

Episode 1: Dr. Todd Golub Talks about Maximizing Your Impact on the World through Bold Science Transcript

[00:00:00.280] - Speaker 2

Hello, listeners. This is Camilla joining you for our first episode of Luminaries of the UCCC. We are thrilled to have our first guest with us, Dr. Todd Golub. And this is a partnership with the Committee on Cancer Biology, who brought him back as a speaker. So we are so thrilled to have you here. And you don't need much of an introduction, but if you would, for maybe our listeners like myself who are new to the cancer research workforce, please tell us who you are.

[00:00:37.440] - Speaker 1

First, wonderful to be here. I'm Todd Golub, founding faculty member and now Director of the Broad Institute of MIT and Harvard, which is a new-ish, almost 20-year-old collaboration between Harvard-MIT and the Harvard hospitals.

[00:00:54.090] - Speaker 2

Amazing. Congratulations on that. The director position is fairly new.

[00:00:58.870] - Speaker 1

Over the past three years? Yes.

[00:01:00.350] - Speaker 2

Yes. Congratulations. That is absolutely amazing. Can you share with our listeners maybe what made you want to become a cancer researcher?

[00:01:11.390] - Speaker 1

I would answer that in two ways. I think there's cancer research and what's exciting about cancer research. And there's also just being part of the ecosystem of caring for patients with cancer. And I was stimulated in different ways in both of those areas. So maybe I'll unpack that a little bit. I think first I was drawn to cancer medicine and caring for patients when I was a student here at the University of Chicago and Pritzker School of Medicine, where Doing a sub-internship in pediatric oncology was just really motivating and intense and helped me realize that this is really

what I want to do. I liked that emotional intensity. I thought it was really meaningful that the attending physician on the ward at that time, when one of the patients on the floor died, the attending broke into tears himself I thought, How many careers are there that have that emotional intensity that it brings you to tears? I was drawn to that emotional intensity to cancer research. Then on the research side, there's almost nothing as exciting as making a discovery for the first time ever. Even if it's a small thing, I just remember the thrill of, wow, no one's ever done an experiment like this.

[00:02:50.220] - Speaker 1

No one's seen this result before. I don't know what it means, but that's pretty exciting. And a lot of that traces back to the University of Chicago as well. And we can get into that further later in the podcast.

[00:03:03.020] - Speaker 2

Oh, absolutely. We will, because you yourself have made wonderful, amazing, ground-breaking discoveries. And you, Chicago, has a long history of being very dedicated and involved in cancer I'm in research, so we are so thrilled to have you here. And I am not a physician, not a researcher, not a clinician or surgeon, so I have to say that. But I would say working with my colleagues in Comer, and some of them are pediatric oncologist, it is a very high emotion and high reward job. I mean, at the end of the day, it is a job. It's also what you give your life and your passions to, right? So thank you for sharing that with us. I want to congratulate you as well for being our first guest and alumni star for the University of Chicago Medicine Cancer Center's 50th anniversary seminar series. So hooray. And can you tell us about when you were at Chicago and in what capacity and what it was like?

[00:04:07.520] - Speaker 1

So I was at U of Chicago as a medical student. So this was 1985 to 1989, straight out of college. Thrilled to have been accepted here and to join my class. And I felt like it was a particularly good fit for me because of the long tradition of Thinking about clinical care and research together. Having these two disciplines joined at the hip at U Chicago was really important. So U Chicago was the right fit for me for sure, because in addition to learning the blocking and tackling of medicine, there was this constant aura of research going on in the background. Being exposed in the process of learning about medicine to learning about research in a place that was

filled with luminaries and a history of luminaries that might no longer be active at the university but were legendary, nonetheless, that was pretty meaningful. During medical school, I was engaged in research projects. I worked in the laboratory of Shutsunliu and Ben May, and that was really stimulating. And that's even an interesting story in itself, because when I was in college, I went to Carleton College, a small liberal arts college, I worked in the laboratory of John Tomosco, who was a student of Shuzunliu, who himself trained with Charles Huggins.

[00:05:59.920] - Speaker 1

And so there's this long lineage of Huggins to Lyao, to Tomasco, to me. And so that was a thrill just to be in that lab at U Chicago in the first place.

[00:06:12.280] - Speaker 2

Wow. I mean, what a great pedigree that you are a part of and contributing to. And I read one of your biographies, short biographies. I don't know if you have a full book. If you do, I'll read it.

[00:06:25.660] - Speaker 1

Not yet? Not yet. And probably never, but that's okay.

[00:06:30.060] - Speaker 2

But it shared that you deeply care about trainees and training the next workforce in cancer research as well as patient care. Can you talk to us a little bit about why training the next generation is so important?

[00:06:45.990] - Speaker 1

It's so important. It's probably the single most important thing, because if you think about it, there's a limit to what any one individual can do. And so if you really want to maximize your impact on the world, you need to think about, Where am I going to get an amplification effect? Where can I get a catalytic impact on the world? And one way, it's not the only way, but one way to do that is through trainees. And so if you can stimulate and encourage trainees to stick with it because research is often really hard, then you've really done something. Because there are all kinds of reasons why people feel like, Oh, I don't think I could do this. They have imposter syndrome. It's too hard. There's a lot of failure. There's a lot of discouragement,

discouraging things that you happen. And so if there aren't people there saying, No, you can do this. You've got what it takes. And don't worry, things may seem dark now, but it will get better. Trust me, then you've really done something important.

[00:07:58.060] - Speaker 2

That I can say that the Cancer Center U Chicago could not agree more. Can you give us a ballpark estimate of how many trainees you have worked with, trained, had in your lab?

[00:08:11.850] - Speaker 1

That's an interesting question. To be honest, I've never counted them up, but there are probably 100 people that have passed through my lab over the years, ranging from postdoctoral fellows to graduate students and medical students to young scientists, physician scientists, to be straight out of college. I particularly like working with those youngest people because they're the most undifferentiated in their career path. And so really encouraging someone to go into medicine, biomedical research, that's a point you can have a lot of impact.

[00:08:58.740] - Speaker 2

I I feel the magic of working with traditionally aged, like end of undergraduate degree, like 2-4 years after. And just the amount of creativity. My background is actually in Student Affairs Administration. And working with those students, I was like, you have so many ideas that are helping push your field forward. I work mostly with engineering students. And it's because you don't have all the baggage to put a word on it, but you can see the future, the possibilities, and grow the field.

[00:09:41.760] - Speaker 1

Yeah, I think that's an insightful comment. There is a bit of a paradox in there because the university setting, and I would say in particular, academic medicine, is a pretty hierarchical environment, where there are professors that are senior professors, junior professors, and then people in various states of their own training. And yet, almost invariably, the best ideas come from the youngest, earliest career people. And So I think encouraging young people, early career scientists to say, No, coming up with those really good transformative ideas, that's your job. That's your responsibility. Disability. And don't be passive and wait for someone with gray hair

to do that. That's your job. The job of the gray-haired person is to help encourage you to have those ideas. But I think our system isn't always optimized for bringing out that creative thinking and ambitious thinking from early career scientists. I think too often the advice that trainees get is, Oh, that's too ambitious. You should scale down and focus. And I think we should be doing the opposite. We should be not encouraging people to be scattered in their thinking, but encourage people to think ambitiously and boldly and to take risks and to only work on the things that are most important, not projects that are likely to succeed, but who cares?

[00:11:30.120] - Speaker 1

To me, that's the worst... I tell people that come through my lab, the projects I hate the most are those that are successful, but nobody cares because they're just incremental advances and not really moving the needle. So I think the aspiration for students and trainees and everybody all the way up to senior faculty should be to work on things that really matter and take some risks that it may not work out as planned for any particular project, but it's far better, in my opinion, to work on something really important and have it not work out than to have a career doing incremental things that are successful by some measure, but just don't actually advance the field.

[00:12:25.370] - Speaker 2

I love that. I think that might be the title of the episode.

[00:12:29.670] - Speaker 1

Well, we'll see. I think I'll also admit that that's easier said than done. Sometimes the funding agencies don't see the world that way. Sometimes funders tend to reward incremental, safer science. And that gets people, I think in particular early career, scientists shifting from this ambitious creative, bold thinking to a more conservative, constrained view of what they do. I think that's not good. And so part of what I like to try to do is undo some of that thinking and bring back the audacious creative, bold, imaginative thinking that students often go into the field with.

[00:13:16.310] - Speaker 2

I think that's a great transition. If you'd like to share with our listeners a little bit about the breakthrough work that you did, maybe as an early career academic medicine faculty member in genomics and cancer research.

[00:13:29.920] - Speaker 1

So I was fortunate, just as I was becoming a junior faculty at Harvard Medical School and the Dana Farber Cancer Institute, that there was just becoming available new powerful genomics technologies that had not yet been brought to bear on studying cancer. But even before that, as a postdoc, as a pediatric oncology fellow, I was starting to use some of the power of genetics and genomics that seem really old fashioned today, but at the time we're cutting edge. And found that if you bring together powerful technologies and the study of human patients, that's a really powerful combination. Because if you start with a disease that a patient has and work backwards to the mechanism, you know you're working on something important. There's a lot of value also in starting with on the biology side, just understand cell biology at its fundamental form and then ask the question, in what ways are these fundamental processes aberrant in disease like cancer? But it's super powerful to start with a patient and work backwards to the root causes, genetic causes of their disease. Where did that thinking come from? That was, in large measure, stimulated by people at U Chicago, in particular, Janet Rauley, where as a postdoc, one of the, I think, still most important discoveries that I was fortunate to be part of was the discovery of what's now while still the most common gene fusion event, chromosome translocation in childhood cancer, the fusion of two transcription factors that we did in collaboration with Janet Rauley.

[00:15:43.880] - Speaker 1

And That was, I think, important because it's now come to become standard of care for children with acute lymphoblastic leukemia pretty much around the world. So that's exciting. But maybe even more important to that, it taught me the lesson, Oh, we should figure out how to do this at real scale. So that project and that discovery, it was like a four-year thing to discover the basis of one child's leukemias. That was great. But if every genetic discovery takes you four years, it's going to be a long haul. But fortunately, Right at about that time, and this is now late '90s, mid to late '90s, new genomics technologies, DNA microarrays, specifically, were becoming available. And that technology suggested, Oh, maybe you don't have to measure just one RNA species at a time. Maybe you could do thousands at a time, and that would be a radical way to approach a problem. And so that thinking, bring technology. I wasn't a technology person. But I think I had enough

sense to see that technology and computational biology, not a computational person either, but the integration of technology, genomics technologies, computational science, and a deep understanding of cancer biology and cancer medicine.

[00:17:31.200] - Speaker 1

If you could bring those things together, that would be really powerful. And so starting in the late '90s, around 1997, I started bringing together some of my friends from the Dana Farber, and we would go over once a week to the MIT campus, to the Whitehead MIT Center for Genome Research, where there was lots of technology development and some computation going on, but they didn't know anything about cancer. We didn't know a whole lot about these technologies or computational biology, but we said there's going to be something interesting at that interface. Let's create a self-appointed group that would take this on in a multidisciplinary way. And that started with a couple of people, then a few more people, and it grew totally organically. We didn't ask anyone's permission to do it. We just started doing it. We started meeting together in a group meeting on Tuesday mornings. This then became the basis for, in part, of starting a new institute called the Brod Institute, which would come to be an institute jointly across Harvard, MIT, and the five Harvard teaching hospitals, that by design would be a connector between those institutions where there was opportunity for collaboration and between disciplines that were really needed to come together, not just like Noah's Ark, I'll get one, two of every kind and something magical will happen.

[00:19:19.460] - Speaker 1

But because it was clear that to solve the real problems facing biomedicine, in particular cancer research, it was going to require bringing people together across disciplines, across departments, across universities, because the cancer problem was too hard for any one individual to solve alone. And so this became the Brod Institute. And I'm proud that the cancer program, which continues to meet on Tuesday mornings, now over 25 years later, is an important part of the Brod Institute going forward.

[00:20:00.540] - Speaker 2

Wow. I'm just in awe. I think our listeners will hear that in my pause. Thank you for mentioning the sheer importance of interdisciplinary and multidisciplinary science and research, because like

you said, cancer doesn't stop at your institution's doors, and the research shouldn't either. So thank you for that.

[00:20:27.500] - Speaker 1

I would just add also there that I mean, interdisciplinary research is hard. I mean, it sounds obvious. Yeah, of course. Why wouldn't you want a computational person, someone from physics background, and an engineer, and a cancer biologist, and someone with expertise in cancer medicine to work together? Yeah, no one's going to say, Oh, no, that sounds horrible. But all those disciplines speak different languages of sorts. They have different cultural norms. They have different concepts of what constitutes progress. They have different... A software engineer thinks about how do you conceive of, launch, and execute a project that's very different than how a cancer biologist might approach it. And so even just the concept of let's plan a project together takes a lot of investment to in willingness to learn each other's languages. Otherwise, you can be in the same building and speak past each other for years. And so investing in how do you interact with people across disciplines. And I would add to that, increasingly at the Bird Institute, we're interacting across academia and industry. And there, there can be even a more profound cultural distinction and language barrier because the work is different and the expectations are different.

[00:22:08.700] - Speaker 1

And so I'm finding that it's really important to invest the time to figure out how do you really productively partner, for example, with scientists in a company that have a different pressures, personal pressures, than people working in the academic world. We have our pressures as well. If we don't mutually invest in understanding what our worlds are and what the currency is of our worlds, which are different in academia, where the currency is largely publications, and the currency of what progress in a company looks like, then again, we'll just talk past each other and not have a long term partnership. But if you can get that to work, it can be a real thing of beauty, because then you're bringing together complementary capabilities and expertise far beyond what either one could do on their own. And that's exciting to see that happen.

[00:23:08.450] - Speaker 2

Yeah. Thank you for bringing that into the conversation that if it's meaningful fruit fruitful, thought out, and people have the desire to speak similar languages or add to a new language together can create this beautiful tapestry, right? If not, it's yarn all over the floor.

[00:23:29.040] - Speaker 1

And part of that, That's correct. But some disciplines approach a problem not by saying, let's think through the whole thing in advance. They might say, Well, let's just get going and try something, and we'll iterate along the way. I don't want to spend a week, a month, a year planning what to do, trying to get that planning perfect and then execute. I want to just get going, do something and we'll take it from there. And if it doesn't work or we're heading the wrong direction, we'll do a course correction midstream. Others would say, Well, that's crazy. That's work without a plan. And they're more comfortable saying, No, let's have 15 meetings to think about it and abstractly and plan. Because sometimes things don't go according to plan anyway. So why are you doing all this abstract thinking? Both approaches have their merits for different types of projects. And if you're really serious about having a multidisciplinary team, you have to be open to those differences in perspectives. Otherwise, it's not going to work.

[00:24:44.810] - Speaker 2

Absolutely. I want to move on to the next question. But before I do that, I also want to mention that the University of Chicago Medicine Comprehensive Cancer Center, one of our previous directors was Dr. Michelle LeBeau, and she was a trainee of Dr. Raleigh. So very deep connections across that pedigree that are in our cancer center. So thank you for bringing that in.

[00:25:11.570] - Speaker 1

Well, Michelle is wonderful, too, and I've had many interactions with her as well.

[00:25:16.740] - Speaker 2

This is just a little preview. Don't know if I'm going to cut this or not, but look forward to a podcast this year with Dr. Lebeau. So I'm looking forward to it. I have not had the pleasure of meeting her yet, but I've heard nothing but wonderful things.

[00:25:31.630] - Speaker 1

Well, I look forward to that as well.

[00:25:33.170] - Speaker 2

Thank you. So you've talked a little bit about where you are now, but what do you do? What do you do there? What does your research look like now?

[00:25:45.940] - Speaker 1

Well, at the moment, I'm doing two things. I'm still running my own lab, which I think is an important part of being an institutional leader to try to stay current with what's happening, and in my case, focusing primarily on cancer research. So there, I'm blessed with having some amazing team members in the lab that are doing exciting work. And I have the pleasure of serving as the Institute Director at the Broad, and that consumes a lot of my time and energy. And I see my role there as not telling people what to do, but trying to make the broad more than the sum of its parts. And that means encouraging people to collaborate with each other, finding opportunities for interactions between different brodies, as we like to call ourselves, and helping to see where there are opportunities for new scientific advancements that might not be obvious when everyone's got their head down, focusing on their thing. And then, of course, helping to find the resources, the financial resources, to help scientists be successful in their work and to help oversee an administration whose job it should be to make scientists successful. And that culture of we're all here to support the scientists is a culture that I think is very important.

[00:27:21.750] - Speaker 1

Sometimes in academic organizations, it can feel the other way around that scientists are given certain rules that they... Of course, you need rules, but we try to have a culture at the broad where we try to get to the answer of yes when a scientist wants to do something non-standard, unprecedented, and try to make it possible for them to do that. So I think my role is largely to get out of the way and to reduce the amount of friction that scientists come up across in pursuing their ideas and encourage them to think boldly.

[00:28:10.820] - Speaker 2

Beautiful. Yeah, that's it. No notes. Being at the head of this wonderful institution, the Brode Institute, what is one of your successes that has happened over the past year that you're really proud of, whether it was something you did directly or you got out of the way for.

[00:28:43.450] - Speaker 1

I think a really important victory, I'll call it, is that we made it through the pandemic even stronger than we went in, I would say. Because particularly for an institute that brings its strength from people coming together across the Boston biomechanical ecosystem. The pandemic sent everyone home and into their corners. And so we got out of the practice of coming together. And that's such an important part of not just the physical act of being together, but the spiritual part of coming together, that I was worried that if we didn't recover that spirit, we'd have a big problem. So I'm really proud of the fact that Brodeys didn't forget that coming together as a community was a really important part of the work that we do because now people are energized and really poised to take the institute to the next level.

[00:29:56.940] - Speaker 2

That's awesome. And I think that goes to our last question of, where do you hope to see cancer research, care, discoveries, and advancements go in the next 50 years?

[00:30:07.350] - Speaker 1

Well, that's a really big question.

[00:30:08.850] - Speaker 2

I know.

[00:30:09.850] - Speaker 1

I would answer that by saying that I don't think there will be a single direction or discovery. But I will say that we've tended to think about patient care as one thing, and then there's a separate thing, which is research. And we're not learning enough from the patient care experience. And so what I'd like to see for the decades ahead is that, of course, we increase the pace of making discoveries and new treatments for patients. But I think that one way that that's going to happen is by figuring out how to turn our health care system into more of a learning system. When we treat patients and follow them, that's an amazing data set, that particularly with new machine learning methods and new molecular biology methods that are increasingly powerful, we could be learning so much more from patients than we are now. And so I think that's got to be a big push for cancer research in the years ahead, that we more effectively learn from patients to make

discoveries, and we more effectively translate those discoveries boundaries back to patients in the context of clinical trials and so on. Of course, that's always been the objective, but now I think we have new tools and can design better clinical trials based on molecular characterization of patient groups, which will mean smaller trials executed more quickly.

[00:31:50.940] - Speaker 1

I think that iterative cycle of learn, do a clinical experiment, learn some more, use that to inform the next generation of drug discovery grounded in cancer biology, I think that's going to really accelerate dramatically.

[00:32:08.230] - Speaker 2

Well, I look forward to your leadership in that effort and the Brode Institute's involvement in the next 50 years of cancer research, patient care, cancer biology, biomedical workforce, et cetera. There are so many words I could say, right? So that's all our time today. I want to thank you so much for joining us and sharing your story and how U Chicago was an important part of that with our listeners. So thank you.

[00:32:37.680] - Speaker 1

Well, thank you for having me. And it's exciting to have done this podcast because it was a good reminder to me of how formative U Chicago was, really, in setting me on this course that I feel really privileged to be on. So thank you.