Daniel Douek, M.D., Ph.D.

Behind the Mask

May 27, 2021

Barr: Good morning. Today is May 27, 2021. My name is Gabrielle Barr, and I'm the Archivist with the Office of NIH History and Stetten Museum. Today I have the pleasure of speaking with Dr. Daniel Douek. Dr. Douek is the Chief of the Human Immunology Section at the National Institute of Allergy and Infectious Diseases (NIAID). Today he's going to speak about some of his COVID work and experiences. Thank you very much for being with me.

Douek: Thank you.

Barr: To get started, can you speak a little bit about the study in Canada that looked at antibody reactivity to SARS-CoV-2 in unexposed adults and infants under six months?

Douek: Well, what that study showed was that these adults, some of them health care workers, using certain assays, looked like they had antibodies to SARS-CoV-2, even though they were not exposed or infected. They are actually antibodies that are cross-reactive with the four endemic human coronaviruses that give us the common cold. That's what that study showed. The question is, do those antibodies affect someone's response to a SARS-CoV-2 vaccine or infection? The answer is probably not, but it's of interest. Certainly, it would be interesting to see whether other human populations have antibodies to the endemic coronaviruses or maybe even other animal coronaviruses, and whether that affects their response to SARS-CoV-2. It has led to some interesting future work that we're embarking on.

Barr: Can you speak a little bit more about this future work?

Douek: Simply, there are so many coronaviruses in nature and three of them have recently spilled over and caused horrible infections—the most recent one [being] the pandemic, and then there was MERS [Middle Eastern respiratory syndrome] and SARS-1. My interest is really how much this has happened, and we just haven't noticed that there's been an attempted spillover, but people may have managed to control it because they have some of these cross-reactive antibodies. That's really what we want to find out.

Barr: Are you surprised at the high percentage of people that had these cross-reactive antibodies?

Douek: No, I think most people have them.

Barr: What has been your role in developing and testing COVID-19 vaccines?

Douek: I work at the Vaccine Research Center (VRC), where Barney Graham was essentially responsible for developing the sequence of the vaccine that is produced by Moderna. He did that with Kizzmekia "Kizzy" Shanta Corbett, based on a lot of previous work, so he's really the core of the effort, but all of the labs at the VRC have been involved in one way or another. My role has mostly been in some of the preclinical work in non-human primates and looking at the antibody responses to the Moderna vaccine, and now some of the variant vaccines that Moderna is producing.

Barr: Interesting. Can you talk a little bit about your participation in the AS03-adjuvanated soluble prefusion S protein vaccination formation trial by Sanofi Pasteur and GlaxoSmithKline?

Douek: Well, I've been involved in non-human primate preclinical studies, and my lab really is responsible for measuring the virus load in these challenge studies to see how effective the vaccines are. Those results, I'm pretty sure, are not public information yet. Because these are public companies, I'm not allowed to give the results yet.

Barr: How does your lab go about measuring the viral load? Can you speak about your methodology?

Douek: You have heard of the PCR [polymerase chain reaction] test that people use to see if they're infected with SARS-CoV-2, [where they] stick a swab in the nose. That PCR test gives you a plus or minus, yes or no—you're infected or not infected. Our assay is kind of a version of that, but it's a sort of step up because it's quantitative. It's a PCR that tells you how much virus you've got. We employ a lot of other tricks and techniques to make it very, very specific and as sensitive as possible.

Barr: How long did it take you to develop this assay?

Douek: Not that long, really—a few weeks. We were in a hurry. We just took great care to make sure that it works. We had all these little tricks; we had to try out different things, which involved sticking swabs in our own noses and seeing how that affected stuff. But yeah, just a few weeks.

Barr: That's very interesting. What has been your experience testing the vaccines against the variants, such as the B.1.617.1 variant and other variants?

Douek: Again, I don't think those are published yet, so we can't talk about them. My experience, though, is that it's fun. I've got to say, it's a bit exhausting, because every time you think you've seen the last variant, there's another variant.

Barr: Do you have to change your assays for each variant?

Douek: Well, we check whether we have to. And so far, thankfully, we have not had to, but that's a very good question. If there are changes in the genetic code of the virus then we would have to, if it would affect our assay. There's a meeting a couple of times a week of this group called SAVE [SARS-CoV-2 Assessment of Viral

Evolution], and it's organized by DMID [Division of Microbiology and Infectious Diseases] at the NIH. It's a fabulous meeting. There are a few hundred scientists from all over the world who meet early on a Friday morning. There are different groups, and there's one group which tells us which variant is being tracked. One looks at it in vitro. I'm in the in vivo group. Friday morning, I find out what kind of work I might have to be doing the next week. Life at the moment—I mean, science is usually pretty fast moving, but with this everything changes every day. It's amazing.

Barr: Have you been looking at the variant in India that unfortunately has claimed so many lives?

Douek: We will be doing that in the coming weeks, yeah.

Barr: How many variants are out there that you've been looking at?

Douek: Well, we've been looking at the variant that originated in India, which is called 617. We've been looking at 351, which originated in South Africa. There's a variant called P1 that originated in Brazil. We're looking at those three, mainly. How many are out there? Hundreds, really, of different sequences. What's important is which ones are the most relevant ones—which are increasing in frequency and could possibly cause the most problems when it comes to the vaccine, and which variants are most resistant to the vaccine-induced immunity? That's the important consideration.

Barr: In your group, you test in vivo against animals. What types of animals do you use?

Douek: Generally non-human primates. That's only part of the work. Most of the work is in humans.

Barr: Is it a different process in non-human primates than in humans? Do you do anything different amongst the groups, or is it exactly the same?

Douek: Oh no, there's a lot of differences.

Barr: Can you talk a little bit about what some of those differences are and how you go about it?

Douek: When you're dealing with humans, there are an enormous number of very important regulations to make sure that they're protected in every way possible, and that there's no abuse. I mean, the same thing happens with animals, but of course the considerations are different.

Barr: Yes, definitely. What have you learned to date, and what challenges have you and others you work with had?

Douek: Challenges? It's just an enormous amount of work. It's fast moving. We see challenges not as obstacles—they're opportunities. I have to say, we're having a fun time doing this. There's a horrible pandemic going on, but this is our job, so to have this opportunity to make a difference to human health worldwide is a real blessing.

Compared to so many people whose lives have been adversely affected, the only way my life has been affected is that I'm working all of the time, which isn't so bad.

Barr: No. Can you speak a little bit about some of the people you supervise in your lab that are helping with some of these studies?

Douek: My entire lab is involved. I have postdocs, technicians, and students who do a lot of the bench work. We do a lot of sequencing, so I've got a sequencing core, and they're always sequencing viruses. Each time there's a new variant that comes in, they sequence it. Then I have a bunch of bioinformaticians who analyze a lot of data. They're all teleworking at the moment. Everyone's involved. Because there are restrictions on the number of people who are allowed to be in the lab at any one time, it's a 24 hour-a-day, seven day-a-week operation, so it's shift work. Everyone's just working amazingly hard and they're all very dedicated.

Barr: That's great. How long does it take to sequence a variant?

Douek: Three days.

Barr: That's really fast.

Douek: It is.

Barr: How long is the analysis process and what does that look like?

Douek: Oh, I have no idea because I'm not a bioinformatician, but I understand the sequencing and molecular biology and stuff in the lab. Then it goes on to a big machine, which does the sequencing. Then this ton of data is uploaded to these huge servers up the road in Rockville, and then my bioinformaticians connect to those. Then I don't know what they do, but they use these computer programs, and they basically look at the sequence of nucleotides, the genetic code of the variants, and then they match it to existing viruses, and they see where there are differences. That's how we decide which are mutations and which are not.

Barr: Have some vaccines worked better than others against certain variants?

Douek: We know from some of the work in South Africa that the AstraZeneca vaccine had trouble against the variant in South Africa, the 1.351. Protection there was poor. Some of the protein ones looked okay. Certainly in vitro work suggests that, even though the South African variant and the Indian variant are to some extent resistant to vaccine-elicited sera, some of the mRNA vaccines like the Moderna and the Pfizer could probably do pretty well. I mean, what people need to understand is that the important thing is not protection from infection, it's protection from severe disease, hospitalization, and death. Most of the vaccines will probably do pretty well against that.

Barr: That is a really good thing. Can you talk a little bit about how the vaccine platforms developed for SARS-CoV-2 may be modified to tackle other types of coronaviruses or diseases?

Douek: We work a lot with the Moderna vaccine, the mRNA vaccine, and the beauty of that is that you can change the sequence so quickly in the event of a new pandemic threat, for example. I think that technology is going to revolutionize the world of vaccines really. It's amazing. It could be applied to cancer vaccines—all kinds of other things.

Barr: That's exciting. Can you speak about your collaboration with the Sheba Medical Center in Israel and your part in facilitating the relationship between NIH and this Israeli hospital?

Douek: I was doing a sabbatical in Israel at the Weizmann Institute last year on cancer and the microbiome and the pandemic hit. I called a friend of mine who was originally introduced to me by another researcher at the NIH. He's at the Sheba Medical Center. He's an HIV doc. I suggested we work on coronavirus together. In Israel, they've done an amazing job of vaccinating people, test and trace, and all of that. We're still working together and having a lot of fun, so it's great. Hopefully, I'll be able to go back when we're allowed to travel.

Barr: They donated a lot of samples to NIH. Can you talk about that?

Douek: Yeah. They sent us a lot of interesting samples and we're analyzing them. We're analyzing T cell responses, B cell responses, people who are infected with HIV—all of that kind of thing. Very interesting. There are no more samples coming because there's basically no one who's infected, which is a good thing.

Barr: That is really good. Where are you getting a lot of your samples from now?

Douek: A lot of them are from the vaccine studies that Moderna is doing with the new variant vaccines. There are convalescent people in the United States, so that's where most of the samples come from. Then we have collaborations internationally, so all over the world as well.

Barr: Have you been involved at all with any of the booster shots that Moderna and Pfizer are working on?

Douek: Yes. Those are a couple of the trials that we're working on with the Moderna vaccines. We'll be looking at the B cells, the cells that make the antibodies, to see how the boosters affect that.

Barr: We're going to shift from you as a scientist to you as a person. What personal opportunities and challenges have arisen for you due to COVID-19?

Douek: Well, I mean, challenges—it's just trying to get all the work done. As I said, though, it's fun. It's kind of nonstop.

Barr: How do you manage? Your work is very important for the world population so that people have the vaccines tested and have [access to] them. Do you have a certain method you use that helps you get things done?

Douek: Well, the only method is working really hard and cheering on the people in my lab as much as possible because it's tough for them. Just trying to keep everyone happy and focused and to be understanding that everyone's being pulled in many directions. And opportunities? Well, I'm working on a virus that I was never working on before. I'm thinking a lot more about pandemic preparedness. Maybe it'll change the direction of my research in the future.

Barr: I saw that you wrote something in the beginning of the pandemic about health policy through the lens of immunology. Would you continue thinking in those sorts of ways?

Douek: I'm not a policy person. I'm a lab person, and what I would like is for the policy people to come to the scientists like me for some advice, and for the politicians to listen to the scientists like me, so that I can then get the funding to do the science that I love to do. I think that's how it should work. If they want to know about science, I'm always here.

Barr: What do you think has been learned about pandemic preparedness, and how would you want to continue working with that?

Douek: Well, one thing that we've learned is that we can make a highly effective vaccine in months against a global pandemic, which is remarkable. I mean, just unbelievable. We know we can do that, number one. Number two, it will happen again—there will be another pandemic. I don't know if it'll be the coronavirus, flu, or anything like that. I still think it's early days, but we know we can do it. The world of scientists came together in such a remarkable way. When this is over, we've got to sit down as scientists and think, "What did we do well, what did we do badly?" Politicians need to do it too. Whether they do it or not, I don't know. I hope they do. But as scientists, we need to do that and get ready for the next one.

Barr: You've worked a lot with AIDS and HIV in your career. Has taking a break and working on COVID-19 made you look at AIDS or HIV differently and given you ideas as to how to go back to that once the COVID-19 pandemic is over?

Douek: No. No, I think it's the other way around. I think working on AIDS and HIV so long really put us in a very good position to attack coronavirus. Maybe when I go back to working on HIV a lot more, when this pandemic is over, I'll realize that it did affect my thinking. But at the moment, I think I'm so focused on coronavirus. But we'll see. We'll see.

Barr: Definitely. What is something that you enjoy doing that's made the pandemic more tolerable?

Douek: Well, it's not intolerable. I mean, I like doing the work and then I've got a few hobbies. I like to garden and grow vegetables, that kind of stuff.

Barr: This is a fun question. What disease do you believe needs more attention in terms of developing a vaccine that does not already have a vaccine in the works?

Douek: Well, there are diseases where there are vaccines in the works, but that should deserve a lot of attention. Malaria, for example. We really need an early effective vaccine for malaria. There's a lot of great work being done—a lot of that at the Vaccine Research Center. Bob Seder is doing some remarkable work on that. Malaria, TB [tuberculosis], diarrheal diseases of childhood—there are a lot of diseases which need our attention that affect human health in dramatic ways.

Barr: Is there anything else that you would like to add as an NIH scientist, but also as a person living through the pandemic?

Douek: Just to reiterate that the science matters. Science saves lives. Invest in science.

Barr: Well, thank you very much for all the work that you and your lab are doing. We really appreciate it. And I hope that you all continue to stay safe.

Douek: Thank you.

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