

Vaccine Research Center  
National Institutes of Health  
Oral History Project  
Interview with Dr. John Mascola  
Conducted on March 21, 2022, via Zoom by Holly Werner-Thomas for  
History Associates, Inc., Rockville, MD

THOMAS: Okay. Great. My name is Holly Werner-Thomas, and I'm an oral historian at History Associates Inc. in Rockville, Maryland. Today's date is Monday, March 21, 2022, and I am speaking with Dr. John Mascola for the Vaccine Research Center with the National Institute of Allergies and Infectious Diseases, which is part of the National Institutes of Health, or NIH. The NIH is undertaking this oral history project as part of an effort to gain an understanding of the Vaccine Research Center's work. This is a virtual interview over Zoom. I am at my home in Los Angeles while Dr. Mascola is in Bethesda, Maryland. Before we get started, can you please state your full name and also spell it?

MASCOLA: John Robert Mascola. J-O-H-N, R-O-B-E-R-T, M-A-S-C-O-L-A.

THOMAS: Thank you. Dr. Mascola is the director of the Dale and Betty Bumpers Vaccine Research Center, or VRC, at the National Institute of Allergy and Infectious Diseases, NIAID, National Institutes of Health. He joined the VRC in 2000 as a founding investigator and served as its principal deputy director from 2000 to 2013. Since then, he has also been chief of the virology laboratory at the VRC. Since 2005, chief of the humoral immunology section. Dr. Mascola has been the recipient of many awards and honors throughout his career. Most recently, both the NIH Director's Award for outstanding efforts leading to successful development of Covid vaccines and therapeutics and a presidential commendation for Covid-19 vaccine development, Operation Warp Speed. Dr. Mascola has additionally been elected to the American Society of Clinical Investigation, the Association of American Physicians, fellowship in the American Academy for Microbiology, and in 2017 was elected to the National Academy of Medicine. He received his MD from Georgetown University School of Medicine and a B.S. from Tufts University.

THOMAS: Like I was saying, I want to start by asking you to describe your background in relation to your career path. What inspired you, who influenced you, if anybody? Things of that nature.

MASCOLA: Well, my background is as a physician. I got my medical training at Georgetown University and then went on to train in internal medicine and infectious diseases. When I was training in infectious diseases in the late 1980s and early 1990s, the AIDS epidemic was first being recognized. So, I'm quite sure that seeing the first early AIDS patients who did not do well and seeing a viral disease that could destroy the immune system without a clear understanding of what was happening or how to benefit those patients really inspired me toward a career in infectious diseases, and, more specifically, towards a research career in viral immunology.

THOMAS: Did you have any support? And what was it, say at school or at home? Or was this all just later as a young professional, as you say, as a physician? Or did you have anybody, a mentor, say, for example, were there clubs or competitions in science? What were the resources that you had?

MASCOLA: I think the resources were really part of the training that I undertook in infectious diseases, which at the time was through the United States Navy, because I went to medical school on a United States Navy scholarship, and I was training at the San Diego Naval Medical Center, and later at the National Naval Medical Center, Bethesda. As part of that training, there was a strong emphasis on research. <My mentors in infectious diseases encouraged me to go into research and really gave me the opportunity to move from clinical training into laboratory-based training where I could acquire the skills that I acquired over the years to become a laboratory-based researcher.

THOMAS: Can you tell us just even one story about those days? You know, your work in the laboratory at that point? Describe either an average day or a story that stands out?

MASCOLA: In standard medical training, one often does the clinical part of the training first. And certainly, I had an active clinic of HIV-infected patients. In the early days, we had limited treatments. And so many of my patients would progress to illness because it was in the days just before we had really effective triple-drug therapy.

At the same time while I was training in the laboratory, and part of that laboratory training was to work with HIV in the lab and to grow it and study it. I began to study how the immune system interacts with the virus, and why the immune system is ineffective against the virus. So, putting those two pieces together, the clinical experience and my early lab experience really sort of fortified for me that a career studying this virus and the way the immune system attacks the virus was something that I was highly interested in.

THOMAS: So, clearly the VRC was first announced in 1998, and it was created really to focus on HIV. Of course, it's been expanded many times over to include research on everything from Ebola to malaria and, of course, SARS. How did you yourself come to work for the research center? And what were your initial goals?

MASCOLA: So, the center actually opened in 2000. In the late 1990s, NIH advertised that it was building this new Vaccine Research Center. At the time, I was an infectious diseases physician doing research at the Walter Reed Army Institute of Research. That's local in the Bethesda area. So, I think the attraction of that center at NIH was that first of all, it was a brand new center at the world's premier research institution. It was focused on vaccine science and on HIV, which were my particular areas of interest. I was immediately attracted to apply. And was fortunate to be one of the first group of investigators that were selected to really get the VRC started and going.

THOMAS: Again, could you tell us a story about those early days? What was it like? What did you find when you got there? Who was there?

MASCOLA: We had the opportunity to start from the very beginning. The very earliest days, the building that I'm in was a shell of a building. We spent a lot of time working with the architects to outfit the building. So, it was a unique experience to be able to build something from the ground up. When we first occupied the building, five floors of research space, there were a handful of people in the building. You'd walk around and hardly anybody working. I had a chance to start a lab from the beginning, to

help hire staff from the beginning, and see this handful of people become, first fifty, a hundred people, and then over the years to where we are now, almost 500 people. It's really a fantastic story of starting something at the very beginning and seeing it all the way through.

THOMAS: Who was there with you at that point? You know, obviously you said like a much smaller staff, for example.

MASCOLA: Yeah. Well, the founding director was Gary Nabel, and a handful of people came at the very beginning. Several of the principal investigators. Mario Roederer, Peter Kowng, Rick Koup, Danny Douek, Bob Seder, Barney Graham, Nancy Sullivan, all came very early on with the first group of investigators, and many of them are still here.

THOMAS: What was the thinking—this is a very broad question, but the original focus was on HIV, of course. What were some of the discussions around that crisis at that point? Because at that point, you know, well into the '90s, HIV and AIDS have been around for quite some time, and I remember in my own lifetime the protests, the Reagan years, you know, all of that. What was the atmosphere around the disease itself that you were focusing on?

MASCOLA: The focus for us was on vaccines. When we were starting in the early 2000s, there had been tremendous progress in antiviral therapies, which was, of course, critical. People were able to control their infection and begin to lead more normal lives. but there was still something on the order of 5,000 new infections a day in the world. The epidemic was pretty much unabated in the whole world. Our focus was on HIV and on HIV vaccines, and there was a lot of optimism that if we really focused our attention on that and brought to bear all of the tools that we could bring to NIH, that we could make an HIV vaccine. A lot of the early discussion was what kind of tools we needed, and we realized that we needed tools that were not just laboratory-based, but we needed the ability to make new vaccines and test them in the clinic.

We began to build all that infrastructure. That means not only the laboratories, but to have a place where we can make a vaccine, what's called a "clinical product" that can be tested. We needed a vaccine clinic where we could actually test the vaccine, and an immunology clinic where we could take blood from these people and test. We built this whole infrastructure where we could discover something, design it, test it, and evaluate it in people all under one umbrella. Sometimes we call that translational research. You can translate what you discover into a research product, and that was the whole model we built to be able to more quickly study HIV vaccines.

THOMAS: Just one more question regarding sort of the initial stages as the center got up and running in the early days. How did you hear about—I know it sounds obvious—but how did you hear about the Vaccine Research Center? Obviously, there was an announcement, it was a presidential effort, I believe. But also, just within your own professional community. You know, did they approach you, somebody approached you to come onboard? Or what was the process there?

MASCOLA: I think when NIH makes a major announcement to build a new center, it's news. We read international journals called Science and Nature and New England Journal of Medicine, which carried

the most impactful stories. And those journals had a big, whole-page advertisement about this NIH vaccine center. It was really the talk of many of my colleagues in the infectious diseases world about this new center, and I think several of my mentors and the senior scientists around where I was working encouraged me to apply.

THOMAS: As you say, no surprise there. But I just wanted to understand the details a little bit. Before we jump into a lot of questions regarding Covid and the last couple of years, there's a large amount of time between the late 1990s, early 2000s, and the last two years. Can you give us an overview of your responsibilities and your career at the center over the last, say, 20 years or so? Before Covid.

MASCOLA: I started at the center as one of the investigators. I ran a laboratory studying the immune response to HIV, but I was also the initial deputy director to the center's director, Gary Nabel. From an early stage, I not only ran a laboratory and did research but was involved in the scientific administration and leadership of the Vaccine Research Center. That gave me a perspective and a hand in shaping the center. I continued to run my laboratory over all of these years, and that grew and we evolved our interest.

But I was also able to, with some of the other founding investigators, shape this whole center in the way we wanted it to be. To be able to do translational research and clinical trials and make clinical products. Over the years, we became more and more capable of discovering something. It would either be a new type of vaccine or sometimes a new type of antibody. We did both types of work. Making it in the clinic, doing what's called a "phase one study" in people where we first test it to see if it looks promising, and then studying it in detail. We began to do more and more of that with different types of HIV vaccine products, different types of HIV antibody products. That really took us all the way through the mid to later 2000s.

The other part that I would add is as we did that, and we built that structure; we realized that we could apply it to other diseases. It was a very effective structure because we could do this translational research as well as discovery. Early on we had smaller programs in other virus diseases. Studied Ebola and influenza. But we grew those programs, and we grew the center to be able to study HIV still is a major focus but major areas of focus on other respiratory diseases like respiratory viruses of children, Ebola and Marburg that cause lethal diseases. Other viruses that sometimes are less well known. West Nile virus. We studied the early SARS viruses. The center grew in the scope of activities and the other viruses that we were studying.

THOMAS: I want to dive in now to the last couple of years, but keep in mind this doesn't have to be completely chronological. I definitely want to get to the heart of the issue here. I want to begin by asking you how you learned about the outbreak in Wuhan, and what was the center's response?

MASCOLA: I heard about the early cases of pneumonia in Wuhan from, I think, early reports in the scientific literature in December 2019. First there were cases of an unexplained pneumonia that clearly might be human-to-human spread that was causing severe disease. As soon as that happens, we get concerned that there may be a new virus. Viruses are common causes of those types of syndrome. The scientific community, particularly the global health/infectious disease community was anxiously

watching what was happening and really waiting for the very first evidence of what the cause was of this pneumonia. That evidence came out in early January 2020 when the sequence of this new virus was published on public websites. What we can do is we can go onto a website. We can pull the RNA sequence, the code that was published. When you look at that code and you can line that sequence code up to all the viruses that we know about and do a simple computer program which sorts all the sequences and tells you what the closest sequences are, right away you could see that this was a coronavirus and that the closest known viral member was the SARS virus where there was an outbreak in about 2002.

Right away we knew there was a new coronavirus, and it was causing an outbreak. I think within a few days or a week, the senior investigators in our center, all of us got together. We had some discussions about what we should do. We had previously responded to an Ebola outbreak. More than one. And done work on vaccines and antibodies. We responded to Zika and worked on a Zika vaccine.

Very early on, it wasn't clear that this new coronavirus was going to be a big outbreak. We took a little bit of time to say can we really put the resources in to make an impact here? But I think within a week or two weeks or three weeks, it became clear this was a major epidemic. And we agreed that the center would devote a major portion of its resources to help out, try to understand the virus and try to design a vaccine. So that was really by, I'd say by January 2020, we were essentially "all in" as a center to respond to this new epidemic.

THOMAS: Before I ask you further about that moment, I wanted to go back a little bit. You mentioned SARS from, I think 2002, which I clearly remember as well. Can you just address that a little bit in terms of why that version of SARS didn't become what this has become? And still is with us so much.

MASCOLA: The first SARS virus caused pneumonia, and actually could be lethal in about 10 percent of the cases, but the outbreak was limited. It lasted for a couple of years and eventually died out. The infectious disease/global health community watched that with a lot of interest. Because it was a new coronavirus, it caused infections of people. It caused lethal infection in some people. But one example, we're not so sure what to do with it.

But then in 2012, another coronavirus infected people, which we called MERS. Middle East Respiratory Syndrome, which was also a coronavirus. That also was lethal in some people. Even though it didn't emerge as a global epidemic, there continued to be MERS cases over the years. Now we had two examples of this category, we call it a family of viruses, coronavirus is a family. We had two examples of this family of virus infecting people with a brand-new virus.

That was enough for us to start a program of coronavirus research. That was started by Dr. Barney Graham here. It was a small program, just a few people, but we realized that we needed to understand that virus and be prepared in case there was another virus that would emerge and be prepared, in a way, to say that we understand what these viruses are, how they attack the immune system and how we might design a vaccine.

THOMAS: Then continuing onto Ebola, and I think H1N1 [influenza] was 2009, if I remember correctly. I should remember because I had it. (Laughs) I was living in Turkey at the time. It just flew through the crowds. In any case, again, a lot of worry. A lot of panic. Public health panic at those moments. And yet there was the ability to shut it down, as it were. Can you talk about those diseases, as well, a little bit, and your reaction there at the center?

MASCOLA: Yes. In each case where there's an outbreak, I think the lessons that we learned over time was the importance of being prepared. It's really too late to see a new outbreak and to begin to study it at that point in time, and to hope that you're going to be able to respond quickly enough to have some kind of an intervention. In our center, we focus on either vaccines to protect, or antibodies against the virus which can be used either as a therapeutic or a prevention.

We started working on Ebola and Marburg and that whole family of viruses at the very beginning days of the Vaccine Research Center. That was work by Gary Nabel and Dr. Nancy Sullivan, who's here, because they knew that there were periodic outbreaks of these type of viruses. Therefore, there would be more. There would be others. So, when there was an outbreak in 2014 and then a larger outbreak in the western African region in 2018, we'd already had vaccine and antibody programs for Ebola. And so, we quickly went into action and eventually developed both a vaccine that is now well into development. But probably most importantly, we developed an antibody that can be used to treat Ebola virus disease and was used in the Democratic Republic of Congo outbreak and was shown to reduce the lethality of Ebola if we use it to treat early. So again, it really was about having a scientific program early on where you can move quickly when there's an outbreak.

Similarly, we had an influenza program. We were studying the virus and we were thinking about vaccines. When the new H1, the 2009 version of H1 came out, we very quickly developed a DNA-based vaccine for that and began to study how—what we did for influenza, because there are currently influenza vaccines out there, we began to study how we could develop better influenza vaccines. What are called universal influenza vaccines. So really, it was about 2009 where we started this new, broader universal influenza program here at the center.

THOMAS: So it was actually 2009. And how much of all of these efforts were based on the original HIV? Obviously earlier you talked about modeling.

MASCOLA: Yeah.

THOMAS: Is there anything you wanted to add there?

MASCOLA: Well, everything that we've done at the center has some basis in our early HIV work. In part, scientifically, the way we approach a problem. We study a pathogen, usually a virus. We also study malaria and tuberculosis, but we study it at the most detailed biological level. For a virus, we study it how the immune system responds to the virus. How the virus causes disease. We study the atomic level structure of the surface proteins on a virus because that's what the immune system has to attack. We learned that those approaches can be translated from one virus to another.

Then the other part is that the infrastructure that we built, the ability to make our own product and do what we call a “first-in-human clinical trial” by quickly testing a new product, was something that we could also apply to other viruses. We applied really the entire capability and structure of our center from HIV to other viruses and other pathogens.

THOMAS: Again, a rather broad question, but I’m wondering, how would you characterize the last two-plus years now? Maybe describe the first month of shutdown. I don't know that you did shut down there, given your work. But two years ago, precisely this month, for example. And then broadly speaking, you know, characterizing the last couple of years.

MASCOLA: Well, I would say that from the time that we first understood that Covid was a worldwide epidemic, even before it was formally declared a global pandemic by the WHO, we went into full action and commitment to vaccine development for this new disease. And that was on top of everything else we were doing. The last two years has been incredibly intense. I think almost everyone at our center to some degree has been involved in the coronavirus effort. We were a pretty busy center before that. We never did shut down because we were doing coronavirus work. Staff continued to work. We had to physically distance, so the research staff went on shifts. Three shifts a day. Early morning, late day into the evening, and evening overnight. I think maybe only over the last couple of months has that intensity started to come back slightly towards normal. I think for everybody involved it has been intense. Sometimes exhausting, but also very exhilarating and gratifying when things that we’ve contributed to actually make a difference.

THOMAS: Let’s talk about that. Talk about leading the efforts, then, at the NIH to develop a vaccine.

MASCOLA: Our coronavirus vaccine work really emerged from a small group of people that were already studying coronaviruses. I think it’s important to recognize the importance of the foresight of Barney Graham and his group to say that we need to know more about this family of viruses, coronaviruses. Because as we discussed before, we had already seen the SARS, the original SARS, and we had seen MERS. If there are two viruses from the same family that have emerged to infect people in the last twenty years, we shouldn’t be completely surprised that there’s a third. We have that kind of foresight, and we had, at the same time, I’d say in the 2018-2019 timeframe, we had become more attuned to the fact that we wanted to be able to respond more quickly if there were a new outbreak. As I said, we had responded before to Ebola and to Zika. But it takes time. It takes time to design a vaccine, to bring it to the clinic, and we wanted to accelerate that.

We began establishing collaborations to allow us to respond more quickly and one of those was to work on a new vaccine platform called mRNA, which people now know has been used for coronavirus vaccines, but mRNA before coronavirus, before Covid, was a relatively untested platform. It was new. As scientists, we knew that platform had tremendous potential. We began studying it, and we began working with companies that could do mRNA vaccines. In our case in particular, we worked with Moderna. Even before the Covid outbreak, so in 2019, we were planning what we called “demonstration projects” between NIH and Moderna to see how quickly could we make a vaccine if we saw a new virus. Could we get that vaccine into people, the first human testing, in six months or three months or even less than that? And so, we were planning these demonstration projects. When this new novel

coronavirus emerged, we immediately turned our attention to all of that planning, and to use it and apply it to this new coronavirus. That's one of the reasons that NIH and Moderna were able to very quickly and eventually Pfizer and BioNTech were able to very quickly get mRNA vaccines into people and developed so quickly.

THOMAS: Super interesting. I had not heard yet about the demonstration projects. When did you say those started?

MASCOLA: We started those discussions in 2019. The intent, the thinking is that response to a new epidemic virus is really dependent on being prepared. Preparedness then allows rapid response. That preparedness has a lot of different elements to it, but it means understanding a particular family of viruses, understanding its biology, its immunology. Understanding how the immune system would protect itself from that virus. And understanding what kind of vaccine one would use in that particular case. If you understand those elements, one could very quickly move a vaccine into people.

We were planning a demonstration project for a different family of viruses, different than coronavirus. The idea was to take a brand new viral sequence, something that we hadn't seen before, and do a clinical trial in less than sixty days and to see if we could actually do that. For the novel coronavirus, it turned out that in working with Moderna, from the time that we saw the sequence to the time that we're in a human clinical trial was, I think, 62 days.

THOMAS: I wanted to ask you about this. What appears to be speed-of-light process from the outside. People talk about the miracle of the vaccine, and you're addressing that now, but if there's anything you want to add in terms of being able to develop a safe and effective vaccine so quickly, or a vaccination strategy as well.

MASCOLA: As I mentioned earlier, we had been studying coronaviruses since the early 2000s. We had been thinking about vaccines for coronaviruses for many years. We actually made a, for the original SARS, we made a DNA vaccine in 2004. DNA vaccines are not very different than RNA vaccines. They're very similar technologies. So that goes back to 2004. This technology that was new to most people was not new to us. We understood how it worked. In parallel, companies were developing and optimizing mRNA as a platform and were learning about it and were doing lots of phase one trials. There was about a decade of experience of early-stage trials with mRNA to show us that it was safe, and it could work.

We paired all that information about this new platform, mRNA, with all the information we had from the first SARS, and from MERS, and from this new coronavirus. Even though it was rapid, really what was happening was we were taking more than a decade of scientific experience and leveraging all of that information to move very quickly on a vaccine platform that we understood. We chose RNA for the very specific reason that it's fast and flexible.

The other point I would make is that this very rapid 60 days means it's 60 days until we're in a phase one study. A phase one study is essentially a safety study in people. It says you have a new vaccine. It hasn't been tested before in the human population. We start with a small group of people. We first do some testing, assess the safety of the vaccine, and then move incrementally from there. And so, the standard



clinical processes were in place. We were just able to jumpstart the ability to get the vaccine into the human clinical trials phase.

THOMAS: Were there issues at all with the safety and effectiveness from the clinical trials? Any setbacks?

MASCOLA: The vaccine proved to be very safe, very well tolerated, and that bore out as millions of people were vaccinated. Of course, the effectiveness, you don't really know until you do the big trials. What we look at in the very first trials - is what kind of antibody response does someone make, or what kind of immune response does someone make, when we inject them with this vaccine? And those early data were very encouraging. We had a sense, and actually even before the human trials, we do the same thing in small animals where we test the vaccine. Each time we looked, we were seeing very strong, very robust immune responses against the coronavirus. We were optimistic that that would translate into people, and that that would translate to clinical protection. Of course, you don't really know until we finally got the results at the end of 2020, which showed that the vaccine was indeed effective.

THOMAS: Throughout our conversation, we've been talking about what your work is built on and what's come before and all of that, but what about technologies? I'm curious what technologies in the course of your career have developed outside of your field that have then influenced your field?

MASCOLA: Many technologies have increased our ability to understand a virus and to respond very quickly. A couple of those would be, that we can now find a new viral pathogen that infects people and sequence that virus' RNA literally in a matter of days and make that data publicly available on public websites that scientists can see and then analyze that data and essentially in minutes to understand what a new pathogen is. Compared to years ago when one might have to culture a virus or spend weeks and weeks in the laboratory, you take that whole process of identifying a new pathogen down to a few days. So that's one. We can work with the genetics of a virus very quickly. Once we have the genetics of a virus, we can start to make the proteins of the virus independently, one at a time. So, we can take it apart.

The other new technology is something called cryo-electron microscopy. Which is a way to study the way the virus looks at the atomic level. It's essentially a very, very powerful electron microscope, and one can see the spike proteins on the virus in enormous detail. You can magnify something on the matter of a million-fold. And so, scientists can look at it on the computer and see exactly what it looks like. One can see how that viral protein would attach to a human cell. So, we have all of that technology. That's called structural biology. We look at the structure of proteins. We can also study the immune system in ways we never could. When we test a new vaccine in people, we can actually isolate the antibodies that a person makes and look at them in molecular detail.

All of this work used to take weeks and months, and we would be studying things by maybe reacting some serum with some viruses in the laboratory. Now all of this is molecular or atomic-level detail. So bottom line is that one can see an antibody attaching to the protein of a virus, and can see it physically, and can see it in atomic-level detail. So you know how things are working. When you know how things are working, then it gives you a framework to say well I need my vaccine to do this. I need it to make this

antibody so that this antibody can block the virus here, and the virus can't attach to itself. All of those technologies emerged over the last 10 years, and they can all be applied to the development of coronavirus vaccines.

THOMAS: That's really astonishing. Taking that information, just one more question regarding sort of the day-to-day of the last couple of years. Most people I talk to, most professionals I talk to when I'm interviewing them, when I ask about the last couple of years, talk about Zoom meetings, and we all know that. But beyond the Zoom meetings, you're actually doing this research. What did that look like for you and your team during the last two years?

MASCOLA: Well for us, there were people in the laboratory all the time. We were trying to do this research which was critical at a time when we had a disease that we didn't understand very well. In the early days, we didn't really fully understand how it was transmitted, or its full level of contagiousness, the best way to protect ourselves. There was no vaccine. We had to find a way to continue work, and everybody at the center who was working in the laboratory wanted to continue to work. While we were physically distancing, wearing highly protective masks, and taking all the right precautions. So, there were Zoom meetings, for sure. There was a lot of time spent in the laboratory talking to people and figuring out how to continue the research. How to design the vaccine, how to test the blood samples, how to look at the atomic-level structure of the virus and get all that work done.

THOMAS: I have a couple of technical questions. From my end, they're technical. And I hope they don't sound naïve, but they might. You'll tell me. I wanted to ask you to talk about the process of identifying an antigen. One of the things that I read in, I think it was, it might have been an NIH blog interview. I'm not sure right now. But it's a quote. "We vaccinate using part of a viral protein that the immune system will recognize as foreign." Of course, right, we all know that. "The response to this viral protein or antigen calls in specialized T&B cells, the so-called memory cells, and then remember the encounter." Okay. So that's kind of basic public understanding. Can you talk about that more technically for more specialized audiences than I am?

MASCOLA: Sure. That quote on the NIH website describes the process of designing a vaccine and how it works. All of that depends on a deep understanding of the particular virus. Exactly what the virus is. How it attacks the immune system and how the immune system protects itself. So, each of those elements are, generally speaking, years of work to understand what I refer to as the biology of something. So, we have a new virus. Coronaviruses have been out there in the world for years. There are a few family members that infect humans, but a new one comes up. It comes up in some animal species. And that animal species then transmits it to people. If we don't have all of the elements of understanding available to us, it could take years to even begin to design a vaccine or to respond to that. So, what we do is we study other family members of the coronavirus family. We already knew for coronaviruses in general what the viruses look like. We knew that there was a spike protein on the surface. We knew what the spike protein looked like exactly for cousins of SARS CoV2. We knew what it looked like exactly for SARS. We knew what it looked like for MERS. For some of the coronaviruses, we knew how the immune system attacked those viruses. We knew that if we were to design a vaccine for the original SARS, what antigen, what part of the virus we would use. It turns out that the part of the virus that

makes a very good vaccine is that surface spike protein, that's just on the surface sticking out because that's what the immune system recognizes.

We already knew all those things for this new virus, and we were immediately in the process of applying all that area of knowledge, but just applying it to this very specific new virus.

THOMAS: I was going to ask you, but I think you've answered that question, about the process of understanding the surface proteins of this virus. Is there anything you want to add?

MASCOLA: Well, here's an interesting story is that when we and other scientists studied SARS and then MERS, in the scientific literature, the level of interest in those viruses was pretty nominal. So, we could publish a paper; some of my colleagues did this, to say, "Hey, there's a common cold coronavirus out there, it causes just cold symptoms." It has a name most people haven't heard of. It's called HKU1. But we all get it. We studied the structure of the surface protein of that virus, and we can see it in beautiful atomic-level detail, and we know how it works. And that's interesting. It was actually published in a very good scientific journal. From the public perspective, nobody would ever know that. Scientists took notice. Maybe a few scientists. That kind of information was absolutely pivotal. If we didn't understand a cousin of this new coronavirus, we would have been many, many months behind. So, what turned out is when this new virus was identified, we could express the surface protein, the spike protein of SARS-2 and study its atomic-level structure. We had that I think by mid-February. There's a brand-new human disease, and we understand that spike protein and its atomic-level structure details within six weeks. That's all based on the fact that we were already studying cousins of the virus.

THOMAS: Yes. So, in the same I think post or article, and you've talked about this somewhat so far already. But learning about the outbreak in Wuhan and accessing the sequence, it sounds like that was just available publicly. Or at least within the scientific community via the Internet. Is that correct?

MASCOLA: Yes.

THOMAS: Okay. Amazing. So, it says here, I think you said, "Literally within days we started making the vaccine in the lab." I'm wondering again if you could describe a little bit further those moments. Looking online and working with your team. What people said, what they thought. You know, that kind of thing. If you could just describe that time.

MASCOLA: There were a small group of scientists at our center led by Barney Graham as the principal investigator and Dr. Kizzmekia Corbett as the hands-on lead investigator. And literally working with a small group, a handful of scientists, some of whom were student scientists, post-baccalaureate, just out of college. They had been studying MERS and other coronaviruses. So, you can imagine the level of intensity and excitement, scientific excitement, when this group of people is seeing—so they are making, for example, MERS vaccines, and studying other coronaviruses, figuring out how to make a vaccine—when they see that there is a new coronavirus infecting people and they can see the sequence. Immediately, in the laboratory. Modern technology allows one to make a gene in literally a few days. You can synthesize a gene. Immediately one synthesizes this gene that makes the spike protein of

coronavirus, and we could put it into RNA, and we can start testing it, and we can have cells kind of churn out and express the spike protein of coronavirus so we can study it.

Literally within a few weeks, we have all kinds of studies going on this new virus. It was both a level of scientific intensity and excitement because we knew it was important. This group of people knew what they were doing could have major public health implications, but it was also something completely new. It's what scientists go into science to do is to discover something new. Here's a brand-new virus, and every day is a new discovery. It was a very intense, exciting first couple of months.

THOMAS: Incredible. Can you talk about working in partnership with Moderna, and why they were and are the right company?

MASCOLA: A large part of the reason, and the genesis of our collaboration with Moderna was the platform mRNA. In the vaccine world, the traditional way to make a vaccine, there are a couple of traditional ways. In vaccines that we all get, if you take polio as an example, it's the polio virus that's grown in culture and it can be killed and activated chemically. Or in the earlier days, it was attenuated. It was actually called live attenuated oral polio vaccine. Those are traditional ways. Sometimes one can make a protein. Like the hepatitis B vaccine is just a piece of protein of hepatitis B. That's a bit more modern approach.

All of those approaches take some years to develop. For years we had interest in DNA and RNA vaccines. That was a focus of our center's work. It turned out for a lot of scientific reasons that RNA is quicker and probably has advantages over DNA as a vaccine platform. It's quick to make. It gets into the cell very quickly, and it can turn the cell on to make proteins very quickly. So, we were very interested in RNA, but it wasn't easy for the companies that had adopted RNA technologies to get it to work. RNA is fragile. It doesn't last very long in the lab. It will break apart. It's not easy to get RNA into the cell. Once you get it in the cell, the RNA has to tell the cell, "Here, make this protein." And there's a lot of pieces there.

It actually took five or more years of work to optimize RNA. To actually get it to be a good vaccine platform. So Moderna, BioNTech, and a few other companies were working very hard on that. Essentially, those companies were formed based on scientific discoveries about RNA vaccines. These companies dedicated themselves to figuring out how to turn that scientific discovery into something that was actually useful and usable as a clinical vaccine product. And it really only in about 2019 had, a few of the companies, Moderna included, made enough progress for anyone to be confident that an RNA vaccine could work. But it was because we were following the progress and working with them for a number of years that we knew when the new coronavirus came out, we could take advantage of that platform and it would be likely—we didn't know for sure, we thought it would be likely—that RNA could serve the purpose for a coronavirus vaccine.

THOMAS: I want to tell you that I actually had the opportunity to interview Robert Langer at MIT for another project, the Lemelson MIT Project in September 2020. At the time, I believe they were still in trials for the vaccine.

MASCOLA: Yep.

THOMAS: Yeah. But my question is, because his work on delivering mRNAs, tiny particles without destroying them, began in the 1970s. And of course, Dr. Karikó was in the news regarding this vaccine with her work with Dr. Drew Weissman. However, when I spoke to Dr. Langer, and I know this is true for Dr. Karikó, they had trouble receiving grants, receiving acknowledgement from the scientific community that what they were doing was legitimate, even, much less important. Dr. Langer told me he was also denied faculty positions. It's kind of trailblazing work, but I'm just wondering, in your opinion, how does that lack of ability, what seems to be lack of ability to recognize innovative thinking, affect these kinds of scientific breakthroughs?

MASCOLA: It is absolutely true that the scientific field didn't recognize the importance or, for example, the early work on the lipid nanoparticles to formulate RNA or the early work of the importance of Drew Weissman and Kati Karikó, where they figured out really how to make RNA into a vaccine through some fancy molecular biology called "nucleoside silencing". The reality is that they published that work in pretty high-level scientific journals. Their work was funded by NIH and by other institutions that fund risky, novel ideas. And not all of these risky, novel ideas pan out, but this one was fundamentally important. I think there's two ways to look at it. Sure, there was some skepticism and early slowness in the appreciation of this work, but the system that the United States and other parts of the world have for public funding of research is critical. Likewise, if you look at our center, we're a publicly funded research center. We've been doing DNA vaccines and working with RNA collaborators for more than a decade. And some could ask, why are you doing that? There's not enough scientific rationale, it's risky, it's untested, but we have the ability to do it because of public funding.

I think part of the story here is the importance of publicly funded scientific research and the importance of continuing the ability of allowing scientists to innovate. Then together with this sort of biotechnology world that can take fundamental discoveries like RNA and begin to optimize them for clinical use. Both of those came together just at the right time, really just in the nick of time to allow rapid development coronavirus vaccines.

THOMAS: Sticking with this kind of in-the-public-eye type of work, and publicly funded public health, of course, I do have some questions about that. One is, you know, whatever your comfort level in asking this question is fine. I wanted to ask if you could describe your work at the NIH under the Trump Administration and challenges. Obviously, the CDC has been in the news since that time. And I know there are differences between the CDC and the NIH. But could you describe that? And maybe also versus the Biden Administration, or previous administrations to Trump?

MASCOLA: One of the interesting things about being at NIH is that as a research institution, we are generally shielded from the political vicissitudes of any given administration. And in particular, when there's, and there has been very strong NIH leadership under Francis Collins and Tony Fauci, who directs our institute. We were given complete encouragement and support to go full speed ahead on coronaviruses from the beginning, and that didn't waver. It has not wavered throughout the prior administration, the current administration.

I think the CDC is in in some ways a more difficult position because from the public perspective, if we're studying the details of the molecular basis of an RNA vaccine, or the structural basis of the spike protein, that's interesting science. At the end of the day, what do people really know? They know that we designed the vaccine. Which is true. Dr. Graham and colleagues and others designed the antigen that is the current vaccine. So that is a success, and people can take credit for that success.

When one is making public health policy, like the CDC has to do, in a rapidly changing environment, it is difficult because there is so much uncertainty on which to make the recommendations that one has to do the best they can. Then when things evolve, sometimes people perceive, oh, you changed but really most of the time what's changed is our understanding of the biology of the virus. That changes pretty rapidly when you have a brand-new pathogen.

I think from the NIH perspective, we were in really good shape with the level of support. The only other thing I'd add is that many of us worked on the Operation Warp Speed teams, which was a different aspect of the research. It was more of the implementation. There, likewise, especially in the earlier days, there was just, there was very strong support for vaccine development and also for drug and antiviral development. It really didn't matter so much what the administration was because the level of support, both funding-wise and structural support to get the job done was just there.

THOMAS: What about in terms of the public? And again, differences between the CDC and the NIH. But one thinks of the anti-maskers, or the antivaxxers, you know. So, because public health ultimately and of course vaccination depends on everybody working together and some level of cooperation, and there has to be trust. Scientific communication, as you said, is tricky. Sometimes it's, quite often it's left up to the mass media to interpret, and they don't have the expertise. Is there anything you want to talk about there? How do you address those issues, especially with regard to vaccination?

MASCOLA: I think for those of us in the vaccine field, there's always been a recognition that there were a group of people who are vaccine hesitant. And some were outright anti-vaccine. And that's some minority of people, whatever that percentage is. I think what was distressing to see was the politicization of that with misinformation and sometimes intentional misinformation, in particular by people with MD or PhD after their name. And to see that happen and to talk about things that, or to say things that are not true or not based in our current understanding of the biology of the virus was distressing. Because it is very hard to expect a layperson to discriminate between really conflicting information when people who should be credible are telling them completely different things. It's much easier for me as someone who studied viruses for 25 years, and who studied RNA vaccines for a decade, to be confident. But then, we then depend on communicating that. Some people did a very good job communicating that, and I think most people understood it, but when there's a competing narrative of misinformation, it increases the amount of vaccine hesitancy. I think that's what's happened.

THOMAS: So how do you build a vaccination strategy based on what you just said? And just in general, as well.

MASCOLA: You meant to overcome vaccine hesitancy? I frankly don't know. The level of political discourse in this country doesn't really currently allow for a very effective strategy to deal with vaccine hesitancy, I don't believe.

THOMAS: Fair enough. Covid-19, of course, like HIV, has had a disproportionate impact on more marginalized communities, and not just domestically. Can you take a moment to talk about health equity?

MASCOLA: Yes. We've learned many things from the coronavirus pandemic, but among them is that every virus has a different biology in that the way it infects people and causes disease, that we don't always understand why a virus causes disease in one person and not another. What we learned in this particular case with this particular virus that causes Covid, that there are certain underlying conditions and factors that predispose people to more severe outcomes. They include certain medical comorbidities, including things like being overweight, having cardiovascular disease, having hypertension, having diabetes. In as far as some of those conditions disproportionately affect some parts of the population, they suffer worse outcomes from the virus. There's a lot there for the public health community to learn from and to address over time. It's beyond my area of research expertise. Certainly, it's a critical part of responding to new outbreaks. Because anytime a virus causes illness, we call that being pathogenic, that means that it's going to affect people differently. We need to understand what the factors are and address them. If it turns out that hypertension, diabetes, and overweight are factors that are problematic, then those are things that can and should be addressed more readily to protect those populations from potential detrimental effects.

THOMAS: Then of course the research. There's research on what it's built upon, but then there's also been a lot of inspiring news coming out of the massive amount of research, just in the last couple of years, toward this disease and how it might affect other diseases. I read that one of the most important pandemic breakthroughs was the discovery that 15 to 20 percent of patients over 70 who die of Covid-19 have rogue antibodies that disable a key part of the immune system. They're called autoantibodies, which attack a protein called interferon, that acts as a first line of defense against viruses. First of all, how would you describe this discovery? And then after that, of course, talking about some of this news that I'm referring to, whether it's developing an HIV vaccine or potentially targeting cancer, things of that nature?

MASCOLA: The first principle here is an understanding, again, of the virus biology. How does the virus infect a person? How does it get in? How does it do damage? And why is that damage different in some people and not others? This novel coronavirus, SARS COV2, has a really diverse spectrum of clinical manifestations. Someone can be completely asymptomatic, or almost asymptomatic. Maybe have a runny nose, maybe have a sore throat. Someone else can have severe pneumonia that is so serious that they can't respirate, they can't breathe, and they need to be ventilated and may die. Why is it so different in different people? There is just, I'd say, an emerging understanding of that problem, that issue. We call that scientifically, we call that the pathophysiology, which stands for the disease physiology. What is the pathophysiology that's different in one person to another? And one of those factors is what you just cited. And I'm sure it's not the only one. But the human body has different sort of levels of immune protection. There's this very early level which says hey, there's a foreign invader

here and I'm going to put a bunch of chemicals down to kind of slow it down. And that early response, if that early response is slowed or defective, which it is in some of these cases, it allows the virus to get in more quickly and replicate to a higher level. And that can be very damaging. So, two years into this disease, where we have a more solid, but I would say, incomplete understanding of pathogenicity of this virus.

THOMAS: Then what about the research toward coronavirus now being potentially used, especially with RNA, toward things like will there really be an HIV vaccine? What are the implications for other diseases?

MASCOLA: Yes, I think there's two levels to think about when we think about what we've learned from Covid. One is the appreciation that work on HIV in particular, and all the technologies and scientific advances that were built over twenty years of studying HIV, were really critical to the rapid understanding of this new virus, SARS COV2. And so, can it now work in reverse? Can we take all this understanding that we've gained from how a vaccine can work on SARS COV2 and apply it back? And by the way, it's not just vaccines. It's also antivirals, monoclonal antibodies and all the other therapies that have been developed. Can we turn that back on HIV and other viruses? And so that's happening. I think there is a burgeoning understanding of how to better protect and treat viral diseases. If we think about it, if one gets sick and goes to the doctor, one can get an antibiotic for a bacterial disease, like strep throat. But if the doctor says you have a virus, what happens? Usually, they send you home and say take some Tylenol. So, we don't really have very good treatments for most viruses. But that's changing. HIV changed that for chronic viral disease. Hepatitis C, we have treatments now. And I think the future is that we will have treatments for viral diseases. Better treatments as well as better vaccines.

The other parallel part of that story is that we should be able to respond rapidly if you have a new viral outbreak, regardless of what family of viruses it is, but that takes preparation. That's maybe a longer story and a longer answer. But we talked about a decade of progress in coronaviruses, starting with Drew Weissman and Katie Karikó and starting with early work on mRNA. If that wasn't done, then you wouldn't have the coronavirus vaccine. If we don't do that kind of preparatory work for other virus families, and really understand the biology of other virus families that could infect people, then we won't be able to respond rapidly enough.

THOMAS: Could you give me an example? If there is one right now?

MASCOLA: I think an example is that there are about 25 or so virus families that we know of that infect people. A virus family is a whole category. So, a virus family includes SARS and MERS and SARS-COV-2, for example. That's a family of viruses. There are probably hundreds of other coronaviruses out there. So, we now, because of Covid, understand quite a bit about this particular virus family. If another coronavirus were to emerge from bats or mammals into people and infect them, you can imagine we would respond pretty quickly. But there are families of viruses. Most of those names are a bit scientific. Paramyxoviruses or arenaviruses or Bunyaviruses that have the potential to infect people and cause disease. People have heard of Lassa fever, relatives of Ebola and Marburg, for example, and many others, where we don't understand nearly as much as we do for coronavirus. So, the research to understanding the virus, relatively speaking, the laboratory research, is a relatively small investment



compared to what you need to respond. So, we think, my colleagues and I think, that pandemic preparedness, doing the basic biology, the research into the major virus families that could cause outbreaks, is well worth it. But it takes this public funding commitment to do some risky, innovative research in ways that don't always, aren't always obvious right away as to why it's going to be helpful, but [will] pan out in the long run to make sure that one doesn't get surprised.

THOMAS: Super important. I wish that could be communicated with the general public on an ongoing basis. Because that would help prepare people for the idea, too, I think.

I always like to ask about biggest successes. I mean, we've been talking about something here that's obviously a very big success. What about setbacks? Have you experienced setbacks? Or I don't even know if you would describe them that way. Some people do not. What happened and what you learned from those things and how you knew to move on.

MASCOLA: There are always setbacks in science. We have developed vaccines or antibody products that didn't work as well as we had hoped. One of the things that we try to do scientifically is say if we develop a product or do a scientific experiment or a clinical trial, that we design it in such a way that we learn as much as possible. And so, while one may not have a successful product, we have scientific knowledge that will help us design a product next time. So, for me, I've studied HIV for most of my professional life, and we still don't have an HIV vaccine. So clearly to me, that's a setback. Now an HIV vaccine, it turns out, is much more complicated than a coronavirus vaccine. There are a lot of reasons for that. But we actually understand the difference much better now. We understand why the immune system can effectively protect against a coronavirus, and why the immune system has so much trouble against HIV. So, we can use that knowledge to try to make an HIV vaccine. We also, we developed, we can develop antibodies as therapeutic products. So, some of my colleagues, Nancy Sullivan and her colleagues, developed an antibody that can treat Ebola virus disease. If a person is treated early, it can dramatically reduce the mortality. We developed an antibody against HIV. And we were hoping that it would prevent or block infection if we gave that antibody to people who were at high risk of acquiring HIV. And the antibody turned out not to work very well in a large clinical trial. You could consider that a setback, but what we learned is that the reason it didn't work very well is that some of the viruses in the community were evading the antibody. We need a better antibody. We need a broader antibody. So, you learn as you go. You take the setbacks not as a final failure, but as a way to figure out the path forward.

THOMAS: Great. Obviously, I want, I always ask about successes in general, and of course we've been talking about the coronavirus. When did you know, when did you realize, however, that your vaccine would work?

MASCOLA: I would say that we were optimistic it would—I wouldn't say highly optimistic. We were optimistic it would work after the phase one trials where we drew blood from volunteers, we studied the blood in the laboratory, and we saw these very high levels of antibodies that were directed to the spike protein and that we knew that those antibodies would block attachment of the virus. That's a very good sign. Did that tell us for sure that the vaccine would work clinically? No. You know, I think we were quite optimistic. What we didn't know was what does optimistic really mean? Does it mean the vaccine

would work 50 percent, 70 percent, 90 percent? And, of course, we didn't really learn that till December of 2020. But what I would say there is, there was this enormous effort to do the right kind of largescale clinical trials that we call placebo control phase III vaccine trials. Those were very expensive and took an enormous amount of infrastructure, and hundreds of thousands of people to perform. And it wasn't really, and then there are data safety boards that look at the data independently. And it wasn't until the independent data safety board broke the code and said, "Your vaccine works, here's the data," that we knew for sure. But I'm proud of the way we approached it. That we built all of the infrastructure quickly, and we did it in the right way with the right safety configuration involving all the regulatory aspects. And yet still were able to learn by the end of 2020 that a vaccine was effective.

THOMAS: I'm just curious. How do you find people to participate in the clinical trials? Because on the one hand, we've talked about vaccine hesitancy, and this would be the opposite, before anything's even been proven safe and effective?

MASCOLA: Finding people to volunteer for any given trial really varies a lot depending on the situation. In the case of Covid, there were many, many people who were very willing to volunteer. We use a process called informed consent, where we explain to them that we are asking them to be administered an experimental vaccine for which we do not know its overall efficacy. We have safety data in hundreds of people, but not more than that. And that we're going to draw their blood and follow them very closely. But there was a huge interest for vaccine volunteers for the coronavirus trials.

THOMAS: That's good news. I have a question for you. Before I ask it, though, I want to ask if there's anything else that we haven't talked about that you really feel is important to add about the coronavirus research or the last couple of years or even the long span, the last 20-plus years of your work.

MASCOLA: I think we've covered a lot of the major elements, so I'm pretty comfortable. I can't think of a major gap.

THOMAS: Good. So, I want to ask you a couple of more general questions. One is just about scientific discovery in general. Which is, you know, it's often messy. It's built upon what came before it, but there's a lot of teamwork involved. And that's not typically the, it's kind of not the popular image that people have of scientific discovery. So, I'm wondering what role does collaboration play in your process?

MASCOLA: Modern science is highly collaborative because it's become so technical and so sophisticated that the expertise to do what one wants to do doesn't lie in any one place. If we take this coronavirus vaccine as an example, on one hand we need to study the genetic sequence of the virus. That's molecular virology. That's people with certain molecular expertise. On the other hand, we want to study the atomic-level structure of the spike protein, which is a protein on the surface. And that takes structural biology expertise. On the other hand, we want to quickly make a vaccine as a clinical product and test it in a phase one trial. That takes biomedical engineers to make a product, and that takes clinical scientists to actually do a phase one trial. When one looks at major scientific developments, if you look at who's involved, it's more and more commonly large consortium of scientists and clinical scientists and laboratory scientists working together to figure something out.

THOMAS: What would you tell young scientists or students who want to be scientists, what would you tell them today? What advice would you give to encourage them to seek out necessary resources or to pursue their goals, for example?

MASCOLA: I have never hesitated to encourage young people with an interest in science to take on that career. I would often tell them that getting a PhD, for example, can be a long journey. Getting an MD and going into research can be a long journey. It's really important to enjoy the journey. One has to have a love of learning the biology, and a love of discovery. Certainly, especially in the early days of science, it's not a highly lucrative career, so you really have to love it and enjoy it. What I can say now to young people is that this really is a golden era of scientific research and in particular, in the realm of infectious diseases and understanding human immunology. It's just blossomed, really exploded scientifically. There's all kinds of opportunities to make progress and to make a difference, whether that's in infectious diseases, whether that's in oncology or what we call immune-oncology and therapeutics. There's just a vast area where young people can come in and make a scientific difference.

THOMAS: Then in terms of mentorship, we talked early on about you had good structure and advice given to you as a young professional. Can you talk about your own role as a mentor, and what the role of mentoring means in science in general?

MASCOLA: Yes. At our center, at the Vaccine Center, we really emphasize mentorship as a key part of our public health mission. I think most academic institutions do the same. Here at NIH, we happen to take a lot of post-baccalaureate students who have finished their degree in college, and they're considering a career in biomedical research. Many of them are trying to figure out exactly how that career will be shaped. Should they get a PhD? Should the PhD be in microbiology or immunology? Or should they get a medical degree? Or should they get both, an MD and a PhD? How should they shape that career?

They come here for a year or two, and they do research. We pair them with a scientist working in the lab who's experienced. Let them work on projects, one or two projects, where they get to work in the lab, understand the science, the scientific terminology, the scientific techniques. Generate data. Contribute to a paper. Present a poster. Go to a major meeting. Give talks. We practice the talks with them, and let them participate in all steps with us. That is probably, I'd say for most scientists, one of the most enjoyable aspects of what we do every day.

THOMAS: A couple of more questions. I meant to ask this earlier. It's always interesting to ask people what motivates them, what inspires them and also, what bores them.

MASCOLA: Discovering something new motivates most scientists. There is a "eureka!" moment when in the laboratory or in the clinic you see something that scientists have not seen before or understood before. When we were working on HIV early on, we discovered an antibody that would work very effectively against HIV. And when we first saw that in the laboratory, it's something we had not seen before, and the scientific field didn't really understand could exist. So those types of eureka moments that scientists really live for to see.

And at the end of the day, it gets back to what I always talk to students about is understanding the biology of something. The biology of an infectious disease's pathogen is complicated. There's a puzzle of it, and a puzzle is never complete. We never fully understand all of the biology of anything, but we can fill in a lot of those pieces. In some cases, we understand it so well that we can treat it; we can prevent it; we can cure it. It's really about understanding the biology of something.

What's boring? Very little. Science is one of the most gratifying careers. A day is never boring. There are administrative functions. Making sure the budget is balanced. You know, those kind of things can be mundane, but those are small prices to pay for the more gratifying moments.

THOMAS: Wonderful. I can understand that. I think we can all relate to that. This is an institutionally oriented question. I read in the strategic plan for 2020-2025, that major goals of the center include developing and implementing strategies for workforce equity—we talked about health equity—and of course women, people of color tend to be typically underrepresented in the field of science. Do you care to address that in terms of the center?

MASCOLA: Yes. Workforce equity continues to be a major problem in science. And I think that is reflected on the intramural campus at NIH, as well as other places. Although there's been a lot of progress recently. I think, at least from my perspective, and I haven't done a real survey of this, we're making more progress in gender equity than we are in racial/ethnic equity. But what I can say is that this is something NIH leadership has made as a major priority. Most of the laboratories, included our center, have their diversity equity inclusion [DEI] committees where we meet with our committees frequently and come up with short and long-term strategies on how to improve the workplace environment and address equity issues. While it's important to address them at leadership levels, of course, so that there's equity at that level, we also have a big emphasis at the student and younger scientist level, where I can see progress being made. If one looks at just a photo collage of young scientists coming into NIH, you can see progress. There's a lot of emphasis there in trying to engender broad interest by young scientists to come to NIH and to train. Because those post-baccalaureate students I mentioned, we really want that pool of young scientists to reflect the community at large.

THOMAS: One more Covid question, and I think we can wrap it up. I wanted just to ask you about long Covid, and whether or not this is a surprising development.

MASCOLA: Long Covid is real. It's a physiologic entity, and it's not surprising. Because we now understand—you know, I say not surprising, I don't mean to be glib. Given our understanding of the pathophysiology, the disease-causing potential. We know that the virus gets into the system, replicates widely throughout the body, attaches to cells throughout the body, attaches to cells on the blood vessels, in the kidney, in the muscles, in the heart, in the brain. And when a virus gets into a cell it causes damage. So, if you understand that biology, the first thing is, as an infectious diseases physician, I want a vaccine right away. This concept that I'm better off getting natural infection is just a misunderstanding of the reality. Yes, most young people will fight it off and not have that damage. But the damage potential from a Covid infection far, far, far exceeds the potential risk of getting vaccinated. Long Covid, I think, it's not, we don't fully understand it, is just a manifestation that the virus does as it replicates throughout the body while the immune system is attempting to fight it off.

THOMAS: That's fascinating and a little alarming, to be honest. Is there anything that we haven't talked about you want to add? Anything I haven't asked?

MASCOLA: I don't think so. I think we've covered things pretty broadly.

THOMAS: Well, it's been a real pleasure to talk to you. Just on a personal note, I'm super grateful for your work.

MASCOLA: Well, thank you. It's a pleasure to talk to you. They were great questions. I enjoyed answering them. And it's always nice to hear thanks. And I pass them on to all the people I mentioned who were working shifts in the lab.