistry lab. And one of them was this guy named Ralph Baric, who worked on coronaviruses. This was 2004. And when I when I eventually moved the SARS Coronavirus, one the original SARS outbreak was in 2000 to 2003. So it was right after the outbreak. He had all kinds of tools to work with in the lab. He had funding and I had been working on very basic biology and I wanted to do something more applied. And so I joined his lab in 2000 for working on SARS Coronavirus, one or SARS Coronavirus, as we call it at that time and have really have miraculously stayed in the field since then.

Dana Rampolla: 6:33

That's interesting. I can only imagine what your dinner table conversation looks like.

Charles Schelle: 6:37

We have we have right now we have a 13-year-old daughter a 10-year-old son and they are the most well educated on Coronavirus, biology and genetics little kids I think that exist in the world rightnow. That's awesome. That was wondering if maybe the two of you have like a double helix in your wedding bands or something.

Unknown: 6:55

No, we don't. We don't but we certainly do talk shop at home a lot. So as as hard as it is to run a lab. It's hard to run husband and wife both to have labs and and my wife sees patients as well. So we both rely on each other for a lot of help and talking ourselves off the ledge a lot of times at the end of the night when we had a rough day.

Dana Rampolla: 7:15

Well, you mentioned a minute ago that that that was SARS Coronavirus-1. So Where where are we now tell tell me about how you've been in the lab how you've done your research and I know that we're a couple of iterations beyond one right.

Unknown: 7:31

Exactly. So SARS Coronavirus-1 emerged in the outside of Hong Kong in the Guangdong Province of China in 2002. In 2003, it went away so it was extinct. It doesn't exist in the wild anymore in its current form. The virus is being used in labs. So we study in the lab as as a model to understand these really highly pathogenic Coronavirus. One of the other things that really is important is that we knew about coronaviruses before SARS-1 so there was four other or at least before SARS-1 there was two other seasonal coronaviruses that give us a cold in the winter. We knew about they have just weird names, so I won't even mention them. But after SARS one people started looking for other coronaviruses and they found two other ones that happen to be also around in people that we didn't even know existed until then. So there were discovered but have been there a while. And so we knew after SARS, one that we had four other seasonal coronaviruses that give us a cold in the winter. So and they just have mild you know we get a runny nose. It's not flu, it's not rhinovirus or RSV. It's another cold and that about 30% of the viruses are coronavirus is when you get them in the winter. And so in so I humbly was working on SARS coronavirus, one when I was here and started my lab. And then in 2012 another coronavirus emerged called which we now called MERS, which is Middle East Respiratory Syndrome Coronavirus. And it was it a it emerged from Saudi Arabia where the first cases were identified. And so that virus turns out to be very different in the same general family as SARS-1 and SARS-2 but a pretty different virus. It's endemic in camels, it turns out been there for decades. And it luckily it only it only jumps to humans very rarely. So there is human, camel-to-human spread. It's in the kind of in the nose and the nasal passages of camels. So you get kind of snotty camels and they can spread it to people. But it doesn't spread very well person to person, which is good because it's about 35 percent lethal when it does. So that one was also just as I was getting my lab going and really understanding how to be a professor and have a lab myself and we have a new virus kind of jumped dropped in our lap. And so we of course worked on this new Coronavirus for a while including SARS one and we were happily working on both of those for many years. We started working on influenza flu in my lab also. And then in December 30 2019 There's a report out of out of China. I know that there was this strange emergence of cases that were retrovirus restoration origin in Wuhan. And ever since then, it's been a very strange ride. And hopefully, we're doing good work in the lab.

Dana Rampolla: 10:16

So what in terms of literally being in the lab has anything changed for you in terms of like, the precautions you take how you're conducting your research?

Matthew Frieman: 10:26

So the biggest difference now is that people care about what we do. So before, before COVID-19, there was very hard to get funding for this, this family viruses, there was a bump of funding for SARS one, so in the Coronavirus field, and then there was a bump of funding after MERS in 2012. But otherwise, after that, it was very, it was very hard to get money. And so one of the really dramatic changes is that now people care about this family of viruses. And so we have we're well funded, that allowed me as a as a professor to expand the lab. So we went from three people to 12 people over the last few years. And we've been able to do all kinds of really, I think impactful things where my basic -- my love is in basic biology, so we study kind of the basics of the virus, what the viral proteins do, and how the replication of virus replicates in cells, and in mice. But we've also been involved with all kinds of therapeutics for drug development, and antibody development and vaccine development. That is, I think, been pretty remarkable to be a part of where something we do in the lab really hasn't affected a human, which is not what we were doing before. So this applied part of the lab has been really fun to be a part of.

Dana Rampolla: 11:42

Before we get into more of the technical talk, let's talk a little bit about what a normal day looks like for you. Because if we backtrack, you are also a teacher, you're a professor here at the university, you're doing your research, you've shared with us that you're a family man. So what is the normal day look like?

Matthew Frieman: 11:59

So a normal day, so every day is a little different, which is, you know, makes it interesting. The normal

day is wake up around 6: 12:04

30 or 7, get dressed, get the kids, if it's during the school year, get the kids dressed and off to school. Our kids go to elementary middle school. So we've the last few years have been driving them both ways. And so we, between my wife and I, we kind of trade off our early morning drop-offs no matter whose day it is. And then

usually in lab between 8: 12:28

30 and 9-930, depending on the day. In the last two and a half years, it's been very busy. So a lot of Zoom calls like everyone else in the world, and living yourself in one of these little screens on our computers. And then it really integrated with lab. So I have with all these people in the lab, I meet with everyone once a week, various amounts of time. So it's talking to whoever I need to talk to you that day who was on the schedule, it's pulling them into meetings and phone calls with companies we're working on or other labs we're collaborating with, to share data and talk about results and, and what the plans are for the disk experiments. So it's a pretty busy full day. And then hopefully, I have time for lunch in the middle of the day. And usually my desk for lunch and our home, again, depending on the day, but it's usually by six o'clock. And then dealing with kids for after school activities. And my daughter is a gymnast, she does gymnastics five times a week on a gymnastics team. So we're playing carpool, my soccer play -- my sons play soccer. So we, you know, are spread pretty thin at night, have dinner, and then I ended up working for several hours at night after the kids go to bed until I pass out and you go to bed to

Dana Rampolla: 13:42

Start it all over again.

Matthew Frieman: 13:44

So it's been it's the last, you know, two and half years have certainly maintain that schedule. I think it was I this is essentially the schedule, I worked full time anyway. It's just now gotten a bit busier. And I never thought I would be as busy as I ever was now.

Charles Schelle: 13:59

Yeah, I can't imagine like with something like this, where it's changing, and it's evolving with all the variants. So there's always a little bit of more behavior characteristics you hear about in the news freaks out people in it in a different way. So I'm not sure how you even stay on top that between talking with fellow researchers, or just like being so involved in something then all of a sudden, you're seeing like a CDC news alert, and you're like crap, like what just happened to this virus?

Matthew Frieman: 14:23

So it's certainly been a roller coaster. I think that what we've certainly seen in the last two and half years is just this evolution of this outbreak. From the very beginning of 2020. It certainly seemed like this was going to be a problem. And I don't think any of us rationalized rationally thought that it would be where we are today. But it certainly was going to be an outbreak of some sort. And the early cases in the United States, if you remember were really hotspots of cities. So there's a big outbreak in in, in New Orleans. There's a big outbreak in New York City especially. And we in those early days, you know, as a lot of preparedness, it was trying to figure out what was going on where, who had where the cases were, how bad it was, how the hospitals were handling them, when it was very clear that it was a respiratory virus, and it was spreading very well in the air, how to handle precautions for respirator, you know, aerosol protection, getting suits, getting PPE, so getting all the suits and gloves and masks around the hospitals. And the labs where they needed to be was a big push at the beginning. So I was on one of the task forces here at University of Maryland hospital, to figure out how to handle these patients. Luckily, here locally that experience with ebola patients and ebola training for a long time,

so they kind of knew how to handle this kind of highly pathogenic kind of people. And it was just kind of waiting for this flood of cases early on, that was the, at least the early days. And the mix of being on Zoom and being on phone calls. You know, all day long, trying to figure out what was out there who we're going to work with. Everyone wanted to collaborate. And because there was not very much Coronavirus expertise out there, because the field had been very small. There was a lot of my fellow colleagues and virology and other scientists calling and wanting help. What do we need to know? How do we set up a lab? How do we do this safely? Can we have your protocols for how to work in the lab? We work in a kind of biosafety level three lab and BSL three. So what precautions do you need? What cell lines do we grow this virus and you know, all these things that go along with doing it safely, which was really the early days most important for how to work on this as a scientist, the the really key parts about just getting getting samples and be able to do this in the lab.

Charles Schelle: 16:42

Let's jump to present day and some of the things that are on people's mind. So one topic that's dominating the news right now is this number of people who have either unknowingly contracted COVID or might have somehow avoided it altogether. The White House estimates that about 70% of people have had the virus. Well, first off Dr. Frieman, are you one of the lucky few?

Matthew Frieman: 17:03

I am. I amazingly enough, I've never had -- not I have not been affected. Our whole family held out for a long time and two of them through the family got infected right in June. The other two of us haven't. So it's been a it's been strange. And we easily also could have been infected. So the number could be higher, I easily could have been infected and not known it. Been asymptomatic, not had any respiratory symptoms that were evident and still been infected. So I imagine that there's a good cohort of people that are like that as well.

Charles Schelle: 17:33

Yeah. So how fascinated are you about the people like yourself with their genetics, and what it may mean if they actually have successfully defended this

Matthew Frieman: 17:43

So my wife is a geneticists. So we talk about virus? this a lot. But I think it's actually a combination of things. So its behavior is certainly one. So I'm a vigilant mask wearer. I wear masks at stores, we my kids wear masks in school every day. My wife wears a mask at work all the time. So why. So part of that is certainly behavior based. So putting yourself in places where you're not exposed, you're not at the group's without a mask on is like just one layer of protection is important. I was also vaccinated early on just like everyone else, as soon as I could get vaccinated, we did as soon as my kids get vaccinated, they could, they did. So that was also part of protecting us in that sense. But there's certainly a another level of genetics and immunity that are important for all of this. One of the important things I think for the vaccine response is that just because you get vaccinated doesn't mean you have really high antibody levels in your blood that protects you from this from any of the strains, especially the current ones. So that's why it works as a population base level, not as an individual level. So that's certainly why the push for getting people to be vaccinated as many as possible is important. And it's still kind of hurts to hear people say that they're afraid of the vaccine or don't want to get vaccinated for one reason or the other. Because we need everybody to be protected at some level and if you're not vaccinated, you certainly are going to be infected much easier than someone who's vaccinated.

Charles Schelle: 19:03

Alright, you know, I don't know if I told this story on the podcast before but I think I'm in that population of I'm pretty sure I got it at some point but there was no way to verify that I got it at the time. Because I distinctly remember, it was January of that year. There wasn't any confirmed cases in Maryland. I just traveled back from Texas and I worked for a state agency down the street where people were still going to China for business so between those two factors and where I was around and everything between airports, and I had this very severe I

guess cold if you wanted to call it at the time that put me on the couch where I could like sleep for six hours get up do a little bit of stuff and then sleep for another two hours and just like sleep for eight hours it just felt like you know dead. But but I was like I think I have it but everything's telling me that that I don't have it because nobody else has it. So I was like wasn't sure what to do. So I'm like, Just took you know normal cold medicines, flu medicines and Gatorade and hope to get through it, but not that that should be off the shelf recommendation for anyone listening today, but you know, I'm sure there's a lot of people who weren't sure, you know, was it pneumonia or something else at the time?

Matthew Frieman: 20:14

Yeah, absolutely. And there was very few, very little ability to test early in 2020. There certainly were cases going around. The first ones were in Seattle, and around Washington in Washington State. But because of that travel history, with people going to China and being back again, that easily could have been, you know, early cases, there definitely are a lot of evidence of things going on in January or February when the case numbers were pretty small around the country.

Charles Schelle: 20:38

And so now we have therapies like Paxlovid, and a pre-exposure prophylaxis called, I think it's pronounced Evusheld? And so then we also have drug cocktail. So what do you think about what's going to be in our medicine cabinet in a few years when it comes to battling COVID?

Matthew Frieman: 20:56

So I think we'll be much better prepared than we are now. Right now we have Evusheld, which is the monoclonal antibody. It's actually two monoclonal together. We worked on that one, actually, with AstraZeneca. In the lab, that one is still works against the variants that are out there. Now, a new versions of all these monoclonals are certainly coming out. In the very near future, Eli Lilly has a new one, that's to be coming out soon, we worked on the early Regeneron antibodies, which don't work anymore, because the variants evolved away from them. So there's been a whole series of these and I think they'll only get better and better and broader and broader so that they are harder to escape from, as the new variants emerge, so they should work longer in for variants in the future. For Paxlovid, that's the it's a protease inhibitor. We worked on the early generation of that one with, with Pfizer, and we're working on future generations of them as well. And so that one is also works very well, there's been very few mutations in the site that it binds in the virus to inhibit it, there'll be additional drugs that are coming online in the very next year to, you know, several years, again, that work against multiple things, multiple variants that are very agnostic. So as broad as possible. And all of these, the really important thing is accessibility. So we can work on the lab as much as we want, we can develop new ones, we're on a very large new project developing novel antivirals for a whole bunch of viruses. But the trick is to get them as early as possible in humans. So they need to be easily accessible, they need to be there. And so hopefully, that in addition to developing new ones, the really the production side of it is as important as anything, to be able to have them write the pharmacy when you're sick to get them that day. So you start as soon as you know, you're sick. And that will certainly help in the future.

Charles Schelle: 22:39

Yeah, and it's really interesting with with some of these that you've worked on, they're battling it at different stages, you pre or I guess, during and post, potentially, and they're targeting different types of patients, right?

Matthew Frieman: 22:53

Right. So certainly some of them are only allowed for, for elderly patients or people that are proposed to have suppose to have severe disease. So this is the again, the limitation of with the way you do clinical trials, but also limitation of production and availability. So all these things kind of go into the mix of of needing multiple things on the shelf. Before COVID-19 we didn't have anything ready. We had Remdesivir, which was worked on as an ebola drug, but it also worked against coronaviruses. So it was done my my old bosses lab at UNC Ralph Baric.

Molnupiravir is the other one that's dealt by Merck, that was also actually worked on in Ralph Baric's lab. That was the next to come online. Both of those are injectables, so you have to be in the hospital to get to get them. But as well as the monoclonal you have to be it's an injectable, you have to get an infusion. So the next range are the ones that are easy to take. So pills. So Paxlovid, that is a pill. And all of the ones that we work on in the lab, now are all oral dosed. So they're easy to use. And it doesn't make sense, actually, for us to be developing them and testing them if they're not able to be easily used. A lot. Some of that is chemistry. So you can find ones that work really well. Injectable, but don't work well as an oral drugs right now. And that's just a, just it's really hard to make them work as an oral drug A lot of times, but at least once you find the right target, then you can you can make sure that it's that it still works as an oral drug. So we'll have more of these and layering these on, combining them together, so they're harder to evolve away from is really the future of where we're going.

Charles Schelle: 24:23

Right? Well, yeah, I was about to say you make it sound so easy as you kind of backtrack for a second. But But why is it so difficult, both logistically and scientifically to find that magic pill that everyone's been, you know, hoping for?

Matthew Frieman: 24:36

So the problem is that viruses are smart. They're there. This is the thing I think is most amazing about them. They are the parlance for the neurologists as nature's toolkit. So they've had much longer to figure out how to get around our own cellular defenses, then we knew they existed. So they are very every single part of the virus whether it It's protein that the virus makes the way that the virus gets into cells, the receptor it uses to get in the immune response that they induce how fast they kill the cell, how slow they kill the cell, all of those things go into how our body reacts to them. And they are really magical little things to evolve and to change when we throw up some defense. So just like we're doing vaccines, now, again, the all the vaccines that are out there right now, the spike protein that's in the vaccine, whether it's the RNA vaccines, or the newly approved Novavax vaccine, which we worked on, they are all to the original isolate of SARS. So the SARS-2, so that Wuhan strain, Wuhan-1 strain. The virus is moving around right now this called BA.5, or Omicron, is the spike protein on the surface of the virus is very different than the original spike protein that we all knew about before. And so that's why the current vaccines while they still work, you need higher antibody levels in your blood to be protected against them. And so they find ways around us and it's and you know, kind of making them seem human at some of the by evading us, but they make a lot of copies of themselves, every time they go in a cell, they change a little tiny bit. And the ones that change a little tiny bit in the right way to get around the antibodies that we have, or the drug we're taking are the ones that survive. And those are the ones that are spread person to person. And that's the one that goes around the world. And so all of these variants are kind of lightning bolts in the midst of everybody being infected. And every once in a while you get the right meat from the virus side, you get the right mutation and the right person who's able to spread it to two people or eight people and make it easier and easier for that virus to go. So it's there, they really are remarkable little things. And we use them to tell us as much about the cell and learning new about way new proteins work in the cell and the way the cell grows in response to any kind of pathogen as much as it is helping us to develop therapeutics against them.

Charles Schelle: 26:56

And for some of the therapeutics you're you're working on, or the at the clinical trial stage yet for humans. And can anyone participate at this point, or I guess, sign up.

Matthew Frieman: 27:06

So the ones that we're working on that were developed in the lab are still early stage preclinical development, we have some we have one project in the lab that's working on actually not targeting the virus itself, but targeting the host. So this is a project that actually started as a yeast project. So using a lot of the same tools that I learned in graduate school, I took back in the lab and use them now I won't belabor the point of the details of it. But we basically have a target that we know of in the cells that we've been able to develop a drug against. And we're trying to make that drug better and better. But this project was initially funded by Emergent Biosolutions. So

they have a good home in Baltimore, across the city. And then now it's picked up by a company called Akito Pharma. It's a development project. And so we're working with them and, and other labs on campus to try to make this drug better and better. And maybe eventually, it'll be into humans at some point. That's the goal, certainly. But we have learned a lot along the way about how to target this one type of protein that we're targeting. But it's on the host side, not the virus, so things that target us. And the really interesting thing about that is that going to this idea of broadly acting drugs. It doesn't just work against coronaviruses, or SARS one and MERS and SARS still works against flu, it works against ebola works against Marburg. And so by targeting really these kind of these little pinch points in the cell, you can target a bunch of different different viruses. So that's I think, where one of the other angles in the future is by not just making the drugs that we are developing against the viral proteins better and better, but targeting proteins that are in our cells already. So we can protect against a whole wide range of things exciting.

Dana Rampolla: 28:43

How exactly does a coronavirus of any sort that you've talked about actually result or cause a disease?

Matthew Frieman: 28:51

Oh, good question. So I'll give you the short version. I teach this in a lecture in the graduate school. So I won't give you the long version. But basically, the gist really any virus kind of works the same way. So there they have to get into cells -- replicate. So all of them either stick to the surface of the cell by sticking to the membrane, so I was gonna ask you there is a wide variety and do you see that they'll kind of lipid soap bubble on the outside of the cell, or to a protein that sticks out of the surface of a cell. And then they get inside by a variety of mechanisms. But they're pulled in. Oftentimes they forced their way in and then they dump their genetic material into the, into the middle of the cell in the cytoplasm. So coronaviruses use RNA. Other viruses like cytomegalovirus use C use DNA. But that's what their gene their genome is encoded in. And then after it makes all of its viral proteins and it takes over the cell in a way that that makes more of the virus than the virus leaves. And oftentimes it kills the cell as it's leaving or soon after. So it uses up all the energy that the cell has and the cell dies, or the cell dies on purpose trying to kill the virus. But all of that together leads to an immune response in our, in our, in this case in our lungs. And so you get a tons of virus being made in your lungs, they infect all the cells that are able to be infected by the virus, you get death of those cells, your body recognizes that the cells are dying and it's trying to clean up the debris and all this gook that's in your lungs. Part of that's making more mucus, so it kept it like you cough it up. So that's why you get kind of a cough and as part of it, a lot of it is you get inflammation so you get all your immune cells rushed into your lungs trying to help you clear this thing that's in your lungs. And all of that together makes you feel bad. So you get a whole you know, your everyone has had the flu before it knows it's like a whole body illness like you're you're just exhausted, your joints are sore, your nose is running, like everything just hurts muscle ache. So you people get a wide variety of symptoms from from COVID-19 from SARS Coronavirus-2 the same way. And you really have this whole body response often. Hopefully, for most people, it's short term. So it only lasts a couple of days, or maybe a week. Other people you have a lot of people have a cough that lasts for you know, two, three weeks. And then there's this really strange syndrome called Long COVID, which we don't really understand much about, but we think that it is this inflammatory response to your body's responding to the virus. And that inflammation affects all parts of your body, whether it's your brain and you get neurons that are inflamed and, and parts of your body that's that are inflamed, that really make you kind of this COVID fog that people talk about. It's brain fog. Really tired for a long time. And so there are certainly symptoms you have people have that lose their tastebuds. They lose their taste and their smell. So all of that goes into this really kind of really remarkable response that this little tiny virus, it's really annoying causes in people and to me, of the, from the human side of it. There's such a wide variety of symptoms. in other different virus studies that you've done? Or is that unique to COVID? So it's I mean, you certainly get people get wide variety sometimes to you know, chickenpox or influenza or flu or a regular cold right people can be knocked down for a couple of days or you know, have a runny nose for one day or feel really bad for a week. So one of the really remarkable things about COVID-19 for SARS Coronavirus-2 is that it's we've never seen it before. So we don't have any our body we don't anybody, anybody any antibodies to it in our body. We don't know, our body has no memory response. So if we get infected with flu as an adult, you've been infected with that a couple other times you've been vaccinated, hopefully vaccinated with it over

over your lifetime. So your body can respond fast to that. For SARS Coronavirus-2, we've never seen it before the seasonal coronaviruses that I talked about, they don't really cross react, they don't recognize the antibodies in your your immune cells recognize this new virus. So it's you get this kind of massive response in your body like this is something new we've never seen before. And it throws the gamut at it. And that really is part of this kind of big rapid response that we see, to this really remarkable new thing.

Dana Rampolla: 33:09

I think it's interesting to how some people have such a mild reaction, and especially now I guess it's a byproduct of these new variants. But people have I want to say kind of the same thing that people were getting two years ago to the variants where they've been vaccinated been boosted my son's been vaccinated, boosted twice, and he's gotten COVID for the second time now. And he was terrible. The second time I you know, and my brain is saying, Well, you've had it before, you should be able to overcome it more quickly. But it doesn't. I don't think it manifests the same in one person or multiple people.

Matthew Frieman: 33:45

Right. So there's multiple things going on there. So part of it is that is that just because you're vaccinated doesn't mean you have a good antibody response against the vaccine. Right? So again, this is why you rely on all your friends around you and your close contacts to be vaccinated as well. So as a community, you can limit the amount of virus that's circulating. Part of it is that the new variants are a bit more resistant to the antibodies from the being vaccinated already. And even people who had Omicron in January are getting reinfected. Now with this new strain, we call BA.5, because it's pretty different than the BA.1, which is the one we call the first one. So they're, they're, you know, they're evading our immune response right now. And the other side of it is that if you're depending on your comorbidities, so if you have diabetes, or heart disease, or or you're older, so over 65, all of these things matter in how you respond to any pathogen, especially this and we know all of those groups have generally less response to vaccines as well. So you layer on all of these other issues and you can really, you can the therapies that we have may not be as protective as someone who's, you know, 22 and being vaccinated and you know, as happy go lucky as they can be. So all of this together makes for a very interesting two and half years.

Dana Rampolla: 35:05

Yeah, I bet I bet. Well, important to understanding these diseases has been the development, the characterization and utilization of mouse models of disease for both SARS COVID-2 and MERS correct? So how have the rapid and successful development of these models allowed you and your colleagues to unravel the cellular and physiological basis for disease of these viruses?

Matthew Frieman: 35:28

So we do use mice in the lab, we use them for SARS-1 and for MERS and SARS-1 and we use them for a whole variety of reasons. So one of the basic things is to understand just how what kind of disease these cause. And we always try to relate this to humans. So we can't use humans in the lab. So we use mice. Hamsters are also a model. We don't use them in my lab. But people use hamsters for SARS-2 research as well. They are kind of in the middle between mice and humans in their type of disease, they get they transmit virus really well, which is interesting. So you can follow transmission that way. But for mice, we use them to understand the difference in in replication of these viruses. So some of these variants cause a lot of disease in mice, some don't. Some of that is reflected in humans, and some isn't. So we try to be as realistic about what we can learn in these models, compared to humans as we can, but we use them a lot for therapeutic development. So we've tested a lot of Novavax vaccines in these in these models, we work with them on their vaccine, which is, luckily had EUA approval last month, which is awesome to be a part of that kind of group, work with them on new booster vaccines now to see which ones to switch to. But we do that we do a lot of drug work with Gates Foundation, and NIH and BARDA, and DARPA testing new combinations of drugs in them or repurposing drugs that are on the shelf to see if they will work. So we've done a lot of that with some really cool data coming out now about new drugs that we already know about, but that we've shown are actually very effective against MERS, SARS

and SARS-2. And we do them, we also test them for antibody. So while we do a lot of antibody testing in a petri dish with human cells in a dish, we test them in mice as well to see how well they protect in an animal. And then each one of these is with whether it's a company or with other labs, they're always layered upon other data that everyone else has. So for the same study, so looking at cells, looking in mice, looking at all kinds of immune response changes. And so all of that together really tells us a lot about the viruses, the variants, particular but also the therapeutics.

Dana Rampolla: 37:25

So in reading about some of your your studies online, I've saw that you said that there's a critical piece of the research. And that's the synergy of in vitro and in vivo models. So can you explain what that actually means in lay terms?

Matthew Frieman: 37:40

Sure. So that was kind of what I was getting at. So the in vitro is all of the cells in the cell culture that we do in a petri dish. So we have cell lines that grow either infinitely in a dish so we can keep growing them and growing them or growing them. We have cells that actually look like little lungs. So we have, we're working actually with a scientist named Meg Scull, who's a professor at University Maryland, College Park, she has a model where she can take human lung cells and grow them, basically, in a little, well, a little petri dish, where there's air on the top, and there's media on the bottom, just like in our lungs, and they look like mini lungs. And so we can affect those cells, and then test drugs and therapeutics, but also really look to see how those cells that look like the inside of our lung, they have cilia that beat back and forth. And they have mucus, and it's actually really, really interesting and cool to look at. They, how they respond different viruses and variants to see if any of the new variants are kicking off a different immune response. Or maybe they're quieter, so they're maybe have less immune response so that they can cause illness, but not make us feel as sick but still spread easier. So we don't know we're sick longer. So all of these things are kind of how we use the cell culture models. And then the in vivo side is mice. So that's the mouse models that we use in the lab to figure out what these things really do in in an animal.

Dana Rampolla: 38:59

Interesting.

Charles Schelle: 39:00

Yeah. You know, with everything that's going on with with how COVID-19 has changed, and then the, I guess, the return of some other viruses, you know, observers thinking like it's almost like a game of like, date marry dump where it's like all the all three things are almost like inevitable, but between the possibilities of a harmful variant, the return of monkeypox or a polio or brand new virus that we haven't heard of, you know, which one kind of keeps you up at night?

Matthew Frieman: 39:32

Well, I certainly I think we're not working on anything else other than coronavirus. And so that's certainly the one I'm I'm worried about the most. I'm not as worried about polio. This, you know, there's been a small outbreaks in New York, I want people to get vaccinated. I certainly think that all of these things show that that educating the public about science and what we what they should know about from their own human condition and to get vaccinated are things that we have very good vaccines for, is, it's hard to watch people who don't want to do that for their benefit. So that's certainly difficult to see that people don't get vaccinated for polio. Even when there's a very safe and good vaccine that we can use for it. Monkeypox is certainly not something that was on my 2020 list of 2022 list of things that were going to come out. There's been a series of outbreaks in West Africa over the last five years, and we should have been paying more attention to these kind of things. Unfortunately, we weren't because they weren't on our doorstep. But now they are. And we're seeing a really large cluster of cases around the world with monkeypox. Again, the good thing for monkeypox is that we have a

vaccine, we have a smallpox vaccine that works. It's not like the old kind, where you get a scar on your arm,. It's injectable, and you get a good response to it. So the doses are finally being released and spread around the country in the US and the world. To be able to vaccinate people that should be vaccinated against small against the smallpox vaccine protects against monkeypox. We also have a good drug that works on monkeypox as well. There's not as many doses, but people should certainly be vaccinated for against with a smallpox vaccine if they're in one of these groups that is more susceptible or more affected by it. And where we see clusters of cases. So all of these are not good things. They, they, they certainly are things that we need to follow. And I worry as school gets back in session and especially monkeypox as colleges get back in session where it's seems to be, it's certainly connected to close skin contact and sexual contact. So colleges are not the best place for people making smart decisions. So I worried that we're gonna see a lot of cases as colleges start up again. But there's always this extra thing that's out there. So things that we don't know about just like SARS-2, and I would give talks all the time talking about SARS-1 and about MERS and saying that we need to prepare. The reason we work on these things is because we need to prepare for the next one. And we had that happen for SARS-2. And we had three coronaviruses in between 2003 and 2019. So 16 years, we had three emerging highly pathogenic coronavirus has come out, we stopped the last. And so again, like we're need to prepare for the things that are coming in the future that we don't know exist yet. But at least we can work on the things that we do know exist and prepare for those families of viruses that are going to come later.

Charles Schelle: 42:31

Right. So how do I guess quote unquote, we prepare like is that a a an onus on the scientific community or government response or mixture of all the players and getting ready for either, you know, the return of a classic or a variant or something new?

Matthew Frieman: 42:50

So there's multi pronged approaches. So part of it is research. So we keep doing what we're doing. We try to make the animal models better. We try to develop new therapeutics for things that we know. One of the big pushes on at least for the coronavirus side is to make vaccines that are pancoronavirus. They work against all kinds of coronaviruses. We know that there's animal coronaviruses out there, there's bat coronaviruses, where clearly SARS-2 came from. And there are so we want things to work against the things that aren't new people yet that we know that there's a hotspots of jumping into humans, and we want them to work against all of these kinds of things. But the other part, which is as important, if not more is the public health side of this. So we have to build public health infrastructure to develop clinics and distribution networks. And really just the public health officials that are involved with the response, like on the ground, the COVID-19 pandemic has been really bad for them, it's been really hard. And there's been a big loss of people that are public health workers over the last two and a half years, whether they're nurses and doctors and hospitals that have been burnt out over this crazy response, whether it's people who are out there trying to do vaccine campaigns and just been, you know, parts of the country, that door shot in their face, and they just don't want to do it anymore. All of that's really hard. And the US has had a, you know, based around the world, even a, you know, potentially a Okay, response, a lot of fault. But okay, a lot of parts of the world aren't nearly as where we are they don't have doses of vaccine, they don't have anything. Right. And so it's really I think, we we have to think more than just in our neighborhood, but still protect people on at the same time. So I think that it's going to be we're not, you know, we you know, there's some people who say we're in a worse position now than we were before. I think we know more. And I think it's certainly people are more vocal now than ever before about the difficulties that came with this outbreak, and both political response and, and community response. So if it ever happens, again, where we have this kind of really global response and pandemic that at least we know where the problems exist. I don't -- I'd be surprised if we find new problems. That's not true. I'm sure there'll be new problems. But I think that we know of the problems that exist. And hopefully, we have people around and the guts and the money and the funding and the support to really fix those problems.

Dana Rampolla: 45:12

Let's change gears for a minute. Before we sign off, the University of Maryland School of Medicine was awarded $1.25 million in matching funds from the Maryland Innovation Initiative Fund administered

administered by the Maryland Department of Commerce. Can you tell us how this number will increase when combined with private philanthropy and what those funds will be dedicated to? And will it help your research any?

Matthew Frieman: 45:36

Absolutely. So we're really excited about this. And only part of that goes to us but we're the. Part of this goes to, is matched by the it's called the Alicia and YaYa Foundation. So I'm the officially the are soon to be officially the Alicia and YaYa Foundation Professor of Pathogen Research. It starts the Center for Pathogen Research that I'll be heading. And it was basically it was provided by Debbie and Marco Chacoan, who are incredible supporters to the university. Marco was the CEO of Paragon, which is right here in the BioPark are now was bought by Catalent. And I've known him for several years, even before SARS-2. And so that work will go to part of that money goes to where the money for us goes to an endowed professorship for me. So some of that money goes to the lab every year to support whatever we want to use it for. So will be for research and for, for hiring people in the lab to work. But it really allows us to expand beyond what we're doing now. So to get equipment in the lab to get new techniques in the lab, and really broad in the interest of what we're doing. Still staying with coronaviruses. But what the Center for Pathogen Research does, which is the kind of broader scope of this is that it brings together all of my colleagues around here around the university so that we work on immunoogy or genomics or other viruses. And we're just getting it off the off on the table now, but really on getting all these people connected through a named Center, which I think will be great. And I'm really looking forward to figuring out how to use this in the future to really connect parts of university that we hadn't really been connecting with very well before. So it brings all this together and with really a focus right now of Coronavirus research, but ultimately looking at other viruses and other pathogens as in the future.

Charles Schelle: 47:27

When do you think that could I guess officially launch?

Matthew Frieman: 47:31

So we are we are talking about details now about bringing who's going to be involved and how that's gonna go. So it should be sometime later this year when we are really officially launched and and really putting the pieces together.

Dana Rampolla: 47:44

Can't wait, will that be within an existing building? Is it a new, physical?

Matthew Frieman: 47:50

So right now it's just a it's just on paper. So it's all its center, really just bringing people together under a title. But in the future, it would be wonderful to have, you know, to this really to be a big thing that we expand to and we get really much large funding to build, you know, a building or a floor of a building where we have all these people house together. And I think the really important part of it is that scientists at work in a vacuum. So while I like having four walls around my lab, and I often tell people like all I ever wanted was to just have four walls, leave me alone, and I'll produce data and give you something in the future. It really is the connecting all the pieces together. So I know what I do really well. But I know what I don't do really well. And so to be able to bring in people that are expert experts at drug design or immunology, or vaccinology, or other viruses, all of this is are things that are fantastic to have a connection to. And that only enriches all of us in this group to get better at what we do. It looks really good to have funding agencies so we can write grants that are really connecting all these groups together. But it also just It stimulates ideas and it stimulates brainstorming about things that not all of us are experts in in this group. And so all of that together, it's I'm just really looking forward to the future about what we can do with it.

Dana Rampolla: 49:06

Well, congratulations. That's awesome. Okay, well, Dr. Frieman, thank you for being here. Before you go. I want to ask you one last thing. So what are we doing in the fall? What should we be doing to protect ourselves? What do you expect in terms of possible new boosters coming out those sorts of things.

Matthew Frieman: 49:23

So I always like the Yogi Berra line, the "I don't make predictions, predictions, especially about the future." But I think what we do know, one is that there will be boosters available soon, with a new strain of, of Omicron in them, whether it's a combination or not. That's what's being worked out now to see which works best. But we certainly will have Omicron based boosters in the fall and that will protect us against the current variants and hopefully build on the and broaden the the coverage that we have now, currently. So that's certainly gonna happen. So that's an easy one. Hopefully everyone gets boosters as well only about 30% of the populace isn't in the US actually got their third dose. So we really need everyone to get more doses. Even if you've been vaccinated, you know, twice and then infected, you should still get boosted. So that's certainly something to do to really bring up your antibody levels to protect from infection. Now, for schools and all of our community as the fall and winter goes on, I think it's we will certainly see increases of cases as people get back together. And as schools reduce their masking requirements, and people go back to their normal activities after the summer. So I think we'll still see cases, whether we'll see a big giant spike in the winter, like we saw last year, because Omicron came out of nowhere, I don't know, I wouldn't be surprised if we saw another thing that we don't know is going to emerge from another lineage of coronaviruses, of of SARS, to just like Omicron came kind of out of left field. So it would not surprise me if we saw something else. The goal, though, is that with drugs online, with booster vaccines online, that whatever comes, we are ready to at least try to minimize cases and severity of disease. And what you see in the hospitals is that everyone that goes in the hospital, almost 100% is not vaccinated. And so the way to give your keep yourself while you may feel really crappy at home, and be on your couch for a week, with a really bad cough and sore throat, you're not sick enough to go to hospital. And so that's the goal. It's going to be it's hard. And really, for any virus, it's hard to protect from infection and transmission. But you really want to just minimize and shorten the amount of time that you potentially have transmitted for it, you're able to transmit. So that's the goal of all these vaccines. And so I think we're getting there for the fall in the winter, I think we rely on our, you know, friends and family to be as honest as they possibly can, if you know if someone is sick, and they're going to come over your house and they have a cough, like you know, you don't take that you don't let them over. You have rapid test them, we have tests all over the place. So those things I think can be really strong mediators to reduce the amount of virus we have around. But I just like everyone else, I want us to go back to normal, whatever that meant means and to be able to walk around without a mask and go into stores and shop and go to dinner and feel comfortable and not scared. Or kids go to school and feel safe. So all of that I think we're getting really closer to not sure if we're there yet, but I think we're getting there. So fingers crossed that we have a nice kind of quiet and, and boring winter, which would I would love.

Charles Schelle: 52:27

Yes, let's hope. Well, the one thing we know for certain is that the University of Maryland Baltimore is very lucky to have you, and your expertise and your contributions to this field is just remarkable. I've learned so much today. I feel like you should charge me for one of your classes.

Dana Rampolla: 52:43

And here we are on a late Friday afternoon. So thanks for joining us. Please get home to your family, enjoy them and stay healthy.

Matthew Frieman: 52:50

Thank you very much.

Charles Schelle: 52:53

Our next Change Maker in October will be Judy Postmus, who is the Dean of the University of Maryland School of Social Work. October is Domestic Violence Awareness Month in the Dean's research has focused on intimate partner violence with a focus on financial abuse, she'll point out some potential signals of distress and how to empower these victims. Also October means Halloween. And we couldn't resist sharing the haunts and the history of Westminster Hall and Burying Ground at UMB. We will have a special Twitter Space in October to talk about the hall, the burying place of Edgar Allan Poe and the catacomb tours. Keep an eye out on the UMBaltimore Twitter account for more information once we have a date set, as well as our website umaryland.edu/pulse. And we'll also release it as a bonus episode, too. And by the way, welcome to all of the new UMB students and employees this fall semester. And welcome back to all of our returning students and listeners. And make sure you tell a friend about the UMB Pulse podcast and subscribe to us on Apple podcasts or wherever you'd like to listen to us right now. And with that, thank you for listening to the UMB Pulse.

Jena Frick: 54:03

The UMB pulse with Charles Schelle, Dana Rampolla and Jena Frick is a UMB Office of Communications and Public Affairs production. Edited by Charles Schelle sound engineering by Jena Frick marketing by Dana Rampolla. Music by No Vibe. Recorded in the University of Maryland Baltimore Community Engagement Center.