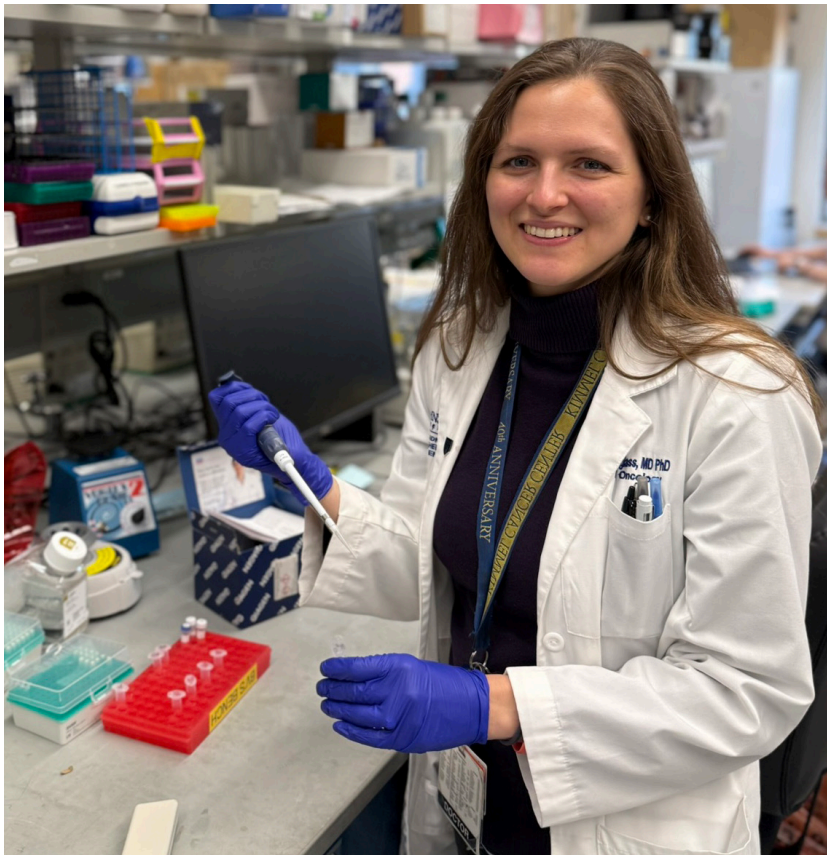

Jacqueline Douglass

Medical Oncology Fellow, Ludwig Johns Hopkins

Could you tell us a bit about yourself, your educational background, and how you got into medicine?

I was born in Charleston, South Carolina, but I spent most of my childhood in Memphis, Tennessee. Both of my parents were in the Air Force, so when I was younger, we moved around quite a bit. My dad studied electrical engineering and worked as an Air Force pilot then commercial airline pilot. And my mom

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trained as a pharmacist and a dentist. I have one younger sister who now works in tech. Math and science were my favorite subjects in grade school. I went to undergrad at MIT, where I had diverse interests, but ultimately decided to double-major in chemical-biological engineering and economics. I didn't know what career I wanted to pursue for most of my undergrad. I had interned in finance, including at Lehman Brothers in 2008. I ultimately decided against this career path, not so much because of the market crash but because I felt that the people I worked with in finance did not seem very fulfilled by their jobs.

When I came back for my senior year at MIT, I had to take one more biology class to complete my degree requirements. I had two excellent professors teaching this biology class, and they seemed so happy and enthusiastic about what they were teaching, which was a refreshing change from what I had observed in finance. I realized I needed to reconsider my career path. I had done lab research earlier in undergrad, and I decided to get involved in research again which made me remember how much I enjoyed wet lab work. Additionally, during my senior year, I was able to shadow a radiation oncologist, which was a pivotal experience. I felt that he had an incredible job being able to care for and guide cancer patients while at the same time working closely with physicists and other physicians, and using sophisticated machines to provide treatment to patients. Based on these experiences, I ultimately decided to pursue a career as a physician-scientist.

After undergrad, I stayed at MIT an extra year to get a master's degree in chemical engineering. And then I spent a year at the NIH in the Intramural Research Training Award program, where I did full-time research for a year while applying to MD/PhD programs. I ultimately did my MD/PhD at Johns Hopkins, where I also trained in internal medicine. I'm currently a medical oncology fellow in my second year, and I'm back in the same lab as my PhD lab, doing similar research.

Tell us about your research ...

All nucleated cells in the body express peptide-HLA complexes on their surface as a way for the immune system, and specifically T cells, to sample the contents of those cells. This is a way for T cells to know which cells to kill. So, for example, a virally infected cell will display viral peptides on the cell surface and invite T cell-directed attack. In cancer cells, mutant peptides derived from mutant proteins can be displayed by HLA on the cancer cell surface. These mutant peptide-HLA complexes are potentially an ideal target of therapy as they are a truly cancer-specific, cell surface marker.

Peptide-HLAs are typically a ligand for T cell receptors (or TCRs). However, antibodies have some distinct advantages over TCRs, so we are trying to make antibodies that mimic

T cell receptors, in that they specifically bind to these mutant peptide-HLA complexes. Then when we identify a given antibody, we can transform it into various T cell-based therapeutic agents such as bispecific antibodies or CAR-T cells. Specifically, we are interested in targeting common mutations found in what are called driver genes (that is, oncogenes or tumor suppressor proteins), as these same mutations are found in many cancer patients and the cancer cells depend on the presence of these mutations for their tumorigenicity. The ultimate goal is to create a panel of these antibodies that would be grafted into an optimized therapeutic format and then could be used in an off-the-shelf manner to treat patients with one of many cancer types.

What interests you about this subject?

I find this an exciting project because it presents major challenges but has the potential to be useful essentially for all cancer types. Nearly all cancer cells contain mutations in their genome, so this strategy could be a completely novel class of anti-cancer drugs, one that is broadly applicable.

How does your background in economics play into your research when you think about things like accessibility?

As a physician when I'm caring for a patient, my goal is to pick the safest and most effective therapy for my patient. However, my economics background does make me concerned about the accessibility of these therapies, as well as the ability of our healthcare system to shoulder the costs of such expensive novel therapies. For example, from a societal perspective, can we afford to give every cancer patient a $500,000 CAR T-cell therapy or a $200,000 course of bispecific antibodies? There's a big price tag on these novel immunotherapies, and I think we as a society will have to think about whether our healthcare system can afford such therapies. I am, however, optimistic that as these therapies become more ubiquitous, with manufacturing optimization and economies of scale, we'll be able to bring down their costs substantially.

What are your favorite avocational activities?

As far as hobbies, I'm married and I have two young kids, a two-and-a-half-year-old son and a three-and-a-half-month-old son. My husband is a resident in a surgical field who works even longer hours than I do. So, currently, my main hobby, if you would call it that, is spending time with my sons. But I also really enjoy physical fitness. I like cycling and running, and at least once a week I try to attend this hot yoga class called yoga sculpt that involves cardio and weights and music. The class is really fun and an excellent workout. I think it's important to have time to myself to focus on my physical and mental fitness.

What would be your advice to young women who are trying to decide what they want to do and are maybe worried about not being able to have a family and be a successful physician-scientist?

I'm not going to lie, it's tough. When I was in my 20s, I didn't make career decisions based on perceived future limitations from having a family because it seemed so far in the future. I also underestimated the time-commitment that comes with having kids and running a household. Now, my advice would be that if having children is a priority for you, it does require significant sacrifice but that shouldn't be a deterrent. The sacrifice comes in several forms—financially, for childcare expenses, time-wise, in caring for them or doing extra childcare related chores, and, to some degree, career-wise because it is very difficult for both parents to have high-powered careers in academic medicine while permitting one of them to be available for daycare drop off/pick up, dinner time, doctor's appointments, sick days, etcetera. Picking a partner who will share responsibilities is critical. Also, getting help from family if you can is a big plus. For the first two years of my older son's life, while my husband and I were both in residency and often both working overnight shifts, our moms took turns staying with us to watch him, which was a tremendous help. I do anticipate things will get easier as they get older and are more independent, so this time when they are little and need so much is temporary. One piece of advice I've heard is that you should make family planning decisions around what you want your Thanksgiving table to look like in 20-30 years, which I think is wise. Additionally, the level of joy I get from my sons is incomparable to anything else. It's a lot of work, but anything that's important and meaningful is going to require effort and sacrifice and that's very much the case when having kids.

What's the best career advice you've received?

I think the best advice is something that Bert Vogelstein said, which was something to the effect that "ideas are cheap, but your time and focus are very valuable." In science, it's important not to overcommit to too many things and instead focus on just a couple projects so that, ideally, you can see those to fruition. I tend to be the type of person who gets excited about new ideas and novel projects, but I find it easy to become overextended. While I do think it's important for trainees to hedge their bets by having a couple projects, perhaps something safer and something riskier, if you have too much going on, you won't be able to think deeply about any one problem.