

Interview with Dr. Geoffrey Krampitz

Colin Yost, Class of 2023



Geoffrey Krampitz, MD, PhD is a hepatopancreaticobiliary surgeon with an extensive background in surgical oncology, stem cell science, and cancer immunotherapy research who recently joined the faculty here at Thomas Jefferson University as an Assistant Professor of Surgery. After earning his BSE in biomedical engineering at Johns Hopkins University and before starting medical training, Dr. Krampitz worked in consulting in the San Francisco Bay Area and eventually helped launch two internet startup companies in Silicon Valley. He then went to UC San Francisco for his Master's degree, where he investigated the role of HIF1-alpha in stem cell differentiation. Dr. Krampitz received his medical degree from and completed his surgical residency at Stanford University, where he also received a PhD in Stem Cell Biology and Regenerative Medicine. He later completed a complex general surgical oncology fellowship at MD Anderson Cancer Center. During medical school at Stanford, he studied VEGF signaling in adventitial stem cells after vessel injury and its contribution to neo-intimal hyperplasia. During his general surgery residency at Stanford, he completed his PhD thesis investigating pancreatic cancer stem cells and developing novel immunotherapies. His current research focuses on identifying the key elements of programmed cell removal and “don't-eat-me” signals that can be targeted for clinical applications.

What made you interested in pursuing surgery?

My interest in medicine and surgery, in particular, started when I was very young. I am originally from Costa Rica. I actually lived on a coffee plantation in Guanacaste, Costa Rica, where I had a picturesque life living in the jungles and rainforest. My dad was an American who moved to Costa Rica, and he was interested in oil exploration and mineral exploration. He had businesses all throughout South America, Latin America, and the world. He had gold mines around the world, and one of them was in Costa Rica. He had sold [this] gold mine to another person, who was also an explant to Costa Rica, and that person defaulted on the payments. My dad was in the process of reclaiming the gold mine equipment, and part of that involved an inspection. My mom went down [to the mine] as did my dad, and when they arrived, they were confronted by the person [he sold it to] and his girlfriend, who then murdered my mother and father. Their death provided a huge impetus for me to evaluate medicine, surgery, and, initially, trauma surgery, as a calling of mine.

In many ways I wanted to prevent others from enduring the same loss and hardships that resulted from [my] loss. I initially wanted to do trauma surgery because it had that direct connection to what had happened to me, my siblings, and my family. Also, growing up I didn't have family members in medicine or in surgery, so the closest contact I had through college and then as a pre-medical student applying to medical school were the shadowing

opportunities that I had in the emergency room, which led to shadowing opportunities in the operating room with the trauma surgeons. So, to me it felt very natural, not only from an inspirational perspective, but also from an accessibility perspective, too.

During medical school at Stanford you founded the Medical Mentorship Program and worked with the Latino Medical Students Association. Could you speak more on those experiences?

I mentioned earlier that I didn't have any direct family ties to medicine. Coming initially from a very disadvantaged background, I think mentorship was hugely important. At Johns Hopkins, making it into and throughout graduate school, and getting into medical school and during medical school, mentors played a huge role [for me]. At every point along the way, I think mentorship has been the foundation of my success. So, I certainly recognize that, and realize that there are a lot of really disadvantaged folks going through similar struggles to those that I went through. I just wanted to help in some way to alleviate that. At least, provide a path. I think when you're climbing up the ladder you really want to be able to reach down and help the next person up the rung. So, that's what I wanted to do, and that was the inspiration for founding [the Medical Mentorship Program].

When I got to Stanford, there were a lot of individual mentoring programs, but nothing really cohesive with a unifying message. What I did was try and organize some

of those already existing programs and also expand that to help a lot of people, [which] was certainly a huge team effort. [The program] was able to reach a lot of the community colleges and other colleges in the Bay Area to provide one-on-one mentorship with Stanford medical students, develop workshops for improving applications, facilitate bridging that gap, and try to get more disadvantaged students to apply to and get into medical school.

Are you still connected with the Medical Mentorship Program? Have you been able to find ways to incorporate advocacy as you've progressed through your medical career?

Yeah! I still have ties to that program, which is still going on at Stanford. It's essentially part of a larger organization within Stanford. I think one of the things that I wanted to do was not build something that was a one-off that was going to die as soon as I left. Part of what I wanted to do was to build a lasting legacy, so to speak, where that could continue on. I still go back; a couple of years ago I went back and gave a talk to the new crop of mentees, and I think that certainly recharged my batteries, so to speak, [getting] to reconnect with the real people that I wanted to help along the way.

You worked in Silicon Valley before starting medical school. What did you do there, and what did you learn there that informs your medical practice today?

I went to Johns Hopkins for college, and I majored in biomedical engineering, so I had a lot of computational background. When I finished college, I wanted to take a year off between college and medical school. At this point, it was the late nineties, and it was the height of the dot-com boom, and I really wanted to go out to San Francisco and see what the excitement was about. I moved out there and initially worked for a consulting company. Then, as a result of that opportunity, I got involved in a couple of internet startup companies in Silicon Valley. What was intended to be a one-year break while I applied to medical school turned into a six-year hiatus where I became immersed in startup culture and what it takes to build a startup company and wearing many hats. You train as an engineer, but you're also in many ways a businessperson as well, and you learn a lot of those skills. While working with clients - you're representing the company. You're not only doing the technical aspects, but also a lot of the other soft skills that come with building a start-up company. Those were extremely helpful skills to have regardless of what you go into.

After working in Silicon Valley, you pursued a MSE in

biomedical science focusing on stem cell research. How did you decide to pursue that degree, and how did it influence your decision to go into cancer research?

At the end of six years, the companies were doing very well, and they were sold to larger entities. At the end of that, I decided that six years was long enough to put my real calling on hold. So, I went back and worked in a lab at UCSF, where I did my Master's thesis, and really got back into the research world, specifically in stem cells. That's really what started my interest in stem cells - working in Dr. Susan Fischer's stem cell lab at UCSF. After that point, I went to medical school at Stanford and continued my real love for research while I was there. I did a Howard Hughes fellowship year during medical school there and worked on VEGF signaling in heart valve development, and that led to looking at VEGF signaling in adventitial stem cells. [I looked at] tissue-specific stem cells in the vasculature and how they respond to vessel injury and contribute to neo-intimal hyperplasia - which is a big problem with cardiac stents and vascular stents in general - and tried to figure out ways to mitigate that. That led to a couple of other research fellowships and foundational fellowships that really helped propel my research work.

What made you interested specifically in surgical oncology and hepatopancreaticobiliary cancer?

When I was in medical school, I developed another mentor-mentee relationship with a surgical oncologist, Dr. Jeff Norton, who is a legend in his own right. He has one of those larger-than-life personalities, and it's very difficult not to become engrossed by his personality and his energy, drive, and commitment to patients. So, while I was rotating on his service, I really started to evaluate what I wanted to do and what aligned with my own research interests that I had developed over time, and I felt that surgical oncology really fit the bill. It aligned my interests in stem cells, cancer stem cells, and immunotherapies with my love for doing complex operations and helping people. Additionally, being inspired by someone of that caliber drove me to do surgical oncology, and in particular, pancreas and pancreaticobiliary surgery.

Your current research interest is in programmed cell removal and immune-mediated signaling. What got you interested in this specific area of oncology?

I stayed on at Stanford for my residency, and during residency I worked with Dr. Jeff Norton and Dr. Irv Weissman. I took some time off during my research years in residency to get a PhD in stem cell biology and regenerative medicine in Dr. Weissman's lab. One of the projects I did was looking at cancer stem cells

within pancreatic neuroendocrine tumors, which hadn't been discovered yet. Part of that was driven by my own interests in pancreatic neuroendocrine tumors and Dr. Norton's expertise in that area as well, but we also had a very prominent member of the community that was afflicted by a pancreatic neuroendocrine tumor, and that was Steve Jobs. He was one of the big reasons why I took on that project as well, trying to figure out not only what these tumorigenic cells were and how they behaved, but also how we could target them and potentially find additional therapeutic avenues for this type of tumor.

That was one of my main objectives during my PhD and it all tied into this molecule that Irv Weisman discovered to be a "don't-eat-me" signal. His lab identified CD47 as a cell surface molecule that was initially looked at as a cancer stem cell marker. What he quickly found was that it was expressed not just in cancers with a stem cell component but also in all the other cancer cells that we tested. CD47 acts as the "don't-eat-me" signal, so it interacts with SIRP receptors on macrophages and basically inactivates macrophages from performing phagocytosis. This is one of the ways cancer cells are able to evade immune surveillance, and by blocking CD47 signaling, we were able to essentially re-awaken the immune system, uncloak the cancers, and allow for immune destruction of cancer cells. We demonstrated this *in vitro* and *in vivo* with animal models and across many different cancer types. This combined work by many talented people in Dr. Weisman's lab demonstrated the preclinical evidence for the efficacy of CD47 therapies, which lead to the creation of Irv's company Forty Seven, Inc. [The company] is now carrying out the clinical trials that will hopefully be bringing this to market soon, and the early results are very promising.

Can you talk about your decision to pursue academic medicine and what brought you to Jefferson?

I'm really excited about being here at Jefferson for a lot of reasons. My passion is in trying to bridge science and surgery, so [after residency] I wanted to continue my surgical training, and I did a fellowship at MD Anderson in complex general surgical oncology, which was a tremendous experience as well. I was able to connect with James Allison, Padmanee Sharma, and Anirban Maitra about what it takes to do high end science, and they provided some real insight into taking the next steps toward that goal. I became even more convinced that I wanted to do both [surgery and research]. I came out of MD Anderson with great training in surgical oncology and a specific interest and focus in hepatopancreaticobiliary surgery, but also wanting to do cutting edge research. When I was coming out of fellowship, I was looking for

a job that would provide both of those and [Jefferson] did just that. It's a tremendous institution that has a commitment and real expertise in both the surgical aspect and scientific and research aspects of pancreas cancer. Being able to operate with Dr. Charles Yeo and Dr. Harish Lavu and learn from them on the operative side and then also do high-end research with Dr. Scott Waldman and Dr. Jonathan Brody and the rest of the scientific community here [made it] a no-brainer to come here. I felt like this was a tremendous opportunity for me to operate at a very high end on both of those aspects.

I think equally exciting to me is the opportunity to re-engage with medical students and residents. Perhaps the only disadvantage of training at MD Anderson was the paucity of interactions with residents and medical students. I really missed the teaching and team dynamic from my previous experiences at Stanford. I'm looking forward to re-engaging with the medical student and resident community. I think trainees provide a boundless source of energy and enthusiasm and ideas. You are really the engine for academic medicine and discovery. So, I'm really excited to be at a place that has such strong medical student and resident communities.

How do you see cancer treatments and surgical oncology changing in the coming decades?

I've always seen surgical intervention as being the cornerstone for cancer treatment. I think there's always going to be a time where surgical intervention is warranted. The indications may become more specific, but I think taking out the primary tumor is always going to be important. I think that a lot of targeted therapies that are being discovered and, in particular, the immunotherapies and checkpoint inhibitors, of which CD47 is one, are going to play a larger and larger role. Especially as we figure out how cancers protect themselves from such powerful therapies, we'll be able to do combination therapies that really allow us to push the envelope and - hopefully, at one point - make each individual cancer a more manageable disease. My focus is on pancreatic cancer, which is one of the most challenging cancers. I'd like to be part of what I think is going to be a real revolution in the next decade or two in how we treat pancreas cancer.

What are some barriers that you see to people accessing these advancements in cancer treatment? What are your thoughts on how to help overcome these barriers?

I think a lot of that really comes down to health policy. I fully recognize that developing these drugs and making these new discoveries - taking a discovery from inception

to putting it in the human - takes an enormous amount of effort and an enormous investment. So, I fully understand the more practical aspect of drug development and discovery and the need for investment in research and development. But then, you make a point about this being accessible to people, which I think is multifaceted and very complicated. Otherwise it would already be solved.

I think it goes hand-in-hand with industry, which has recognized that in a lot of ways. A lot of pharmaceutical companies have outreach measures to make their drugs more available to a broader portion of the population, especially the uninsured or underinsured. There's also a policy component, whether we talk about how we restructure our healthcare system or our insurance system in such a way that more people have access to coverage. So, I think it will require cooperation from the pharmaceutical industry, the insurance industry, healthcare providers, and government. There's the corporate level on the drug development and pharmaceutical side, the insurance industry and making sure that reforms are made there - [so] more people have more access and better quality health insurance - and then the governmental side, essentially facilitating. I think the government works best as a facilitator of these different processes.

Now that you're a practicing surgeon and a researcher, could you discuss work-life balance and how it's changed throughout your career? What advice do you have for medical students interested in surgery?

Yeah! I think that's an interesting topic. I kind of view it as a triangle. You have your clinical aspects - taking care of patients and operating - and that's certainly paramount because it's how you affect your patients individually and their families. You have this tremendous impact on those people every day, and it's extremely rewarding. That's one of the things that fuels surgeons: to be able to make that difference for that particular person and [give them] the chance to heal. Everything that we've all essentially aspired to be as doctors - that's what that opportunity allows. Another apex of that triangle is the research component, and that's how we touch the lives of the broader population. The discoveries you make in that area are potentially the ones that are going to impact the most people. So, that has obvious importance to it. And the other side of that triangle is family. I think those are the triumvirate of success or happiness, and I think that you have to figure out a way to nurture all of those areas, and it's not easy. At times, one will suffer at the expense of the others, but you have to figure out a way to make that one area not be neglected for too long. That is

where the balance comes in.

I'm not really sure "work-life balance" is the right term. I think you're always in a state of imbalance, and you just have to find a way where that imbalance is somewhat shared. I think at times family life is going to suffer a little bit, but you have to figure out a way to recharge those batteries, to replenish that, and to re-water that tree. And, similarly, I think there will be times where you'll cut back on some of the patient work that you'll do - or, sometimes, the research aspects - to make room for the other of the three pieces. I think the idea that you can have all things at all times is probably a disservice to people that are hearing that advice and going into medical school thinking that's possible.

I don't mean to suggest that it's not a worthwhile endeavor. I think that it's one that you have to go into with eyes wide open. It all becomes about time management. I think the more that you do, the more focused you become on the things that you want to focus on, and the things that you previously engaged in but weren't really at the core of who you are or what you really enjoy go by the wayside. And I think that's good in a lot of ways, because it really allows you to focus on the things that are important to you.

What do you like to do outside of work?

I used to be a competitive weight-lifter, and I even won a national championship in powerlifting. I still enjoy lifting from time to time, but I no longer compete. Now the bulk of my time is spent with patients, in the lab, or with my family. I have a daughter and a baby boy, and they keep me and my wife pretty busy at home.