Mario Roederer, Ph.D., NIAID
Oral History
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Interviewed by Gabrielle Barr, Archivist, Office of NIH History and Stetten Museum, NIH

Barr: Good afternoon. Today is January 7, 2022. My name is Gabrielle Barr. I'm the Archivist at the Office of NIH History and Stetten Museum, and today I have the pleasure of speaking with Dr. Mario Roederer. Dr. Roederer is the Chief of the Immunotechnology Section at the National Institute of Allergy and Infectious Diseases (NIAID). Today he's going to be speaking about some of his COVID-19 research experiences. Thank you very much for being with me.

Roederer: It's my pleasure.

Barr: When did you join the team that assessed the efficacy of Moderna's mRNA-1273 vaccine and what was your role in the series of the initial studies?

Roederer: Well, I've been involved in the whole vaccine project from the beginning. All of us at the VRC [Vaccine Research Center] made a decision to join forces and address the pandemic together. We all lent our own experiences. My role was to help with the animal models, the nonhuman primate model for infection. We had to do the initial setup, define how to infect the animals, and [define] what the output variables are because animals don't get sick with COVID. Then we designed the experiments to test whether or not the vaccines and monoclonal antibodies could protect against the limited viral replication that happens in these animals.

Barr: How did you find what type of nonhuman primate was best for the study?

Roederer: We did not test different models. We have a lot of experience with the rhesus macaque model. That's the one we've been using for our studies on HIV and basically every other vaccine that we work on or disease that we work on here. It's just natural to choose that and work on it. It was a very good model in terms of the immune responses that are generated.

Barr: Can you talk a little bit about—you said you had to see how to infect the animals? How do you determine what was working and some of your points of reference that you learned over the course of your studies?

Roederer: Right. We had to decide how to instill the virus into the animal. We tried things like intranasal or intratracheal administration, or both. We had to decide how much virus to give the animals because if you don't give enough, then you don't see any replication, but if you give enough, then you see replication. We had to decide which time points at which we're going to assess replication—day two or day four, day seven or day 14 or day 28. Initially, we went out much longer. Then we realized that the monkeys just don't get sick, and they control it quite readily on their own. We shortened the timeframe of the experiment and really focused on the first week. You can see viral replication in the lungs; you can see viral replication in the nose quantified by PCR at those sites. Then it's a matter of determining what is the most consistent outcome variable. As we encountered

different variants, we had to repeat that initial pilot study on every variant that we were using in our studies, whether it was beta, or alpha, or omicron, or the original Washington.

Barr: That's interesting. Did you notice any differences when you administered it in different ways, like intratracheal, intranasally, or muscularly?

Roederer: Well, we didn't try muscular because the main route of infection is through the airways. But yes, you get different amounts of virus that are later generated in the nose or in the lungs. When we did the intranasal infection, we didn't get very good infection of the lung. Or if we did the lung infection, we didn't get very good infection in the nose. We ended up doing both at the same time we infect the animals, to cover all the bases.

Barr: That's interesting. Were you also involved in administering the vaccine to all these animals?

Roederer: Well, I don't know what you mean by involved. We (the PIs) don't actually do anything directly with the animals. We design the experiments and the people who work in our labs do those. But yeah, our personnel administer the vaccines or the monoclonal antibodies to test whether or not they can totally prevent infection—something that would be a great result but given the high dose of infection, would be unlikely. The [interventions] are designed to reduce infection and reduce viremia. In general, what we find is that the vaccines, in fact, generate an immune response that can significantly reduce the amount of viral replication, which we take to be equivalent to reducing symptomatic infection in humans.

Barr: Can you speak about why vaccine-associated enhanced respiratory disease was a concern when the vaccine was still being tested?

Roederer: Yes, that goes all the way back to the 1950s from initial studies on RSV, respiratory syncytial vaccine, where it was basically an inactivated virus that was given to thousands of kids. It went through all phase one, two, and three level experiments, and only when it was released was it found that it actually can, in some rare cases, enhance disease when kids got infected later on. It's been kind of a ghost that has hung over the vaccine field for 50/60 years. But it's never been seen in a viral vectored or RNA or DNA vaccine. It was only seen in one case in that protein vaccine. That was probably because–you could talk to Barney [Graham] about this—the vaccine was improperly inactivated. It generated T-cell responses that may have been responsible for the enhanced disease. When we started this vaccine study very early on, we looked for those kinds of responses that might be indicative of an enhanced disease. We never saw them in the monkeys. So that gave us confidence to move forward with the RNA vaccines. We've done that also with the protein vaccines [for COVID]. When we test those, we look for the T-cell responses that are harbingers of that enhanced disease. We never saw that.

Barr: That makes sense. Well, that's a good thing that it is such a low probability. What were some of the obstacles that you and others in your lab faced when you were creating these animal models for the vaccine?

Roederer: The animal model is difficult because it has to be in a biocontainment facility, which our contractors set up. There's a very limited amount of space, and that limits the size of the studies that can be done. You can't use as many animals as we would like in a typical vaccine-challenge study because it's in these biocontainment

facilities. Then there's the challenge of doing this entire research under the guidelines of the pandemic of having to be [socially] distanced. You can't have very many people in the laboratory at the same time, and they have to be fully masked at all times. Then finally, the whole thing of doing the collaborative work by Zoom was challenging.

Barr: What was your reaction when you learned Moderna received its emergency use authorization in December of 2020?

Roederer: Well, like everyone, we were pretty happy. I was proud for the people who developed the vaccine and proud to be associated with that group and part of that group.

Barr: Did people like friends and family or people in your community ask you a lot of questions about it along the way?

Roederer: Absolutely. All the time, once the people in the community realized that I was involved. I live in a condo building nearby NIH and they asked me to give a talk about the development of a vaccine. I had to do that and also explain what COVID was and how we could prevent it and so on. And yes, and my family and friends asked me questions all the time about "What should I do?" or "Should I get boosted or not?" or "Which vaccine should I try to get?" and so on and so forth.

Barr: Do you ever feel like it's a lot of responsibility on you? I feel like sometimes people ask me things and I wasn't even associated just by working in NIH and you hate to be responsible for people's choices.

Roederer: Yes and No. I'm careful to try and tell them a I'm not a medical doctor, but I tell them what I would do if I were in the same circumstances. Or I'll tell them what I did do in the same circumstances.

Barr: You've been involved in evaluating the efficacy of the vaccine against all the subsequent variants. You alluded to it a little bit earlier. How do you think the vaccine efficacy and durability can be improved as the virus continues to mutate?

Roederer: Well, one thing that's becoming clear now is that if you've had the full vaccination and the booster, you're pretty well protected against the variants in terms of death or hospitalization. We've also been doing studies in animal models to try to assess whether or not we need to have variant-specific vaccines versus the original Moderna vaccine. I think that the data is coming in that as long as you just get the booster, you're in reasonably good shape.

Barr: That's interesting. I was reading that a lot of the response doesn't really seem to target any of the T cells. Is that a major concern or something that's being looked into further?

Roederer: No, I think that the antibody response here is really the key. T cells are good for possibly [if] you might want good response and T-cell response for durability. But it's unlikely that they're playing a direct mechanistic role in protection.

Barr: How did you contribute to a study that looked at…? Well, I guess before we dive into further research, can you talk a little bit about what it was like to work with so many of your NIH colleagues who all attend to their own areas of research in relatively normal times? On the Moderna study, there were quite a lot of you on that study.

Roederer: It was fabulous because we met almost every day by Zoom. We had at least three or four different series of one-hour meetings every week. There was a lot of interaction. We saw a lot of each other and got sick of a lot of each other [laughs] during that time, but it was all by Zoom. Learning how to do that was interesting as well, rather than meeting in person, but I think it was a fabulous experience. I mean, we knew that what we were doing was important and would have a direct impact on the vaccine, and that's a feeling that you don't get very often.

Barr: Did you feel like you got to know any of your colleagues better?

Roederer: Well, we've been together for about 20 years. It's hard to say that we get to know each other better. In some ways, yes, because you always get to know a little bit more. But in fact, we've been a team here for about 20 years, most of us, so it's hard to improve on that.

Barr: How did you contribute to a study that looked at the efficacy of an adjuvanted soluble protein vaccine against SARS-CoV-2, and how does this platform compare to the mRNA platform?

Roederer: Well, again, my role in those is mostly to help design or implement the animal experiments. The adjuvanted protein is what we hope will be the eventual vaccine for the world because it's cheaper to manufacture and easier. But it looks like it doesn't give quite as good responses at this point, or the protection isn't quite as good. The protein vaccines have been around for almost 100 years whereas RNA vaccines are very, very new. They've only been around for about 10 or 15 years.

Barr: Will you please explain the technique that was developed called molecular indexing of proteins by self-assembly, and how this technique helps profile autoantibodies in patients with COVID-19. How does it compare to other techniques used? You were a part of that.

Roederer: Again, this is not really something that I played a direct role in. Ben Larman at Johns Hopkins did. It's basically a new technique to assess the antibody repertoire at a very wide, broad level. I don't want to speak too much because I didn't play a direct role in that.

Barr: That definitely makes sense. In what direction do you think SARS-CoV-2 vaccine and monoclonal antibody research needs to go? Or is there a certain aspect or path of vaccine development for this disease that particularly interests you?

Roederer: Well, I think that, in general, the vaccine effort for SARS-CoV-2 is much like any vaccine effort. In other words, you have to develop a little bit more potent antibody responses that will persist for a lifetime and not

wane over the period of six months or a year. It's really a matter of determining how to generate very potent and long-lasting vaccines, I think is where the field has to go. The other area is to develop pan coronavirus vaccines that are not just SARS-2, but SARS-1 and MERS [Middle Eastern Respiratory Syndrome], and eventually some of the other coronaviruses as well, and hopefully those that cause the common cold that have been endemic for 50 years or so in the population.

My own interest has been—I have people who are working on the monoclonal antibody side of things to look for monoclonal antibodies that are more broad than just SARS-2 or more broad than just specific variants, but that are targeting regions that are conserved across all the coronaviruses and try to reach into those and explore that effort.

Barr: Are you involved in any of the other vaccine initiatives?

Roederer: Oh, yes, absolutely. My lab has worked on HIV mostly in the animal model—the SIV, simian immunodeficiency virus—for 20 years. Bob [Seder] and I have co-led an effort in TB for about 12 years or so. That's very active. I have also an effort in equine encephalitis virus [EEV], which is considered a bioterrorism threat virus. The work there is actually very similar to the kind of work that my laboratory is doing in coronavirus where we're trying to identify monoclonal antibodies that can protect against multiple different [strains] of the equine encephalitis viruses, and not just strain specific. So yes, it's similar in some ways to many of my projects. The SARS work that my laboratory does has really keyed off the work that we've done in in SIV and EEV models. Finally, my lab is involved in defining an animal model for human norovirus infection and in testing vaccines against Nipah virus – a possible pandemic virus.

Barr: That's very exciting. In addition to being a scientist, you're also a person who's been living through the pandemic, what have been some personal opportunities and challenges for you presented by COVID-19.

Roederer: I think that the real challenge for me has been reduced attention span. Because I don't attend meetings in person and we all get to sit down and fiddle with these things [holds up a cell phone] during our meetings, my attention span has decreased significantly. I'm not really able to focus for long periods of time like I was a couple of years ago. I think the real challenge now will be relearning those techniques, relearning how to focus. It's not really COVID fog, because I don't have COVID, but it's related in the sense that we have to relearn how to communicate in this hybrid world without as much interpersonal contact.

Barr: What was it like supervising people, especially those in the lab, during the pandemic, when you were not being physically able to be with them?

Roederer: You have a tremendous amount of guilt because you're not able to go in and help them out. I haven't been in the lab in 10 or 15 years, but I never previously felt guilty about not being able to go into the laboratory and help people out. I always assumed that I could, if needed, but now with the [social] distancing and so on, it just wasn't possible anymore. I had to stay home and telework. It's really a tremendous amount of guilt for not being in-person on campus or being down the hall where you provided advice. Early on, we devised some techniques—we had weekly social meetings where it was like a happy hour time, something where it was not

necessarily about science. We were just talking about the struggles of having to be quarantined or at home very early in the pandemic, and what people had to go through. We had these weekly meetings for a while until people settled into the whole new reality. Running a lab by remote is not difficult per se, but I think there's a lot of social aspects that I think are not something that I would have expected to come up.

Barr: What were some of those aspects?

Roederer: Not seeing people day-to-day in person. I think I've become cognizant that there's a lot of value to the person-to-person meetings and interpersonal interaction for running a lab. But it's also true in meetings. This is something that I've known for a while with meetings. People said already 10 years ago, "Why don't we hold these meetings by phone, teleconference, or by Zoom, or so?" And we all kind of disparaged that and said no, the interpersonal context is very important, but we couldn't really quantify it before this. But now that really has come up in in our day-to-day life between our families and our friends, and our co-workers in our labs, where all of these are now happening by Zoom. We see the impact on our interpersonal relationships, and that is something that I think we didn't expect but saw a little bit of from having these meetings that we'd go to in-person rather than having by teleconference.

Barr: Definitely so. I think everyone's feeling that situation. Is there anything else that you would like to share about your work with COVID-19 or your experiences during the pandemic?

Roederer: I just wanted to say that I feel like I hit the career lottery by being here at the VRC—really at the epicenter of all this. It's been a fantastic environment, a fabulous environment. I have so much respect for my colleagues who did all this work.

Barr: Definitely so. Thank you for all your work and I wish you and your lab all the best, and I hope that you continue to stay safe as well with all this omicron [variants] out there.

Roederer: Well, thank you very much.

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