Seder, Robert 2021

Dr. Robert Seder Oral History

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Dr. Robert Seder

Behind the Mask

December 10, 2021

Barr: Good afternoon. Today is December 10, 2021. 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. Robert Seder. Dr. Seder is the Chief of the Cellular Immunology Section at the National Institute of Allergy and Infectious Diseases [NIAID], and today he is going to be speaking about the way he and his team have contributed to various vaccines and antibody treatments against SARS-CoV-2. Thank you very much for being with me.

Seder: My pleasure.

Barr: When did you become part of the team that looked at the efficacy of the Moderna, also known as mRNA-1273, vaccine against SARS-CoV-2 and what insights and expertise did you feel that you could offer this rather large cohort of government and industry scientists?

Seder: I became engaged in mid-March of 2020 when it was clear that SARS-CoV-2 was a major global health problem and that we (the entire Vaccine Research Center (VRC)) would all have to be engaged in all aspects of the vaccine development – from the preclinical stage to clinical development. In terms of pre-clinical data that would inform clinical development, the VRC has substantial expertise in using non-human primates (NHP) to test vaccines against infections. Thus, we developed a large team which included most of the principal investigators (Danny Douek, Mario Roederer, Nancy Sullivan, Barney Graham, Eli Boritz), post-doctoral fellows, students, and personnel from the animal core. The nonhuman primate model is especially useful and relevant for vaccine development in humans for a variety of reasons. Non-human primates are outbred, and the immune responses generated are often are similar to what would be induced in humans with the same doses of the vaccine. Moreover, they have similar innate immune systems to humans and thus are a good model for predicting safety of the vaccine and provide insights into the mechanisms by which the vaccine induces adaptive immunity. The also allow us to sample blood and tissue compartments such as the airways which are important for understanding how the vaccine is mediating protection following challenge. We have used the non-human primate model to develop vaccines against Ebola, TB, malaria, and other viral infections including MERS. Thus, we designed a series of studies in NHP over 12-18 months that we thought would address the most important questions as the pandemic evolved.

Barr: How come, in some cases, nonhuman primates have experienced lung inflammation after receiving the vaccine? And were there any reports of humans experiencing this or is this common across vaccines?

Seder: We didn't see very much inflammation by the vaccine in the primates.

Barr: You've continued to assess the effectiveness of the vaccine against each of the variants of concern that keep popping up. Can you talk a little bit about how you and your group have been going about doing that?

Seder: The first study we did in April of 2020 was to demonstrate that the Moderna mRNA vaccine was safe, immunogenic, and protective in non-human primates. At that time the FDA was requiring safety, immunogenicity, and protection data from non-human primates prior to initiating Phase 3 vaccine studies in humans against COVID. We showed that the Moderna mRNA vaccine was safe, immunogenic, and highly protective in both the upper and lower airways against the WA-1 strain. These data were published in the New England Journal of Medicine in July of 2020 and preceded the initiation of the Phase 3 study at the end of July. There was great excitement by all of us at the Vaccine Research Center as it provided clear evidence for very high level protection in what we considered to be a predictive animal model.

Based on the protection by the Moderna mRNA vaccine in non-human primates, we then set up a series of studies that we felt would be important to guide human vaccine development through the pandemic. The first study was to define the immune correlates of protection. This refers to measurements of antibodies or T-cells in the blood or airway mucosal tissues following vaccination and determining whether these would predict protection following challenge. Understanding immune correlates of protection is a key aspect of vaccine development as it be used to assess the likelihood of whether a vaccine will be protective and can be used by the FDA to make decisions on licensing vaccines. To assess this, we gave various doses of the Moderna mRNA vaccine to generate different immune responses and protective outcomes. We showed that a specific titer of neutralizing antibodies against SARS-CoV2 in the blood measured after vaccination was a correlate of protection. This finding was subsequently substantiated in humans and remains the primary measure of predicting protection. In our animal studies, we also showed that it took a higher amount of antibody to protect against infection in the upper airway (nose) than in the lung. The implications of this finding was that it was easier to protect against severe infection in the lung than mild infection in the upper airway. We felt that this was an important finding at the time as it would explain why most vaccines, even those that had relatively low levels of neutralizing antibody responses were protective against severe disease in the lung, but that the more potent vaccines such as the mRNA vaccines would be better for protecting against symptomatic upper airway infection. These data would also have implications for how vaccines may prevent infection and/or transmission.

Another important consideration for vaccine development is the durability of immunity and protection. We thus vaccinated animals with the Moderna mRNA vaccine with the same dose and regimen as used in humans and followed them over six to twelve months. We measured immune responses in the blood, lung, and upper airway over this time period and then could determine if the vaccine was protective following an infectious challenge. These studies on the durability of the vaccines became very informative as the pandemic progressed, as it was clear in humans that the immune responses following the mRNA vaccination given twice began to wane and there were new variants emerging that showed reduction of antibody neutralization. Because we had these animals vaccinated and we are following them for a long time, we could assess whether boosting the animals six to eight months later would improve immunity and protection against variants of concern. These boost studies were performed in March of 2021 and were the first to show that boosting animals with the approved Moderna RNA vaccine was able to significantly increase the immune responses against all variants tested and confer protection against a variant challenge. Importantly, we compared boosting with the original Moderna mRNA vaccine to an mRNA vaccine matched to the Beta variant which was circulating at the time. At that time a major question was whether the vaccine needed to be changed to match the variant. The data showed that the neutralizing antibody responses following boosting with the original mRNA vaccine or the variant mRNA vaccine were similar at least over 4-8 weeks in non-human primates. A key scientific finding was that the original vaccine regimen induced a population of memory B cells that were cross reactive against the original WA-1 strain and multiple variants including Beta. This explained why boosting with either the original vaccine or a variant-specific vaccine were comparable since they were both able to expand this pool of primed memory B cells. These boost data showing high level neutralizing antibody responses and protection following challenge in the non-human primate model were presented to the Israeli government in late July of 2021 as they were confronting waning immunity following mRNA vaccination in their older age population and increased hospitalization which led them to consider boosting their population. Indeed after our meeting and presentation of the data in non-human primates, later that day, the Israel government approved the boost for their country. Approximately two weeks later, in a follow up call with them, they noted a reduction in hospitalizations in those that were boosted. This highlighted how we were able to generate scientific data to support clinical decision making and then in real-time assess the clinical outcome. The results from our non-human primate studies were also conveyed to the U.S. Government as they were determining whether to procure more vaccine for boosting the U.S. population. In addition, they were deciding on whether a change in the vaccine was needed to match the variants or whether the existing approved vaccine would be sufficient. Ultimately, the decision was made to purchase more of the original vaccine and with the data from Israel demonstrating that boosting improved immunity and protection, the FDA recommended boosting in the late fall of 2021.

An important lesson going forward for future pandemics is that thinking ahead by having animals vaccinated that could be followed over time and boosted could provide real-time scientific data for informing clinical decisions in humans.

Barr: Definitely. I had two subsequent questions based on what you just said. Why are homologous boosts more effective than heterologous boost in protecting against the disease and variants?

Seder: What you're referring to is the question: After people received the first two immunizations of the Moderna mRNA vaccine, would simply giving them another shot of the same vaccine (homologous boost) be as good as changing the mRNA vaccine boost (heterologous boost) to match a variant? In our studies in March 2021, we directly compared boosting with the original mRNA vaccine versus boosting with an mRNA vaccine matched to the Beta variant which was circulating at the time. Now, we are doing that same comparison using the original vaccine boost versus and Omicron variant boost. Our data comparing the homologous boost versus heterologous boost with the Beta variant showed them to be comparable for increasing neutralizing antibody responses at least over a short period of time (4-8 weeks). It is possible that over time there may have been a differences in the antibody responses by the heterologous boost. The major scientific finding was that both the homologous and heterologous boost were increasing the frequency of memory B cells that were generated by the original vaccine and were cross reactive against the original WA-1 strain and other variants. It remains possible that an Omicron boost may improve the response based on boosting cross-reactive B cells generated by the original vaccine, and priming additional B cells specific for Omicron only. So far, our data in non-human primates suggests that essentially all of the boosting occurs from already primed B cells, and we generate few new B cells against a variant only.

Barr: One thing that I thought was interesting was in one of your studies you saw that the South African variant was more resistant to neutralization than the Delta variant. Can you comment why there's an increased time lag for some of the vaccines to kick in as well as a decrease in the robustness of the response of the vaccine against the variants?

Seder: As the pandemic has progressed, all of the variants have a number of mutations which can lead to reduction in the ability of vaccine induced antibodies to neutralize the virus. This can in turn alter protection. The mutations may also change functional properties of the virus so they are more transmissible. In late 2020, our colleagues in South Africa isolated a new variant now called the Beta which had a specific mutation called 484. The concern was that there was a five -fold reduction in the ability of our antibodies in blood to neutralize the Beta variant compared to the original strain. This reduction in antibody neutralization against a variant of concern with multiple mutations was a potential harbinger of things to come and caused a lot of "angst" amongst those of us working around the world. At that time, another variant called delta was also isolated and shown to be more transmissible. Thus, Delta quickly became the dominant variant around the world and was associated with increased hospitalizations in elderly people. We had a group of animals that were vaccinated with the Moderna mRNA vaccine approximately 1 year ago and when we challenged them with Delta we were able to show that there was protection against severe disease in the lung, albeit delayed compared to studies when challenge was done much sooner after the vaccination and with other strains. Moreover, there was with minimal protection in the upper airway. The protection in the lung provided some assurance that our current vaccines may work well against this variant against severe disease but highlighted the importance that boosting would have for optimizing protection. Finally, Omicron has the most mutations of any variant. The concern is that it might further limit the ability of our antibodies in our blood to neutralize the virus. So we needed to learn would be the implications in terms of requiring additional boosting or new vaccines to match the variant.

Barr: How is NIH and Moderna working to make the vaccines more effective against the different variants and have longer durability? Durability has been one issue of concern.

Seder: What happens is when new variants of concern are identified, we work closely with Moderna to have them make a new vaccine to match that variant. They did this with the Beta and more recently with the Omicron variant. The RNA technology allows you to make these vaccines very quickly, and so they are an ideal platform for rapid translation. Then, we quickly test these new variant vaccines in various animal models to see if they are immunogenic and protective following challenge. As most people have already been vaccinated, a key aspect of our studies is to have animals that have been vaccinated with the original vaccine and then use them for boosting with these new variant vaccines. This is the best way to model the new vaccines rather than testing in unvaccinated animals which now represents a very small number of the population.

Barr: How do you hope that the mRNA platform will be used to protect against other diseases, and what do you think is promising about this new technology?

Seder: The new technology is very flexible, so you can make the RNA vaccines relatively quickly and you can package in the RNA vaccine, perhaps, multiple targets. mRNA induces broad-based antibody and T cell immunity, so it has advantages for "potentially" mediating protection against a variety of infectious diseases. Most licensed vaccines against virus and bacteria mediate protection by generating antibodies. For COVID, neutralizing antibodies have been defined as a correlate of protection. T cells may also have a role in protection against COVID and this would likely be against lung infection. T cells are important for protection against infections such as TB and malaria and are used in cancer vaccines. An advantage of mRNA vaccines is that they can package multiple antigens which may be important for infections such as TB and malaria in which you may need broad T cell immunity against more than one antigen. I work on tuberculosis and malaria vaccines, so we will start to look to see whether RNA vaccines will be useful. An important issue with TB and malaria vaccines is they require a high frequency of T cells in the lung and liver respectively where the infections are initiated. It remains unclear whether a vaccination with an mRNA will induce T cell responses of sufficient magnitude, quality, and breadth at these tissue sites. This may require a change in the route of vaccination.

Barr: Before we move on to some of the other vaccines that you have been a part of, can you just say what your reaction was last December when you saw the Moderna vaccine being administered to the general population?

Seder: One of sheer and overwhelming delight. I was especially proud of all my colleagues at the Vaccine Research Center, who played prominent roles in the leadership through Operation Warp Speed and through various scientific groups. This included Barney Graham who conceived of the design of the mRNA vaccine for SARS-CoV2 based on his years of studies with other coronaviruses. Kizzmekia Corbett was the post-doctoral fellow in his laboratory who focused on this work. John Mascola, Richard Koup and Julie Ledgerwood all had leadership positions in Operation Warp Speed as well as Adrian McDermott who led the analysis of immune responses. Danny Douek worked most closely with me in leading the non-human primate studies. Matt Gagne, Juan Moliva, Danielle Wagner, Barbara Flynn , Kathy Foulds and Shayne Andrew all played a critical role in performing the immune analysis. We also had outstanding effort by JP Todd for managing all the vaccine studies in non-human primates. There was a communal aspect to all of us at the VRC working on this. There was also a wonderful aspect of working with our colleagues cross the world in what I would consider the greatest global scientific collaboration.

Barr: In addition to the Moderna vaccine, you've worked on others. Will you please speak about your contribution to the formulation of a rejuvenated soluble protein vaccine, and how does this vaccine compare to some of the other COVID vaccines that are in existence?

Seder: Yes. I've spent 20 years studying protein and adjuvant vaccines for HIV, flu, and other infections. When Sanofi was developing their COVID protein vaccine, they wanted us to test it with two different immune stimulators called adjuvants. So we performed a non-human primate study and were able to show that the immune responses with the SARS-CoV-2 protein vaccine – the antibodies were quite good, and we were able to get high level protection. That facilitated the initiation of their clinical trials. Novavax has a protein vaccine that has very high-level efficacy in humans, and my guess is that when Sanofi has the phase three data, their vaccine will be highly protective, and so I think we'll add another vaccine that could be given and used around the world. Similarly, the Vaccine Research Center developed a S2P SARS-CoV-2 protein vaccine that we licensed to Medigen and this was ultimately approved for use in Taiwan. Thus, the VRC had a major contribution for two different vaccine approaches.

Barr: What are the advantages and disadvantages of the different platforms?

Seder: mRNA vaccines elicit antibodies, CD4 and CD8 T cell responses. Protein vaccines elicit potent antibody and CD4 responses but low to undetectable CD8 T cell responses. This is the major difference. Both vaccines are advantageous in that they can be given repeatedly. Viral-based vaccines such as Ad26 or ChAdOX developed by Janssen and AstraZeneca respectively are able to induce antibodies, CD4 and CD8 T cells. Such vaccines elicit lower antibody responses than mRNA or protein vaccines, but usually better CD8 T cells. A disadvantage of such these vaccines is that they may be limited in their ability to be used continuously for boosting since they elicit immune responses against the adenovirus.

Barr: Are there advantages to using that platform?

Seder: The mRNA and protein/adjuvant vaccines induce higher antibody responses than the Johnson and Johnson vaccine or the AstraZeneca vaccines. A notable feature of the adenoviral vaccines is the ability to rapidly induce antibodies and T cell responses with a single administration. Perhaps in the future the best option is to combine vaccine platforms termed heterologous prime-boost immunization whereby mRNA, protein or adenovirus vaccines are used in combination. This type of approach can often elicit higher immune responses than using one of the vaccine platforms only. This type of approach may be important depending on the infection and they type of immune responses required.

Barr: Can you please speak about how SARS-CoV-2 spike ferritin nanoparticle vaccine is constructed, how it works, and how you and your lab have been involved in assessing this type of vaccine's efficacy in hamsters and mice?

Seder: That vaccine was developed by our colleagues at the WRAIR [Walter Reed Army Institute of Research], and they used a ferritin platform that was originally developed at the Vaccine Research Center for influenza vaccines. They adapted that ferritin protein to make a nanoparticle vaccine. We helped them with some of the animals studies and provided challenge viral stocks. I would urge you to speak to them because they developed it. I would note that the some of the people developing this vaccine were trained at the Vaccine Research Center.

Barr: That's wonderful. That must make you all feel very proud that you trained people so well.

Seder: Yeah. I think one of the legacies of the Vaccine Research Center will be the training of enormously talented people that went out and made major contributions. A prime example of this is Jason McClellan who worked closely with Barney Graham in developing an RSV [Respiratory syncytial virus] vaccine and subsequently the SARS-CoV-2 S2P vaccine.

Barr: Are there any vaccines being developed that would not only protect the individual but also not allow them to spread the virus? And why is the latter mission so difficult to achieve?

Seder: That's a very good question. What you're asking about is a vaccine that would prevent infection and transmission, and so my sense is that that might be a delivery issue for a vaccine. The first goal is to prevent serious disease in the lung, and we've been very successful at that. The second goal is could you limit infection in the upper airway so you wouldn't get sick at all or transmit it to someone else. The question becomes whether that would be achieved if you could give a vaccine which would induce higher responses in the upper airway. That might involve a different route of delivery where you might give the standard intramuscular vaccine to give you circulating antibodies that protect you against lung disease and some protection in the upper airway, but then you might have a second immunization that would boost immune responses in the upper airway to limit or prevent infection and transmission. That's a different goal, and something that we're actively working on.

Barr: Are there efforts to target other parts of the virus other than the S-protein or other parts of the human cell?

Seder: Yes, there are efforts to make vaccines that target other proteins and generate T-cells against those proteins, and that's based on the fact that the T-cell responses are highly conserved against variants. There's a lot of effort in developing vaccines to induce T-cell vaccines. It is important to emphasize that antibodies are the first line of defense. T-cells might come in later to kill the virus and to limit severe disease or death, but right now, I think first and foremost, antibodies are primary immune mediators. I think it would be unwise to develop vaccines that depending solely on T-cells.

Barr: Will you please discuss a study that you are a part of that looked at in vitro and in vivo functions of SARS-CoV-2 infection enhancing and neutralizing antibodies?

Seder: We did not do much direct investigation into antibody-mediated enhancement. That work was done in a collaboration with my colleague Bart [Barton] Haynes at Duke. He had done some elegant work and isolated a series of antibodies that could be highly protective and also ones that he found that had very little protective capacity. That's really his work, and he could explain it best.

Barr: Will you please discuss what was learned about the virulence and transmissibility of the variants in a study that you were a part of that looked at SARS-CoV-2 variant prediction and how RBD62 has promise for future drug and vaccine designs?

Seder: That's again a study that I urge you to talk to my colleague Danny [Daniel] Douek. He has been working on this for a long time with his colleague Gideon Schreiber in Israel. Gideon developed a molecule that would bind to ACE2, so it would presumably block any coronavirus. They've completed some nice animal studies to show that treatment with this reagent can limit infection. I think that is something that you should talk to Danny about to give more detail to what the possibilities are of using that for people who are infected and possibly using it as a preventive measure over a short period of time that might work against any possible coronavirus. There's potential excitement there.

Barr: Definitely. How have you applied your knowledge from years of working on vaccines – you've worked on a lot of different vaccines against malaria, HIV, cancer, TB.

Seder: I think we apply kind of a common set of questions. The first question we look at is: What is the type of immune response that we think will be needed to protect you? The second question is: Where does that immune response need to occur? Based on that, we then start to look at what type of vaccines and routes would best induce those immune responses. If it's an infection where antibodies are the primary mediator of protection, then protein-based vaccines, or mRNA vaccines, would be something you might consider right away. The mRNA vaccine is probably easier to manufacture quickly than a protein based vaccine. If T cells, and especially CD8 T cells, are important, you might consider adenovirus vectors or live-attenuated vaccines. The mRNA vaccines may also be considered. A key question about T cells is whether they are required in tissues and if so, would this alter the route of immunization? Thus for TB vaccines or malaria vaccines where T cells are required in the lung or liver in high numbers, we have shown that intravenous vaccination is much more protective than IM [intramuscular] or SQ [subcutaneous] administration. This may also apply to tumor vaccines.

Barr: Have you been involved in any other COVID-19 research or initiatives?

Seder: I was on Operation Warp Speed in the group focused on pre-clinical studies, and then became a member of the SAVE Network which was put together to track variants and then determine how this influenced antibody neutralization and protection following vaccination. There are three calls a week for the SAVE group. There's now one or two calls a week for what was called Operational Warp Speed – it's now called BDT. Those are the two major groups that I'm involved with. The SAVE group is also an outstanding collection of scientists around the world.

Barr: What was it like to be part of the Operation Warp Speed group and who was involved on the calls?

Seder: Oh, it was fantastic. The vaccine effort was led by John Mascola, my colleague and the director of the Vaccine Research Center. We had calls every Thursday night. It was an incredible network of really highly talented people across the spectrum from basic science to clinical trials. Everybody worked very hard and very collaboratively. It was just a wonderful group. Over the last 18 months through all these calls, we all bonded together through the experience. It evolved from the discovery of the vaccine to the early trials of the vaccine to the final efficacy trials in both adults and children. It was the evolution of science through translation playing out in real time. Simply amazing.

Barr: What would you like to look at next in terms of SARS-CoV-2 or delve deeper into?

Seder: So I am looking to get back to my work in developing vaccines for malaria, tuberculosis, and cancer. We have some exciting new data showing that we can prevent malaria with a monoclonal antibody. A lot of this work was done during COVID, which was challenging but underscores the commitment to continue research and clinical development for other really important diseases.

Barr: That's exciting.

Seder: It's very exciting. It always looks like we're done with this, but now Omicron came up and so we have these studies, but I think the final studies I'll do related to SARS-CoV-2 will be this: Whether you can alter the administration of the vaccine and maybe give it by an aerosol or an intranasal route and if that might limit transmission. If we could do that, that would help not only against SARS-CoV-2, but you could use it for influenza and other upper respiratory pathogens. That's a basic question that I spent a lot of my life looking at: how changing the route of vaccination might be optimal. That's kind of what I have as the final study, and then I have very good colleagues that will stay intimately involved in this work: Nancy Sullivan, Mario Roederer, Danny Douek, Eli Boritz, Masaru Kanekiyo and Peter Kwong and the entire VRC, there'll probably be a pan-coronavirus effort. If they need my input for designing nonhuman primate studies, I'll be available, but I think I'm looking forward to getting back to what I was doing before.

Barr: What has been most exhilarating or rewarding for you working at NIH during the pandemic?

Seder: Just the incredible professionalism and skill and competence of my colleagues at the Vaccine Research Center and colleagues around the world. You just can see that when you get people coming together that are really smart and dedicated that are focused on a problem, it is just extraordinary. Not only is the work of the highest quality, but they're doing it 24/7. The only thing that's changed is we're generating high quality work in a very rapid time frame. We've been able to adapt quickly and our collective efforts have in some ways saved the world – it has just been extraordinary for the speed and the success of the vaccine. I think this is something that all of us globally who worked on COVID will have a common bond that will remain over the course of our lifetime. This has affected all of our lives, and I suspect that a lot of my colleagues will stay in this area of research the rest of their careers.

Barr: In addition to being a scientist at NIH, you're also a human who's lived through the pandemic. How has the pandemic affected you personally with challenges and opportunities?

Seder: I think the one thing about the pandemic is it's changed life for all of us. We are both sitting here remotely, and this limits direct face-to-face interactions, which I think is still important. However, through all these Zoom calls, you end up getting to know people really well around the world which has been great. I think what is notable about COVID is the intensity and amount of information that is developing every day. Thus, we need to constantly adapt to the new information and make changes to our ongoing studies. I don't think any of us mind working 24/7, which is what all of us have been doing during the pandemic, but I think a lot of us are a bit tired because you're constantly looking at data that is coming fast. It's human data; it's animal data, and to trying to keep up with it all and integrating it is intense. That's what I think is different about it, but the immense joy is getting to know these really brilliant scientists and clinicians around the world and seeing what they do. I am always amazed by how quickly new viruses are identified and then the rapid work to establish how vaccines responses may be impacted by mutations they harbor. Scientists thrive on the unknown and I think to some extent we are in some ways “addicted” the changing information and figuring our solutions.

Barr: This is one of the last questions, but how have you kept up the morale of your lab who's been working so hard? It’s been a different situation for them.

Seder: That’s a really good question. I had my lab out for dinner last night and talked about that and said that I was really proud of them and that even though I wasn't there face-to-face, I'm doing my best and I'm thinking about all their projects. They've been able to all work and maintain really a high level of productivity in all of their projects. I think it would benefit if I was there more and in the lab more face-to-face, but I do think they've done a great job. All of our projects were maintained while I was doing COVID vaccine work, and I don't think any of our work suffered, so while it's been exhausting to keep up all the projects, hopefully next year we'll get back into a regular routine.

Barr: This is my last question. Do you have anything else that you would like to share about your COVID-19 research or experiences or your thoughts on the pandemic in general?

Seder: I want to highlight some thoughts that relate to my colleagues at the Vaccine Research Center who worked 24/7 for the last 2 years. They are an extraordinary group of people who have made a significant contribution to global health. Moreover, this accomplishment extends to all scientists, clinicians, and health care professionals around the world. It has been an honor and a privilege to be involved in the VRC effort. It does tell you that when you work together and collaborate, things like this can happen. I think at the end of it, we'll all look back and say, “We did what had to be done.”

Barr: Well, thank you very much for all you do, and I wish you and your lab continued success and continued health.

Seder: Thanks very much for taking the time and interest in our work.