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The Bancroft Library

University of California
Berkeley, California

Joseph DeRisi

Joe DeRisi: From Sandler Fellow to UCSF Professor of Biochemistry

The Marion and Herbert Sandler Oral History Project

Interviews conducted by
Martin Meeker
in 2018

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It is recommended that this oral history be cited as follows:

Joseph DeRisi, “Joe DeRisi: From Sandler Fellow to UCSF Professor of Biochemistry,” Marion and Herbert Sandler Oral History Project, conducted by Martin Meeker in 2018, Oral History Center, The Bancroft Library, University of California, Berkeley, 2019.

Joseph DeRisi in his lab at UCSF

Photograph courtesy of UCSF

Joseph DeRisi is Professor of Biochemistry and Biophysics at the University of California San Francisco and co-president of the Chan-Zuckerberg Biohub. Professor DeRisi is a graduate of UC Santa Cruz and Stanford University. In this interview, DeRisi discusses his educational background, including his term as an early Sandler Fellow at UCSF. He provides an overview of some of the high-profile research conducted in his lab at UCSF, an account of meeting and getting to know Marion and Herb Sandler, and a discussion of the role of the Sandler Foundation in supporting scientific research.

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Project History: the Marion and Herb Sandler Oral History Project

Herb Sandler and Marion Osher Sandler formed one of the most remarkable partnerships in the histories of American business and philanthropy—and, if their friends and associates would have a say in things, in the living memory of marriage writ large. This oral history project documents the lives of Herb and Marion Sandler through their shared pursuits in raising a family, serving as co-CEOs for the savings and loan Golden West Financial, and establishing a remarkably influential philanthropy in the Sandler Foundation. This project consists of eighteen unique oral history interviews, at the center of which is a 24-hour life history interview with Herb Sandler.

Marion Osher Sandler was born October 17, 1930, in Biddeford, Maine, to Samuel and Leah Osher. She was the youngest of five children; all of her siblings were brothers and all went on to distinguished careers in medicine and business. She attended Wellesley as an undergraduate where she was elected into Phi Beta Kappa. Her first postgraduate job was as an assistant buyer with Bloomingdale's in Manhattan, but she left in pursuit of more lofty goals. She took a job on Wall Street, in the process becoming only the second woman on Wall Street to hold a non-clerical position. She started with Dominick & Dominick in its executive training program and then moved to Oppenheimer and Company where she worked as a highly respected analyst. While building an impressive career on Wall Street, she earned her MBA at New York University.

Herb Sandler was born on November 16, 1931 in New York City. He was the second of two children and remained very close to his brother, Leonard, throughout his life. He grew up in subsidized housing in Manhattan's Lower East Side neighborhood of Two Bridges. Both his father and brother were attorneys (and both were judges too), so after graduating from City College, he went for his law degree at Columbia. He practiced law both in private practice and for the Waterfront Commission of New York Harbor where he worked on organized crime cases. While still living with his parents at Knickerbocker Village, he engaged in community development work with the local settlement house network, Two Bridges Neighborhood Council. At Two Bridges he was exposed to the work of Episcopal Bishop Bill Wendt, who inspired his burgeoning commitment to social justice.

Given their long and successful careers in business, philanthropy, and marriage, Herb and Marion's story of how they met has taken on somewhat mythic proportions. Many people interviewed for this project tell the story. Even if the facts don't all align in these stories, one central feature is shared by all: Marion was a force of nature, self-confident, smart, and, in Herb's words, "sweet, without pretentions." Herb, however, always thought of himself as unremarkable, just one of the guys. So when he first met Marion, he wasn't prepared for this special woman to be actually interested in dating him. The courtship happened reasonably quickly despite some personal issues that needed to be addressed (which Herb discusses in his interview) and introducing one another to their respective families (but, as Herb notes, not to seek approval!).

Within a few years of marriage, Marion was bumping up against the glass ceiling on Wall Street, recognizing that she would not be making partner status any time soon. While working as an analyst, however, she learned that great opportunity for profit existed in the savings and loan sector, which was filled with bloat and inefficiency as well as lack of financial sophistication and incompetence among the executives. They decided to find an investment opportunity in California and, with the help of Marion's brothers (especially Barney), purchased a tiny two-branch thrift in Oakland, California: Golden West Savings and Loan.

Golden West—which later operated under the retail brand of World Savings—grew by leaps and bounds, in part through acquisition of many regional thrifts and in part through astute research leading to organic expansion into new geographic areas. The remarkable history of Golden West is revealed in great detail in many of the interviews in this project, but most particularly in the interviews with Herb Sandler, Steve Daetz, Russ Kettell, and Mike Roster, all of whom worked at the institution. The savings and loan was marked by key attributes during the forty-three years in which it was run by the Sandlers. Perhaps most important among these is the fact that over that period of time the company was profitable all but two years. This is even more remarkable when considering just how volatile banking was in that era, for there were liquidity crises, deregulation schemes, skyrocketing interest rates, financial recessions, housing recessions, and the savings and loan crisis of the 1980s, in which the entire sector was nearly obliterated through risky or foolish decisions made by Congress, regulators, and managements. Through all of this, however, Golden West delivered consistent returns to their investors. Indeed, the average annual growth in earnings per share over 40 years was 19 percent, a figure that made Golden West second only to Warren Buffett's Berkshire Hathaway, and the second best record in American corporate history.

Golden West is also remembered for making loans to communities that had been subject to racially and economically restrictive redlining practices. Thus, the Sandlers played a role in opening up the dream of home ownership to more Americans. In the offices too, Herb and Marion made a point of opening positions to women, such as branch manager and loan officer, previously held only by men. And, by the mid-1990s, Golden West began appointing more women and people of color to its board of directors, which already was presided over by Marion Sandler, one of the longest-serving female CEOs of a major company in American history. The Sandlers sold Golden West to Wachovia in 2006. The interviews tell the story of the sale, but at least one major reason for the decision was the fact that the Sandlers were spending a greater percentage of their time in philanthropic work.

One of the first real forays by the Sandlers into philanthropic work came in the wake of the passing of Herb's brother Leonard in 1988. Herb recalls his brother with great respect and fondness and the historical record shows him to be a just and principled attorney and jurist. Leonard was dedicated to human rights, so after his passing, the Sandlers created a fellowship in his honor at Human Rights Watch. After this, the Sandlers giving grew rapidly in their areas of greatest interest: human rights, civil rights, and medical research. They stepped up to become major donors to Human Rights Watch and, after the arrival of Anthony Romero in 2001, to the American Civil Liberties Union.

The Sandlers' sponsorship of medical research demonstrates their unique, creative, entrepreneurial, and sometimes controversial approach to philanthropic work. With the American Asthma Foundation, which they founded, the goal was to disrupt existing research patterns and to interest scientists beyond the narrow confines of pulmonology to investigate the disease and to produce new basic research about it. Check out the interview with Bill Seaman for more on this initiative. The Program for Breakthrough Biomedical Research at the University of California, San Francisco likewise seeks out highly-qualified researchers who are willing to engage in high-risk research projects. The interview with program director Keith Yamamoto highlights the impacts and the future promise of the research supported by the Sandlers. The Sandler Fellows program at UCSF selects recent graduate school graduates of unusual promise and provides them with a great deal of independence to pursue their own research agenda, rather than serve as assistants in established labs. Joe DeRisi was one of the first Sandler Fellows and, in his interview, he describes the remarkable work he has accomplished while at UCSF as a fellow and, now, as faculty member who heads his own esteemed lab.

The list of projects, programs, and agencies either supported or started by the Sandlers runs too long to list here, but at least two are worth mentioning for these endeavors have produced impacts wide and far: the Center for American Progress and ProPublica. The Center for American Progress had its origins in Herb Sandler's recognition that there was a need for a liberal policy think tank that could compete in the marketplace of ideas with groups such as the conservative Heritage Foundation and the American Enterprise Institute. The Sandlers researched existing groups and met with many well-connected and highly capable individuals until they forged a partnership with John Podesta, who had served as chief of staff under President Bill Clinton. The Center for American Progress has since grown by leaps and bounds and is now recognized for being just what it set out to be.

The same is also true with ProPublica. The Sandlers had noticed the decline of traditional print journalism in the wake of the internet and lamented what this meant for the state of investigative journalism, which typically requires a meaningful investment of time and money. After spending much time doing due diligence—another Sandler hallmark—and meeting with key players, including Paul Steiger of the Wall Street Journal, they took the leap and established a not-for-profit investigative journalism outfit, which they named ProPublica. ProPublica not only has won several Pulitzer Prizes, it has played a critical role in supporting our democratic institutions by holding leaders accountable to the public. Moreover, the Sandler Foundation is now a minority sponsor of the work of ProPublica, meaning that others have recognized the value of this organization and stepped forward to ensure its continued success. Herb Sandler's interview as well as several other interviews describe many of the other initiatives created and/or supported by the foundation, including: the Center for Responsible Lending, Oceana, Center on Budget and Policy Priorities, Learning Policy Institute, and more.

A few interviewees shared the idea that when it comes to Herb and Marion Sandler there are actually three people involved: Marion Sandler, Herb Sandler, and "Herb and Marion." The later creation is a kind of mind-meld between the two which was capable of expressing opinions, making decisions, and forging a united front in the ambitious projects that they accomplished. I think this makes great sense because I find it difficult to fathom that two individuals alone could do what they did. Because Marion Sandler passed away in 2012, I was not able to interview her, but I am confident in my belief that a very large part of her survives in Herb's love of "Herb and Marion," which he summons when it is time to make important decisions. And let us not forget that in the midst of all of this work they raised two accomplished children, each of whom make important contributions to the foundation and beyond. Moreover, the Sandlers have developed many meaningful friendships (see the interviews with Tom Laqueur and Ronnie Caplane), some of which have spanned the decades.

The eighteen interviews of the Herb and Marion Sandler oral history project, then, are several projects in one. It is a personal, life history of a remarkable woman and her mate and life partner; it is a substantive history of banking and of the fate of the savings and loan institution in the United States; and it is an examination of the current world of high-stakes philanthropy in our country at a time when the desire to do good has never been more needed and the importance of doing that job skillfully never more necessary.

Martin Meeker, Charles B. Faulhaber Director, Oral History Center, UC Berkeley

List of Interviews of the Marion and Herbert Sandler Oral History Project

Ronnie Caplane, “Ronnie Caplane: On Friendship with Marion and Herb.”

Steve Daetz, “Steve Daetz: Values and Leadership at Golden West Financial and the Sandler Foundation.”

Joseph DeRisi, “Joe DeRisi: From Sandler Fellow to UCSF Professor of Biochemistry.”

Stephen Hauser, “Stephen Hauser: Establishing the Sandler Neurosciences Center at UCSF.”

Russell Kettell, “Russ Kettell: A Career with Golden West Financial.”

Thomas Laqueur, “Tom Laqueur: On the Meaning of Friendship.”

Bernard Osher, “Barney Osher: On Marion Osher Sandler.”

John Podesta, “John Podesta: Building Infrastructure for Progressive Politics with the Center for American Progress.”

Anthony Romero, “Anthony Romero: Leadership of the American Civil Liberties Union in Times of Crisis.”

Michael Roster, “Michael Roster: Attorney and Golden West Financial General Counsel.”

Kenneth Roth, “Kenneth Roth: Human Rights Watch and Achieving Global Impact.”

Herbert Sandler, “Herbert Sandler: A Life with Marion Osher Sandler in Business and Philanthropy.”

James Sandler, “Jim Sandler: Commitment to the Environment in the Sandler Foundation.”

Susan Sandler, “Susan Sandler: The Sandler Family and Philanthropy.”

William Seaman, “Bill Seaman: The American Asthma Foundation.”

Paul Steiger, “Paul Steiger: Business Reporting and the Creation of ProPublica.”

Richard Tofel, “Richard Tofel: The Creation and Expansion of ProPublica.”

Keith Yamamoto, “Keith Yamamoto: The Sandler Foundation and the Program in Breakthrough Biomedical Research at UCSF.”

Interview 1: May 2, 2018

01-00:01:58
Meeker: This is Martin Meeker interviewing Joe DeRisi for the Herb and Marion Sandler Oral History Project. Today is Wednesday, the 2 of May, 2018. And we are here at Professor DeRisi's office at UCSF [University of California San Francisco]. Thank you very much for joining us today. We begin interviews the same for everyone. And that is, tell me your name and date and place of birth.

01-00:02:19
DeRisi: Sure. My name is Joseph DeRisi. I go by Joe. I'm a professor here in the department of biochemistry and biophysics at the University of California, San Francisco. And I'm also the co-president of the Chan Zuckerberg Biohub.

01-00:02:31
Meeker: Where were you born?

01-00:02:32
DeRisi: I was born in Los Angeles.

01-00:02:35
Meeker: In what year?

01-00:02:36
DeRisi: Nineteen sixty-nine.

01-00:02:37
Meeker: Nineteen sixty-nine. Tell me about your first interest in science as you recall when you were growing up.

01-00:02:46
DeRisi: I think my first interest in genetics and molecular biology and the kind of science that I do now really started forming when I was in junior high school to high school area. And, it was especially motivated by the AIDS [acquired immunodeficiency syndrome] epidemic. So, as a kid growing up during the early eighties, the AIDS epidemic was front and center on every newspaper and *TIME* magazine. And it was the talk of the town.

And, I was struck by the fact that, for a good period of time, nobody knew what caused it. And, that was kind of bizarre to me. How could we have all this technology and science and all these advances in genetic engineering and so on, and yet not know what the cause of a disease was? And so, this whole concept of a mystery infection has stuck with me ever since I was a kid.

Now, I've gone on to work on things that are similar in nature—that is, diseases of unknown etiology, and developing tools to make that process better and faster. If we had the technology that we have today and the methods today back then, at the height of the AIDS epidemic, I see no reason why it

wouldn't have taken less than twenty-four hours to figure out what this was instead of years.

01-00:04:04
Meeker: That's fascinating. So, tell me about your engagement with science and genetics as early as junior high school and high school. Were you taking classes? Did you feel the curriculum at your high school was giving you the education that you were hungry for?

01-00:04:20
DeRisi: Yeah. I was a public high school kid in Sacramento, in the Carmichael area of Sacramento. And, our classes were great. We did traditional fly crosses where one kind of fruit fly versus another with white eyes and red eyes and sort of do the Mendelian genetics of those experiments. And those experiments were a lot of fun and really illustrated in real ways genetics and how genetics works.

And so, I found those to be very stimulating and motivating. But, I don't think anything was as motivating as the headlines that were going around at the time of the AIDS epidemic and so on. There was no advanced genetic engineering training at the time at the high school level. And many high schools today don't even have that. But, I felt that the grounding I got in my public high school education was excellent and prepared me well for launching into a career in that area once I went into my undergraduate education.

01-00:05:21
Meeker: Were you asking these questions of your teachers in high school? There's this virus out there. No one seems to understand what it is or where it came from.

01-00:05:32
DeRisi: If I asked those questions, I don't remember their answers. And, if they did answer they probably weren't that satisfying because the tools and technologies were, compared to today, pretty crude and pretty simple. But I thought we had all the technology at the time. And so, I think it highlighted for me the first time that I realized that there was gaps in the knowledge of science, that it wasn't all known, that everything wasn't in the *Encyclopedia Britannica*. I guess today it's like Wikipedia. But at that time we actually went to the books. And that science wasn't complete. And so, I think that was my first awareness that there was something more to do.

01-00:06:13
Meeker: So you go to UC Santa Cruz for your undergrad education. I guess you would have started in 1987?

01-00:06:20
DeRisi: Nineteen eighty-eight.

01-00:06:20
Meeker: Nineteen eighty-eight? Okay. What drew you to Santa Cruz?

01-00:06:27
DeRisi: UC Santa Cruz is probably the most beautiful school in the whole UC system, without a doubt. It's got the redwoods. It's got the mountains. It's got the ocean. It's a small town. It's by the shore. It's just an amazing place. And I was also drawn to the science there. When I went around and did the college tours, interviewing with different professors that were there and hearing about their work, I was just really struck by all the cool stuff going on, in particular the people like Harry Noller, who was one of the master scientists working on the ribosome, and others. I thought this is a place that I could totally be.

And I also thought that Santa Cruz offered exceptional opportunities for undergraduates to do research in the lab, and that an average person coming to Santa Cruz would have a chance to get in the lab. And I felt some of the bigger schools with tens of thousands of students, it would be harder to get that kind of opportunity. So I thought Santa Cruz offered the whole package.

01-00:07:24
Meeker: Did you already have an agenda in mind by the time that you got to Santa Cruz?

01-00:07:26
DeRisi: Absolutely, yeah, absolutely. So I had two major interests—genetics, biochemistry, infectious disease—without a lot of opportunity to be able to do it, obviously. But, that idea was in my head. But I also loved computers. I'd been programming since I was in sixth grade. And, I've always had computers in my life. And there was no such thing at the time as bioinformatics. That major didn't exist. The discipline basically didn't exist in real words.

And, so I actually launched into a major in biochemistry and molecular biology. And alongside that, although I didn't finish a major in computer science, I took that whole, the majority of that curriculum, into upper-division courses. So, algorithms, computer science, linear algebra, discrete applied mathematics, all those things that the CS [computer science] majors took, I also took because I knew that this is going to be important. But there was no way I wasn't going to be blending computer science with biochemistry and what I do.

01-00:08:35
Meeker: How did what attracted you to Santa Cruz in the first place play out in terms of getting lab time, maybe having closer relationships with professors?

01-00:08:42
DeRisi: Yeah, it worked great. There were opportunities to join labs as undergraduates. And I took advantage of those opportunities. I was able to get into a lab pretty easily. And, it was a great experience. It really galvanized me for the future that was to become.

01-00:08:59
Meeker: So, the lab experience, was this something that you stuck with, the same lab, throughout your entire undergraduate period?

01-00:09:05
DeRisi: Yes. I worked for a number of different individuals in little stints. But I had one major lab that I worked for. And, when I wasn't working for the teaching lab under a guy named Mike Dalby or some other individuals, I worked for a professor named Larry Peck. He was originally from Harvard, and he came to Santa Cruz. He eventually went on to become a lawyer. So, he left science to do other things.

But while he was there, and when I was there, I was in his lab, and together with a bunch of other undergraduates. So, it was mostly undergraduates in the lab. It was one graduate student and, like, ten undergrads, which is very different than a place like UCSF.

And, it was a great learning experience because you got a lot of hands-on, personal attention from the professor. I learned a lot of techniques, a lot of rigor, how to keep a notebook, how to do meticulous experiments and repeat them. And that was actually where I was able to participate in writing a manuscript. My first scientific publication came out of my undergraduate career there. And it was a great learning experience all around to learn all aspects of doing science.

01-00:10:12
Meeker: What was the topic of that first paper?

01-00:10:14
DeRisi: It was on RNA polymerase III transcription in *Xenopus*. It's a pretty detailed, niche area.

01-00:10:24
Meeker: Okay. So, tell me about your decision to go to Stanford. Were there many different options for you, I would guess?

01-00:10:30
DeRisi: Sure. After graduating Santa Cruz I took a year to be a technician in the same lab. So, I was employed as a technician, so different than undergrad research. Now I was just employed as a technician in that same lab, in Larry Peck's lab, where I continued doing that research. And, at that time I applied to a bunch of different graduate schools all across the country. I toured around maybe seven or eight of them, I would say.

And, I was struck by the fact that I amazingly got into most of them. And, in fact, I hadn't thought about applying to some of the larger, more top-tier schools, including UCSF and Stanford and things like that, until Harry Noller, one of those professors that I had worked with there at Santa Cruz, said why

aren't you applying to those places? And so, I got some good advice. I applied to those places.

And, Stanford was a convenient choice because it kept me in the Bay Area. But also, while I was there doing interviews, I met this guy, Pat Brown, who's the lab I ultimately joined. And, one of the things that struck me when I was having conversations with the professor on interviews was just how freaking smart this guy was. I thought, this guy is sort of off the charts. And I want to go to the place where I'm surrounded by the smartest people I can find. And this guy is kind of off-scale. So how can I get in this guy's lab?

01-00:11:53
Meeker: What told you that he was so off-scale?

01-00:11:56
DeRisi: It's just a number of things. Just having conversations with him, he was describing a technique for mapping genetics between related individuals that might have inherited diseases that was completely different than anything I'd ever heard, and just so radically different. And he also worked on HIV, back to my original interest in infectious disease, as well as related viruses.

And he was the guy who had figured out fundamental mechanisms of how HIV integrates its DNA in the genome of the host, the enzymatic reaction that actually does this, this enzyme called integrase. He was one of the key people in the field that figured out the biochemistry of how that actually works. And inhibiting, of course, integrase, is now one of the preferred ways that people use anti-HIV drugs. So, his fundamental work led eventually to therapies that are actually in the field, even if he didn't develop those therapies himself.

And so, I thought I've got to go work for this guy. He's got it all. He's doing all this cool genetic stuff. He's got technology. He works on infectious disease. This is someone I've got to be around.

01-00:13:06
Meeker: Well, and he's pretty widely known now for his Impossible Foods.

01-00:13:10
DeRisi: Impossible Foods, yeah, exactly, and also open access publishing.

01-00:13:14
Meeker: Well, and so both of these have a social mission as well.

01-00:13:18
DeRisi: He always had a social mission. That was always pervasive in the kinds of things he did. And, he always infused his science with that social mission and a sort of unshakeable ideology that he knew what he wanted. He knew what was right. He took the high road. And it didn't matter if people didn't agree with him or looked down upon him. He was going to do the right thing.

01-00:13:44
Meeker: Do you recall some examples of—

01-00:13:46
DeRisi: Oh, many times, yeah, unlimited examples. For example, in the beginning, he did this whole open access publishing thing. And, I'm sure you're familiar with the open access publishing issues. But, the core issues is why should we as scientists give our science to be the private property of a publishing house in perpetuity even though the taxpayers paid for it? And you as a citizen, why should you ever face a paywall to get the science that you already paid for with your taxes? That doesn't make any sense. Why would we give the record of our scientific progress to a private corporation forever?

So, that fundamental problem doesn't make any sense, especially in the internet age where the physical act of printing ink on paper doesn't matter anymore. That's, I think, one of the core issues. And so, that rang true with me, too. I thought, well, that's really amazing. And I remember going with Pat Brown and Mike Eisen, one of the co-founders of *PLOS Biology*, to the, at the time, the preeminent electronic publishing house, which was based in Stanford, HighWire Press. And they published some of the original electronic journals and were pioneers in the field. We're going to talk to these people and tell them why we should make an open access journal. And HighWire Press would be the perfect place to do it. It's at Stanford. Everything's there.

And, at the end of the pitch, in this guy's office, who I don't remember who was running HighWire Press at the time. But whoever saw us at the time explained to us how we really should go back to the lab and not worry our pretty little heads about this, that the publishing houses control everything, and that the scientists don't control publishing, and that this wasn't our deal, and that if we try to do something open access, the publishing houses would just crush us. And they controlled our careers.

That was the explanation we got. I'm paraphrasing, obviously. But, we were so angry coming out of that meeting, and Pat in particular. And, on the way back to Beckman Center from this office across campus, I remember him saying, you know, we've just got to do it ourselves. We're going to start our own journal. We don't need them. We don't need this. And in the end we'll crush them. And he did.

01-00:16:16
Meeker: What did he start?

01-00:16:17
DeRisi: So, he started *PLOS Biology*, the family of journals that you see down there. And, the PLOS family of journals, including *PLOS Biology*, *PLOS Medicine*, *PLOS Tropical Diseases* and *PLOS ONE*, became the largest scientific publishing house on the planet in terms of biomedical research and open access publishing. And HighWire Press is a faint shell of their former shelves.

They've mostly imploded, as far as I can tell. And, open access publishing has taken over as the way to do science because it is the right thing to do.

01-00:16:53
Meeker: At what point in your education did you decide that, as a career, you wanted to be a scientist running a lab?

01-00:17:00
DeRisi: Well, back in junior high, working on—

01-00:17:03
Meeker: So, it was that early, huh?

01-00:17:03
DeRisi: Oh yeah, no question. No, I was set on being a genetic engineer of some sort. And, I didn't know all the right terms. But back then I called it genetic engineering. And some of it is. But, biochemistry and molecular biology and infectious disease, together with bioinformatics, that blend, I was going to do that. There was no question, junior high on. There were a lot of kids going to college not knowing what major they wanted to be or what they wanted to do, and they're going to explore. That was never me. There was always a laser beam that I was walking.

01-00:17:40
Meeker: So, as I understand it, the way that education goes for scientists is you get your PhD. And then you spend many years as a post-doc in someone else's lab, building your publication résumé before a faculty position might become available and you can establish your own lab. I believe the Sandler Fellowship is something that intervenes in that and creates a different path. Can you tell me about your application for this new fellowship program? Because I think you were probably the second or third person to get it.

01-00:18:13
DeRisi: Third.

01-00:18:16
Meeker: Yeah, can you walk me through that process?

01-00:18:18
DeRisi: So, first of all, you don't apply for the Sandler Fellowship. You can't apply for it. You have to be nominated by someone else, typically your research advisor. And, at that time, I was doing a collaboration with friends here at UCSF, in particular Professor Ira Herskowitz, who's also another famous professor from UCSF and one that I hope you have some oral history on. I don't know if you do.

01-00:18:46
Meeker: I don't know. [The Oral History Center did not conduct an oral history with Professor Herskowitz.]

01-00:18:47
DeRisi: It's a shame if you don't.

01-00:18:49
Meeker: Is he still active?

01-00:18:50
DeRisi: He died. I think he died in 2003 or 4—you'll have to check—of pancreatic cancer. So, in the late nineties, I was doing a collaboration between the Brown Lab and Ira Herskowitz on the process of sporulation in baker's yeast using this new technology, DNA microarrays, that I helped pioneer while I was in Pat's lab, which was an offshoot of many different things I was working on there.

01-00:19:20
Meeker: Can you define what the DNA microarray is?

01-00:19:21
DeRisi: Do you want me to go back and do that?

01-00:19:23
Meeker: Yeah. I'd like to know what that is.

[Side conversation deleted.]

01-00:19:56
DeRisi: So, I joined Pat Brown's lab at Stanford to work both on infectious disease, like HIV, or the rodent version, MLV, something similar. And, I was also working on a genetic mapping technique technology that Pat had invented called genomic mismatch scanning. And, the readout for this technology was going to be difficult. We needed to look at many different parts of the genome all at once to be able to read out the result of this genetic scanning technique that he had created.

And so, that was a missing part of the technology. Pat had recruited a mechanical engineer to help work on creating some sort of system that would put lots of pieces of DNA on a nylon membrane or a glass slide or something that then we could assay. At that time, people were doing dot blots, putting DNA in nylon membranes, and then hybridizing radioactive DNA to it to see which pieces stuck. And it was slow and time-consuming. And you could only kind of do one at a time. And we wanted some way that we could do multiple ones.

And so, I worked next in the same bay as this other guy, this mechanical engineer. And, he had some limited success putting some DNA on glass slides. And he immediately saw commercial potential for this and vanished overnight to go start a company and leaving the lab with sort of a half-finished prototype of something that would make little DNA spots on glass or nylon membranes. And, it didn't really work very well. And the techniques to make

the slides and the techniques to do the hybridization and all that stuff were pretty shaky at the time.

And so, Pat came and said, “I know this is tough, this guy’s left. But, could you pick up the pieces here, see what you can do?” He gave me a pep talk. I thought really all was lost. And so, I really got into it, actually and then started building these robots. So, I built a robot to make some arrays. And then I built another robot. And then I wrote the software. And then I developed the slides. And so I really started pushing that technology as the major focus of my thesis and got the technology working reasonably well enough that we were able to do a whole bunch of other kinds of experiments I hadn’t even anticipated.

And then a lot of collaboration started forming immediately, collaborations with the NIH on cancer, collaborations with others looking at yeast, and basically any organism you can think of. And, the other thing we did is, motivated by these ideas of open access, is I put directions on how to build the robots on the web. I said I’m not going to start a company. I’m going to put directions on how to do this open source-style. So I put the software out there. I put a guide that you could follow where you could just build one at home in your garage, and put that out there on a website.

And, that was great. I got a lot of attention for that. And also, people built these arrayers—we called them arrayers—all over the world. And, I was invited to come build some in other countries and things like this and help out. And then we taught a class at Cold Spring Harbor showing people how to build them. And so, that turned into a class that Jim Watson recruited us to do, actually, at Cold Spring Harbor. And so, that was a lot of fun. And we had great participation from all of our colleagues. People like Pat Brown and David Botstein and others all contributed to making this a big success.

And, it was at that time where we were doing basically genomics. And, UCSF at the time didn’t have much genomics. There wasn’t a lot going on in genomics here at UCSF. And, among the places I interviewed for either fellowship positions or post-doc jobs and so on, I was invited to come give a seminar by Ira Herskowitz, my collaborator here at UCSF, in the towers, in HSW-301.

And at that time they had this bizarre system where they had this acrylic yoke that you put around your neck that held a microphone in front of you. These lavalier microphones didn’t exist at the time. Or UCSF was too cheap to buy them. I don’t know which. But it was this bizarre, ancient contraption from, like, the sixties or something. And, he gave me this. It’s a giant acrylic plastic yoke you wear across your neck and shoulders. Weird, because the microphone it held was big.

And, he gave it to me in front of the audience. And he said don’t make any jokes about this thing because you can’t make a joke that no one’s already

told. Everybody's heard it all, okay? So, just put it on and get with it. And then, I didn't really understand it. I put it on. And I grabbed it. And I thought it was flexible. And I pulled it, and I snapped it in two. I broke it in two right in front of this packed audience. And everybody erupted in applause. I finally broke the yoke, and they never used it again. And I carried the microphone by hand. So I did the one thing that nobody else had done.

01-00:25:17
Meeker: I'm tempted to see this as a metaphor, too.

01-00:25:19
DeRisi: It was. And it was a way to, "I'm going to do things at UCSF that have never been done." So, it was after I gave that talk as a graduate student, giving the seminar which, by the way, not a lot of graduate students get invited to give that Tuesday biochemistry seminar. They're usually professors that get invited. And yet I was a graduate student giving this. So, I already knew that this was kind of a big deal and that I'd better do well.

And I guess I did well because after that Ira came down to the lab at Stanford. In fact, he's known for whistling as he walks. And, I was in Stanford. I was at Saturday. I was working in the lab. And I heard whistling down the hallway. And then in walks Ira Herskowitz on a Saturday at lab, no appointment, just shows up and said I want to tell you about this fellows program that we have and that Pat's nominated you for. And, here's what it is. It's an independent position. It's not a faculty position. But we give you a salary and some supply budget. And you'd be embedded in with a bunch of other labs. But you'd be your own thing. Does that appeal to you? You should come up and do this.

I thought, that is a great idea. So, I came up and met the people here at UCSF, people like Doug Hanahan and Alan Frankel and Peter Walter and others, John Watson, and many other people that influenced me here. And they all thought it would be a great idea. And then another special person I met when I came up to talk to people here about this fellows person was a guy named Don Ganem, who's now vice president of Novartis, infectious disease. And he's an infectious disease clinician. He was on the front lines of the HIV epidemic. He's one of the heroes of that story for his work on Kaposi sarcoma and so on.

And I met this guy. And I had the same reaction that when I first met Pat, too, like oh my God, this guy is so freaking smart. I have got to go to where the smartest people in the world are. And, so that led me to choose UCSF over the other options I was presented at the time. And it was the right decision. It was a great place to be. And I think it was soon after that that I was asked to give a little scientific presentation to the donors that backed the fellows program, who I'd never heard of, I didn't know anything about. And it turned out to be Herb and Marion Sandler.

01-00:27:41
Meeker: Tell me about that. What were your first impressions of them?

01-00:27:45
DeRisi: I had never given any scientific presentations to philanthropists or donors. I was never given that opportunity at Stanford. The graduate students never interacted with philanthropy or donors. That was a different world to me. So, I didn't even know what I was doing. And I was struck by the fact that there were these two individuals at the back of the room that were asking all the tough questions. Marion Sandler was knitting away at the back, as was her habit. And she would interrupt me constantly asking questions.

And I thought, I haven't been grilled this hard by almost anybody in science. And yet I'm getting grilled really hard by these two bankers, as far as I could tell. But their questions were insightful and on point. And it was really an interactive, really fun meeting but also stressful. I had a lot of anxiety about it because I felt like I was constantly being judged and put on the spot.

01-00:28:43
Meeker: What were you presenting?

01-00:28:44
DeRisi: I was presenting the work I was doing with Ira Herskowitz on our work on sporulation in yeast and how we're using this new technology, DNA microarrays, to obtain all this genome-wide data in a way that no one else could do at the time.

01-00:28:55
Meeker: Had you, at that point in time, really started to think about ways in which to communicate your research to a non-expert audience?

01-00:29:04
DeRisi: Not really. I don't think I was a very good speaker at the time and didn't really practice or know how to do that very well. So, I was just winging it.

01-00:29:17
Meeker: Yet these non-scientists, these bankers, as you said, were following along and asking incisive questions.

01-00:29:23
DeRisi: Absolutely, yeah. They asked great questions. I think I made a good impression because they didn't kick me out.

01-00:29:31
Meeker: Where was this?

01-00:29:32
DeRisi: This was at Parnassus in the chancellor's conference room.

01-00:29:35
Meeker: Okay. So, there were a handful of people in attendance?

01-00:29:38
DeRisi: Oh, there were the advisors there, and people. And I didn't know them. I didn't know who the chancellor's people were. I didn't know the chancellor. I didn't know the deans. I didn't know the chairs. And the whole hierarchy was a mystery to me. I was just invited to come, show up, now go away.

01-00:29:54
Meeker: So, after you go away and you come back to your lab that you've established, tell me about what you accomplished.

01-00:30:00
DeRisi: Well, I was just starting at the time, so I was just getting going. My laboratory was put next to Peter Walter's in the old HSW and HSE towers at Parnassus. And, those facilities weren't nearly as nice as what we have here at Mission Bay. But they were packed full of great people. And it was this tight packing and really close interaction that I think was excellent. It led to a lot of collaborations. I learned a lot from the labs around me.

But, I also learned a lot from the other professors that were there, like Don Ganem. We immediately started up a collaboration with Don to start looking at infectious disease, in particular two post-docs in his lab. Dave Wang is at Wash U now. And Laurent Coscoy is at Berkeley now. And, with those people we began looking at ways we could apply this genomic technology not just for studying baker's yeast and basic biology, which was fun, but also to more apply problems like infectious disease. Could we use this technology to diagnose infectious disease?

And, this spoke to my sort of like original motivation for getting into science. How do we use technology to go after diseases of unknown cause? Could we use the technology to discover not just what's known but something that's unknown? And, Herb and Marion played another role in this because it was at that time we thought, well, how could we get this technology going? We're going to need a grant. We don't have any preliminary data. What if we apply for one of these Sandler grants, these internal Sandler grants here at UCSF? There's a variety of different ones, the sort of Program in Breakthrough Biomedical Research, PBBR, as well as Sandler asthma grants, because they had a specific interest in asthma given that Marion suffered from asthma.

And so, Don and I, together with his post-docs, we wrote one of these short grants for asthma research, actually, to see if we could develop a DNA microarray that would be able to read out different respiratory infections. And we could then think about trying to figure out if people with asthma had their exacerbations caused by certain kinds of viruses. There's all kinds of different respiratory viruses. What if it's one kind of virus that's really doing all the damage here? And we wanted to sort of explore associations between different viral infections in asthma.

That was the original intent. But the real motivation of the grant was to build this thing, build this new kind of arrayer, again, a new arrayer, and build a chip that would have all the known viruses ever discovered on one chip. And this thing was called the virochip. And, we built that chip and started working on asthma with a pulmonologist here at UCSF like Homer Boushey and others. And our early experiments demonstrated to us that we could take samples from patients and we could tell what virus they had by putting it on this chip, not using any of the other conventional diagnostics, straight from the patient's sample without having to culture the virus, which is a big advance.

So, those early publications reflect that. And, Michael Bishop actually helped us communicate one of these key publications to PNAS. He was the communicating editor on that. And it was very soon after that, because this was around 2002, 2003, in about spring 2003 I remember sitting at the dining table looking at the newspaper, in the Chronicle, and it says there's a weird unknown respiratory infection in Hong Kong. Like, what is this thing? Unknown cause but caused severe respiratory distress. And we just made a chip to look at respiratory infections. So, that's it. How do we get in on this, because this is what our chip is for?

Through Don Ganem's connections and the fact that Julie Gerberding was the head of the CDC, who was formerly at UCSF, we were able to make the right connections and to get on those global emergency calls for what we now know what SARS. And on those global emergency calls with the CDC and others, there was no emergency operation center at the CDC at the time. It was these conference calls, basically. We said we have this new technology. If you can send us a sample from a patient or any kind of material that you have, we can put it on this chip. And maybe we could help you figure out what this thing is.

And so, eventually we were able to get a sample shipped to us. And that arrived on a Saturday, actually, which was difficult to get deliveries here. The Mission Bay campus had just been built, so there was only one building here, Genentech Hall. It was a giant construction site. There were no other buildings around. We flagged down the FedEx driver because he didn't know where the building was or anything. And we were able to get this basically unmarked white box that had SARS in it. But no one knew it was SARS. No one knew it was a virus. No one knew anything about it at the time.

01-00:35:15
Meeker: What was the sample?

01-00:35:17
DeRisi: It was pieces of lung tissue supernatant from cultures that had lung tissue in them, basically a variety of different pieces of material the CDC had imported in from Hong Kong. And, we put the sample on our virus chip together with Dave Wang and Anatoly Urisman and others and Don Ganem. We were all

there on Saturday. And we worked kind of all through the night, twenty-four hours. And, in the morning we scanned the result on the computer. And we had a positive hit. We had a hit on the chip. And it was a combination.

The hit indicated that the thing in the sample had to be some kind of mixtape of cow, bovine, bird and human coronavirus, but all coronavirus, but not just one kind. Not just human, not just bird, not just cow—it was a weird mix. And so, it just screamed this was something different. This is a novel coronavirus. And we subsequently got additional information that confirmed that.

We sent that information to the CDC. And at the same time they had electron micrographs that had pictures of something that looked like a coronavirus. So, coronavirus here. Our genetic data said coronavirus. And then there was a couple of other little pieces of information that all came in around the same weekend. And they all triangulated on novel coronavirus. That meant we had it.

And so, we assisted in the discovery of this novel coronavirus by providing this key piece of information. It wasn't us alone. There were others involved and other pieces of information that triangulated. But it was one of the most thrilling moments at the time.

01-00:37:03
Meeker: But also scary. I mean, discovering a wild novel coronavirus—

01-00:37:08
DeRisi: Yeah, but it's what we wanted to do. It's what we built the technology to do. And, when you build the technology like that, and you think that it might be applicable someday, you never know if it's ever going to be applicable. What if there's never an infection that needs this kind of technology? What if we built a hammer and there's never a nail? And it was miraculous that we got the Sandler grant. We built the technology just in time for the nail to show up. And then we were able to pound it back down. That was amazing. That was a lot of luck.

01-00:37:42
Meeker: The thing about the Sandler Fellowship, even before this grant, is I think the description is "sheltered independence," right, so that you're not necessarily a post-doc working on another research agenda. And that early on you do make this shift from spores to actually thinking about the real world and broader issues. If you had been in another person's lab, do you think that you would have been given the freedom to make that leap?

01-00:38:16
DeRisi: Well, I don't know. I don't think so. I think that you're always working for someone else's agenda on somebody else's grant. And that's the way post-docs generally work. I think kind of the unbridled freedom just to do whatever the hell I wanted was key here. Now, the danger is, a fellows program like

that, and others have said this, too, is they give you a lot of rope, a lot of slack, to do what you want. And you can easily hang yourself with that same rope. And so, having too much freedom can lead sometimes to option paralysis where you don't really know what to do. There's so many things to do you don't do anything. You don't end up getting anything done.

And so, finishing projects is really important and being able to follow through. Do you have an idea? You said you can do it? Are you going to follow through and do it? And, if you have a lot of freedom, I could do this today, or I could do that today. And maybe nothing ever gets done. And there's no product to show for it at the end of the day. And so, I think the fellows program is great for individuals that are able to follow through, see a goal and work towards that goal, not give up, not facing adversity, and resilience from failure, and just push through. And, it's not for everyone.

01-00:39:31
Meeker: I've also read that mentorship is an important component of this. And I would suspect that mentorship maybe helps those who have really great ideas stay on track and keep focused.

01-00:39:42
DeRisi: Yeah. And the post-doc is a great format for that. And you can have a really close relationship with mentors. I used my fellow position to have many mentors. So, instead of being a member of one lab, I had this whole department of different people in the biochemistry department to be my mentors as well as people outside the department like Don Ganem. And so, everyone from Liz Blackburn to Peter Walter to Ira Herskowitz to Doug Hanahan, all these individuals, Cynthia Kenyon, all participating as mentors and giving me advice. And I think that was incredibly valuable.

01-00:40:19
Meeker: Did you get to the point of meeting more one-on-one with Herb and Marion as their support for your research continued?

01-00:40:27
DeRisi: Well, I certainly remember having many of these scientific sessions where we have to present the results to our donors, in this case Herb and Marion. And so, I participated in many of those. And then occasionally I got invited to their apartment here in San Francisco. And, they held many dinners with their scientific advisors and/or distinguished scientists that they just found interesting or just people that were interesting at their apartment. And, I remember many of those dinners and lunches being really fun and interesting.

They of course had a rule that you can only have one conversation at the table. And so, that led to highly structured discussions. They weren't just social events. And there were a lot of memorable dinners and lunches there with meeting distinguished scientists that I probably wouldn't have met otherwise, people like Eric Kandel and other luminaries, Phil Sharp, many, many famous

people in the field, but also people involved in policy. I had lunch there, and the guest was Jerry Brown. I had lunch with the governor. That was fun.

01-00:41:36
Meeker: Did you have an opportunity to talk about policy?

01-00:41:40
DeRisi: He did most of the talking.

01-00:41:43
Meeker: Not surprising.

01-00:41:43
DeRisi: Which is what he usually does. And, we had another lunch with a judge, Thelton Henderson. And he took over health care in the prison system. And that was a big decision, sort of a real policy thing. But, it's way out of my league but really interesting. And so, dinners and lunches like that, fascinating. And so, I felt privileged to be able to be invited to these occasionally.

01-00:42:16
Meeker: Were they asking you to kind of push the social dimensions of your scientific research?

01-00:42:22
DeRisi: They didn't ask me to do that. I was kind of already doing that. I think they helped applaud it. Now, they also played a big role in the open access thing. So, we got this going. Pat Brown started *PLOS Biology* together with Harold Varmus and Mike Eisen. And, my spouse, my wife, Suzanne, was actually I think employee number three at PLOS [Public Library of Science]. And she was in scientific publishing and electronic communication and websites and all that and had a degree in information science.

And so, they hired her to start producing the website for *PLOS Biology* and help run production for the journal. And, I don't recall the exact year. But sometime shortly after 2003, maybe 2004 or so, the business model for *PLOS Biology* was having trouble. And they had initial grants from, I think, the Gordon and Betty Moore Foundation and others to get PLOS going. But those monies were running out. And, it wasn't clear what the business model was going to be and how an open access journal would make it without some sort of revenue stream and advertising and all that stuff.

And, Pat's a visionary, but he's not a business person. Or at least he wasn't then. He is now. And, I was here on a Saturday in lab. And my wife was working on her laptop in my office while I did some lab stuff. And, Herb and Marion happened to come by on Saturday, unannounced, just visited me in the lab. They're lucky I was here, working. I often worked weekends. And I still do. And, they'd never met my wife, Suzanne.

And I introduced her. And then they said, well, what do you work on? And she said I work on this thing called *PLOS Biology*. It's this open access journal. What's open access publishing? She described what open access publishing was and what the economic issues were and what the sort of really moral and ethical issues are in terms of open access publishing. And, they asked a lot of insightful questions. They gave her a hard grilling on the spot. And then, after that, they actually met Pat Brown and Harold Varmus and those guys and got more into it and ended up becoming the primary financial backers of the open access publishing motion.

And they installed their own financial officers at PLOS to be able to engage with real financial discipline at the institution and led to the generation of the business model that actually became super-successful and made PLOS what it is today. So, a chance meeting with Herb and Marion in my office on a Saturday in lab was likely a key turning point in the open access publishing business.

[Side conversation deleted.]

01-00:45:32

DeRisi: And it was really interesting because, at the time, in 2003, before the inaugural issue of PLOS, we were working on malaria, another infectious disease with a large social component, because the poorest people in the world are the ones that suffer malaria. And there are not many large pharmaceutical efforts towards that disease because the people who die aren't the ones carrying credit cards, frankly.

We had done a massive study using DNA microarrays, once again, to figure out how the parasite grows within the red blood cell, what its genetic program is really running when it's inside a human and inside a red blood cell. And, that was a milestone piece of work for us. It was a major paper. And it actually was invited by *Science*. And so, *Science* magazine said we really want this. Tell us when it's ready.

And when it was ready, we sent it to *Science*. And they sat on it for a long, long time, actually. And, I should back up. They initially said, hey, we really like this. And, I said yeah, here's the catch, though. I want you guys to publish this open access. It's about third world health. It's really important. I think you guys should publish this open access and free for everyone. I don't want anybody to hit a paywall when they have to get this article.

And then they sat on that for a long time. A long time we didn't hear anything until ultimately we said, hey, what's up? What's going on? We need to move on. And I got a letter from the editor of Science at the time that basically said we're never going to do this. Open access is a dead issue. The scientists really don't control science. The publishers do. It was the same thing we heard at

HighWire Press echoed again, but this time from the head of the major journal.

And it was a very discouraging article. It was condescending in every way. And, the message in between the lines was, don't worry your pretty little heads about this. Toe the line and shut up. We weren't going to have that. And so, what we discovered through the grapevine of editors is that they were recruiting a competing article that they would publish knowing they would reject ours because we wanted it open access. And they were sitting on it so they could get this other article through.

01-00:48:02
Meeker: Did you see that one in print eventually?

01-00:48:04
DeRisi: Yeah. So, at that point we said this is terrible. We are going to put this in the first issue of *PLOS Biology*, volume one, issue one, number one. And we're going to get this out. And then it became a race to get the journal out because they were trying to race their article out. They came out within a week of each other, basically. And, ours is the one that's cited now, not that one.

01-00:48:27
Meeker: Well, that's what I was going to ask.

01-00:48:28
DeRisi: It's clear which one was more dominant in the end. And so, that came out right here in issue one, number one, volume one of *PLOS Biology*.

01-00:48:37
Meeker: And that's October 2000?

01-00:48:40
DeRisi: This is October 2003, volume one, issue one. This is a collector's item because they only made some print articles as a demonstration to convince people that this was a journal, because at the time the idea that you were only going to publish electronically or something was pretty foreign. You had to have something in print. This is the DNA microarray work on the malaria parasite.

01-00:49:05
Meeker: Is PLOS entirely online now? No print edition?

01-00:49:08
DeRisi: Yeah, there's no print.

01-00:49:09
Meeker: When did you give up the print edition?

01-00:49:11
DeRisi: I don't know when they gave up the print edition. They print limited versions here and there. But, it's not a sustainable model to print paper that people are just going to recycle.

01-00:49:23
Meeker: Two thousand three, that's just a couple of years into your time here, a pretty compressed research schedule.

01-00:49:31
DeRisi: Yep. Two thousand three was a good year for us.

01-00:49:39
Meeker: Well, I think that we don't have a whole lot of time left. And I don't want to keep you.

01-00:49:42
DeRisi: Yeah, what other points do you want to hit? Yeah, we are a little bit over time. Let's keep going, whatever final questions you have. We're on a roll here.

01-00:49:51
Meeker: Okay. I do want to ask a final question. Well, a couple of final questions. But first of all, can you tell me about the continuing relationship with the Sandler Foundation? Have they continued to support your lab here?

01-00:50:04
DeRisi: Absolutely. From time to time we have been recipients of PBBR [Program for Breakthrough Biomedical Research] funds or other things or have collaborated with labs that have PBBR grants. And, I've continued to participate in lunches and dinners with the Sandlers. And, I've also been on the committee for the fellows program. And so, Alan Frankel is the chair of that committee. And, he's done a great job of it. And I've been a strong proponent of the fellows program.

And also, in our discussions with the NIH, we impressed upon them how successful our program was. And it was a conversation I had at the time with Francis Collins and his team leading the NIH that they should do something like this. And they ended up doing it out of the NIH director's office. It was called the Early Independence Award. And it's modeled after the Sandler fellows program here. And it's since become this very, very successful program at the NIH.

So, there's been a lot of downstream impacts from that program and from my interaction with the Sandlers. And to this day we continue to work with the Sandlers on a variety of different things, including rolling out these infectious disease diagnostic systems, no longer a virochip anymore. It's taken on different forms. But rolling it out for clinical utility and making this actually something that's not just at the research bench but like a doctor can order.

01-00:51:30
Meeker: Is this part of the next-gen precision diagnostics program?

01-00:51:33
DeRisi: It is. So, all the things that we discussed before, using DNA microarrays to diagnose infections in SARS [severe acute respiratory syndrome], that's all at the research level. The next question is, well, if you're a patient, and you're sick, and if your doctor wants to order this test, how does that happen? Because, unless they know me and call my phone and we have a steady setup, that's not going to happen. You really just want to be able to put an order in and get the test result back.

And so, DNA microarrays were the way to do it back then. But around 2008, the sort of really quantum leaps in technology in DNA sequencing began to overtake what we were doing in arrays. So, we rapidly adapted and switched our technologies in about 2008-2009 to use what's called next-gen sequencing. And that involved actually a lot of bioinformatics because the sequencing just produces random bits of DNA and RNA sequence. You have to be able to put those together in a giant puzzle to understand what's in there and all the technologies associated with preparing samples and so on.

So, we've been working on that for some time now and have used it to discover a number of new viruses and show that we can diagnose patients. But then, the Sandlers helped fund the real push, which was let's not just go out and try to raise venture capital and start up a company. That would be kind of the traditional Silicon Valley way to do it. But instead, can we just do this at UCSF? Why don't we just do it here? Can't we just run the test here and run it like a nonprofit? We are a nonprofit. Let's just run it here. And that way it'll be open. It'll be transparent. It'll be no black boxes.

The headlines were rife with bad things happening in the diagnostic fields like Theranos and other companies that went down in flames. We didn't want to be that. We wanted to be completely above board, completely transparent, and do the best genomics we could. And so, a former post-doc in my lab, Charles Chiu, who worked on some of the Sandler-funded programs in my lab, and is a clinician in laboratory medicine here, took the charge of that together with Steve Miller.

And we got a grant from the Sandlers to be able to pioneer bot the development, further development of the technology, and launching it inside the clinic. And so, that test exists today for neurological infectious disease, for meningitis and encephalitis. And you can go on a website, and a doctor can order it. And so, I think it's a remarkable accomplishment. You didn't need a bunch of venture capitalists to start up a company and have it be in some black box down in Redwood City. You could do it right here in Mission Bay in the clinic. And now it's a test that any doctor can order.

01-00:54:16
Meeker: So, walk me through what the patient experience would be like with this.

01-00:54:20
DeRisi: Well, the patient experience is pretty transparent. Usually, if it's meningitis and encephalitis, you're pretty seriously ill. Your doctor would do a lumbar puncture to obtain traditional values from cerebrospinal fluid like how many white blood cells there are in there. And, if that indicated there might be some infectious process but they didn't know, they can send that CSF to UCSF, or if they're here already. And then that sample will be sequenced in much the same way that we've detailed in many of our research papers and so on.

And through a lot of bioinformatics one can weed out the human sequence from the foreign sequence and figure out if they have an infection or not. And then, if that comes back with a real infection, depending on what it is, it can be very actionable. There might be a particular antibiotic if it's a bacteria. There might be a particular antimicrobial if it's a fungal species. If it's a viral species there might be a drug for it. There might not be. But then you'd make the right decisions with supportive care.

And so, it potentially can lead to lower cost and better health outcomes together at the same time. So, I think this is an example of how we take bench science and translate it into something that has actual impact on people in real time. The SARS bug was really amazing and was super-exciting. It was probably the most fun thing I've ever done in lab. But there's also a great satisfaction from getting a result on a clinical patient sample. And occasionally you get an email or something from a patient or a visit that says, hey, I'm glad you sequenced me. I might not be here if you hadn't done that.

And so, you can write all the grants you want in the world and get all these reviews on your papers. And people say all these critical things. And all the criticism and negative stuff that comes from doing science is wiped away by a positive comment when you did this thing and you might have saved my life. Or you did save my life in some cases. That is pretty awesome.

01-00:56:26
Meeker: I appreciate the role that the Sandlers have played in funding your work here. But, I suspect a lot of public money has gone into this as well.

01-00:56:34
DeRisi: Sure. We had a variety of NIH grants. All the malaria work was funded on NIH grants. And actually the result of those NIH grants has resulted in a therapeutic that's now entering Phase II clinical trials that we had a major role in called SJ733. I'm hoping it'll make it to market one day. And so, public money funded a lot of that. And we've had grants from a variety of other foundations, public sources, you name it.

01-00:57:01
Meeker: Are there particular issues or stages of research that you're more likely to go to a Sandler foundation that you think they're going to be more interested in funding?

01-00:57:11
DeRisi: I really want to do science that interests me and excites me and where our technology can have a play. And so, I'm not that picky about where the money comes from as long as it isn't dirty money or something like that. But, an example is, you probably remember some number of years ago there was a lot of headlines about bee colony collapse disorder. Honeybees were dying across the United States.

And, when that was happening, in walked through my door at Genentech Hall a representative of the California Almond Growers Association. She had a bunch of free almond cans with her. And she said, you know, bees are really important to almonds. And, something like 85 percent of the world's almonds are grown in the central valley of California. And we need the bees. We're interested in bee health. We think this might be an infectious process. You have a technology to look at infectious disease. Would you please apply for a grant to the California Almond Growers Association to work on bee colony collapse, because isn't it the same thing? Sure, why not?

So, we got a grant from the California Almond Growers Association, which was great. And, we worked on it. And it was a really fascinating project. And we were able to describe several new viruses, a bunch of new infectious agents, including a microsporidium called *Nosema ceranae* that was probably was one of the major reasons bee colony collapse was happening. But it was clear it had to be something multi-factorial. One thing didn't explain everything.

01-00:58:43
Meeker: What are you really excited about right now?

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DeRisi: Well, we are working on a variety of different projects. We just submitted a paper on sharks. And, as you probably read headlines from last thing, there was a big shark die-off in the San Francisco Bay. So, we've been able to illuminate that and figure out what the cause of that was. It turns out it was a parasite. And, so that's really fun. But we're also working on things like Ebola and Zika virus. We continue our work on malaria.

We have exciting new projects in the area of autoimmunity because a lot of things that look like infectious disease aren't and then are instead autoimmune diseases. And sometimes those can be confused with each other. And so, we need ways of ruling out infection and ruling in autoimmunity to be able to treat people effectively. So even though I got into this to work on infectious disease, I can't ignore the fact that there's a problem. And the problem is

autoimmune disease that looks like infection. And so, we have to work on that.

So, we have a bunch of exciting projects in that area. And we work on a lot of other different odd diseases that other people either don't know about or ignore or are just not on their radar.

01-00:59:59
Meeker: Or, as you said, these diseases in animals. There was the boa constrictor research.

01-01:00:02
DeRisi: Absolutely, yeah. We will work on any infectious disease, basically, because even diseases in veterinary animals or domestic pets or livestock or wild animals, you never know where the next zoonosis will come from. And all the recent viruses that we worry about—SARS, MERS, HIV—most all these come from an animal source first, a non-human animal source. And so, we have to pay attention to what's going on.

So, in that same regard, we have to be worried about what the mosquitoes are carrying. So, we have large mosquito surveillance projects up and running now. So, these are all really fun things. And we brought a lot of that to bear on the projects that we're doing now. And I'm doing a lot of this in collaboration with the Chan Zuckerberg Biohub, a new nonprofit institution that is here in Mission Bay that joins Stanford, UCSF and Berkeley all together as one collaborative project.

And, I would have to say, my role as co-president of the Chan Zuckerberg Biohub probably never would have happened had the Sandlers not funded our research and been involved in what we do. And so, I think the involvement, for example, of Mark and Priscilla in science here in the Bay Area is indirectly a result of Sandlers' participation.

01-01:01:34
Meeker: And the Biohub also, I think, includes the social dimension of the scientific work that you're doing.

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DeRisi: Yeah. The Biohub is a proponent of open access publishing and pre-print publishing now, so-called bio-archive publishing. And, it has a lot of the same social agenda. We're working on infectious disease. We're working on basic science. And we're trying to raise the bar in the Bay Area as a whole. And the gemstone of the Biohub program is our investigator program, which is not exactly like, but somewhat similar, to the fellows program in that we give people discretionary money to do their most bold and innovative work outside the confines of the traditional NIH granting system with a lot of technology support and collaboration.

01-01:02:25
Meeker: Well, I think that we can probably end there. I know that you've got a busy schedule.

01-01:02:28
DeRisi: Yeah, we caught a lot of stuff. That was good.

[End of Interview]