

Steve Lewis 00:10

Welcome to Speaking of Mol Bio, a podcast series about molecular biology and its trending applications in life sciences. I'm Steve Lewis, and today I'm excited to welcome Giovanna Prout to the show.

Giovanna is the president and CEO at Scale Biosciences, a single-cell omics company with a suite of fascinating analytical tools and patented technologies. It was a joy to learn from Giovanna about the great work happening at Scale and her vision for the future of the genomics field. Thanks for joining us today, and I hope you enjoy the conversation.

Giovanna Prout 00:49

As the CEO of a small company, for only 50 people, you get to do and wear many hats. That could be from working with the development teams and our product development process. It can be emptying the dishwasher in our kitchen or talking to investors or bankers or analysts or working with the marketing team. So, it's actually a really fun role, because you get to do all sorts of different things and really focus on you know, what's the most important activities for that day, for that week, for that month and year, to help drive the business.

Steve Lewis 01:28

It's always great to speak with CEOs, because it really gives insight as to how varied your day-to-day can be. And it's wonderful to hear too, that you're, you know, really a part of the team, even going so far as to empty dishwasher.

Giovanna Prout 01:43

Of course.

Steve Lewis 01:44

That's great.

Giovanna Prout 01:45

That's the servant leadership right there.

Steve Lewis 01:47

I like it. Now, quantum barcoding, tell me about that.

Giovanna Prout 01:52

Sure. We are a single cell company, and in single-cell omics, you're really trying to barcode cells so you can read out the molecular information from that cell at a unique cell level. And with quantum barcoding, this is our unique technique to have a very large barcode space for single-cell omics, which means we can process lots of different samples and lots of different cells at one time. And it's a combination of serially indexing cells. So you build up an index, so then every cell has a unique index, but also incorporating microwell plates and beads to really expand that barcode space. And so we have a barcode space that's order of magnitudes larger than anyone on the market. And so we felt like

quantum was a really great word to use to define that capability, and it pays homage to some of the IP that we use to create that product, which is quantum barcoding, as it's described in the patents.

Steve Lewis 03:08

I have to say, of many of the companies I've spoken to that sounds the most science fiction come to life in terms of the name of it. So, we'll dig deeper into that as we get into the science part of our session. But who are you? How does somebody come to this space?

Giovanna Prout 03:27

First and foremost, I am a wife and a mom. I am empowered and I'm inspired by my family to do what I do to work so hard. And like many of us, you know, we've been impacted by disease, whether it's been in our families, our friends and so life science tools, that market, is near and dear to my heart. I feel like all of the time that I spend, you know, at the company, traveling is for good, and it showcases to my family, and especially my kids, you know I have three kids that, you know, there's, there's a benefit to working hard, and you can be passionate about your work. So that's really kind of what grounds me in everything that I do. But I started, I guess, in school in bioengineering. And bioengineering was a very specific major for me, because I liked kind of all things science. I liked, you know, core mechanical engineering, but I liked biology, and I liked chemistry, and I think that just feeds into, like, the personality of a CEO, where you like to do lots of different things. And I went to school at UCSD, and my first job in school was at the Salk Institute, and this was at the time of the Human Genome Project. And I was so inspired by genetics and genomics and the Human Genome Project, even in my dorm, I had like the Human Genome Project poster on my dorm wall. And being at the Salk, they were really, you know, at the forefront of using tools, you know, to do their, do their research. I just so happened to be in San Diego, and Illumina was a company that, you know, was starting to really bud in San Diego. And right out of school, I started at Illumina, and this was at a time where, you know, they were just making oligos, and their bead arrays were just, you know, starting to be on the market. And I can't think of another industry that I would be a part of, like life science tools is just like so ingrained in everything that I've done, and right from the start, too.

Steve Lewis 06:08

And then now entrepreneur. Tell me about that?

Giovanna Prout 06:11

I guess the entrepreneur spark started for me when I got my MBA and I went to UCSD Rady to get my MBA. They had a program called lab-to-market. You put together a business model, and you got to develop ideas, and you pitched the ideas. And the idea that I had was a wearable device for fertility tracking. And people really started to get interested in it. And I thought, well, I could, like, start a company around this. And so I started, you know, a very small, tiny company to develop this technology called OvaPal. That's where I really got a lot of experience. And I think that, you know, even though it was a short experience with OvaPal, like, really helped set me up for success in in this role.

Steve Lewis 07:09

Going from OvaPal and you're now at Scale, how did that transpire?

Giovanna Prout 07:15

Yeah, so I was at Illumina for 12 years, and I was running the library prep portfolio at Illumina. So this was all of the upfront preparation to get libraries on the next gen sequencer. And so it was DNA libraries, you know, either in a PCR-free or low input way. It was, you know, total RNA or mRNA. So we had a pretty large portfolio that I managed with my team. And there was a product called Nextera, which is a tagmentation based workflow for library prep. So it uses a transposase or Tn5. And this product started to be used for single-cell. So there was WaferGen, Fluidigm, the C1, that put one cell and one well and was using Nextera to create the libraries after a cDNA conversion. And I started to get really interested and like, what is this single-cell application like? This seems like revolutionary to actually look at like the unit of biology, instead of just mashing everything up together in a bulk way. And Illumina had decided to partner with Bio-Rad at the time for single-cell and 10x was really starting to make some noise on the single-cell side as well. So I actually called up who I knew at 10x and I was like, I want to work for you guys. So they interviewed me, and, like, two weeks later, I was working for 10x as a product manager. That just helped foster, really, my passion around, you know, both life science tools, but specifically in single-cell. I had a very small stint after 10x after being there almost five years at a more of a startup company, pre-commercial company called Deepcell. You know, all of that really helped set me up for this role at Scale.

Steve Lewis 09:22

Now, you mentioned patents earlier in the conversation. Tell me about the core technology?

Giovanna Prout 09:29

So, the core technology at Scale Biosciences is a combinatorial indexing approach, but also leverages quantum barcoding. And the core technology is really, how do you barcode cells in a highly parallelized way, and with enough barcode space that you can process many samples and many cells at a given time? Recently, at AGBT, which is a big genomics conference, technology conference we announced a new core technology called Quantum Scale RNA. And we have a number of products. We actually launched five products that go down to 85,000 cells and 24, or 1 to 24 to 2,000 samples that you can run and anywhere in between, all the way up to a workflow that can process 4 million cells. Two plates of, you know, pipetting and, you know, pooling and redistributing to get to 4 million cells. And you can get up to almost 10,000 samples as a part of that workflow, too, if that's how you want to design your experiment. So really the like ultimate flexibility technology platform that we put out that we can then build different applications on top of. So we have a protein or cell surface protein application. We have an mRNA application, and we can build from there. I did talk in that presentation about FFPE capability, which is, you know, super exciting, because there's so many bank samples out there, and you really want to reduce down, you know, batch effects in your experiments. So if you can write it all within one experiment with one lot of reagents, that's super important. And I also talked about CRISPR applications, so being able to read a guide RNA out with the RNA as well. So a really nice, you know, platform technology that we have, which is instrumentation-free, like very easily to automate on liquid handlers, that we can really build up our portfolio. And when you're a small company in this type of market, you can't just be like a one product company. You have to have lots of different applications in your portfolio.

Steve Lewis 11:55

You're really hitting on something with the platform-based approach really being kind of critical to diversifying even markets that you're in as well.

Giovanna Prout 12:05

Yeah, if you can build a core technology, you can think about those different applications. Maybe more suited for pharma and biotech, or more suited for academia, or think about the lens of areas of research, like oncology or neuroscience developmental biology, which really opens up your market potential when you can address all of these different things, versus just having, like a fit for purpose type of product.

Steve Lewis 12:35

If you can diversify, but really through the technology convergence of what you're building, it definitely opens a lot of opportunities as well. What are some of the tradeoffs that you encounter in your day-to-day role as a CEO, but also technology-wise, in the lab? I imagine one of your tradeoffs was, because you mentioned it earlier, whether or not to perhaps go with an instrument-based approach. What did you land on?

Giovanna Prout 13:09

Fundamentally, when we started Scale, it was all about instrumentation-free. It was about eliminating the activation energy and budget energy to buy a piece of capital equipment, so that was pretty core to the decision that we made in order to barcode cells. What we're not against is leveraging all the different types of liquid handlers that are out there in order to fully automate a workflow. And actually, when you have a specialized piece of equipment, whether it's, you know, generating droplets or vortexing, it's actually harder to integrate in a Hamilton, a Tecan, a Beckman, an SPT Labtech who we partner with, to do a full end-to-end workflow. And our vision of our portfolio was we want to foster these really large-scale experiments, and we want it to take the least amount of time and least amount of hands on time, and be fully automatable so people can think about our workflows and more of like an enterprise scale type of environment.

Steve Lewis 14:26

Orders of magnitude you mentioned?

Giovanna Prout 14:28

Yeah, yeah.

Steve Lewis 14:29

How do you envision enabling orders of magnitude more throughput benefiting your customers?

Giovanna Prout 14:39

I have to answer that question to investors all the time. There's a couple of areas that are really instigating large scale experiments. One of those is the emergence of AI being leveraged in cell

biology. And in order to build, you know, really good predictive foundation models, you need to have a lot of data, and it needs to be good data. And you need a lot of diversity in that data. So whether that is, you know, biological diversity or ancestral diversity, or you know, different drug diversity. That diversity really helps you build those foundation models so you can, you know, do this prediction on the back end. So it's been really cool to see how machine learning has started to really infiltrate the cell biology, cell omics world. So you know that that's one, one area and there's companies like, there's a small little company called Panacent, where they like, adjust all of the public data that's out there, and they can build these predictive models. And it can help you annotate the different cell types, that can actually help you, like identify cell types in less sequencing situations too. So now you're actually saving money because you're using these predictive models. So I'm really excited to see like that, that area help drive these large-scale experiments. Another area is in drug screening. When you think about drug screening, you know, pharma, biotech, have done a lot of, like, high content phenotyping, so they're just, like staining the cells, and they're looking at the phenotypic readouts, you know, with different drugs. And they can do this in like a crazy, ultra-high throughput way. But on the single-cell side, you know, they might only need 100 cells, 1,000 cells per condition, to know if something's happening biologically with that drug. And the current products on the market today kind of don't allow for that flexibility of number of samples and number of cells, really, except for our platform. And so drug screening, where they want to do everything, all in one shot, 10 million cells, like crazy, numbers of drugs, doses, time points, you know, can now do that all at once in one experiment and really reduce down those batch effects. You know, thankfully, with the market where it is today, pharma and biotech, you know, are less impacted, like by the NIH funding and things like that. So it's a really great customer set to have for these types of experiments. And then you pair that with AI too, and it's like, it's really cool. And then we're also seeing doing larger and larger patient cohorts. So a lot of the single cell analysis that has been done today has been on healthy tissue, and it has been done probably on a more narrow set of like diverse samples when it comes to age and gender and ancestry. And so to really understand and get to, like more precision medicine types of applications, you need to add in that diversity, and you need to add in disease as well. And this is another area where perturbations come in, is can you perturb the genome in every way? Like, can you have this huge combinatorial perturbation so you can actually, you know, create these cell models from, like, maxing out the perturbations? You need, like, hundreds, millions and billions of cells to do all of this. So it's not just one application area, it really is a lot of different application areas, and that's why you're seeing, you know, some of the single cell companies like start to talk about million cell products, because that really is where we need to go.

Steve Lewis 18:56

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Steve Lewis 19:56

For somebody who may be listening and maybe new to the space. Can you talk about some of the existing combinatorial index strategies, maybe, as it relates to split and pool steps, and then how Scale's technology is accelerating and increasing the scale?

Giovanna Prout 20:16

So, with Scale Bio, or Scale Biosciences, we always start with fixed cells or nuclei. And by fixing the cells, you can permeabilize barcodes into them, and you lock in the biology. And it allows you to, like easily batch samples and store them over time if you're collecting from like different locations. That's pretty fundamental to any plate-based method, whether it's combinatorial indexing or split pool or some other crazy home brew that someone's trying to do, is really that fixation step. And we've spent a lot of time on that fixation step to make sure it really like represents the true biology of those cells. So once you start with your fixed cells, those go into a 96-well plate, in our case, and there's one barcode in every well of that 96-well plate, so 96 different barcodes. And you not only permeabilize the barcode, but you also do reverse transcription at that step, so that you know you gives you there, takes your mRNA and converts it into your cDNA so you can count those mRNA molecules in those cells. And then you take those cells and you pool them together. And in our case, we've seen that using a funnel plastic, so you kind of like, flip the plate on a funnel and centrifuge is a really great way to get all of the cells out and eliminates some of the pipetting steps. So that's very unique to us. So then all your cells are mixed together and, you know, there's many cells that have the same barcode, because the groups of cells were all in those 96 wells. And then you redistribute them. And in our case, you redistribute them to another 96-well plate. They're 96 macro wells, and this is what we call the quantum barcode plate. In those macro wells are micro wells. Zero to many cells or nuclei will settle into those micro wells, and we apply a bead pool on top of each one of those wells. So one bead sits on one micro well, and the bead is lawned with oligos, and that is your second level of barcoding. And in our case, our bead pool is over 800,000 barcodes, whereas in a typical split pool workflow, you might just have 96 barcodes, or maybe 192 barcode. So those are orders and orders of magnitude more barcodes. And so that really is where we get our scalability, is because of the use of the bead pools as well. And we have a lot of expertise internally on making bead pools. And we are really good at, you know, getting beads in wells and out of wells and you know that that is fundamental to this workflow. And then from there, you prepare your library.

Steve Lewis 23:36

This entire process must cut down on hands on time?

Giovanna Prout 23:41

Yeah, absolutely. I have some, like, really good charts that we show customers. So this workflow is a day and a half. There is like an incubation step as a part of the workflow, which makes it a day and a half. Some of our FAS's, like, the hardcore ones are, like, we're going to get it done in a day. And they can do, like, a really long day, but not most people are like that.

Steve Lewis 24:04

Really find this conversation fascinating in that there's so much more to go, in a way. Do you want to talk a bit about the 100 million cell challenge?

Giovanna Prout 24:16

We truly have only scratched the surface of our understanding of you know, healthy biology, let alone disease biology. And when we were kind of thinking of ideas of getting QuantumScale out to the market as soon as possible, we really wanted to have researchers think big. Like, "What if cost wasn't an issue?" Like, "What would you do? How would you dream of experiments?" And I love pushing that ambition, you know, whether it's whether it's with customers, or, you know, internal to the organization. Then, you know, even my kids too, like I want, I want them to, to be ambitious. And we also thought, you know this, this shouldn't be Scale centric, like, this is a community, and we need multiple tools to work together to really get to these ambitious projects. And so I was at an investor conference in the summer, and, you know, I have connections with Ultima, because, you know, the degrees of freedom and life sciences, life science tools is, you know, maybe one like, we've all worked together, you know, over the last two decades. And so we sat down with Ultima. And we're like, "I have this crazy idea. Like, let's get people to say, you know, they want to do millions and millions, hundreds of millions of cell types of experiments. Let's do this together." And they're like, "We're in let's do it." And we, like, executed on this so quickly. This is probably like a career highlight project for me and we announced this, and we got so many submissions for projects that really had never been seen before. CZI took note of this, and we'd been talking to them, and they really wanted to participate and fund some amount of these projects, which was amazing, and that's what they did. And so we were able to announce that CZI was going to fund. So the researchers got to do this for free, basically, these projects. I was actually at the single-cell genomics conference, it was in Greece this year, and I got to announce it early to the audience, and it was like it was so fun to be on stage for that. And we had over 140 projects from around the world, almost a billion cells that were submitted that we got to choose from, and it was just such an example of like, where the market was going. And so we selected projects. There was 14 projects that we selected. They varied across, you know, refining cell atlases, large patient cohorts, big drug screens, and we're running them in the lab right now as a part of our services. So, it's been great to, like, talk to these customers and experiment with design with them, and, you know, actually get to run, run their projects and then deliver the data back.

Steve Lewis 27:40

That is so cool. And I have to imagine really inspiring too, because you're getting to read those applications and I love the thought exercise of just, if there were no constraints, what would we do?

Giovanna Prout 27:56

I like that philosophy because I think we just inherently put constraints on ourselves, you know, whether it's personally or professionally, and to be able to just like, step outside those constraints for a minute and say, like, "What could be done?" It's really exciting.

Steve Lewis 28:12

This has been a really fantastic conversation, and I greatly appreciate your time today. Across the conversation today, is there anything that we didn't touch on that you'd like to highlight for our listeners?

Giovanna Prout 28:26

Maybe one thing to highlight is the life science tools market is really getting a beating right now. And, you know, being a part of that market and a community as a part of that market, I think we just still need to, like, really charge ahead and really continue to innovate, and, you know, not let any of this slow us down, because that's, you know, bad for science, it's bad for discovery. And, you know, maybe it's me just, you know, proclaiming that we are dedicated to doing that and hope that others, like, follow along. And we've seen others follow along with that too, but we can't, like, give up when there's a hard market, because these are the times where, like, we really just have to, like, have our grit and get through it. And it's going to take the life science tools community together to do that.

Steve Lewis 29:20

Absolutely. And for maybe some of the newer or earlier scientists in their career, just feel confident that biotech is cyclical always.

Giovanna Prout 29:32

Yeah. Yeah. Definitely.

Steve Lewis 29:35

I love that call to action.

Giovanna Prout 29:35

Don't be scared of it. Yeah, for sure, it's the most awesome industry.

Steve Lewis 29:40

So the next kind of question that we always ask is, what have been the keys to your success?

Giovanna Prout 29:48

It's intertwined in a lot of things. I have not succeeded in a lot of ways in my career. Whether it's like not getting a job that I really wanted, or, you know, had, like, not a great boss that, like, really undermined me. What you know makes me, is just like my persistence and building of my maturity over time to say, "Let me learn from this, and let me just do the best job that I can do moving forward." That kind of dedication to that for me, I think, has really helped me. There's also a point in my career where I did really let go of what I am trying to achieve, and really, really focused on, like, what is my team trying to achieve, and what is my company trying to achieve? And that was a really hard transition for me, you know, just being, like, really ambitious early on in my career, where is all about me, but I definitely went, went through that, and it's so much more like rewarding on the other side of it, and there's so much more that you can achieve with that mindset. I think there's right time and right places sometimes too, and right background. You know, I had this kind of multidisciplinary background. You know, this opportunity just happened, you know, to be open, and it was in San Diego, and it just felt like very serendipitous. So sometimes it's just like, you get lucky, and if you have the background and the experience and the drive, you know, it can, it can all work out. So those are some of the components I think, that have, have gotten me to where I am. It's funny to like think of it as like, you know, what have

you done to like, become successful? Like, really, what is success? You know, I think I've done some really amazing projects and have impacted the industry. Whether that's successful or not, I don't know. It's not, not for me to decide.

Steve Lewis 32:13

I think your servant leader approach is very much on display in that answer. And I think it's wonderful to highlight how self-reflective and persistent dedicated you have been throughout your career. And I think for folks who may be also entrepreneurs or budding scientists in the space, it's really important to kind of hear about how over time, you don't necessarily know where you're headed in the moment, but you can find yourself, for example, as the CEO of an early-stage startup. Our final question is, for those scientists who are earlier in their careers, what advice would you give them?

Giovanna Prout 33:08

Work hard and smart. At least in this industry, you really need to be thinking about how you're making an impact to the company, to the project. And really, like, pour your heart into it. Like believe in it and work really hard at it. And maybe that's a generational thing. I feel like, you know, in my generation, when we were, you know, starting early in our careers, like I was working 14 hour days like we would, we would never leave work, and it was our life. And I don't know if that was right or wrong, but you just like so believed in what you were doing, and you wanted to make a difference, and, you know, be a good collaborator and a good team member, and learn and be curious, and, you know, push the status quo. All of that will help you just see the bigger picture and, you know, improve in your career. Don't just think that things are going to land on your lap, because that's, you know, not typically, how the world works. And, and I say this to you and I say this to you know, new scientists, you know, thinking about careers like, I say this to my kids all the time, whether it's about math homework or some other project, like, it's about working hard and working smart and really just believing in it.

Steve Lewis 34:38

That was Giovanna Prout, President and CEO of Scale Biosciences in San Diego, California. Speaking of Mol Bio is produced by Matt Ferris, Sarah Briganti, and Matthew Stock. Join us next time for more fascinating discussion about the wide world of molecular biology, until then, cheers and good science.