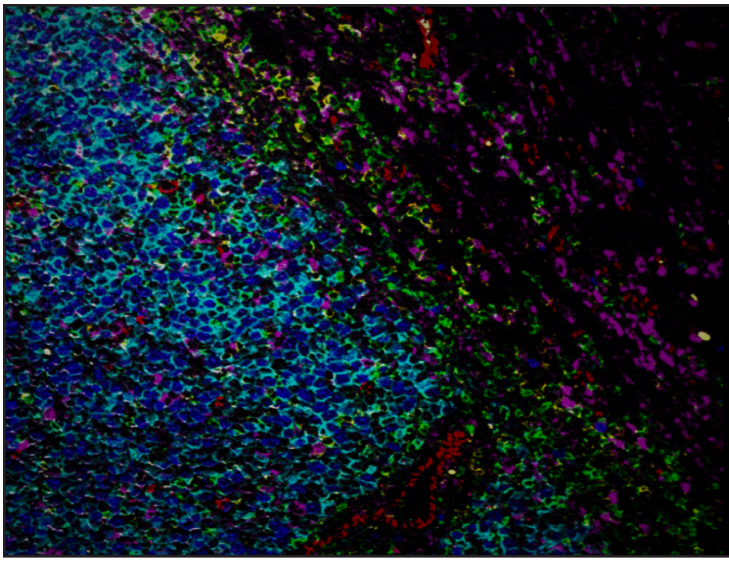

IONPATH

Visualization Drives Analysis Drives the Cure

By Josh Wolff

I approached an unmarked building. Darkened windows obstructed any further observation. When I entered the clandestine edifice, I wasn't sure what to expect. The walls were empty. The area was spacious. There was plenty of room to grow.

On the coffee table adjacent to where I was seated, there were copies of the three most recent issues of Nature. "Modelling in 3D: Advances in Organoid Models for Cancer Research" was emblazoned on the front cover of Nature Reviews: Cancer. As in most cases, one is left to imagine, to read, about what this technology might look like, how it came about in the first place, and what it might mean for the field and the world. In this instance, however, all I had to do was turn around. Behind me were devices at the cutting-edge of spatial analysis. IONpath's imaging device enables breakthrough measurements and analysis of tumor microenvironments. In doing so, it aims to advance the entire field of immuno-oncology.

Harris Fienberg approached me energetically, hand outstretched.

"Coffee OK? Always very caffeinated here."

What follows is a memoir of sorts, interview-style, which details Dr. Fienberg's journey from an undergraduate to a co-founder of a multi-million-dollar company that promises to change the way we understand and analyze cancerous tissue.

I began as you would expect:

***Q:** "After completing your undergraduate degree, what did you do?"*

"After I completed my undergrad, I spent most of a year cycling around South America. Then, I ended up in Switzerland for a couple of years. I did a Fulbright fellowship where I studied evolutionary biology. Then, I worked at a drug company called Actelion where I worked on making new antibiotics. That experience at Actelion taught me that I knew nothing about industry or private companies. I was 23 or 24 – a student up until that time. It was really cool to work in that organization because I saw the way these folks were using science to advance these bigger goals. It was interesting because you come from this academic background where it's very, very individual focused. It's all about you, your project, your success. At the industrial scale, it's all about working as a team and

common goal. There the common goal was developing new antibiotics, which was something that I really believed in. And that gave me the desire to join private industry. I realized it wasn't such a bad or scary thing.

"Then I completed my Ph.D. at Stanford. I worked in a lab under Garry Nolan, who is a phenomenal professor. He has this reputation for bringing out all of these amazing companies from his lab. There's been maybe a dozen companies that have spun out of Gary Nolan's lab."

Q: *"Is that why you chose him?"*

"Yeah, by then, I knew that I had this desire to work in private industry, either in diagnostics or on a device or on a drug. That [working on something non-academic], for many academic institutions is verboten. I felt, at least, that it was something that was frowned upon. But at Stanford, that is not the case. It is very much a part of the DNA of the institution. I told Gary, when I got to his lab, that I was very interested in being part of a start-up or a company afterwards, and he exclaimed, 'That's great!' Garry was incredibly instrumental in setting me up with opportunities that allowed me to come into a place where, by the time I was in my postdoc, I already had a lot of experience working with companies. This gave me the background to do what I'm doing now."

Q*: "How else did he integrate you into industry?"*

"The research in his lab is very focused on new applications. When I got there, there was this new technology called CyTOF (cytometry by time of flight) that he was working on. At the time, it was brand new and he had the first one in the world outside of the lab of the founders. It allowed you to look at 35 different proteins simultaneously. It was a really fancy flow cytometer. It was amazing to see the energy around this new technology. When a fellow in his lab started working on this new imaging device, I grew super excited about what it was going to be and how it was going to work. That ended up starting me on my current journey."

Q: *"Do you remember the specific time when you realized that this was it?"*

One was Michael Angelo, a clinical fellow in Gary's lab at that point, who is an incredible guy. He earned his Ph.D. in electrical engineering, is a board-certified pathologist, and is a force of nature. When he started to use this thing and talk to me about it and tell me what it was doing it, it sounded so incredible. I had never used it before nor knew if it worked, but I trusted him. He and Sean Bendall, another guy he worked with, are now both professors at Stanford in the Department of Pathology. It is pretty unusual to go from your postdoc to a PI (Principal Investigator), but these guys are incredible. Sean pioneered the CyTOF approach and published the first papers for that technology in Science and Cell. I knew that Sean and Mike were excited about it, and then – and now – I had an extraordinary amount of respect for those guys. They mentioned they were looking to start a company, and I said, 'Where do I sign up?' I turned down six-figure job offers, but I had a conversation with my wife, and we discussed what I really wanted to do, and she could tell how excited I was about the technology. She encouraged me to go and do it. 'What's the worst that could happen?' she asked. I became a postdoc in Mike's lab, which was basically a supply closet – then, he was a 'clinical fellow plus.' Sean had just started his lab – he had one postdoc. The team was great, and the technology was great. I wanted to be a part of it.

"Normally tech companies start in a garage. So, biotech companies start in a closet?"

"Ha, ha, yeah, this was a toxic waste supply closet, yeah. I'm not sure if we quite have that origin myth – these were two professors at Stanford. But there wasn't a lot of infrastructure to start."

Q: *"How were you able to do this kind of research at Stanford in this makeshift area?"*

"That's what I think is so cool about how Stanford's set up. It was technology development, so it was way too early to be a company. The way Stanford works with this stuff is that they encourage faculty to file for patents. Sean, who had a lot of foresight, filed a patent early and wrote 3 to 4 fundamental and very well thought-through patents at Stanford that have since been granted and give the company wide protection to continue to develop this technology un-impinged by competition. Stanford owned all the intellectual property, but they had a process whereby they could

license the IP from Stanford and form a company. Stanford still receives money from the success of the company, and they receive a percentage of the sales of the company. Stanford is financed through a few of these incredible arrangements, whether it's the Google algorithm or a few of the monoclonal antibodies. Stanford is basically helping to fund these very early technologies that can be spun out into companies. Then there is private investment that accelerates them and makes them into something useful. It is a very cool model and I know a lot of other universities have tried to replicate it but so far haven't had the success that Stanford has had."

***Q:** "Do you think that has to do with culture?"*

"I think that it's partially culture, and also the Office of Technology Licensing at Stanford is incredibly professional and thoughtful. They have a wonderful team for doing this work, and they balance the needs of the university and the needs of these private companies, which is not an easy thing to do. It's also being in this ecosystem that Stanford's developed where there's all of these kinds of methods to bring technology to fruition."

***Q:** "Ah, I see. So, when did you decide to move out of the closet?"*

"Well, we had to get funding. The team had professors, but none of us had any money. We're certainly not going to fund the company. I think we each put in a thousand bucks to start out to cover some legal fees, and Gary put in some more money. We pitched to venture capital, we explained our crazy idea – a type of mass spec (spectrometry) to do imaging, and we have this one paper. This is going to be a big deal. We found these very thoughtful early stage venture capitalists who were not on Sandhill Road. They worked for smaller firms but were willing to take a chance on the company. They brought a lot of expertise in building a company and have been extraordinary mentors to this day. These folks helped me and the rest of the company to get up to speed and transition to this stage as an organization and become a company with revenue."

***Q:** "I've heard before that there are two types of venture capitalists, the traditional life scientist and the tech-oriented Sandhill Road-type. How did you balance those two?"*

"Yeah, now there's been this new category that has emerged focused on tools and diagnostics. They are focused on this area and really understand the business. That's who we ended up partnering with."

***Q:** "OK, so as you're building this, your company is funded, and then what are your next steps? Was getting there easy?"*

"[Getting funded] was easier than I expected. We had this extraordinary technology – and still do – and the technology was not invented in a vacuum. It was invented to solve a problem we had in Gary's lab. This made for a clear pitch to the investors because we made the company to solve a widespread problem. We explained that we were bringing the technology to a place where it can address those problems. It wasn't easy, but it was perhaps more straightforward to raise money than other companies. We raised a few million dollars, which sounded like a lot of money at the time.

"We started to hire a team, and that's the place where we really lucked out. Our first few hires were incredible. Our first hire was a woman by the name of Rachel Fink, who was our Director of Bioinformatics. She had never worked at a start-up before, but she had been transformative for the company since day one. In addition to owning all the software in bioinformatics, she put in all the processes we used today. She is very process focused. Her joining the company was an amazing stroke of luck early on, as she put in place many processes that I would not have even thought of, and she's also an amazing bioinformatician. She has built this group under her that works on bioinformatics, software engineering, and the cloud software for analyzing data – it's a huge scope of work. I did not even appreciate how hard it was until we were working together for a couple of years."

"Right now, we do software, hardware, and all of the pathology. We were able to recruit the former medical director of the pathology group at UCSF, Jessica Finn. Jess is a powerhouse, and brought in several clinical-oriented processes, which has been incredibly useful as we work with pharmaceutical companies.

Q: *"There were several business models you could have chosen. You could have licensed out the instrumentation, you could have licensed the software for the instrumentation, you could have licensed the patent – it seems like you took the most ambitious approach by developing the whole platform. Why did you take that route?"*

"Our business model came naturally. We had this background as scientists, and we had this problem we were trying to solve. We realized we needed an instrument that can read these slides, but we also realized that the instrument was a sliver of the equation. You also need all of the reagents [for the instrument], and the reagents have to be well-validated. I spent 3 of the 5 years of my Ph.D. validating reagents. We realized that if we centralized the validation of reagents, which a lot of companies do not do, then it will become much easier to publish. Publications then end up driving adoption of the technology. It's a win-win for the customers and the company. Finally, you get these images from the device, but what do you do with them? How do you analyze that data? We decided we needed to also support our customers in this area too. If we were our customers, we thought, what would we need? We would need a reliable instrument that was great at producing data, reagents, and the software analysis. Without all three of those things, the system wouldn't function. It had less to do with ambition and more to do with being thoughtful regarding what we would need and want to be successful if we were the ones on the other side of this technology. We have both a service-based model and product-based model. Our third early hire was Jason Ptacek who ran research services and had a lot of background working with that.

"These were the first three hires in 2015. By 2016, we had 12 people, by 2020 we had 55."

Q: *"What has been the biggest growing pain or scaling issue that you have faced?"*

"There hasn't been a single one, because at every phase there are different challenges. The first one encountered was hiring. Unless you've been in the position of hiring many people, you do not realize how specific many of the skillsets you need, and how challenging it can be to bring in talented, self-motivated people who are willing to do the work needed. We have striven to create a workforce that is more broadly reflective of the world, which is another challenge we took on.

"One of the things I love about my job is that I have these incredible tutors and I get to be curious. I get to go someone's desk and make them explain something to me for an hour." Harris chuckled a bit. "That's such a cool thing about the job – every day, I get to learn about really cool stuff. We work on mechanical engineering, electrical engineering, firmware, software. We have incredibly patient employees who have been really generous with their time. They have taken me through what the electrical components of the instrument are, how they work together, what requires thought regarding this. It's really fun to have these people who are very well trained, very experienced, very thoughtful, who are basically teaching an idiot how everything works. I've done most peoples' jobs at this company pretty badly at one point or another. It's given me an appreciation for how difficult everyone's job is. I actually have not attempted software engineering – I know nothing about that one. I haven't worked on CAD models or wiring diagrams, but I have been involved in understanding what is going well and what isn't going well in engineering and helping to bring in new folks to solve these issues. This requires understanding the engineering issues at a pretty deep level. I've done the same thing in sales and marketing. The place where I do have background is on the applications and reagents side, so I've done all of that stuff to various degrees.

"The key to doing this job well is to be willing and excited to find someone who is much better than you at each task. Our scientists are better scientists than me, our sales and marketing people are way better sales and marketing people than me, our engineers are certainly way better engineers than I could ever be in a million years. That's what it means to build an organization. You find people who are more skilled, more thoughtful, brighter than you are, and you bring them in to make a great team. The alternate – to bring in people who are worse than you in everything – and that makes a very bad company."

Q: *"How was that transition from fundamental science research to the head of an organization?"*

"For me, it was a lot of fun. I have worked with great

scientists. Sean Bendall is a great scientist. Mike Angelo is a great scientist and great engineer. Working with these people made me realize that I was never a great scientist. I'm a good scientist, and I probably could have had a career in academia if I really wanted to, but I knew I would never be as good as those guys. It was great to transition to this other area because I love doing what I do. It's interesting, you get to learn about this great technology all day – you get to be this professional student. It was a natural, fun transition. It's probably harder for those who are great scientists or great engineers. Mark Andreessen once said that a great C.E.O. should be in the top 25% of several different areas. For me, this describes my skillsets very well. I'm better than average at sales, marketing, science – around four to five areas where I am pretty O.K. That made it natural to transition to this role and work to hire people under me."

Q: "Alright, last question. You're on your deathbed. You're reflecting, and you're very proud of this. Why is that?"

Harris paused for a moment. "I helped build a great company with people who really liked working there. If everyone who works here ended up starting their own organization, their own companies, using this as a springboard to be successful – I would love if that was my legacy. If I was on my deathbed and I looked at IONpath and realized, this was the best part of people's career and they used this as a springboard to do better things, that would be amazing."

"So, kind of, in a way, Stanford and what Stanford was like for you and your company."

"Yeah! Exactly!"

Josh Wolff is a staff writer at PROBE Magazine.