

Dr. Andrew Redd  
Behind the Mask  
April 9, 2021

Barr: Good morning. Today is April 9, 2021. My name is Gabrielle Barr. I'm the archivist for the Office of NIH History and Stetten Museum. Today I have the pleasure of interviewing Dr. Andrew Redd. Dr Redd is a staff scientist for the National Institute of Allergy and Infectious Diseases. He is also an associate professor for the Johns Hopkins School of Medicine and a visiting scientist for the University of Cape Town where he is currently. Thank you very much for speaking to me about your COVID research.

Redd: Sure, happy to do it.

Barr: My first question is: when did you and your team begin thinking of and putting together the study that is looking at whether the variants of SARS-CoV-2 eluded the protective immune responses of someone who had either recovered from COVID or had been administered the vaccine?

Redd: The main part of the study we started back in April or May of 2020. That was when we realized that people were going to start using convalescent plasma to try and treat SARS-CoV-2 infection. What we decided to do was collect samples from possible convalescent plasma donors. People who wanted to come in and give plasma so that we could get a better idea of what their immune response to COVID was. We've done multiple experiments and multiple projects on this larger group of patients to try and get an idea of what the immune response is. That was work that was done starting in May all the way until the end of last year.

For this particular study at the end of last year, we started hearing the reports of the new variants that had emerged in Britain, South Africa, and Brazil. So, from our original data, from our original work, we wanted to say we had data that we could go back to and see if the immune response in the T cells or in the white blood cells was affected by the mutations in the new variants. This project really started at the end of last year, beginning of this year and happened really quickly because we had laid all this good groundwork of data and work in the year before.

Barr: That's really great. Can you relay how you structured this study and how you went about conducting it, including your methodology and the types of equipment you use? Also, how many variants did you and your team look at?

Redd: I'll answer the second question first. We again started this in the sort of beginning of 2021, we looked at the three main variants that have been identified at that point, the one from the UK, the one from Brazil, the one from South Africa. As I said the methodology of this was as the virus is going to continue to mutate and evolve, we wanted to get an idea if the immune response is going to be ready for those mutations. We just happen to be lucky that the data that we had generated in our earlier study looking at the white blood cell, T cell responses, to the virus generated the

type of data where basically what we did is we found out on the virus itself where the white blood cells were targeting. Because we knew where they were targeting, we could then go back and say—we just were in this unique position where we knew where it was targeting. We said, “We can look to see if those mutations in these new variants fall within those same areas.”

For this actual study, the equipment used was essentially our computers. We took our old data and the new data that had been identified and then just matched them up. But to get that original data on where on the virus your immune cells were going to be targeting, that was actually really interesting work that was done by our collaborators, which is Immunoscope. They're a company that's a biotech company that's based in Singapore and San Diego. They have a really interesting technology that allows you to do something called tetramer staining, which is what allows us to figure out where on the virus the different white blood cells are going to attack. Their version of tetramer staining is what we did with them in 2020.

Barr: Interesting. How did you decide on analyzing the blood samples of 30 people? Were there other qualifications that the people had to have other than recovering from COVID?

Redd: Yes. Because this project is from a larger study looking at a large group of convalescent plasma donors, we selected these 30 on three criteria. One is they had to have enough cells so that we could actually see this. We needed to have the right types of cells; so that was the first criteria. Then the second is we wanted to see what the response was in people who had a strong immune response versus people who possibly had a weaker response. So, for that we selected from all of our group that we had, and we split them up into what is called a tertile. We said how much antibody to SARS-CoV-2 do you have, just total amounts, and then we separate into three groups: low, medium, and high equal groups. We selected 10 people from each group; that was so that we could get an array of strong responses and weak responses and sort of in the middle responses to get a better broader idea of what the immune response was going to be. Those were the criteria that we used.

Barr: Interesting. What challenges have you encountered? Did you find anything to be surprising?

Redd: The challenges, I think, for this particular [study] weren't that hard. I mean one of the great things about what's been happening with SARS-CoV-2 research is that people are sharing their research as it's happening. Because of that we got the mutations as soon as people sequenced them. We could see, instead of having to wait for six months for a paper to be published, that information was made readily available and so we could use it to do our analysis. That was really good.

I think one of the big surprises was that I was partially expecting that these variants would have some effect; that there would be mutations that were found in the same places where the white blood cells were targeting. I think I was very surprised that essentially, we found only one mutation that was in one of the places where we target, and it was probably a minor mutation that doesn't affect how the white blood cells would react to it. That was somewhat surprising and also

very encouraging because I think it shows that the T-cell response with a white blood cell response in people who have previously been infected.

Now we know from some work by other people [that] vaccines as well seem to remain fully intact or virtually fully intact against these new variants. Now as new variants are continuing to evolve, which they will, I think that is really encouraging that you will have this second layer of immunity to protect us from any of those new variants in in some form or fashion.

Barr: Yes, that was actually going to be my next question. Can you elaborate further on what you have found in your study: that the T-cells, like you just said, largely protected those who had either recovered or have been vaccinated? Can you elaborate further on what you mean by protection? Does that mean you never get COVID again or does that mean not get very sick?

Redd: To answer your question, to be honest, we don't really know. One of the things is we don't yet know what part of the immune response protects you from infection. We know that things like neutralizing antibodies, which we've all heard a lot about, are almost certainly protective. If you have a neutralizing antibody and you have enough of them in your body, that's going to stop the virus from ever getting into a cell. I like to think of it like a baseball game; neutralizing antibodies are a strikeout. You never even get on the base. It's, "Go back to the dugout; you're done."

However, the immune response is not just one thing. You have neutralizing antibodies. There's also binding antibodies, which bind to the virus and either recruit [them] to being eaten by phagocytic cells—so white blood cells that come in and just eat things—they also can find other antibodies that can bind to infected cells and say, "Hey, something's wrong with this cell" and recruit things to come and kill it. In addition, you have these T cells, and the T cells are more of what we call the adaptive immune response. They have evolved in our bodies to be able to find cells that are infected with a virus, take those cells, kill them, and then recruit other things to that area to say, "Hey there's an infected cell here. There are probably other ones in the same neighborhood. Let's find those guys and kill them too." So, the T cells we found most likely wouldn't prevent the virus from getting into the body and maybe infecting a cell or two or the first couple groups of cells.

However, one of the good things about T cells is your immune system uses them to remember what you've been infected with. It's called your immunological memory. What the idea is that if somebody had gotten COVID or vaccinated, six months later once we reopen and we can go and do things, if they happen to run into somebody who has COVID, maybe the virus gets in, starts replicating, but those T cells—that memory will pop back up really quickly, find the infected cells, kill them, and in the meantime, it'll tell the rest of the immune system that fights COVID. They'll say, "Hey, this thing is still floating around out there. You guys need to make sure that that the antibody levels are up, and the cell levels are up. We're probably going to see this again, so we need to be sort of vigilant."

I'm simplifying it, but that's sort of where the protection is. So, the T cells themselves don't prevent you from getting infected but almost certainly would prevent that infection from becoming established. This would be the first sort of barrier. And then if it became established, it would kill it off faster and in a more uniform way so that you don't get sick. That is the hope and I

think that the data we have as well as the data of others would suggest that that's what the case is.

Barr: That's very interesting. Do you believe based on the findings of your study that any public health policies would be established?

Redd: I think one of the things that our data will help support is there's a big question now in the public health field and the public in general of are these vaccinations enough. So do the vaccines we have and/or previous infection enough to protect you from a new variant or new variants. There's a lot of people who are saying things like look maybe we're going to need a booster dose of vaccines or maybe we'll need to have a new vaccine every year or something like that. I think what our data does is put the brakes on that a little bit and say we don't know. There's the data out there, in my professional opinion, is not conclusive enough to say we're going to need that booster doses or we're going to need to make sure that we get a vaccine every year or something like that. I think that we still have a lot to learn about the virus before we can say we're going to need that.

This data I think sort of says and encourages or supports the idea that we may not need a booster dose or at least not one in the in the near future. I personally think that we should take the new variants, one of the other things that is happening is people are taking the new variants and updating the vaccines and I think that's a very good idea. We should update the vaccines and if it's found to be just as effective then let's use the old and the new so that we cover all our bases. But that doesn't mean we need to do a booster shot, that would mean we'll update the vaccines. Let's get everybody vaccinated around the world. Then we can start thinking about booster vaccines if we need them. We just don't know yet.

Barr: Yes. Can you speak a little bit about who your team was comprised of and what your role was on your team with this study?

Redd: Sure. Obviously like lots of things these kinds of studies take a lot of people. Our larger study was really coordinated by the Johns Hopkins School of Medicine. They are the people who started the convalescent project to get plasma donors for clinical trials and to treat people. One of our partners is Dr. Aaron Tobain, who's a pathologist at Johns Hopkins School of Medicine. Another pathologist, named Evan Block, really brought us in early on. And then our expertise where we come in is: I'm a virologist so I was sort of coming in from the point of view of a virologist. Our group does a lot of work looking at antibody responses in infectious diseases and viruses, viral infectious diseases in particular. We sort of oversaw the sort of virology, basic immunology part of it. One of our collaborators, Evan Block, introduced us to the folks at Immunoscape, which is the biotech company we worked with on the project. They really brought their technology of using these tetramer staining, and a machine called the scitok machine that allowed us to really dig deep into these white blood cells. That was really done by them. It's been great. It's been a great collaboration between the groups. And then there have been some fantastic people in our lab who've worked on multiple areas of this, Drs. Tania Bonny and Sarah Benner, in our lab who are two post-docs who've worked on this project. My job again was to sort of be the virologist and

help coordinate things and then when the new variants came out then I sort of helped to lead that analysis.

Barr: That's very interesting. Can you envision subsequent studies based on your research?

Redd: Yes. I think one of the things we will need to do is continue to monitor the virus as it evolves around the world and in particular to see if new mutations we find are starting to build up in these areas where the white blood cells are targeting the virus. If we see that build up, that's the kind of thing where we'd say, "Okay now we need to start thinking. Maybe we need to get a booster vaccine or something like that." We need to continue to monitor and that's part of it.

Another area that we're looking into is there seemed to be places in the world, or people, who even when they get exposed to COVID don't seem to get sick. They seem to already be just totally fine. What we really want to know is in those people what is it about their immune system that allows them to prevent getting infected or getting sick from COVID. Looking at some samples and things from before the epidemic to find if there are people who have pre-existing immunity, I think that's one of the areas we're really interested in looking at in particular. We're working with some people in Uganda to look in Central Africa and see what the responses are there.

Barr: Why Uganda and Central Africa in particular?

Redd: For a couple of reasons. One is before COVID a lot of what our lab does is international. We're the international HIV lab and so we do a lot of work in Africa and in Uganda in particular. NIAID has an International Centers of Excellence in Research location in Uganda and we actually help run that. That's one of the big reasons we work in Uganda. We know a lot of stuff and people in Uganda.

But second, one of the really interesting things about COVID is everyone was very worried about what would happen when it started spreading in Africa because of the lack of health infrastructure and things like that. Everyone was worried that there could be massive problems and those things other than in South Africa as a sort of anomaly. In most of central, west, east Africa, sort of right across the middle of the continent, the rates of deaths and infections of people who have symptomatic infections appear to be very low, whereas in the United States we've had 500,000 plus people die from COVID. In a country like Uganda, which has, I think, 60 million people—it's a relatively large population or maybe it's 50 million—they've had less than a thousand deaths. Part of that is maybe there's a little under reporting of the deaths. But we think actually it may have to do that the population is very young, but we think it also may have to do with the fact that there may be some sort of pre-existing immunological state or pre-existing immunity that is protecting the population as a whole. Again, I want to stress that they have had COVID deaths. There have been people who died of COVID in places in Central Africa. The numbers are just much, much lower than we had thought. So, trying to figure that out, I think, is going to be the next step in the research we're doing.

Barr: That will be really interesting. Another one of my questions is based on what we last talked about. How has your work with HIV influenced how you have thought about and approach SARS-CoV-2?

Redd: I would say the three main ways. One of the things we learned early on in the HIV epidemic is that no infectious disease is just in one country. One of the things about HIV and one of the real failures we did in the United States and the resource-rich world [of] Europe and America was in the beginning of the HIV epidemic we said, “Oh, it's only gay people” or it's only this, it's only people who are IV drug users. Then when it started going bad in Africa, we said, “Well that's not our problem, that's Africa.” What we then saw is that virus doesn't know borders. It's going to continue to spread and continue to get worse until the entire world takes it seriously. Once that happened then we started getting headway with HIV.

What we've learned from COVID is the same thing. If in the beginning people said, “Oh well, it's a problem in this part of the world in China or it's a problem in Italy or we don't have to worry about it here.” What we've now learned in the very hard way is that viruses and infectious diseases do not know borders, and so that when you ask what about HIV that's sort of the biggest lesson. When I look at COVID and I look at the worldwide pandemic I try and look at it from a world view, not from what's happening in my hometown or what's happening in my state or my country. It's what's happening around the world because we're not going to be able to fix COVID until we fix it everywhere.

And then the second thing is a lot of what I study is how HIV evolves within people, but also within populations and in particular when you have multiple variants of HIV in one person or in a population. When the [COVID] variance started being reported, I really fell right into what I study. What really bothered me is a lot of the reports that came out were gloom and doom; oh, we have these new variants, and the sky is falling. It was not based on enough data. I tried to say okay, knowing what I know about HIV and how it works, when you have two different variants and more than one variant, what are the sort of questions we need to ask? And one of those is do you see this escape from white blood cells, which in HIV we actually do see. It's called T cell escape and it's a big problem in HIV infected people. So that's one of the reasons why my brain sort of went to that when I heard about the variants. It seems that that's not the problem that we have here.

Barr: That's at least a positive thing. Are you involved in any other COVID related initiatives?

Redd: No. Most of the ones I've looked that I've been part of is this big study on convalescent plasma. The other thing that I've been doing, as I mentioned a little bit about, is how the research community has been sharing research at just a breakneck pace. I've been working with some people at Johns Hopkins on something called the National Coronavirus Research Compendium (NCRC). It's a group of scientists and researchers at Hopkins and other places who are trying to take all of the research that's being published and put out in pre-prints, etc. and identify papers and research that we think is really important for public health. And then working with students and some post-docs and med students and things like that, we write short write-ups of these important papers and then put them online so that the regular researcher or the public health expert or doctor doesn't have to try—and as I like to think of it, there's so much research that's

coming out, it's like trying to drink from a garden hose. What we do is we select the interesting stuff and write it in a quick way that you can just go through it and say okay that's what I need to know, and this is not being written by media people. It's being written by actual scientists, who are not going to lie but tell you the important things, not just whatever's flashy.

Barr: Yes. Have you been able to continue any of your HIV research at this time?

Redd: For the first part of the epidemic, no. Everything was COVID. If you weren't doing research on COVID the NIH and all the laboratories were, "Look if you're not doing COVID stuff you need to stay home." And so I did as much as we could to continue that work and particularly, we want to make sure that people who are on therapy can stay on therapy. We're not going to cure COVID and then come back and find HIV 10 times worse than we left it. So that's all continuing but really, I haven't been able to dig into my research until about a month and a half ago. I was able to get vaccinated because obviously we're rolling out vaccines in the United States, and I work in a lab that studies COVID, so we were eligible. But that also allowed me once I became vaccinated to travel back down to South Africa, which is where I am now, so that I can restart those HIV programs, because unfortunately COVID did not make HIV go away. It may actually make it worse in the short term. All of us who study other diseases know that when we're done with COVID we still have tuberculosis, we still have malaria, we still have cancer, we still have heart disease. As great as we're doing with vaccines and things for COVID as they're rolling out, we're all going to have to get back to work quickly unfortunately.

Barr: Can you speak about some of your personal challenges as well as opportunities that COVID has presented?

Redd: Personally, because I do a lot of work in Africa and particularly in South Africa and Uganda, because of that I spend a lot of time traveling. I'll spend months down here working on the projects that we have. One of the hardest things for me has been early on in the epidemic, I was brought back to the United States because we're worried about the epidemic, etc., and I couldn't get back to the people I work with and the projects I have and that personally was very difficult.

But that being said, I luckily still had a job. My family and my close friends, although I've had some friends who have gotten COVID and some of them gotten very sick, luckily no one has passed away. My parents, who are elderly and at risk, have not contracted COVID and now are both vaccinated, which was a huge relief. Personally, like everyone it's been tough, but we'll get out of it and then we do. As long as people are healthy and safe that's what the key is.

And then opportunities. It's been a really nice opportunity to work with some new people. I've studied HIV my whole career and so it was nice, I mean from an intellectual point of view to really step away from something and as a virologist study a new virus. And then also just to see what the scientific community can do when you put us all in one goal. You give people the resources to make big discoveries, guess what, we make big discoveries. We can move quickly if need be and it just takes financial resources from government. And it takes the drive, which obviously COVID provided the drive.

Barr: Yes, definitely. This is a fun question. What is one way that the South African COVID experience has been different than the American COVID experience for you? Is it very different there?

Redd: I actually don't think it's been as different as people think. The one difference I think is here [South Africa] when the epidemic first started going up in the first wave the country, I think, did the exact right thing. They did a real hard lockdown. They said don't leave your house unless you're going to the grocery store or unless you work at a hospital. We want everybody to just stay at home. No one's traveling and no one's doing anything. I think that they did have a bad first spike, but I think it kept it from being overwhelming the country. I think it was really, really smart to do. Then when they came out of that first lockdown and first wave, I think they were doing the right things.

Whereas in America we would go through a wave and then as soon as we started coming down people were like, "Just throw open the doors; let's get started!" And then instead of us having waves we had a wave to a plateau and then a wave to a plateau and a wave to the top. Then eventually we got vaccines and they started coming down. So that's, I think, one of the big differences, that in the U.S. we sort of did a lot of half measures and what we learned is that half measures may get you over the peak, but it's going to keep you on that plateau. And here they learned that what full measures will do would get you back down into really low rates, which is where we are now.

I think that's one difference between the two. I think we could learn from the other. The South Africans very early on were monitoring the virus and sequencing it and looking for mutations. There were some colleagues that I've worked with here at UCT as well as in Kwazulu-Natal, which is on the other side of the country, where they were looking for these mutations. They were saying, "This virus is going to mutate. Let's screen it and see if we can catch it early," and they did. That allowed us to identify this South African variant very early on. Because of the good scientists they had down here in South Africa they were able to do some of the initial basic virology and immunology really quickly so that everyone around the world could say, "Oh, they've got this variant." They're like well, it seems to avoid neutralizing antibodies so maybe we need to take that into consideration. That's also been something that's really nice about the COVID experience here in South Africa.

Barr: It's very interesting. Is there anything else that you would want to add as an NIH scientist, but also as a person who's living through this pandemic like everyone else throughout the world?

Redd: I would like to add from my perspective, the virus has become so widespread in the world and because we have people who for some reason don't want to take the vaccine or are hesitant to, I would encourage everyone please get vaccinated. Because the virus has been spread so widely around the world, I think what we're going to find is that COVID, SARS-CoV-2, is here to stay so it's going to be what we call endemic. We have four coronaviruses that spread seasonally, and they just cause the common cold. That's what you know. We know most people who get it, that's



what they get, and I feel that SARS-CoV-2 is going to become the fifth one and that it's going to continue to circulate around the world. I think because of that we need to plan on that. So if you're one of these people who says, "Well, I'm not going to get vaccinated because herd immunity is going to make this go away," I don't think it's going to go away. And you're either going to get vaccinated and protect yourself or someday along the road you're going to get it. And trust me when I tell you again, I've had friends who've gotten very sick, and the vaccine is what you want. You do not want to get this virus. I would encourage everyone just please get vaccinated so we can all go back to doing fun things like going to concerts, which I missed so much, and going to the movies and going out to dinner, seeing friends and family and being able to hug people, and all those things that we've all missed for a year and a half now.

Barr: Thank you very much and I wish you the best on your research and I hope that you and your family continue to stay safe.

Redd: Thank you so much, Gabrielle, for giving me this opportunity.