Innovation Conversations: Dr. Claire Fraser

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Trey Powers: Welcome back to Innovation Conversations, a special series of Sterne Kessler's IP Hot Topics podcast. I'm your series host, Trey Powers, a director in Sterne Kessler's litigation and biotech practice groups.

For our fourth episode, we're delighted to be joined by a true innovator, Dr. Claire M. Fraser, director of the Institute for Genome Sciences at the University of Maryland School of Medicine. Dr. Fraser was a pioneer in the early phases of the Human Genome Project. She also led the teams that sequence the genomes of several microbial organisms in the early days of whole-genome sequencing, including important human and animal pathogens that helped launch the new field of microbial genomics and revolutionized the way microbiology is studied. She is the recipient of numerous awards and is the current president of the American Association for the Advancement of Science. Welcome Dr. Fraser and welcome to all of our listeners.

Dr. Claire Fraser: I'm happy to be here.

Trey Powers: You've been involved in a lot of innovation throughout your career. I believe you're an inventor on something like four dozen issued patents, which is a huge number, especially in the biotech space. Are there any particular innovations that you are a part of that you're especially proud of?

Dr. Claire Fraser: Yes. Great question. I think the one patent and the one effort that I was involved in that makes me most proud was work that was done in collaboration with colleagues at Novartis Vaccines going back now over 15 years ago. And this was to develop the enabling technology for what has become known as reverse vaccinology, that's starting vaccine development at a new place beginning with a

genome sequence of a pathogen, which basically gives you a parts list of all possible vaccine candidates and taking that through to development. And this work resulted in marketing of a vaccine against meningitis V, which is known as Bexsero. This prevents invasive meningitis. It's particularly of concern in young children and this new vaccine received breakthrough therapy designation from the FDA, not once but twice. So, for me, this effort was really meaningful because it took the work I was doing in genomics and translated into a real-world product that has had a profound impact.

Trey Powers: Wow, that's great. Claire, in a previous conversation, I think you mentioned something to me about doing some hiking in Yellowstone many years ago to look for biotech tools. Why would you expect to find laboratory tools on a hike? Can you set the stage and tell our listeners the story?

Dr. Claire Fraser: Yeah, I'm happy to do that. That was a really great experience. As your listeners may know, a lot of the reagents that formed the basis of the entire field of molecular biology, Taq polymerase is an example that's used in PCR. These are enzymes that have come from really unusual organisms that live in extreme environments like the hot springs at Yellowstone. And again, this goes back a number of years to the late 1990s, the Department of Energy had become interested in the genomics work that we were doing, and they were particularly interested in exploring some of these bacteria that are called extremophiles because they live in these extreme environments for a couple of reasons.

One was to see if there were other novel enzymes and other proteins waiting to be discovered that could be used to advance the field of molecular biology, but the other reason was these organisms derive their energy very differently from organisms that live in more temperate environment. It's all chemical energy and back 20 years ago, this was of great interest to the DOE.

So, set out in Yellowstone with a couple of colleagues who had done this kind of bio prospecting before. We were collecting from some of the prismatic pools. These are the brightly colored hot springs that you see in Yellowstone. I didn't actually do the collecting. I was just along as an observer, but I remember my colleagues had on steel toed boots with heavy rubber boots on top of those because the heat and the acidic environment is highly corrosive, and they were very gingerly reaching over into the pools to collect water samples that we ultimately then characterized with genomics. We didn't necessarily find anything new that made it into a molecular biology reagent catalog, but we learned a tremendous amount of information about how these extremophiles not only survive but thrive in what many people would think to be inhospitable environments.

Trey Powers: Claire, you are smack in the middle of some of the first whole-genome sequencing efforts and first author on several of the papers published disclosing the first complete genomes ever sequenced. Can you explain the importance of these

early sequencing efforts? Why is it important to know the genetic sequence of a microbe?

Dr. Claire Fraser: I think it's only been in retrospect that we've really been able to appreciate the impact of that work that we started now 25 years ago. When you have a complete genome sequence in hand for any organism, whether it be a microbe or whether it be humans in the work that has come out of the Human Genome Project, what you basically have is a parts list in terms of the biology of that organism. You are then able to think about the biology of an organism by looking at its parts and with microbes that has been extremely important. A lot of the work that I've done has been on microbes that cause disease. And as we just talked about earlier, when you know all the genes and all the proteins that they encode in a disease-causing organism, you potentially have in front of you all of the vaccine candidates and all the therapeutic targets for that particular pathogen.

So, what a genome sequence does is enable one to fast forward. It doesn't necessarily give you all the answers, but it gets you to a new more informed starting point to go forward and carry out translational research. And I think we've seen over and over again now over the past 25 years how powerful that kind of information is because as scientists, we can only study what we know. So, before genomics efforts, so much of the biology of organisms was unknown because the genes and the proteins hadn't been identified before.

So, it's having a genome sequence is such an incredibly important starting point because you now know all of the potential vaccine candidates, all of the potential therapeutic targets. If you're looking at a pathogen you know all of the biochemical pathways that might be exploited in agriculture, if you're looking at agricultural microbes. And so, what genomics does is get you to a new starting point, and it's a starting point that's fully informed by knowing all of the genes that you have in your organism of interest. And it means that nothing in that particular organism is unknown. And it has proven over the past 25 years to be a powerful enabler of downstream studies.

Trey Powers: Claire, you've been involved in industry. You've been the president of not-for-profit organizations, and you've been an academic researcher. Does a researcher in these different roles have a different perspective on the importance of patents? Having been so involved in various roles, is there a perspective on the role of intellectual property that you'd like to share?

Dr. Claire Fraser: Yeah, thanks for that question, Trey. I finished graduate school in 1981, which was really coincident with the start of the whole biotech industry. And I've been extremely privileged to have my career move forward in parallel with biotech. And as you say, I've seen this from the perspective of being in academia, from being in industry, I've served on a number of biotech startup boards, and I don't think it's any exaggeration to say that the biotech industry wouldn't be where it is today, and we wouldn't have had so many breakthroughs were it not for the whole patent system and the ability to secure intellectual property rights on new discoveries. And I think it's also interesting that 2020 marks the 40th anniversary

of the Bayh–Dole Act, which was critically important in moving basic research discoveries in academic and government labs into the biotech and large pharma arena. And it's been really remarkable to me to see how the thinking has changed over this 40 years about development of new breakthrough discoveries.

When I finished graduate school, I didn't know anybody who was going into industry. The biotech industry really didn't exist. When you talked about industry it was large pharma. And those that did were considered having gone to the dark side. I think we are in such a very different and more enlightened place now 40 years later where we understand that it is a very virtuous cycle of basic research in academia into biotech spin out oftentimes then into acquisitions by large pharma. And I think society has benefited tremendously from all of that activity. None of that would've happened without intellectual property protection. So, it's been critical and I think it will continue to be going forward.

Trey Powers: Great answer, Claire.

Dr. Claire Fraser: Thanks.

Trey Powers: As a woman, did you feel like there were any particular challenges you had to overcome in your career? And if so, how did you do it?

Dr. Claire Fraser: Yes, for sure there were challenges. Things have definitely improved, but there's more work still to be done always, but early on I would find myself in situations where I was the only woman in a room, and I would look around the room and have this sense that I didn't belong. And I think I've heard and spoken with a lot of other female colleagues about the imposter syndrome, that when you find yourself in a situation like that where you don't see other people like you, it's not unusual to think that maybe you have mistakenly been called to be part of a group, part of a discussion, part of a collaboration. I just forged ahead. My father was a Marine and he instilled upon in me the idea that there was nothing that you couldn't or shouldn't do. And the idea of saying something was too hard was just not acceptable, but I can tell you that there were so many times when I felt like maybe I had chosen the wrong career, maybe I didn't belong. There were also a lot of times when in order to overcome that self-doubt, it was just a fake it till you make it approach. And now, fortunately, with the benefit of many years behind me, I don't suffer from those same doubts anymore. I see less of them perhaps in younger female colleagues, but they haven't completely disappeared.

Trey Powers: We've had some great guests on this program bringing interesting perspectives. Historians studying innovation in Walter Isaacson and the director of the patent office, Andrei Iancu. Claire, as an academic researcher actually doing the innovation, tell us about how you view the US patent system. Is it important to you and how?

Dr. Claire Fraser: As I said before, the patent system is absolutely essential to getting breakthroughs to market ultimately for the benefit of society, but as an academic investigator, to me, I guess, I would say the patent system still seems a little bit

confusing, at times a little bit opaque. I don't know that that's so much an issue with the patent system as it is a shortcoming on my part, but we've asked the patent system to do an awful lot over the last 40 years to keep pace with all of the really rapid new technologies that have been brought to bear to solve some of the biggest world's problems, particularly in the healthcare arena. And so I don't think it's at all surprising that there have perhaps been some inconsistencies, some ambiguities in how intellectual property is looked at, how patents have been granted. But again, I say all of this with the caveat that I'm looking at it from the side of a basic scientist.

Fortunately, I've been able to work with really talented tech transfer officials in the various universities where I've been, but I suspect that the patent office that was set up over 300 years ago when things were much more straightforward in terms of what is and isn't a patent has probably been challenged to more than a little bit of an extent by all of the technology developments. But that said, I still think the patent system is fundamentally sound and is serving us quite well.

Trey Powers: As an academic researcher and from a 30,000-foot view of the US patent system, is there anything you'd like to see improved about the patent system? And do you have any ideas about how we might go about making those changes?

Dr. Claire Fraser: I think that part of what is challenging all of us is the fact that technology is moving so quickly and I'm sure like many federal agencies, the patent office could benefit from additional resources. And ideally, we'd all like to be able to impose the luxury of additional time to deliberate about new technologies, what is or what isn't patentable, but that's a tall order. And so, I think we have to be more pragmatic and just keep moving forward. What I have seen serving on a number of boards, both in terms of large corporations and small startups, is that there do seem to be some inconsistencies in when and how various patents are granted. And from my 30,000-foot view outside the system, it seems like there is an awful lot of time and money that gets spent on patent litigation. But quite honestly, I don't know if that's fixable. Maybe that's healthy and robust part of the patent system, but I just see my colleagues in industry spending a tremendous amount of time trying to harmonize IP rights across institutions, across inventors, across technologies.

I don't know, I guess I would turn around and ask you, and maybe I'm not supposed to be asking you questions here, but as someone who sees all of this from sort of the opposite side of the street, how do you feel that the patent office has done in keeping up with all these new technologies that are coming at it fast and furiously?

Trey Powers: Yeah, I think you're absolutely right to point out that it is a big challenge for the patent office. I don't think Thomas Jefferson could have possibly imagined that we'd be debating about inventorship when an artificial intelligence makes the invention. I think the patent office has done well in general, but certainly challenges exist and will continue to as the pace of innovation increases. Claire,

when you look to the future in biotech, what strikes you as the fundamental problems yet to be solved, or the discovery is yet to be made?

Dr. Claire Fraser: I think one area where there has been some disappointment, but where I think the future still remains extraordinarily bright is with regard to the payoff that have and will continue to come from the investment in the Human Genome Project that was completed about 20 years ago. If you think about all the monoclonal antibody-based therapies that have come from better understanding molecular pathways that are involved in cancer and inflammation and other diseases, I think we've done remarkably well in terms of new products that have come to market. And I think there is just so much more to do in that space. And this is before we've even begun to see what the impact of CRISPR-Cas9 might be in solving fundamental problems in the healthcare arena.

I think the other area where I'm hopeful that there will continue to be a lot of new breakthroughs and a lot of new discoveries is with regard to genetically modified organisms. And I think quite honestly, they have gotten a very bad rap. Maybe the initial rollouts were not as wise as they should have been, but I think it's pretty clear that without continued breakthroughs in agriculture that allow us to deal with the pressures of climate change, increasing temperature, increasing drought, severe weather, we're never going to successfully be able to solve the world's food security problems. And I think those of us in developed countries are in a very privileged position. We have the ability to make decisions about whether we do or do not consume genetically modified organisms, but if you go into the developing world the risk benefit ratio changes substantially. And I think that it's only through breakthroughs with what we have to call genetically modified organisms that we're ever going to address some of these issues.

I think another area which reflects my own current research interests where there's great promise and we're just beginning to see some exciting new developments is in leveraging what we're starting to learn about the human microbiome as a way to influence not only disease but health, and we're just at the start of that journey. And it's really encouraging to me to see how many startup companies, how many small biotech companies have already been created around the microbiome space. Based on my own research, I think there's a tremendous possibility there as well. And it's always difficult when the rate of change is so quick to predict. And I suspect that in five years from now, we'll be looking back at where we are today and what we understand today and thinking that we were really not very sophisticated in our understanding of biology on a grand scale.

Trey Powers: So the pace will be ever accelerating, sounds like.

Dr. Claire Fraser: I think that's right.

Trey Powers: Thank you very much for being with us today, Claire. And before we let you go, I just want to ask you one final question that I think we're going to make something

of a tradition here on Innovation Conversations. Would you please share with our listeners something that they might find surprising about you?

Dr. Claire Fraser: Sure, happy to. When I'm not thinking about science, I'm ballroom dancing. And I started out a number of years ago wanting to learn how to do ballroom dancing more for social situations, but it has evolved into a very strong interest in competitive ballroom dancing now. Think about *Dancing with the Stars*. So, I have two closets full of costumes. I have an entire drawer full of false eyelashes. It's theatrics, it's performance. It's a way to lose yourself in the music. And for me, I don't know that I've found anything else in my life outside of doing science, an activity outside of science, that brings me such tremendous joy and being somewhat competitive, let's say, I do that to win just like anybody who knows me would say, that's sort of my life philosophy.

Trey Powers: You're in it to win it. I love it. That's a-

Dr. Claire Fraser: I am.

Trey Powers: ... great answer. Thanks very much Dr. Fraser. I really appreciate you taking the time out of your day to have this conversation.