John O’Shea, M.D. and Elizabeth Walsh, Ph.D.

Behind the Mask

September 15, 2022

Barr: Good afternoon. Today is September 15, 2022. My name is Gabrielle Barr, and I'm the Archivist at the Office of NIH History and Stetten Museum. Today I have the pleasure of speaking with Dr. John O’Shea. Dr. O’Shea is the Scientific Director, Chief of the Molecular Immunology and Inflammation Branch, and Acting Chief of the Laboratory of Lymphocyte Nuclear Biology at the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS). I also have the pleasure of speaking with Dr. Elizabeth Walsh, who is a team lead as a Supervisory Health Science Policy Analyst at the Office of the Director (OD). Today they're both going to be speaking about some of their COVID-19 initiatives and experiences. Thank you very much for being with me.

O'Shea: Thanks very much, Gabrielle.

Walsh: Yeah.

Barr: To begin, both of you were very instrumental in launching and managing an online platform to submit ideas for tools and strategies to mitigate COVID-19. What made you both volunteer for this endeavor?

O'Shea: Why don't I go first on this one, Beth, because I think I actually really did volunteer for this, and I'm not sure you necessarily volunteered per se? But you can come back and say why.

Walsh: Yeah, I'll add on to what you have to say.

O'Shea: In my case, without sort of going into too much detail, what I would imagine future historians might want to hear is sort of the frame of mind maybe Beth and I both were in. Again, maybe Beth can tell it slightly differently than me. I was born in 1952. I knew at that time that there were plenty of diseases around that could be taken care of with vaccines. On one level, I had a very naive view of how pandemics and the like worked. Mostly, polio was a big threat when I was young, but the vaccine came out and took care of that—and lots of other things. But then I came to the NIH. The year I came to the NIH was the year that the HIV epidemic began breaking—1981. Then during my experience at NIH, we had a number of other things, like Ebola. Suddenly I became way more aware of how tenuous all this is. It was very personal for me, because my mother was in a nursing home at that time. Then at one point—it would have been probably around March of 2020, when the governor said no visitors—I was unable to go see my mother. I'm a physician, and they gave me a fair amount of latitude. They said, “Well, if you know how to do aseptic technique and everything, if you want to, come in and see your mother.” But she said, “No, absolutely not. You can't come in because it's going to be very risky here.” She was watching the news. She was watching Tony [Dr. Anthony] Fauci every day—and I had worked with Tony, and she had known Tony. She had met Tony when I first came to the NIH in 1980s and so she was absolutely thrilled to see Tony being in charge and helping in all the ways he helped. But she said, “No, we don't know how risky all of this is going to be. It seems to be pretty deadly, and I don't want you to come into the nursing home.” I met with her, and I said, “You know, I don't know if I'll see you again, Mom.” But yeah, that was the last time I saw her. I said, “Mom, this might be it. We'll stay in touch, but I will honor your request, because we don't know how dangerous this is going to be.” And she said, “I don't want you to die, and I don’t want your wife to die.” Pretty soon, in April, she did get COVID. She died right away as soon as it came through. It is sad, and it was

dramatic. I became very close to the doctor who was taking care of her, as you can imagine. She was telling me what was going on in the nursing home, and it was terrifying. That's why I volunteered. Beth, you're crying now and I'm crying now.

Walsh: I'm a mess already. You got me.

O'Shea: I really felt compelled to do a bunch of things. I was telling Beth I felt like I was in this movie—sort of a World War II movie of the Blitz in Britain or something. I thought, "Oh, my God, this is terrible. I gotta help in some way." Why don't you take it from there, Beth, and say how you and I got to be partners during this?

Walsh: I just think at the beginning of the pandemic, there was desire across not just NIH but across the nation for everyone to really pitch in and roll up their sleeves to do whatever they could to contribute. I mean, from my perspective, it was a duty I felt I needed to fulfill because I could.

Barr: Can you introduce the portal? Who is it for? How'd you all design it? When did you start working on it?

Walsh: Sure. I think after the declaration of the pandemic there was a bit of a lag before people realized the role NIH was going to play, and was already playing, in the response. But I think once that realization hit, a couple of weeks after the declaration, there was this overwhelming tide of information that started coming into NIH through just any channel that people could find. We really needed a way to be able to sort through that information and make sense of it. I really think it was a reflection of people feeling a little bit helpless, in a way, and just looking for an outlet to feel like they could contribute, and I think the portal kind of provided that. We had a lot of different types of candidates—diagnostics, therapeutics, vaccine targets, homeopathic remedies, and even just a lot of personal stories—that would come in throughout the pandemic. I think it was something that people could really coalesce around and feel like they were contributing to during a time where I think all of us were feeling a little bit helpless in the face of this enormous public health threat. That was kind of the impetus behind it.

Barr: How did people submit it?

Walsh: We created an online form, and we modeled it after a submission site that DARPA [Defense Advanced Research Projects Agency] has for advanced development projects, because we thought there was the potential that some of the information coming in might be more appropriate for DARPA versus NIH. We're more in the research realm; they're more in the advanced development realm—so we wanted to make sure that there was alignment across agencies so that we could really streamline the channels and routing of information. We really wanted to do that. Setting it up really only took a couple of days. I and another staff member, Kamilah Rashid, worked on it, and then one of our counterparts in the Office of Extramural Research, Michael Dorsey, built the actual web form, and I'm sure he worked with some others to do that. It went live in May of 2020, and immediately the amount of information that came in was a little bit overwhelming. We had a group of 15 volunteers with a wide variety of expertise across NIH, and John O'Shea, of course, headed that as the chair of the committee. We had clinical pathologists. We had people with olfactory expertise, since it seemed like there was possibly going to be a taste and smell component to some of the interventions or suggestions that were coming in. We had immunologists. We had people who were familiar with developing diagnostics. We really hit a broad number of areas, because we weren't exactly sure what we were going to get.

Barr: How did you guys go about tracking them? Which ones did you even discuss? I'm sure some of them are very, very relevant, and some may have been off the wall, so which ones did you bring to the table? You said you had so many. Did you review every week or once a month? How did you go about doing that?

Walsh: In terms of the process, we knew we needed to be fast. Every minute counted at the beginning of the pandemic, and I think everyone felt that sense of urgency. The system that we set up wasn't a meeting-based system, so we had a spreadsheet that I would provide to the committee where I would compile all of the responses that we had received on a given week, and then there would be a very quick triage system where we had kind of a voting system set up. We had five people and then the first five to get to a given candidate would say yes or no as to if this is this something that we should continue to look into. If there was consensus that they were all "yes," we would move that forward to a group of NIH-wide contacts—again, in different areas of expertise and work streams—and I would provide that information to them for additional, more specific follow-up. If there was a consensus on "no," then I would triage that, and no further action would be taken. But sometimes we would get a scenario where there were some people who thought it should go and some people who shouldn't. Then John and I would meet and discuss those candidates and make a final decision on whether it would move forward. I turn it over to John to talk a little bit about what went into that kind of decision making.

O'Shea: Sure, sure. The key thing that needs to be emphasized is—maybe a couple of things. One is that for neither of us was this our day job, right? Dealing with COVID as Scientific Director kept me quite busy, and Beth had many, many other responsibilities. Beth, you put this all together with two children, who I'm sure were helping you a lot in this process. But suffice it to say, Beth is an exceptionally organized person, and with exceptionally good judgment. We didn't know what we were going to get. [screen freezes for 23 seconds; no audio] We didn't know how many we're going to get. And to be honest, it was completely terrifying in the beginning. I think the first week we got more than 100 applications, would you say?

Walsh: Yeah, I mean, I think the first week it was about 125 that folks had to sort through on top of everything else that that was going on, so it was not an insubstantial lift.

O'Shea: To a certain extent, these things are a little bit like grant applications—so just like taking on 100 grant applications. I had a lot of ideas on how we should do it, and then Beth told me I was wrong—appropriately.

Walsh: That is not accurate. [laughs]

O'Shea: It's totally accurate. Well, I'm paraphrasing a little bit. Sort of the way I was thinking about it would be more like reviewing papers—reviewers would write, and then we would read the reviews. But I realized right away that we needed to be quick. And we did need to pick the wheat from the chaff quickly. And Beth was exceptionally good at that. But in the early days, she and I went through every single application very carefully. As you said, some of the applications were—how did you put it? "Off the wall." Maybe we would put it slightly more diplomatically, but people did not always have a great deal of scientific sophistication. Maybe Beth will get into this. You could imagine, over time, there were a lot of applications that related to ivermectin and ultraviolet lights. Beth, you took it on a lot of times to go through the applications that probably did not have a great deal of scientific merit. You did that yourself, and then you told me what you did at the end of the week, but it didn't go out to the rest of the committee. We didn't want this to be burdensome for them. We were looking very much for the wheat versus the chaff, and for things that really deserved heavy-duty scientific evaluation.

Walsh: I mean, in the first couple of weeks, I think I sent everything to everyone. But then after a couple of weeks, when it became clear that there were some where the scientific foundation for the idea maybe wasn't there, I was able to sort through those. Those became my children's bedtime stories more or less.

Barr: People had to submit full applications?

Walsh: Basically, there was just a brief justification narrative field. They were allowed 500 characters, and then they could provide a hyperlinked document if they wanted to provide extra information. I mean, sometimes it was obvious from what was submitted in the justification that it wasn't something that NIH prioritized to pursue, and other times you had to read all of the information that was provided to make a judgment call. It was that kind of stuff that was presented to the committee for further evaluation.

Barr: What were some of the proposals that you all considered?

O'Shea: Well, we alluded to the ivermectin and hydroxychloroquine. In a way, I think one of the things that was important was that we pass on all of the information on that we were hearing about. It's very important that NIH took on taking some of these things seriously, just because—who knows? —maybe there was some truth to that. But it's very important for the population of the United States to know that we were taking all these things seriously. The science, in the end, had to rule, and even if somebody thought something was a bad idea, it should be tested rigorously. Those were some of the things that came through.

Walsh: Yeah, in a lot of ways, there were submissions from companies that were a lot more standardized and methodical—the submissions for vaccine platforms, candidate diagnostics, immunotherapeutic, monoclonal antibodies—things that people maybe didn't know about before the COVID-19 pandemic that are now household terminology. But then we would have other submissions that were really a reflection of the broader messaging to the public that was going on at the time, in a time of more political divisiveness where the messaging really wasn't clear and sometimes didn't have a scientific foundation. There were submissions where people would make suggestions about drinking bleach or asking us questions like “What percent bleach solution am I supposed to be drinking?” Then we would have to route that information to public sources for response and say things like, “Please don't drink the bleach.” There were a lot of those types of submissions. There were submissions from individuals whose grandma had a specific tincture that she would always give them when they were sick—maybe it was a ginseng or echinacea tea or something like that. Those things are comfort remedies, which we shouldn't discount, because your mental perspective of health and the potential immune benefits of those items haven't really been scientifically tested either.

Barr: You must have felt very close to those people that would give you so many personal stories from their family.

Walsh: Yeah. I mean, in the beginning, it was harder because you had to just kind of compartmentalize. The information was coming in and you had to stay in the process to make sure that all of the information would flow. It was hard to digest some of the things that were coming in and reflect upon what those really meant to people. But after the first eight months of the pandemic, when things kind of settled in, we had a couple of monoclonal antibodies, we had good prospects for vaccines, and people seemed to settle down. The submissions also kind of settled down a little bit too and declined. You could take more time and think about what led to this person providing this information, and just kind of think about them a little bit more.

Barr: How did people get access to the portal? It's on the public site, but how did everyday people know about it or find it?

Walsh: When people would make public inquiries into NIH through either communications channels that have been long established or just one-to-one communications, they would be directed to the portal. In terms of researchers and companies who are already familiar with NIH and know how to navigate it, they'd be able to find it on their own. A lot of people were coming to the COVID-19 website that NIH had at the time for answers, and we had a link to the portal there, so I think people were pretty aware of it. Some people were very aware of it.

O'Shea: From around the world, right? But again, to Beth's point, it was a terrifying time. And I think the idea that any person, if they thought they had a good idea, had access to give information to the NIH… I mean, I'll give you another example. When the vaccines were starting to come out, and we knew they had to be refrigerated, we actually had a lot of ideas from people—like repurposing ice cream trucks to bring it [to communities]. That's a great idea, right? There were other examples like that, where you think they heard on the news, "Wait a minute, how are we going to get these vaccines that are frozen? How are we going to get them to people?" If you have enough people, you get a lot of good ideas. That's why I think Beth and I get emotional. There's sort of a pride that we were that interface—that people could do that, and we would give them an audience. And even if people didn't follow through, it was, in a way, an optimistic note in a very pessimistic time. Beth, I'm not saying it as well as you say it.

Walsh: Yeah, again, just having that outlet for [finding out] what are good ideas. And like John said, some of these great ideas that were submitted we couldn't necessarily follow up on because it was outside of the NIH purview. But we made every effort, when we thought something was valid or a good idea, to try to find a point of contact inside or outside of NIH to pass that information on to. We weren't always successful in that, but we did try.

Barr: I think your portal is also nice because so often people see NIH as being kind of removed. Even though the American people pay for it, they don't really have access, so it's nice that you show you are actually caring and interacting with them.

Walsh: Yeah. And I mean, that was also part of the reason that we set up the COVID-19 public site, because there can be that disconnect about what we are actually doing and how that is benefitting them. And so, the impetus behind that site is really more to reflect that and to make it personal stories that show the impact it has on different communities and individuals. That is another way we try to connect.

Barr: Have you all done analysis on those who contributed, like a total number? Have you broken it down by companies, scientists, physicians, those in the medical field, and the general public—or any kind of demographics?

Walsh: Yeah, so we haven't done an extensive kind of impact analysis and demographics. I mean, I do have some numbers. We had 1,074 submissions in all, and about 211 of those submissions were sent to various contacts across NIH or to DARPA contacts outside of NIH for follow-up—or at least to make them aware that we received some information that we thought would be viable to follow-up on. In terms of the breakdown, most of the ideas that that we received were for therapeutics. We had about 102 therapeutic submissions that we initially passed on for information. For diagnostics, vaccines, preclinical targets, it was fewer—probably more in the

order of 15 to 20 each. Then there were others that didn't really fit into a category, probably somewhere in the order 40 to 50 of those.

Barr: When did you guys decide to wind down this portal, and why did you make the decision when you did?

Walsh: As we went along, we kind of looked at the need based on the number of submissions. Initially, that was really the only channel for people to provide their ideas for therapeutics or vaccines. Eventually, the ACTIV [Accelerating COVID-19 Therapeutic Interventions and Vaccines] program set up a more structured portal for therapeutics that requested a lot more specific information, and then they underwent their own triage process. But that was a bit later—months later—in the response. There is a bit of a lag there. Once they had their portals set up, there was a drop in the information that came into ours. But in some cases, because people were aware of it, they would still send us the information that we would then transfer over to the ACTIV program. But I think once people knew a little bit more about the pandemic, once there were diagnostics and vaccines, and people were kind of coming to grips with the mitigation measures that are available to us—how we address this, and how we deal with this—at that time, the submissions really, really started to go down. Once we got down to just receiving ten submissions for a month that were really kind of repetitive—a lot of the same individuals submitting the same ideas over and over again—we decided to close it down, which was November of 2021.

O'Shea: If I could interject, that was sort of a sad day for me, to be honest. Part of it was, again, with the dissension early on, we really didn't know how bad things were going to get. There are obviously histories of plagues in the world where half the population dies. In those early days, we really didn't know how bad it was going to be. Our point of view was of saying we want to be in the fight. This is a fight for humanity, in a way, or it seemed like it at the time—and sort of still is. You want to be doing the best you can. But at the same time, as chaotic and terrifying all this was for me, every week I got to see Beth, and we'd sort of talk about the latest. In a way, we supported each other. Beth had two kids, and I'd get to meet them for a short period of time, they'd be jumping on the bed or something. There was sort of a bonding that happens when you're in the trenches—you know, soldiers in the foxhole or something. You think, "Okay, it's really scary out there, but we're going to work together. We're going to try to survive through this." Each week we would meet and do our job, and then, in one way or another, in my mind, sort of support each other. I would try to come up with jokes for the kids. I got a few really good jokes that your kids really liked, right? And they would tell the rest of the family, right? In a way that's emblematic in my mind when I think what the key survival things are. I mean, okay, so we didn't live through the black plague. Thankfully, we got vaccines, and many fewer people died than could have. But we didn't know that in 2020, right? We didn't know that the NIH would generate vaccines by January. If you told me on a meeting that we were going to have vaccines by January, I'd say, "You're crazy. I'm an immunologist. I know how long it takes. I've been involved in drug discovery. No, no, no, we're not going to get vaccines within a year." But we did and thank goodness for that. Then that obviously changed everything. But week after week, in my mind, having a sense of humor, a sense of camaraderie, and a sense of mission were the things that sort of kept you going. Am I being overly dramatic again, Beth?

Walsh: Oh no. Meeting with John was always a bright point in the week because I knew no matter what we had to do or get through that day, it was going to be a positive experience. And I have to say the "interrupting cow" joke is still a perennial in the household.

Barr: What is the "interrupting cow" joke before we move on?

O'Shea: Knock, knock.

Barr: Who's th—

O'Shea: Moo!

Barr: That was a good one. I'll have to use it on my family.

Walsh: No, no, no. Okay, let's try that again, John. Knock, knock.

O'Shea: Who's there?

Walsh: Interrupting Cow.

O'Shea: Interrupting co—

Walsh: Hey! How are you? How was your day?

O'Shea: Okay, okay. We need to work on the delivery.

Barr: Dr. Walsh, can you talk a little bit about how you contributed to the RADx-UP [Rapid Acceleration of Diagnostics – Underserved Populations] working group and what skills and expertise you provided?

Walsh: Yeah, so I entered that project kind of midstream. At the point I came in, they had already kind of set up the program infrastructure and governance, had put out some funding opportunity announcements, and made their first set of awards. Where I picked up was in the coordination and execution of the next couple of phases of that. I would interface with RADx-UP leadership. Our co-chairs there were Dr. Eliseo Perez-Stable and Dr. Richard Hodes. We had a governance committee composed of Institute and office directors that provided the overall strategic direction of the program. I would really work with the programmatic staff who were on the ground developing the initiatives, identifying the next priorities for the program to put out funding initiatives, and then coordinating and overseeing the review process and making sure that went smoothly, reporting out to NIH leadership what the needs for the program were. That was another interesting experience where a lot of the reviews were done by NIH volunteers. The Center for Scientific Review was really overwhelmed, and we really recognized the urgency of setting up these testing demonstration projects in communities that were really in need and didn't have regular access to health care. There was just a massive movement across NIH to volunteer and conduct these reviews really quickly so that we could get these awards out the door, get the project started, and get testing to the people who really needed it the most. It was a harrowing time, to be honest. You'd be doing your kid's pre-K Zoom with one hand, bouncing your baby in a bouncer in the other, and trying to coordinate a review meeting at the same time in collaboration with Scientific Review Officers from across NIH. It was very rewarding, but also very stressful.

Barr: I can imagine, having two kids at home. The kids are different ages. They're so young.

Walsh: Yes, at the time, I had a four-year-old and a six-month-old, so a high-need time.

Barr: Dr. O'Shea, can you discuss how you went about assuring that NIAMS staff were safe during the slow down and shut down of many of the labs?

O'Shea: For better or for worse, we were one of the first labs to shut down. We had somebody who was at a meeting in New York, and he came down and I saw him. And he looked terrible. He looked like he had a fever. This was in the very early days, and we were maybe not paying attention as much as to why this guy didn't look so good. We didn't have testing and all that done, and we learned right away that he got very sick, and it was very clear that he had COVID. It's almost hard to imagine [considering] where we are now, where we were then, right? Now somebody in lab, says, "Gee, I don't know whether this is allergies or COVID." Then you have the rapid test. We have those tests now. We didn't have any of that. Basically, I communicated with people and said, "What do we do? We don't know how infectious this is going to be, what is the right protocol for having everybody [work]?" Basically, we emptied out the 13th floor here. Again, we didn't know how long we were going to be quarantined. I basically went home and told my wife that I thought I was exposed to somebody with COVID. And so there I was, in the guest room of our house, and she would be putting plates in [the door] to me for the next period of time as we communicated. I got a phone call that night from Francis Collins, and he said, "Hey, John, what's going on?" I said I didn't know. We, of course, learned, that person went home and was quarantined, and everybody was safe, but then we had to sort of move to the next phase of how we are going to move ahead.

Basically, everything was shut down. People finished their experiments as best they could, and just got out. I took notes, of course, but I don't know exactly at what point we started coming back in. It was weeks to months before people would come in, but under very limited circumstances. I started this thing that we called COVID lieutenants, where the people who knew they had to come in basically reported to me to if people were being safe. Were they wearing masks? Was there adequate cleaning? In the early days—you have heard this from others—the one thing that Francis did really well, I thought, is that all of the Scientific Directors, Clinical Directors, Executive Officers, would meet on Tuesday night at 6:00. Francis would be giving us an update on all of this. That was really, really wise on his part. In part, because you know Francis. He is an upbeat, positive guy. He could tell you about the most depressing things in the world, and he would make it clear that we're in serious times. But Francis being Francis, there was always an optimistic note. Tony was like the rock. You could see him on CNN. And my mom, as scared as she was, thought Tony would tell you what the truth is. And Francis, same, but a different personality in a way. Really critical for the NIH moving forward. We had the COVID lieutenants who really were very good, keeping an eye on things, making sure everything was under control, reporting back to me. It didn't really begin to open up until we had the vaccines.

Barr: How did you support your NIAMS staff who could not be at the bench or see patients to the same extent at that time? I'm sure a lot of them were coming to you very upset. It's very hard not to do the work you're trained to do.

O'Shea: No, no, no. They're very insightful. To be honest, it continues to this day. As much as in a lot of universities, things have gotten back to normal. They're not really back to normal here yet. For clinical researchers who needed patients to come in for less-than-urgent visits, if they have chronic diseases, we're still not quite up to the usual pace. What we did was have lots of meetings with lots of people at different levels—postbacs, postdocs, clinical teams—just basically talking through things. How are we going to do this? It seemed like there were a million decisions on any given day. We even had an acronym that I put up. It was a silly sort of acronym, but I basically just tried to remind everybody to be safe, respectful, and cooperative. It was really just trying to remind everybody that we're going to get through this, but the only way we're going to get through it is by working together. I spent a lot of time talking to people about their individual problems, and trying to figure out, with my COVID lieutenants, what we can fix and what we can put off. It was really, really difficult in one sense. I mean, obviously, as soon as we got the vaccines, all of a sudden, you could begin to take a little bit of some relief in saying, "Okay, If I go to work, I'm not going to die." For historians in the future that might sound

like hyperbole, but the truth is, we just plain didn't know, right? Beth, you and I were talking about how the groceries would come in.

Barr: We would put something thing down and wash everything down in the beginning.

Walsh: Swabbing down your Amazon packages, and then putting them in quarantine for a couple days before you open them. I mean, yeah, we were really going through the extremes at that time. And it was scary.

O'Shea: What does it mean to have a workplace that's safe? I mean, we always want that. We always do that all the time. But you know, what's the safe working place in a pandemic? There were no rules, right? You did the best you could moving along. And you know, we had no shortage of cases. One of the things that I had to deal with, fairly frequently, were people who wouldn't wear masks. I remember workers who were sort of antagonistic to one of the women who works in my Institute. They were saying, “Why are you wearing a mask?” I can tell you that one of my jobs at the NIH for a while has been as chair of the security committee, CABS [Community Advisory Board for Security]. I called the person who I know is always a good resource in this circumstance, which is Bill Cullen. He's head of security. And I asked Bill how I deal with this. Bill said, “Yeah, I can help you with that. We're going to make sure, when the police go around and they see instances like that, they will say, ‘Look, right now, you’ve got to wear a mask.’” That was the guidance at the time.

Walsh: But I would say overwhelmingly, most NIH employees were really good about that.

O'Shea: No, no, that's right, but there were a few people who really made a lot of other people really uncomfortable. Often, they were contractors who were coming in to do something. They were not NIH employees. It was very frightening, I think appropriately, and very threatening for people, in a way. I don't mean to overstate that. I had to deal with a few people like that, and it was quite maddening.

Barr: For sure. Can you talk about your role in facilitating NIAMS participation in COVID research? There have been a couple of studies that you have been involved in.

O'Shea: Absolutely. Again, people were just more than happy to do it. As an immunologist, you think about looking at responses. We have a group here that that generated so-called nano mice that would make nanobodies. The idea was to use this for HIV, but they pivoted quickly and thought we can have new monoclonal antibodies that you can make in mice. The way so-called antibodies are made is they are usually generated from camelids or llamas. We don't have a lot of camels on campus, and we actually haven't started importing camels onto campus, but what we have are engineered mice that have camel antibodies, and they actually work pretty well. Some of this is being commercialized. All of this stuff happened really, really quickly. Fortunately, a lot of it became moot with the vaccines being effective and then with variants. That moves very quickly. But we also have structural biologists who have provided other insights for different aspects of the virus that you could target—proteases and that sort of thing. People had this sense of being more than happy to help. If there was a project they could get in on, people were more than happy to do it, because, like Beth was saying, there was really this sense of how these are scary times and people really wanting to help.

Barr: JAK [janus kinase] inhibitors are something that's very dear to you for many reasons. What are your thoughts about using these kinds of therapeutics against COVID-19? Baricitinib is one example of using one of these therapeutics but are there others. What further research needs to be conducted?

O'Shea: I was pulled into a couple of meetings, as you might imagine, with both industry and also with NIAID [National Institute of Allergy and Infectious Diseases]. And as you probably know, ACTT 2 [Adaptive COVID-19 Treatment Trial] went forward with remdesivir and baricitinib and remdesivir and dexamethasone. These drugs were tested and shown to be efficacious and ultimately approved by the FDA to have an emergency use authorization. My colleagues at Lilly [Eli Lilly and Company] have told me that the drugs were originally approved for things like rheumatoid arthritis and other diseases, but at this point, more people around the world have taken the drug to treat COVID. It was very edifying to be involved in. And again, it was the sort of thing where I really did feel like everyone said—using the metaphor of the Blitz— "We're working on this together." I really enjoyed interacting with the Lilly scientists and thinking about what they were going to do, how were they going to do it, and how to design the clinical trials. I mean, I was hardly a critical person—they knew exactly, they do clinical trials all the time—but I was involved in those discussions and discussions with NIAID. The one that thing was edifying was that we actually had a preclinical experiment with mice, where the mice had a septic shock model with LPS [lipopolysaccharide] and this sort of thing. We wanted to know whether JAK inhibitors would prevent that. It did, and we published that result. I was able to show that to the Lilly scientists who were working on the big baricitinib trials with NIAID. We at least had preclinical data for this cytokine storm thing, so it's not crazy. That was a big thrill, and it's a big thrill now knowing that. One of the strange things, of course, with the pandemic is that it's not uncommon now to have scientific meetings or even clinical meetings. I just had a meeting today for another related project, and they were scientists from Hong Kong, Vietnam, Europe—all around the world. I remember talking to doctors in India, and we were talking about treating patients with JAK inhibitors for COVID. I never thought in my wildest imagination that I would be in that position. Again, a really scary time, but a time of tremendous optimism, all at the same time.

Barr: You volunteered to help administer COVID vaccines at both NIH and in Montgomery County. Did you receive any training? What was the experience like for you?

O'Shea: Sure, sure. In a way, it's all the same line. I'm a physician and even though I've been at NIH for a very long time, I did all the usual things that docs do—stitches and helped a lot in surgery. I had no problem with needles, I knew a lot about needles. Doctors don't usually give immunizations to patients, but I had plenty of experience with invasive things. Now, having said that, it's been a long time since I've done that sort of thing. But especially after my mother died and knowing that we had something that really was going to save lives, I got a vaccine as soon as I could. But I thought that I wanted to be on the front lines of having everybody have that opportunity. And I can tell you it was a very emotional experience again—people literally would cry. People were so relieved that essentially help was on the way. That was the other part of it. Beth can tell you that I'm not usually so "sobby."

Walsh: It's usually only every other week that you break down in tears. [laughs]

O'Shea: It really was unbelievable. All of the volunteers all saw it. It really was very palpable. Everybody there knew that they were making a difference. Again, forgive my lack of modesty, but certainly at the NIH, there were a number of people who knew who I was and knew I was sort of an important immunologist. There were graduate students, and I would be the one vaccinating them. They would look at my ID and they'd say, "Can we take a picture of you vaccinating me?"

Barr: Oh, that's so funny!

O'Shea: It was great. They would ask if they could post it on Facebook, and I would tell them to check with whomever, I didn't know what the rules are here. But they had my permission. It really reflected that—a really

terrifying time, where suddenly, thanks to science, a lot of people who were immunologists were saying, “Wow! This really is it!” In a way, I wanted to do it for my mother. There was a time where it could be pretty dark and frightening and depressing, but it [vaccination] was really a time of optimism. That’s the other part. I learned right away that I really liked the volunteers. The metaphor I often thought of was if you see a fire, most people run out, and then there’s a group of people who run into it to save lives. I thought, “I want to be the immunological fireman.”

Walsh: I love that. [laughs]

O’Shea: That’s what you and I did, right Beth? That’s why now at this point it seems so emotional. We were the immunological firemen.

Walsh: Well, you didn’t have time process it at the time. We all have families; we all have kids. There was this kind of added stress on all of this as being not consolidated, consistent information coming into them from the normally publicly available sources. You kind of became a source of truth for an extended network of people. You had people—friends, family, people you hadn't heard from in 20 years—calling you for information asking what to do. That added to that experience, on top of everything else. But have to say—I don't think I ever told you this, John—I was really sad when I found out that you were giving vaccinations, and I had already gotten mine. Oh, I would have loved to come in and gotten my vaccine from John O'Shea.

O'Shea: Right, right, right.

Walsh: Through all of it, you had to keep that positive outlook and positive mindset and just find the bright pieces of it for yourself and the contributions that you and others were making—and just the fact that you had the opportunity to do so while some people weren't so fortunate. Some people lost their jobs and weren't able to do anything during this time. I tried to keep the mindset that this was an opportunity to do something really impactful.

Barr: What do you all feel that you learned from all your COVID experiences that you would apply to other situations?

Walsh: Do you want to start there, John?

O'Shea: You go first.

Walsh: I mean, honestly, [I learned about] the importance of community—both the NIH community and the interaction with the broader scientific community and the public—and how all of those pieces have to work together. I think COVID-19 has created a model and avenues that we really need to make sure continue. The level of awareness now of the work that the NIH does and how we contribute to the public well-being is higher than I'm sure it ever has been, and it would be good to keep those lines of communication open. In terms of actual NIH processes, and my own personal perspective, I’ve learned to work more efficiently than I ever have before, just because you had to. You had to cut away the chaff on what you were doing. Otherwise, there's no way you could get it all done. Sometimes, regardless of that, you were still falling asleep after midnight, with your face on your computer. But you had gotten a lot more done in a day than you ever had before in your life, despite all of the competing family obligations and work.

O'Shea: My response is pretty much the same—maybe that's why Beth and I were such a good team. I came away the same way, with this sense of mission of the NIH. I always have loved working at the NIH, because on one level, I knew I was, day by day, making progress that was going to help people. And it did. It doesn't happen quickly. It happened over the course of 20 to 30 years. I actually just submitted a paper that got accepted to Cell, and it's actually the 30-year history of the JAK-STAT [janus kinase, signal transducer and activator of transcription proteins] pathway. There's a tremendous sense of pride. I came to NIH to work with Tony Fauci because I had a patient when I was a resident who had a disease called vasculitis, which was what Tony was famous for. I thought I had to go to the place [he was]. No one knew how to take care of this patient. I ended up calling Tony's lab for advice on how to treat this patient. I don't know if I talked to Tony at the time. I didn't know who he was, and I didn't know if he was important or not. But ultimately, after learning about this, I decided I had to come to the NIH. This is the place to go where medicine is really going to make a difference. That turned out to be true, but the pandemic is like that on steroids. This sense of mission and the sense that what we do really matters. My wife has a number of funny stories. Sometimes when I would go through customs or something like that people would ask why I am coming to whatever country I was going to. I would say, "I'm an immunologist." That would confuse them, and they would ask what I meant. I would try to explain what an immunologist is. The people who understood a little bit would then start to say what their theory of immunology was. There I was just trying to get through a line at customs, thinking I had to listen. Once you sort of explain what immunology is, people have strong opinions of this—not often anything close to the truth. But now it's even more so. Now the whole world knows who immunologists are. As Beth was sort of alluding to, the shocker of all of this is, on one level, I'm prouder of working at the NIH and with NIHers than I ever have been in my life. But I guess I never realized that some people would see us as the enemy. That's just mind boggling. I mean, I get it, because I understand the political framework and all of this sort of stuff. And I know full well that humans are really good at thinking of ways that they hate each other and all of that sort of thing, but humans are also good at pulling it together and working as a team. And we saw a lot of that during the pandemic. I want to think about all the things that will make us work together as a species. That's what I got out of the pandemic: Work together!

Barr: Is there anything else that either of you would like to share about your professional or personal experiences with the pandemic, or just thoughts in general about the pandemic or what you might like to do continue contributing to ameliorating the effects of the pandemic?

Walsh: I think the thing that is maybe a little bit unique to NIH is that we're almost using this as a test scenario. Pandemic preparedness is going to be a part of our culture and mission like it never has been before. This was almost the dry run, so to speak. I think moving forward there's going to be a lot more work and cognizance of that. The pandemic triggered a fight or flight kind of response in us, and I think it's safe to say that we're going to stay and fight and prepare for all the future fights that are coming.

O'Shea: You can see why it was just a joy working with Beth. She's a genius, she's organized, she's got an amazing moral compass. She wants to do the right thing. She kept me on track. I would say what we learned is that it's a very small planet—we thought it was small, but it's really, really small. We better figure out ways of working together. That's the only hope. And we know that we can do that, but we have also learned that we're really good at not doing that. For the historians in the future, who might be listening to this, how did it turn out? Good luck.

Barr: The jury's still out. Well, thank you both for your time and, of course, all your contributions to NIH and the globe. Thank you.

O'Shea: Well, thank you for doing this. This is a great thing. This is really terrific that you're doing this. I'm really very thankful for you making the effort.

Walsh: Yeah.

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