



Quenton Rashawn Bubb

MD-PhD Candidate, Ludwig Stanford

Tell us about yourself, where you come from, where you were raised, your family.

I was born in Brooklyn, New York. I'm a child of immigrants from the island of Grenada. My parents met when they were very young in the church community in St. David's, Grenada. They immigrated to the United States in the early to mid '80s. My mom was a registered nurse, so she was in nursing in Brooklyn for pretty much the entirety of her career. My dad is an electrician. We had a really interesting upbringing because my mom would be working nights sometimes and would sleep during the day. My dad would pick us up from school, and on a week-to-week basis she had different shift schedules. We would oftentimes sort of have to improvise as far as who our main caretaker was. They were a pretty unique team for me and my brother.

Where did you go to college and what was your major?

I went to Johns Hopkins University, in Baltimore, where I studied biophysics. While I was in high school, I had this major dilemma. I knew that I wanted to somehow be in the periphery of medicine, and biology was really fun and cool, but I fell in love with math and physics. At that time, I didn't really know that engineering was an option, but when I was Googling "biology and physics programs," Johns Hopkins Biophysics came up, and I was like, "Oh my God, I could do biology and physics at the same time!" So that's what I really got into in college. Johns Hopkins was a very protein and structure-based program. That was my first deep dive into that sort of thing. It was tough, but also extremely gratifying.

Do you feel like your biophysics background has helped you?

Yeah, absolutely. For my PhD project, I set this ambitious goal to create a CAR T cell that can target three different antigens simultaneously through one CAR receptor. So I had to ask very fundamental questions about what kinds of proteins one should utilize in creating this kind of thing. One issue with using antibody or scFvs to make a trivalent receptor is that they aggregate. They have really sticky hydrophobic surfaces that can make it difficult for them to express. Early in my PhD, I had this wacky idea that, instead of using scFvs, what if we just use the ligands of the proteins that we are targeting. Here you have a folded unit, a globular unit that can fold independently of other globular units, that are attached via linkers and express extremely well. I consider that to be a triumph of my biophysics background and understanding, having intuition about folds for that earlier design.

What led you specifically to cancer research?

I think I took a sort of winding path toward cancer research. I mentioned that I'm a child of immigrants from the island of Grenada and one of the first characterizations of sickle cell disease came from the island of Grenada. Many people in my family had sickle cell disease, so it had always been on the back of my mind. While I was in college, I learned that Linus Pauling wrote a paper on sickle cell disease and put forth some elegant analyses and hypotheses about how the disease works at a molecular level. That I would say is the first time hematology entered my mind's eye. I then received the Marshall scholarship, and I completed a one-year program studying protein folding at the University of Cambridge. Around that time, I learned about potential cures for sickle cell disease, which included gene therapies. For

"I'm oriented toward becoming a physician-scientist. The kind of physician-scientist that I want to be is the hard question right now."

gene therapies to take, you have to get rid of a patient's immune system to replace it with a new one. That includes chemotherapy and radiation, and I initially thought that was ridiculous. Why would a person, who's dealt with these crazy pain episodes their entire life, opt into irradiating their bodies to get a potential cure? Around then, I was exposed to the research of my PhD advisor Agnieszka Czechowicz, who was exploring ways to establish transplants without having to use chemotherapy or radiation. In settings like sickle cell disease, not using chemotherapy or radiation has potential to significantly improve access to cure.

When I got started at Stanford for my MD-PhD after Cambridge, I learned that this transplant problem is also a significant barrier for malignant hematopoietic diseases like acute lymphoblastic leukemia and acute myeloid leukemia. Patients go through this "conditioning process" where they get chemo and/or radiation to clear out their blood system, and then they get a stem cell transplant to give their body a new immune system to add an additional layer of protection against that leukemia. In some disease settings, a significant proportion of the mortality that you see from stem cell transplantation comes from the conditioning itself.

This idea that came together was a collaboration between my main advisor Agnieszka Czechowicz and a co-advisor, Crystal Mackall, to create a cell therapy that



can go into the person, destroy malignant disease, destroy the person's healthy or pre-leukemic, hematopoietic system as a two-in-one. They could get a potentially curative transplant without chemotherapy or radiation, which I thought was a pretty clever approach.

Any avocational interests, hobbies?

I'm one of the biggest jazz nerds that you'll ever meet. I've been into music since I was a young child. My dad is a guitar player and saw it as important for me and my brother to understand our musical selves. So I've been playing piano since I was four years old, and I started playing the drums in high school along with many other interesting instruments. I started playing the harp in high school as well. It's hard to come by a harp these days, so I haven't played it since.

In high school, I started playing jazz music and it has stuck. I consider myself a professional amateur, in the sense that I'm not paid to make jazz music, but I still make it anyway. I'm an avid listener and I try to see as many live shows as possible. So if I'm not in the hospital, if I'm not in the lab, if I'm not playing video games, I'm probably listening to jazz music or making it.

Who are your favorite jazz musicians?

That is tough. When I'm asked this question I always separate it into people who are alive and people who are no longer here. So right now, my favorite musician is Jaki Byard, a piano player who became a master of all the styles of piano. In the middle of my PhD my mom passed away from a uterine cancer. It was tough, as she was in New York, and I was in California. But, around that time, I discovered Jaki Byard, and he has this album called *Parisian Solos* that I probably listened to more than 100 times in the year that she got sick. It's like a tour de force of Jaki Byard's virtuosity. He has these really emotional and experimental ideas and, at least to me, the album represents the ways in which life in its simplest way, can have a lot of rhythm to it. It helped me really lock in on a day-to-day basis, which I think is really important when you're supporting family through crises like that.

And as far as people who are alive right now, ask me an instrument and I'll tell you my favorite player, but I would say that there's a drummer named Marcus Gilmore who I think is one of the best drummers alive right now. He plays out in New York and he makes some really awesome music as well.

What do you want to do next? Do you want to focus on research? Do you want to be a physician-scientist? What are you thinking?

This is the hard question. I'm oriented toward becoming a physician-scientist. The kind of physician-scientist that I want to be is the hard question right now. I hope to enter a residency program that's physician-scientist focused, and it'll likely be in internal medicine, toward hematology/oncology. I'm still brainstorming about whether or not my value is in a lab, in the hospital, in biotech, or a mixture of the three.

So, in a very jazzy sense, I'm improvising, taking it one step at a time. A sort of surprising realization that I had in the last year, I think, is that I've always thought about being a physician-scientist in terms of what I could produce, what can I discover, what therapies can I create, et cetera. I didn't really think as much about the actual facilitation part. How much can I grow scientists to think, create, and discover? That idea has actually become

more valuable to me over time. The idea of not only just having a lab that's working on basic and translational questions, but also having a lab in which I'm fostering young minds and helping them discover.

This has been one of the reasons why I've thought seriously about running a lab. But we'll see how things pan out and how my priorities change as I proceed through my training.
