Vanderbilt Health DNA: Discoveries in Action
Season 2, Episode 1
Blueprint for a Pandemic-Ready Society

Dr. James Crowe: So the capabilities of the human immune system, I would say are, it's the largest information system on the planet. It's bigger than super computers can deal with. It's more than all the stars in the galaxy, the human immune system within your own body is an enormous information system that can deal with anything that comes along.

Dr. Robert Carnahan: Resolving pandemics is always going to be a difficult strategy, right? So we just went through, I mean, honestly, a mind-blowingly amazing scientific response to a pandemic. As I tell people, you're watching science happening in real time.

Dr. Keipp Talbot: How do you communicate risk so that people understand risk without scaring them, but also without them feeling that there's no risk? It was interesting because someone told me, "Only 1 in 100 people die. So that's no big deal." But if I turn it around and said, "You just won a flight to Hawaii, 1 in 100 flights are going to crash. Will you get on the plane?" They're going to say no. And so it's very interesting how we perceive risk.

Clark Buckner: You're listening to Season 2 of Vanderbilt Health DNA: Discoveries in Action. I'm your host Clark Buckner. And the reasoning behind this show's name is quite simple. The path to better health lies in our DNA. Discoveries in Action is about the big ideas and breakthroughs happening right here in Nashville, Tennessee, from Vanderbilt Health. Our drive to discover, care, learn and share is in our DNA. It defines who we are just as your DNA defines you. We're kicking off this season by exploring how we can prepare for the next pandemic. And one of the most critical pieces of gearing up is the immune system.

Let's take a peek into the majesty and potential of the human immune system with Dr. James Crowe, who runs the Vanderbilt Vaccine Center. You might recognize that name if you're a fan of 60 minutes. Dr. Crowe's lab was just featured for its game-changing expertise in MRNA and monoclonal antibodies. Dr. Crowe and his team worked to find groundbreaking, scalable ways to train the immune system with new information, immunological blueprints, to help the body fend off disease. And these immunity boosters are not what's sold as smoothie add-ins. It's the result of decades of science.

Dr. James Crowe: I got my second dose of Shingles vaccine yesterday. I'm getting a little older, I'm feeling a little sore today, a little flu-like. And I've been contemplating, I've been stuck with a lot of vaccines and I participated in a lot of experimental vaccine trials at Vanderbilt. And so part of the question you're asking is, is there a limit to what the human body can do? And do you sort of burn out your system or use it up or make it weaker or do you just keep adding new features like in an iOS app. And the answer to that is it looks like we're not tapping in, but to just a very small percentage of the capability of the

human immune system. Human immune system is far greater than the entire diversity that exists in all the microbes on the earth.

So we can do, going back to the well and stimulating immunity to new pathogens probably almost infinitely, amazing capacity of the human body. The question is, can we prepare the body through vaccines or antibodies ahead of time, rather than letting the full-blown infection occur? Because there is a lag time. That's the issue there's a week or 2 weeks before your body really figures out what's going on. And so the whole idea of vaccinating or treating with antibodies is giving you that several week jump to be prepared yourself and to let your body do the job itself, rather than depending on a medicine.

Clark Buckner: The Crowe Lab worked with DARPA. Yes, the research and development arm of the U.S. Department of Defense. It was for a so-called sprint to find an antibody to fight Zika in 90 days or less. And they came in an astounding 12 days early. That was in 2019. And it was like a fire drill for responding to pandemics. As we heard in season 1 on our episode, Pandemics Versus Prosperity. Crowe and his colleagues have a list of pathogens that they suspect could lead to pandemics or epidemics in the future. They want to find resources. And the societal will to prep now. So we don't have a repeat of COVID-19 in the future.

Dr. James Crowe: We're spending most of our time getting ready for AHEAD100 deploying. And in fact, we've already made best in class antibodies that could be used to prevent or treat 30 or 40 of these diseases. So I'm also looking for partners just to move them forward. We have them in the lab, but they're not being manufactured because we just lack the money, basically. I'm working with a nonprofit and they've raised about two and a half million dollars for a planning phase for the two and a half billion dollar AHEAD100 programs. So we're really looking ahead to develop the prevention for the potential epidemics in the future. We would like to have antibody drugs that could be shipped anywhere in the world on a moment's notice, ready. And so this is called a stockpile, typically. The United States government has sort of prototyped this for Anthrax. We have a stockpile for preventing Anthrax, but there really aren't any other major stockpiles.

So we would make drugs for the 100 things that might cause an epidemic and have them at the ready with the ability to fly them anywhere in the world and use them immediately. And we would already have tested them in human beings to show they're safe. So for two and a half billion dollars for 100 targets, we can have drugs that we know are safe. We would not yet know that they work because each target is about a two billion dollar project. So we're not asking for two billion times 100 because it just, at some point it becomes not plausible. But we're looking to stockpile 100 drugs or antibody cocktails for 100 diseases that are ready to go at about 10,000 doses. Our dream is that we don't actually have pandemics in the future that we would have epidemics. Certainly infections will cross over from bats or mosquito populations into the human population and cause local outbreaks that could spread to larger epidemics. But we need to build a capacity to respond quickly to those local outbreaks and contain them so they do not spread.

And I think of this sort of like having fire alarms in your home, and then you have a fire extinguisher under your kitchen sink, and you have a little pan fire in the kitchen and you put it out and you did have a fire, but not many people were hurt. You need a next level where you have firetrucks in your neighborhood. And after that, you need planes that can cover whole areas. And what we want to do is move the response closer to the kitchen fire extinguisher. where as soon as the outbreak occurs, we snuff it out. That's really the strategy. A lot of lessons in COVID-19 about individual components that work well or not. So for instance, in our type of science, taking the blood of an individual who has survived an infection and making a human monoclonal antibody, that could be a treatment.

We were able to do that in 25 days and to hand lead drug candidates that are antibodies to our pharma partner to start manufacturing them. We did that in 25 days. So that's extraordinary and a very high success. And yet that's not the end of the story. Then you need to be able to manufacture that material safely and cleanly and reproducibly, and then you need to be able to distribute that material to all over the nation. And what about underserved populations within our nation? And what about people in low and middle-income countries? We don't really have a good schematic for how to do that. Individual components, and we learned a lot in this pandemic and we have lots of successes. I think what we need to do now is string them together into an end to end solution where as soon as something happens, the cure or the prevention can be delivered to that small population, that local outbreak, no matter where it is in the world, no matter what their social standing is, communication occurs, and the prevention is delivered immediately.

Clark Buckner: Pandemic response, isn't all blood draws and therapeutics. The response is a complex web of sophisticated logistics, Dr. Robert Carnahan, associate director of the Vanderbilt Vaccine Center explains how everything from shipping and bureaucratic red tape to international treaties impact how scientists and communities respond.

Dr. Robert Carnahan: We had finished the Zika sprint in 2019, and we were planning out 2020 actually. So, the program that has principally sponsored a lot of our rapid responses, DARPA, which is a division of the DOD. So January 14th, we actually had the DARPA program officers at Vanderbilt for a meeting. And we were in a series of all day meetings. And the point of the meeting was, "well, what are we going to do in 2020?" We felt pretty good about what we had done in 2019. We had, as far as we knew, the fastest generation of antibodies, starting with a donor sample to antibodies that we knew were efficacious in relevant animal models. We had done that in 78 days, which we thought was the fastest we knew about. So we were kind of like, "Well, how could we do better than that?"

So we're in the meeting with our DARPA program officers. And we actually got a phone call from our prior DARPA program officer who had moved on to another job, but had all of our cell phones. And he's like, "Have you heard about this thing in China? You guys, that's what you should do for 20-" He knew, we were talking about what we're going to do in 2020, his name's Matt Hepburn. And he said, "that's what you guys should do for your sprint. Your pretend should be this thing. Your pretend pandemics should be this thing happening in China." And we kind of got all, we're like, "Maybe, but at this point it's

only in China and we actually need human donor samples." And there becomes this whole sort of international treaty that needs to be bridged between the United States and the country.

And we didn't know that we were going to get samples out of China anytime soon. We were like, "Well, that was a nice idea. But we already had an idea for this year. We were going to do this, this other viral pathogen. That we're super interested in. We think we'll just stick with that." And then it was about a week later where this headline splashed across the first U.S. Patient, Washington 1, as you guys know. And so as soon as we saw that headline, we were like, "Well, we know what's going to happen now." And so within about 12 hours of that announcement we were like, "Okay, well 2020 is all about us responding." At the time. We didn't know it was going to be quite like this super international pandemic. We just knew that having spent all this time building a rapid response platform, we couldn't not apply it to a problem which had now been in the U.S. Which at the time we suspected would be maybe just a mild or moderate problem, but of course it quickly expanded.

We actually think a lot about those logistic and procedural issues, which is why we have permanent full-time staff who literally will watch the headlines and see where things are happening. Start to help Dr. Crowe and I understand where this is at. And then we think about, do we have connections into that place? And how could we make our way into it? And how urgent is it, right? Is it something where there are things like Rift Valley Fever happening in Kenya and other places where we consider that a really interesting and relevant target that has what we call sort of a pre-pandemic virus. But we take a long-term approach. We need to build relationships and try to make our way in and form mutually beneficial partnerships in a sort of a slow approach, which is different than sometimes where we think, okay, here's a unique opportunity.

There's been an outbreak we probably need to get in there more quickly. How can we get in there more quickly? But we do it all kind of with our own resources, for the most part. When you go back to the societal thing, if I had to say, "Well, what should we do as a society?" If we think the antibodies are something we want to activate in response to infectious diseases, which I would advocate is, not the only tool, but a tool in our toolbox we should definitely be breaking out. We need to work on that because we were left to our own devices, but our best donors actually came from Canada. So we actually had to negotiate an international piece to it, to get those samples in here. It was actually really complicated. We had a wonderful partnership with FedEx that actually helped us bring that in.

So we kind of had to build that ourselves on the fly with help from some institutional folks here at Vanderbilt, which was super helpful. But again, it was a Vanderbilt initiative that helped us identify those donors in Canada and go through the complexity to bring those samples into the United States. So how should we do it in the future? It shouldn't be that way, right? It should be that, the way I think of it is, any place you go there's this box on the wall, it has glass. And it's like, in case of fire, you break the glass. And we should have that, right? We should have that for infectious diseases as well, on an international level. We operate a course through treaties and things should go through their proper paces normally.

But if there is an emergency, there has to be a way to approach that. And what we found out is everyone knows that in the midst of emergency, everyone knows that there needs to be a faster, better way. But if you haven't predefined it, it's not going to happen in the midst of an emergency. The science of course makes it in all the science papers. The science reviewer is not going to let us put in there, you know what was really key here? Is that we made a great connection with FedEx and they were able to go retrieve a sample, which got lost in the Toronto airport. Literally got lost. Those samples got lost.

We were able to activate FedEx. They went and they were finding it. I later on my cell phone got a picture. I'm like, "is this what you're looking for?" I was able to say, "Yeah, that's exactly what I'm looking for." I'm like, "Okay, we rerouted, it's going to be on a plane within an hour. It will be be you guys tomorrow." So that stuff you can't put in the paper, but without that, our sample, our precious Canadian samples might still be in Toronto airport somewhere in The lost and found'

Clark Buckner: The scientific method. We learned it in school. But most of us, or maybe I'm just speaking for me here, have forgotten the details. Advancements and breakthroughs can appear to come out of nowhere because most of us don't spend the time reading academic journals. The reality is though science, like what we've seen in the last 18 months is built on layers and layers of research from all over the country and the world. We're talking decades of teams competing to get published and learning from each other. They watch and explore happenings that most of us don't even know are happening.

Dr. James Crowe: I'd like to think that we've learned a lesson, but this is actually not the first major epidemic that my research group has lived through. We worked on H5 Avian Influenza. We worked on a Chikungunya outbreak, infected a million people in the Caribbean 1 year and many people in the United States. I think 38 states. Zika Virus causing hydrocephalus in children all over South America and infected a number of people in the United States. Ebola has broken out numerous times, is still causing outbreaks in Sub-Saharan Africa today. So you can go on and on. These things have been happening and sort of knocking on the door. We know they're going to happen. And every time we say we've learned our lesson and we don't. So the magnitude of this particular pandemic is pretty scary. And I think if you contemplate the fact that we did have a headstart, there's potential for even larger ones in the future. And I hope that we have some continuity from philanthropists and government visionaries who see this needs to be a full-time ongoing program. Not an episodic.

My entire professional life. I've been watching these technologies develop. Now, to the credit of the biomedical community. We don't just rush these things into people. We spend a lot of time trying to do them, not only effectively, but safely. I think the safety concerns in the research community are paramount. And I think the public probably does not understand that. They probably think we're just coming up with crazy ideas and trying to try them. But the, "First, do no harm" principle in medicine is deeply embedded in the community that's developing new vaccines and interventions. So it's actually slower than it could be. Even in the current management of coronavirus, it could have been even faster, but all of the steps that are conventional and that we know are necessary were taken. So no one skipped

any steps. That's the amazing thing, we could have gone even faster if we skipped steps and we're not going to do that.

And I think to some extent the pandemic was a very confusing situation. That was very much like a world war. There. There was a lot of confusion about what was right. There was insufficient data to make statistically robust decisions about what to do. So decisions were made with the best knowledge at hand, and they weren't always perfect decisions. And I think the public got a little confused. Do the experts know what they're talking about or not? And if they change their mind was the first thing wrong or not? And, and I think a reasoned person does change her mind if she sees new information that contradicts the original decision. So I think it played out okay. But the public is still sort of grappling with their relationship to science and government authorities. And I think that's a fundamental trust level that we have to maintain and build

Clark Buckner: Infectious disease expert. Dr. Keipp Talbot, Associate Professor of Medicine and specializes in adult infectious diseases sits on the Advisory Committee on Immunization Practices, which advises the CDC. From her vantage point during the pandemic, she said she was heartbroken at the divisiveness around masks. Establishing new and more lines of trust is paramount

Dr. Keipp Talbot: Trust and patience are the two things I think we need. Trust first, we lost trust. Somehow there was a lack of trust. And I think some of that was messages seemed to contradict each other. And there was good reason for that. This was a completely new virus that we were learning as fast as we could. The closest virus to this was SARS. What we knew about SARS, some of it held true for COVID, but did not hold true. Some did not. Specifically, you didn't spread SARS unless you were febrile. You had to have a fever to be infectious. It was not the case with COVID-19. And so I think we lost trust really early. And I don't know how you earn that back. You have to earn trust. And so I think that's going to take time to do that. I think the other area is patience.

If you want something delivered to your house, you can get it within 2 hours from Amazon. If you want to watch a movie, all you have to do is click a button on your computer or TV. Gone are the days that you have to wait until Saturday morning and get up early to watch your cartoons. So I think we have forgotten how to be patient. And there was a lot we had to learn. There's a lot we had to learn and a lot was learned in a very short period of time, but I still think people didn't understand that we were learning as fast as we could, and that there were some patience required.

This is so hard for scientists because we are always theoretical. We're always proposing a theory to try to uphold it or shut it down. And so we don't think in absolutes, we think in terms of gray and we don't communicate well. There are a few who do, I mean, there are exceptions, there are always exceptions who are great at talking, but I think this is one of those areas where we really need our social scientists and we need to learn to communicate with them and involve them at every step of the way.

So I think that's an important thing is that we become human and we show our human side. I think the other side is we need to learn to talk with people, not to people or at people, but with people and not

use our medical jargon. And I think we do this somewhat with our patients, if we do it well. My patients joke because I'll say, "Give me a moment. I need to put this into English." It's that idea of taking it from a jargon to how people really talk. And I think we need to practice that and explore it and do more of it. I do think scientists, we kind of live in our science. We live in our head and learning to communicate that is important for us to get our funding and to do our research. But when we learn to communicate it, once again, we learn to do it in our medical jargon and grant language.

So I think it's going to require some practice. And I think it's going to require us to kind of get out of our comfortable zone. I mean, we're comfortable in the lab. I know exactly what I'm doing behind my closed office door. I know how to do it well. But talking with people about my science in English is much harder. And so I think it is going to take some practice. I think we do need to teach science in schools, but we need to teach it in a way that is understandable and approachable and that carries through life. It should always be open to ask questions. You should always be trying to learn something new. I think we also need to teach what's credible and what's not credible science. And I don't know how to do that, once we need our social sciences again.

But I do think we need to be able to discuss science in a way that it's not a political thing or a religious thing. You can have both, you can have religion and science. And so I think that's one of the things that we need to do going forward so that when we do communicate, it's not either/or, it's a spectrum. One of the things that always amazes me, people were like, "I'm not getting a vaccine." Or, "I'm not wearing a mask because I trust God." I trust God. And I wear my seatbelt too. I don't think it's an either/or I think it's part of the spectrum. God has given us these gifts. God has given us these scientists so that we can learn and grow and protect human life. And I think medicine has given us a wonderful chance to protect human life. My life right now is trying to get these vaccines into everyone that will stand still.

Clark Buckner: As healthcare's focus shifted first to keeping people protected from SARS-CoV-2, then to administering vaccinations, the pandemic revealed workforce weaknesses. There's a limited supply of people who can administer injections or take swabs. So as communities roll out COVID centric sites, other routine care went undelivered.

Dr. Keipp Talbot: We also don't have enough healthcare workers out in public health to handle outbreaks. So they have to drop all their regular routine, preventative jobs to pick up an outbreak. And that means we leave other things behind. Perfect example of this is when we were trying to track down all the COVID cases. We quit following up how well kids were getting vaccinated. So kids got behind on their routine immunizations. So if Measles gets introduced into this country, we have a population of kids that weren't vaccinated and are at risk. So we really need the infrastructure to do our regular routine preventative care plus prepare and handle a pandemic or epidemic.

I think the other part of that is we really did a great job funding the science for our vaccines. I mean, it was unbelievable. We took everyone who had a candidate vaccine and said, here's the money. Go. Make it, try it, produce it, everything. We didn't fund any health department to actually give vaccine until long

after vaccine was available. So health departments were completely unprepared. They were getting shipments of vaccine and didn't know how to schedule people.` Didn't know how to get them in. Didn't know how to do it safely. Didn't have the staff to give the vaccines. So I think we have a lot of room to do on our infrastructure for healthcare.

Clark Buckner: The infrastructure that allows scientists to equip the human immune system to respond to pathogens is a heavyweight mission. As we have learned that quest takes cooperation from pretty much all parts of business, government and communities.

Dr. James Crowe: I was at the TEDx Nashville conference one year and all of the astronomers from Huntsville nearby were there talking about how big the universe was. And I said, "Well, inside your body's bigger." It's sort of like, "My system's bigger than your system.", But it really struck me. If you look at the numbers the receptor capability, the diversity in your body and if you take a broader sense, in the human population is extraordinary and much larger than what astronomers would ever look at.

Clark Buckner: We're excited you joined us for this episode of Vanderbilt Health DNA: Discoveries in Action. On the next one you'll hear from some of Vanderbilt University Medical Centers foremost thinkers, to explore what it means to be in and discharged from the ICU. Since technology makes injuries and diseases, including COVID more survivable.

To learn more about the show, check out episode extras and find more information about Vanderbilt health and today's experts visit listendna.com. You can also find us on Twitter @VUMC_Insights and all of your favorite platforms at Vanderbilt Health. And of course, don't forget to follow rate and review the show anywhere and everywhere you get your podcasts like Apple Podcasts, Google and Spotify, we're there.

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