A Conversation with Leonard and Leonore Herzenberg

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Abstract

Leonard and Leonore Herzenberg have left an indelible mark on the fields of immunology and cell biology, both in research and clinical aspects. They are perhaps best known for developing the technologies of fluorescence flow cytometry and hybridomas. Over six decades, they made a number of important and fundamental discoveries in lymphocyte biology by applying these technologies. During this era, they immersed themselves in the sociopolitical environment, interjecting scientific rationale into public discourse about McCarthyism, nuclear fallout, war, genetics, and other politically charged topics. Their unique philosophy has shaped their lives, their science, and ultimately the scientific community. In this Conversation, we explore some of these driving forces and the impact on the laboratory.

INTRODUCTION BY MARIO ROEDERER

Drs. Leonard (Len) and Leonore (Lee) Herzenberg have been supervising a highly productive laboratory in the Department of Genetics at Stanford University for more than 50 years. Len is a member of the National Academy of Sciences and is the recipient of multiple distinguished awards, including the Novartis Immunology Prize (2004) and the Kyoto Prize (2006).

Len and Lee's scientific accomplishments span a diverse range of fields, including genetics, immunology, and biotechnology; these tremendous accomplishments and scientific advances have been reviewed elsewhere (1–4; see also **http://en.wikipedia.org/wiki/Leonard_Herzenberg**). Given the existing literature, I focus this Conversation less on specific scientific contributions and more on the personal lives of Len and Lee and how the political and social environments of the times influenced their research programs and colored their scientific lives.

Nonetheless, the contribution of the Herzenberg laboratory to science should not be understated. The Herzenbergs are perhaps best known for bringing fluorescence-based flow cytometry to the fields of immunology and cell biology. This technology has become irreplaceable in most immunology laboratories. A testament to its power and endurance is that it has not fundamentally changed in the past 40 years; it has simply advanced in terms of speed and capabilities.

The Herzenbergs are also responsible for bringing hybridoma technology from Milstein's laboratory in Cambridge, United Kingdom, to the United States. They recognized its incredible potential for transforming basic and clinical research, assays, and therapeutics; they urged early commercialization and distribution of useful hybridomas. Their laboratory isolated many of the original monoclonal antibodies against human and murine leukocyte subsets, paving the way for decades of research in immunology. Together with Columbia University, Stanford was awarded the patent on chimeric antibodies now used as immunotherapeutics. This patent has become the highest-earning patent in Stanford's history, eclipsing the Google patent.

Len and Lee have a remarkable scientific pedigree. Their early mentors, at Caltech and the Pasteur Institute, comprise a veritable "Who's Who" of Nobel Laureates. Similarly, their trainees include a large group of accomplished and internationally recognized professionals. Certainly, Len and Lee have left an indelible mark on the field, both scientifically and personally, through their technological creations, scientific discoveries, and mentoring of productive scientists and clinicians.

Throughout their career, the Herzenbergs have espoused a philosophy that the science they do belongs to society and to the US government, which has paid for it. They have always been generous in sharing reagents, results, and technology—sometimes to the discomfiture of postdoctoral fellows who had not yet published it! But this philosophy was unequivocally productive, leading to many collaborations and more rapid advances.

I was extremely fortunate to have spent a decade in their laboratory. During that time, I was exposed to all aspects of their program: from basic immunology to clinical research, from technology development to application, from collaborating with investigators around the world on research to working with companies on technology. I was struck by their steadfast commitment to science for the good of humanity, the loyalty to their trainees (past and present), and their drive for discovery.

These commitments pervade their life, both in the laboratory and at home. Indeed, Len and Lee have never divorced work from home or science from politics. They lead by example—not just educating in the lab, but educating the public, becoming politically active, and trying to bring positive changes to society by basing discourse on their knowledge of science. It is my hope that this Conversation reveals some of the driving forces behind Len and Lee's science and illustrates some unique aspects of the program they created.

A CONVERSATION WITH LEONARD AND LEONORE HERZENBERG

Mario Roederer: Hello. My name is Mario Roederer. I'm a senior investigator at the Vaccine Research Center at the National Institutes of Health. I'm here this afternoon to speak with Professors Leonard and Leonore Herzenberg, who are at the Department of Genetics at Stanford University, where they've run a successful genetics and immunology laboratory for 50 years. I did my postdoctoral training with Len and Lee, and I'm pleased and honored to be here to have a conversation with them about the making of their science, not so much the science itself. Len, Lee?

Leonard Herzenberg: It's going to be very interesting. Mario was in this lab for 10 or 12 years, something like that, before he went to the Vaccine Research Center.

Mario Roederer: It was a very productive time in my life. There are a number of unique aspects of your laboratory that I thought would be very interesting for people to hear about. One of them, obviously, is that you're a husband-and-wife team and have been for a very long time. I wonder if you would tell us about how that came about, the evolution of Lee's role in the laboratory, and how you interact in running the laboratory.

Leonard Herzenberg: Lee and I met when I was a senior at Brooklyn College, and Lee was recommended by a friend of mine to be tutored because she had a case of poison ivy and she was falling behind a little bit in her math or analytic geometry, or calculus. We decided she could come over to my house, which was within walking distance of Brooklyn College, and there we studied. We also played around and eventually we fell in love, and many more things came about, including our getting married, having children, and so on.

Mario Roederer: It was an immunological reaction that brought you together originally.

Leonard Herzenberg: Well, intellectual immunology.

Leonore Herzenberg: It was more like analytic geometry.

Mario Roederer: Lee, you followed Len when Len went to Caltech for graduate work.

Leonard Herzenberg: I did graduate work after Brooklyn College. I went on a National Science Foundation fellowship to Caltech.

Leonore Herzenberg: He had one of the first National Science Foundation fellowships. They were very exciting at that time. They started the whole support that followed after that for biology. It was great.

Leonard Herzenberg: Before I actually went to Caltech, there was a summer in between, and that summer I belonged to an organization that we called the Society of Biology and Medicine. It gave a scholarship to the Marine Biology Laboratory at Woods Hole; however, I didn't have to use that. I used the NSF fellowship to pay for that, and this good friend who introduced us took the Society of Biology and Medicine scholarship, so he was also covered. So neither of us had to pay for the summer at Woods Hole.

Mario Roederer: Lee, you didn't start working with Len directly for many years, right?

Leonore Herzenberg: I worked with him at Woods Hole. Whenever I could get into the laboratory—he was in the laboratory full time, from the time he got up in the morning until the time he went to sleep at night, and I just hung out. You don't just hang out; you start learning about it. You start working on it. You hold the pipettes, you mix the solutions, and eventually you just basically do it. It started back in Woods Hole. When we got to Caltech, I tried—he went a year ahead of me, and then it was too lonely and too expensive to be on the other side of the country, so I followed him. The succeeding year we got married. I was all of 18. How I knew I wanted to get married, I don't know. But I knew that I was with the right person. My parents knew also. I think my parents had as much to do with making that marriage as I did myself.

When I followed him out there, I tried to continue school at Pomona, but Pomona was teaching how to become a lab technician for women, and Caltech had Jim Watson, Matt Meselson, and George Beadle. It was one of the most exciting places to be that you ever could be. After 6 months at Pomona, I decided I was spending money to alienate myself from the environment that I really wanted to be in. Now, at 18-and-a-half, we worked this out. We figured out that this wasn't the place to be. Looking back at it, how we ever did this I don't know.

Anyway, I'd come home from school and the first thing I'd do would be to come to the lab, and I'd be there from, say, 4:00 in the afternoon until midnight, when we went home. The next morning, I'd go out to school and then I'd come back and do my homework at the lab, but there were things to do. There were experiments to be had; there were lots of great seminars; there were colleagues. Everybody would come in and talk about science. The kind of science that we did in our lab comes from that environment, where everyone knew what everyone else was doing, and whenever somebody had a new finding they came in and shared it as soon as they could.

Leonard Herzenberg: I want to add something. When I went to Caltech as a new graduate student, I really wanted to do some lab work, and they assigned me to work in the laboratory that was part of Herschel Mitchell's laboratory. I became a sort of postdoctoral fellow of Mitchell.

Leonore Herzenberg: Predoctoral.

Leonard Herzenberg: Predoctoral. George Beadle was the chairman of the Department of Biology, and Linus Pauling was there. He was in the chemistry part of it, and I was in the biology part of it. There were very few students, very few postdocs, and my lab partner who was assigned to Mitchell's lab, who was at the other bench in the same lab, was a fellow who had worked in—it wasn't the Poison Control Centers at that point. What was it, Lee?

Leonore Herzenberg: Al was in the Navy. He had just come back.

Leonard Herzenberg: Al [Alfred G.] Knudson. He became very famous later on for doing many scientific things. He was my lab partner on the other side of the lab. George Beadle was his mentor as the chairman of the department. He was eight years older than we were.

Leonore Herzenberg: Al was.

Leonard Herzenberg: He had a couple of young kids at that point. We babysat these young kids for Al. I can't remember the name of his wife.

Leonore Herzenberg: Paula.

Leonard Herzenberg: Paula. Al and Paula. That's correct.

Leonore Herzenberg: They nurtured us a lot, and that was very helpful. We were just kids from New York. I had no idea what Caltech thought of me at that time. I would love to understand that. As I look back, if I could see me as I was in that environment, this was a very cute kid. I was tiny, not like I am now, but very tiny and just full of vivaciousness and jumping all over the place and really loving to go to the classes. They eventually invited me to just take classes there. They said that was okay. I said I would take classes there because that's what I wanted to learn. But they were only graduate classes, so I was a two-year undergraduate and I was taking graduate classes with Len's classmates. It didn't occur to me that maybe I shouldn't dare to do such a thing because they were intellectually far better trained than I was.

Mario Roederer: It was a fantastic place to be with all those future Nobel laureates. [There were] seven or eight Nobel laureates in that group.

Leonard Herzenberg: Correct.

Mario Roederer: One of the people you interacted with was Barbara McClintock, right?

Leonard Herzenberg: A little bit later on.

Mario Roederer: She was a woman in science, which at that time was fairly unusual at that position.

Leonore Herzenberg: Fairly is not the word. Very, very [unusual].

Leonard Herzenberg: Caltech didn't accept women either as undergraduates or graduate students at that point. Lee was a sort of—what were you called? You were auditing, basically.

Leonore Herzenberg: Yes.

Leonard Herzenberg: The professors said she could also go to the laboratories and she could also take the exams. They gave her letters from the exams saying that she had done extremely well.

Leonore Herzenberg: I got my grades. All A's, but one B.

Leonard Herzenberg: That turned out to be very useful later on when we went—after Paris at the Pasteur Institute, we came back to the NIH, where I was a two-year wonder. That kept me out of the Army, and I carried a pipette for my country. Lee and I found together that Bruce Ames, who had been at Caltech a year or so before me, had a place for a GS8 position. He hired her to be a technician, and then he promptly went off to St. Louis, where Arthur Kornberg and his whole team were.

Mario Roederer: This has been a long battle for both of you: to support Lee as a leader in science, as a scientist, because there was this tremendous bias against scientists and women, something that, to a certain extent, still exists. What was the battle like? Even when you came to Stanford, which was a fairly liberal institution even at that time, there were still hurdles that had to be overcome. Has it been a frustration? Has it led to open doors?

Leonore Herzenberg: It's a good question. Try to remember back; you have to remember into a different world. We were in France, remember, when we went from Caltech, where I was welcomed and I was allowed to take the classes even though the school didn't allow me to. I was treated like a student, and they had the same expectations for me, which was great. That they did this started me off in that direction. When we got to Paris, I was newly pregnant, still morning sick, and Len said, "You know, you can be the painter that you always wanted to be," because I loved to paint, and I like to write. I said, "I don't want to do that. I just want to come to the lab with you."

Jacques Monod said, "You're very welcome in the lab." It being France, there were women scientists in the lab at that time. It was not a shock for women to be in the lab. Mostly they were technicians, but the technicians were very well treated and participated a lot in things.

Leonard Herzenberg: Some of them were very good scientists, though.

Leonore Herzenberg: Madeline Brunnerie and some of the others. Monod did not say, "The men stay here and the women stay there." That happened at Cambridge later on. That's another story.

Leonard Herzenberg: It was important that Monod's mother—was it his mother?—was American.

Leonore Herzenberg: His mother was American. His wife was the head of, I think, the Asian Museum in Paris. She was the head of one of the major museums. He did not see women as second-class citizens. Monod did a lot with me. He would talk directly to me all the time about things. One day he said that you can't grow *E. coli*—you can't grow any organism—there's no organism that would grow on a thiogalactoside, and that just tweaked me. I went out and took some dirt and put it in a flask and put in thiogalactoside, which was what we had in the lab, and put it in the dark in the closet. Two weeks later I opened it up, and opened up the top: "Look at that. They're growing! Jacques, Jacques! Look!"

Leonard Herzenberg: "Smell, smell, smell!"

Leonore Herzenberg: Guess what I did? Before that time we never had sterilized any thiogalactoside solution—

Mario Roederer: Because nothing would grow on it.

Leonore Herzenberg: —nothing would grow on it after that. I did it—

Mario Roederer: Stunk up the lab.

Leonore Herzenberg: —stunk up the lab and made it so that we had to make all the solutions and autoclave them. But it was great.

So the baby was born there.

Leonard Herzenberg: The first baby.

Leonore Herzenberg: They didn't mind that we brought the baby in, and she sat in a carrycot up on top of Len's desk. I would come in midmorning with her and hang out until it was time to go home. It was a welcoming environment in France. We were both at the table at lunch. Lunch consisted of the 10 or so scientists in our group, Jacques Monod on our floor, Georges Cohen, François Gros—all of these people became heads of whatever in France. Upstairs were François Jacob and—

Leonard Herzenberg: Elie Wollman.

Leonore Herzenberg: —Elie Wollman and André Lwoff, who later became Nobel Prize winners. That was lunch. There were 12 of us, 10 or 12 of us, at lunch.

Leonard Herzenberg: We'd all go out to the nearest—

Leonore Herzenberg: We didn't. We ate in the cafeteria there. Remember, we had that table?

Leonard Herzenberg: No, there wasn't a cafeteria there. We brought in our food. Remember that?

Leonore Herzenberg: It wasn't a cafeteria. We had a lunch room. Remember, this was the Pasteur Institute, and Louis Pasteur's big wine vats were actually stored at the back of this glass-topped atrium because they had natural light; they had all glass-topped science buildings. Anyway, the group of us would sit at lunch, and half of lunch was science: whatever the latest finding is, whatever the latest theory was, debating. Ultimately right after, the year after we left, they got the Nobel Prize. But more than that, it was politics. That's the other side of life. That's where all of this began.

Leonard Herzenberg: World War II came just before that. This was only a few years after the end of World War II. It was 1952. World War II ended in 1945 in Europe, and Jacques Monod and several of these other people were in the Resistance during World War II.

Mario Roederer: Did those conversations spur you to become politically active? Because [during] your years here in the United States, you were very politically active.

Leonore Herzenberg: We were already. At Caltech, Matt Meselson, George Streisinger, and Linus Pauling were part of the group that we were part of, and we volunteered at Linus's house as kids. We lugged the cases of soda and set the tables and cleaned up afterwards when they had political parties and things like that. We formed a chapter of the Federation of American Scientists, and I was very active in that. I'd grown up in a neighborhood where politics was politics. I grew up in Brighton Beach before it became a Russian center. There was an immigration wave that changed things. But when I was in Brighton, it was very political. People walked down the street and talked to each other about some latest political thing, "Did you hear that so and so had done this?" Strongly democratic, Roosevelt supporting, some thread of the Communist Party through there, a lot of labor activists and union activists.

Mario Roederer: Then at Caltech, you directly experienced the McCarthy era, right?

Leonard Herzenberg: The McCarthy era began when I was still an undergraduate applying to become a graduate student, and I remember when—I was with my mother in the kitchen—where McCarthy was fought by Eisenhower for the Army. McCarthy was a senator, and he was terribly conservative, radically conservative. It really began there. Then I got this NSF fellowship, which allowed me to go to Caltech, and as I said, the NSF fellowship actually was given out at the point because of *Sputnik*. *Sputnik* was the satellite that the Russians had sent up.

Mario Roederer: At Caltech, though, there were problems. Didn't Linus Pauling have problems because of—?

Leonard Herzenberg: Yes, Linus Pauling's visa was not allowed by the state department because he was in favor of—this was a little bit later—he was in favor of blocking nuclear testing and nuclear bombs.

Leonore Herzenberg: Something was happening at the time; it started at that time. Martin Kamen's visa was blocked. Martin Kamen was another well-known biologist.

Leonard Herzenberg: He was a biochemist at San Diego at that point.

Mario Roederer: Even when you were here at Stanford, you saw the remnant effects of the McCarthyism because the UC system required all of the professors to sign a noncommunist—

Leonore Herzenberg: A loyalty oath.

Leonard Herzenberg: Many of the professors were at the University of California, Berkeley. They refused to sign the loyalty oath, and Stanford benefited from it enormously. The people who were going to Berkeley instead went to Stanford, like [Joshua] Lederberg, who was the chairman of the department.

Leonore Herzenberg: The whole physics department from Berkeley picked up and moved here en masse, as a department. It wasn't that people were disloyal. There was a feeling that the government doesn't have a right to ask you to sign when you are, as a citizen, already loyal. The argument was really the loyalty oath; it was not the issue of whether or not you were loyal. Pauling didn't want to sign this, and then McCarthy came in with his famous "Have you ever been a member of the Communist Party or any group affiliated with it?" You could never answer that question because you never knew whether they were going to unearth some group and say, "You said you never were." "I didn't know that the Daughters of the American Revolution were actually a Communist front organization!"

You couldn't know by what organizations said, anyway. It was a legal mantrap. But McCarthy's idea was basically a political one that he drove. George Beadle was forced to fire the stock department keeper, a man named Paul Orr. He was forced to fire him because Paul Orr had some affiliation with what would be known as an actual Communist group. He was not a member of it, but he had some affiliation with it. The whole story was of people hiring or firing you on the basis of what your past political activities were, not what you did in your job or what you were doing.

Mario Roederer: You continued to be politically active through the 1960s with the Vietnam War and beyond.

Leonard Herzenberg: Yes.

Leonore Herzenberg: When we came here, the first thing we did—there was an attempt by the government to prove to you that you could dig a fallout shelter in your backyard, put a roof over your head in case there was an atom bomb. You could crawl down into that and have enough supplies for a week, and then when you came out, you would be safe. We tried to explain to people that if there was fallout on the ground, it was going to be months and months and that you couldn't put yourself through this.

Leonard Herzenberg: This was the time of John F. Kennedy, before he was shot. He was in favor of building these fallout shelters.

Mario Roederer: Ironically, the measure of fallout underlies some of the technology that eventually became flow cytometry.

Leonard Herzenberg: Correct.

Mario Roederer: There's a big circle here, but we'll come back to that a little bit later.

Leonore Herzenberg: We have to come back to that. It's a good story.

Mario Roederer: It's a fun story.

Leonore Herzenberg: Knowing about radioactivity was something that we as scientists knew about because we were already using radioisotopes. At that time, we used them in very small

counters; you actually sat and fed the counter one tube at a time. Horrors for what we were exposing ourselves to.

Mario Roederer: The political activism was very integral in various parts of your life. Do you think that colored your research? What's the interplay between the way you ran your research program or the projects you did, the people you brought into the laboratory, and your politics?

Leonard Herzenberg: I think it was a lot. The reason we went to Paris, to Pasteur, was because Jacques Monod had been in the Resistance during World War II, so we were attracted to going there and he was happy to get us to come because we were liberals, too. Very liberal.

Leonore Herzenberg: It's a very good question, Mario. I think that the politics certainly colored our associations. When we were at Caltech, the whole bunch of us were all Federation of American Scientists members, and they were the leading people of their time. There were people who we didn't hang out with—

Leonard Herzenberg: Can I interject? Before it was called the Federation of American Scientists, it was called the Federation of Atomic Scientists.

Leonore Herzenberg: That's true. All that stuff ties together with our interest in it. I think it's fair enough to say that our social interactions were also colored by our political thinking. The people who hung together hung together. There was the question of what we would do about this guy in the department who was being fired; there were questions. There were a few people in the department who hung together and were probably more right wing. I hardly remember them now. Most of the active, forward-thinking scientists were forward thinking on all of the issues. They believed women should be admitted to Caltech. Most of Caltech was horribly conservative. It was engineering and was a whole other side of the world.

Richard Feynman was there at the time. It was generally thought that those people who were good scientists and bright hung out with the liberal group.

Mario Roederer: Do you think it's our role as scientists to be politically active or to advocate on behalf of science and health?

Leonard Herzenberg: The answer is yes. It's important that scientists who know an awful lot about medicine and recombinant DNA, dealing with genetic sequencing, and so on—to this day, it's still the liberals who are very much involved with that and the Republicans who are blocking so much of it. So much support for research comes from the NIH.

Mario Roederer: How would you compare the environment now, not just the funding environment, but the support of science at the congressional level or at the administrative level, compared with that, say, 20 or 40 years ago?

Leonore Herzenberg: Support for science now—I was saying the other night that part of what's happened is: We've been forced to work so much harder to get support for science that we don't have time for this. That was not an unintentional result of cutting the funding of science. If you go back to the Reagan era, there were whole discussions of this, and Reagan himself said that they've got too much time to do these things to think about politics. "They should be working harder," and "We're too liberal; we're giving them too much money. We're allowing them to have too much time to do this."

I don't know what that took out of my time—maybe 10% of my time when I was away from the lab. Mainly it took away from sleep and family, so the lab had to go on. Science has to go on; it's an 18-hour-a-day operation. So that didn't stop, but we've reached the point in funding for science where I think we're destroying science, and I think it will take 10 or 15 years to work through the findings that today's scientists have already made, up until today. There will be some more important findings that will be made, but for an awful lot of it, it's going to be just working out and integrating what was found, and then there's going to be no new garden to grow. That's what's really missing: the support for people to do something that nobody thought would work.

Mario Roederer: One of the things I found remarkable when I first joined your lab, which was already a quarter of a century ago, was the number of eminent scientists who had trained in your laboratory. It was remarkable to see the litany of people who had come out of this laboratory and gone on to become fantastic independent scientists. For people who are starting their own laboratories and are tasked with trying to figure out what postdocs to bring in or what students to bring in, what's the secret? How do you identify those people?

Leonard Herzenberg: Nowadays, big labs—we were a big lab. For 14 years—renewed after 7 years—I had what was called an Outstanding Investigator Grant (OIG) from NIH, which allowed me, every year, to say what I wanted to work on. I could bring in people who would work on these projects and support them.

Mario Roederer: So it was the long-term funding view taken by NIH through the OIG that allowed you the freedom to hire excellent people and let them do—

Leonard Herzenberg: It was. The OIGs are now gone, and it's very, very difficult to get grant support for Lee's work, for my work, for the work of my postdocs or graduate students, or medical students.

Leonore Herzenberg: If somebody took a good look at those OIG grants and looked at what was produced during the time of those grants, the FACS [fluorescence-activated cell sorter] was definitely—without the OIG grant it would have been very, very hard to build the FACS. I think most of the people seeing this would know what the FACS is used for, but just for your benefit even, and for their benefit, between using it for all the cancer diagnosis, all the HIV monitoring—

Leonard Herzenberg: Autoimmune diseases.

Leonore Herzenberg: —disease monitoring of all kinds.

Leonard Herzenberg: Diagnosis monitoring.

Leonore Herzenberg: All of those things, and then the stem cells. Irving Weissman also had an OIG grant, and we would not have stem cells today if Irv didn't have the freedom to go and do that. If any of us had to prove to study sections every 3 years what it is that we're doing, this would really be a mess. These grants were—they used a very good panel of people to judge who was going to get them. They were outstanding panels, and they really worked. This is basically what made science what it is today. I'm sure we can find four or five other OIG grants that were used similarly.

Leonard Herzenberg: Hugh McDevitt, who was very important here. You said Irv Weissman. And people like Hiro Nakauchi from Japan, who was in our lab 25 years ago. He's now coming back—

Leonore Herzenberg: We hope. We hope.

Leonard Herzenberg: —to do this with Irv Weissman again, because of state money. Not just federal money.

Mario Roederer: The people [who you] brought into the lab, having been in the lab for many years—it was much more of a family environment in a sense than any other laboratory I have been in. We had journal clubs at your house on Thursday nights at 8:30, which was late for many people, but it was a wonderful time because we would sit back, have a glass of wine or a glass of beer, and it would be an open forum for discussion. That's a journal club that goes way back, right?

Leonore Herzenberg: It doesn't exist anymore. This is one of the things I'm hearing from all over: that the computer has destroyed a lot of this because you take your computer home.

Leonard Herzenberg: Your laptop.

Leonore Herzenberg: It's become like video games. They're social, but in a very different way.

Mario Roederer: Yes. I see that when I read about your time at the Pasteur Institute with Jacob and Monod, and you spoke earlier about sitting around at lunch and listening to these eminent

scientists have these discussions. And then the journal clubs where you have these face-to-face discussions in a less science setting—

Leonard Herzenberg: It was less formal.

Mario Roederer: —personal setting. I think that's very useful. That's certainly something that you espoused, and the society you create inside the laboratory is very important.

Leonore Herzenberg: I would still like to do this. Again, money. If there were enough money to bring the visitors that we used to bring, but there isn't. We still have our regular Monday lunch—well, it's Friday now, but whatever. We still have our regular lab meeting as we always have, and that's sacrosanct. Everybody produces, but it's a smaller lab, and now we try and join up with some of the other labs here at Stanford and have joint meetings. But there's no money to travel with; other people don't come traveling here. Plenty of people come, but really people don't come, and they don't spend the time.

Roy Riblet is back in the lab. Remember, Roy was one of the very first students. He was the first one to get his graduate degree with us.

Leonard Herzenberg: My first graduate.

Leonore Herzenberg: He now comes up here regularly because he has to come up here for family reasons, so he sits in the lab when he's here and now he's become part of the lab. This is great. If we had money to pay for him to be here all the time, that would be great. So much of it hangs on the availability of money. I really hate throwing it back to that because money has never been the driving interest.

Mario Roederer: To fund the face-to-face meetings. Another key part of your career has been the sabbatical that you did in Cambridge, and later you did one at Pasteur. Can you talk about how the sabbaticals you took influenced the development of the science and technology?

Leonard Herzenberg: The only sabbatical I really took that was relevant was at Pasteur, years later.

Leonore Herzenberg: César.

Leonard Herzenberg: Sorry, in England, César Milstein.

Mario Roederer: Right.

Leonard Herzenberg: His philosophy was to keep things very much into himself or, at least, for the English. There was an editorial in *Nature* saying that American scientists are set to take advantage of the English findings of making hybrid antibodies. Actually, we were the ones who—we being Lee and I—who went to a party with César and said, "Why don't you call these things that are just hybrids of B cells hybridomas?" They really are hybrids of tumors, which is -oma, and of normal cells—spleen cells or lymphoid cells.

Mario Roederer: You coined [the term] "hybridomas"?

Leonard Herzenberg: We called them hybridomas.

Leonore Herzenberg: It was at a New Year's party at the Cambridge Club, and we went with César and his wife and a couple of other people from the lab. We got into discussing these, and Lee, being ever so what Lee is, said, "César, we have to name these things. It is ridiculous. We can't talk about them. Let's give them a name." He said, "I don't know what to name them." We threw out two or three names, and I threw out hybridoma. He said, "I like that." So they became hybridomas.

Mario Roederer: This was, I think, a key technology that you brought back to the United States, the hybridoma technology, because that underlies virtually all of biotechnology nowadays.

Leonard Herzenberg: Right.

Mario Roederer: Its specificity brought by monoclonal antibodies allows us to do bioassays. It's in therapeutics; it's in every assay that we do every day. This was in 1976, 1977? You brought the hybridoma technology back?

Leonore Herzenberg: Len understood this; I remember this well, actually. Roy Riblet was asked, as part of his graduate work, to do a hybridization very much like what Milstein did. He took the data; it was rolled up on a tape. Remember how we used to get tapes off the printer? It was rolled up on this tape, and it sat in in the left-hand side of the desk drawer as he pulled it out. His desk was against the wall in the lab opposite the office, the one that Charlie used to be at in the same area.

Leonard Herzenberg: Charlie Shu.

Leonore Herzenberg: Charlie Shu. I would come in there and Roy would open the drawer. I'd say, "Roy, are you ever going to compute that?" He said, "I'm gonna do it. I'm gonna do it. I'm gonna do it." He laughs now; he says, "I left my Nobel Prize in the desk drawer."

He knew that it had worked. He'd looked at the tape, he knew it worked, and he didn't want to be pushed into doing a different project than the one that he was doing because he was going to finish his degree, finally. He felt it would be a distraction to do this. He actually had done the same hybridization that César had done.

Len heard César had done it. Len was interested anyway in learning molecular biology because we really didn't know very much molecular biology at that time. So he worked out for us to do a sabbatical with César at—

Leonard Herzenberg: The Medical Research Council.

Leonore Herzenberg: He worked out for himself to go there and do this. Then I said, "What will I do?" They said, "César says you can work where his wife works, which is in Babraham."

Leonard Herzenberg: A nearby town.

Leonore Herzenberg: We were going on sabbatical with somebody Len wanted to work with, but I figured like everything else, I would be able to work in the lab with Len. César absolutely would not have me in the lab. I think I walked into that lab room maybe 10 or 20 times during the whole time we were there. He would just not have me being there. Nor would he actually have Len in the lab, strangely. Len talked with everybody at MRC and did a little bit of work with this but spent much more time talking to other people. César had a guy there who was working on the hybridomas, and he had developed the famous anti-IgD [immunoglobulin D], but he wouldn't let us work on it. We said, "César, the best way to look at this is to look at it with the FACS. We could really see what it does. We could use it as a staining reagent," et cetera.

César would have none of this. He said, "It's not for that purpose; it's here for basic science, and I want nothing to do with this," basically.

Leonard Herzenberg: I'd like to interject right here that it was then that we were working at Stanford with a guy who was a member of the department, Vernon Oi.

Leonore Herzenberg: He was a graduate student.

Leonard Herzenberg: He was a graduate student, and he was working with Marian Koshland—she was called Bunny—at Berkeley.

Leonore Herzenberg: Dan's wife.

Leonard Herzenberg: Dan Koshland's wife. She ran a very conservative laboratory where people kept their own findings and didn't interact with other people. Vern interacted across the board because he had been in our lab. He was also getting divorced from somebody.

Leonore Herzenberg: He was unhappy and he missed us, and he was the only graduate student who was floating around. At that time, Dick Goldsby and Barbara [Goldsby] were in the lab. It was a good, solid group working in the lab. Pat Jones had come back and was working. The lab was working well, but Vernon was at sea, so Len—

Leonard Herzenberg: I said, "Why don't you come to Cambridge, where we are, and you can stay in the apartment that we had gotten, but there are more rooms in it than we need to use." So he came. Milstein was having a problem with—the hybridomas weren't working

because there was some kind of yeast infection in the cultures. We worked out in Babraham, which is where Lee was, with Milstein's wife, and we made the hybridomas there and read the results on the cell counter or the radiation counter. We took this little motorcycle back and forth.

Leonore Herzenberg: Vernon had got a motorcycle, and he and Len would ride out on the motorcycle.

César quite happily gave us the material. He did not hold onto it, but I don't know if it was quite happily. I never did figure that out. He was a strange guy.

I once had a discussion with him relevant to what we're talking about here. The discussion was, "César, suppose that I know something that I could continue to work on, and you know something that you could continue to work on, and that those two things put together, if we told each what we were doing, would allow us to cure cancer in 5 years. But if we each do it ourselves, it might take us 10 years to get to that point, and only one of us might get there. Or maybe we'd both get there. Which do you think is preferable?"

My answer was clearly: You would pull your information and get there in 5 years because this would be people's lives. No, César said, "Do it separately. Each person should do it separately; then you know what they've done."

He was more interested in knowing what he'd done. We were basically less interested in knowing what we'd done than in getting lots and lots of things done. We took old stories to people. "We worked on that; we contributed to that"—it's amazing, all the different pots that we've stirred over a lot of years.

Mario Roederer: I think an epitomic example of that would be when you came back from Cambridge and you made a series of monoclonal antibodies to the original CD8 and CD5 and allotypes and isotopes, and all of those hybridomas and antibodies you shared fully with whoever asked for them.

Leonard Herzenberg: Correct. That's absolutely correct, Mario.

Leonore Herzenberg: Well, let me finish about César, the lore on this, which you probably don't know. At one point, César had the anti-IgD, which because we were giving out all the other antibodies, he basically had to throw into the pot. He accosted me over this one day. I liked César. We got along. He's an interesting guy, but we had very different philosophies. So he accosted me one day. He said, "You had no right to give out those hybridomas unilaterally. You made a unilateral decision to give out the hybridomas." I said, "We made the hybridomas. We always share everything we do." He said, "You had no right to do that."

I never did quite understand what he wanted by multilaterally—that we would have a big conference and all decide to give them out? It could take us another year to do that.

Mario Roederer: It would just slow things down.

Leonore Herzenberg: It really didn't make any sense. Baruj Benacerraf, on the other hand—one of the few compliments I got from Baruj Benacerraf was, "You guys did the right thing by giving out these hybridomas. It really made the whole difference."

The difference really, for other people who are listening, is that before hybridomas, the use of the FACS was a very catch-as-catch-can operation. You could stain cells, but I had one conventional antibody, which I got by bleeding seven mice and pooling them together, and you had another one by bleeding seven mice and pooling them together. Yours could be different from mine. The meetings were meetings where we were not only arguing the meaning of the science, but whether what your antibody saw was the same as my antibody. Then somebody would finally stand up and say, "Let's get the two antibodies together."

The technology wasn't even possible, and by the time you got it all together you had no more of the antiserum. Len saw this immediately. He recognized this when we got to Cambridge, and

he realized that the hybridomas really were there and that you could make them. He immediately called Eli Sercarz and they set up a meeting in Park City, I guess it was. It was one of the ski places.

Leonard Herzenberg: One of the ski places.

Leonore Herzenberg: We added a session onto that program on hybridomas, and we invited César to speak and I believe he came.

Leonard Herzenberg: And we also invited Klaus Rejewsky.

Leonore Herzenberg: Klaus Rejewsky came. It was a very important set of people who were there. We all talked about the use of hybridomas. At the same time that Len was doing this, he called Bernie Shoor, who was then head of Becton Dickinson. Becton Dickinson were the people who were making the flow cytometry instruments. Len told him that these are going to be FACS reagents. They're going to be important. It took Bernie 18 months to convince the management—what's new? Still the same story. It took him 18 months to convince them to move into this new technology. Finally they did, and they hired Chuck Metzler, who was one of our alumni, and later Noel Warner, also one of our alumni, to build the whole concept and to teach people that hybridomas were better than goat antibodies. They were quite convinced that goat antibodies were the way they were going, and they had made a corporate decision that these were correct and no amount of science was going to convince them otherwise.

Ultimately, that's how it all grew. It was all right before Christmas that year, or before the winter in any event, that Len spent a lot of time explaining to people why hybridomas were really important, what you could get out of them.

Mario Roederer: Other people started making hybridomas, but they weren't quite as generous in terms of sharing them.

Leonard Herzenberg: That's true. We also had meetings galore in which people got together and talked about the future of antibodies, monoclonal antibodies and hybridomas, but people were not sharing them. Bernie Shoor, bless his soul, was very generous, and he also found people who were making hybridomas or monoclonal antibodies from Sloan Kettering. There was a guy by the name of Robbie Evans.

Leonore Herzenberg: The first human ones were made by Robbie Evans.

Leonard Herzenberg: Bernie said, "What can I do to encourage him?" I said, "Give him one of the FACSs that we've made, and let him test them on them, and have him send us some of the antibodies to test on the FACSs we have."

We did that. That generated not only CD4 and CD8 but many of the human antibodies.

Leonore Herzenberg: Jeff Ledbetter had characterized the mouse ones in our lab, so when these came up, Robbie eventually brought them out. We were having a site visit that day, and Jeff was in the FACS room when he tested these first things, and somebody came and got me and said, "You'd better see Jeff." I said, "What's the matter?" Jeff was really having a hyperventilating incident. "They're exactly alike," he said, "I can pick out from these humans exactly from the mouse what these are. I've got anti-CD3."

We didn't have [anti-CD]4; we had anti-CD3, -CD5, and several others. He was so shocked by what he had seen on the screen because they really have the same phenotype. He, of course, did this correspondence between mouse and human stuff, and he did the biochemistry.

It was knowing how to do the work. We had people who really knew how to do the work and who taught each other everything in the lab. There was no such thing as "I have a technology."

Leonard Herzenberg: It was "We have."

Mario Roederer: Let's talk a little bit about the king of biotechnology, which is flow cytometry. The original biotechnology, as you've referred to it, which is correct—it's one of the original biotechnology instruments. What drove the original need? How did you perceive the need for biotechnology?

Leonore Herzenberg: Len has very bad eyes, as you know. He hated microscopy. We were doing microscopy with regular antibodies, and the way that people were deciding that this was a B cell and this was a T cell was by having something that—the antibody reacted with immunoglobulins, and this antibody reacted with something. We didn't even know that they were really T cells, but Th1 was the key antigen. People were looking down microscopes and saying that there are 55% of these cells in here and 30% of those are stained green and those are red. You're getting all these discussions ending in fights. Various people would say, "I saw that there were 80% of those." They were both on the same cell, and other people would say, "No, you really weren't seeing right."

You'd have these ridiculous arguments. Ultimately, Max Cooper and John Carney were considered the authorities; if John and Max said they saw something, that won. But it was horrible. For Len, he was out of the club because he could not deal with the microscope and we had no other way of quantitating what was in a cell suspension. Now we know how many different kinds of cells there are in spleen. It would take a mouse spleen to make a suspension out of it, and they couldn't—it was just chaos. We knew it was chaos. It was not science as we wanted to do it.

Len basically said, "There ought to be a way of counting these things and of measuring the amount of this marker that's on the surface. There ought to be some way of measuring the fluorescence." He heard that, at Los Alamos, Matt Fulwyler and—what's his name?

Leonard Herzenberg: I know the science, and I can't remember his name right at this moment, but I'll come back with it.

Leonore Herzenberg: Anyway, he heard that he had a way of passing cells single file past a light source, and they were basically using a Coulter orifice and seeing cells go past it. [Len] said, "I'm going to go to Los Alamos." This was 1961, roughly. "I'm going to go to Los Alamos, and I'm going to ask those people if they would add fluorescence detection so that we could actually count the number of red ones and green ones." Len went there.

Leonard Herzenberg: This was Los Alamos Biological Laboratory. They said, "It's not in our mission to do that. Our mission was to measure fallout," basically.

Mario Roederer: Radiation fallout.

Leonard Herzenberg: Radiation fallout. Fulwyler had gotten an opportunity to work with a fellow scientist in Colorado, in Denver. I said, "If you could give me the plans for what you've got, I can try and duplicate that at Stanford and do fluorescence-activated cell sorting," which is what we called it by then. They said, "Sure, we'll give it to you."

I took the plans back here, and I found several people who were working for Lederberg in the instrumentation research laboratory. I got them to make another machine like that. I told them what the requirements would be and made sure that they looked at enough cells. That's when Bernie Shoor came in. He was always looking for results that were happening at Stanford since he'd moved out to near Stanford, [to] Atherton. He took a license on this finding.

Leonore Herzenberg: Actually, Bernie came looking for some other kind of immunomeasuring technology, which was not very interesting. I forget which one.

Leonard Herzenberg: His son-in-law.

Leonore Herzenberg: It wasn't his son-in-law, but it was a company son-in-law who was with him. He came to introduce him, and they were trying to do some immunoassay. Len said, "If you really want to do something that would be valuable, you would license this machine that we're building."

By that time, we had built the whole thing. We had actually put cells through it. We knew it would work. He said, "You could license this and build commercial versions of this, and this would be pretty good." The question was how many would sell. Would it be 10, or do you think

we might actually sell 30? There are now 30,000 of them or something like that. There are many different companies making versions of them.

Mario Roederer: What I find particularly remarkable is that, in principle, the basic technology has not changed that much over 45 years.

Leonard Herzenberg: Yes, that's right.

Mario Roederer: It's much more spiffy looking and there are much better electronics, but the basic physics and process of the flow cytometry are exactly the same as when you built the first one in a different building here at Stanford.

Leonard Herzenberg: Yes, correct.

When the Suez Canal crisis came, they cut back—no, how did we get Dick Sweet?

Leonore Herzenberg: It was one of those crises; it wasn't the Suez Crisis.

Leonard Herzenberg: Funding crisis. The company he was working for—Varian [Medical Systems], I think it was—was going to drop the project that we started at Stanford. I called him up and said, "Dick, how would you like to work with us at Stanford, instead of at Varian?" He said, "There's nothing I'd like better than that."

So he came over here to work with us and was the key—

Leonore Herzenberg: This was before Bernie.

Mario Roederer: Dick Sweet had the patent on the ink-jet printer.

Leonore Herzenberg: That's right.

Mario Roederer: It's roughly the same technology of depositing ink drops—

Leonore Herzenberg: It is the same technology. Fulwyler was using Dick Sweet's ink-jet design to deposit the cells. So when you found a cell you were interested in, you could move the stream. They used Sweet's design.

Len talked to Sweet while they were building the machine here, and then Varian took an interest and said that they might build the machine, and they were cut back. This is the standard thing. This is why things like this don't fly in corporate places because it was obviously a 6- or 7-year effort, at least, and somewhere in between somebody's going to change hands in the corporate world. Len was just devastated over the fact that Sweet was going to go somewhere else and do something where he could pay attention to the project. That was when you—

Leonard Herzenberg: I got Lederberg to allow the instrumentation research lab people with whatever his name was—

Leonore Herzenberg: Lee Hundley.

Leonard Herzenberg: Who was the head of that group?

Leonore Herzenberg: Elliot Levinthal.

Leonard Herzenberg: Elliot Levinthal. Yes. And it's now Levinthal Laboratories.

Leonore Herzenberg: Speaking of funding, you'll find if you go to the archives for Elliot's lab—it was a NASA project—if you go and look at his reports, they built the cell sorter. It wasn't that he was stealing credit, but his reports came out because his people were actually doing it. He met with his people and he kept that engineering effort moving, and he was an important part of that in that sense.

Len, who was not an engineer at all, had started it because he knew what it needed to be. This is, again, another one of the problems with biotechnology these days: that the engineers get together and they talk about what they think they can build, and they build it expecting that some biologist is going to use it. The real answer, as we know over and over again, is that the biologists have to drive this. I remember one time in particular when Len went to a meeting, he came back and said, "They can only make it go 10^6 cells per minute." I don't remember what the number was, but it was something like that.

Mario Roederer: A million cells per hour?

Leonore Herzenberg: A million cells per hour, maybe. Len just said to them, "If you can't do that—" They said, "You'll have to defy the laws of physics. We can't do it." Len said, "If you can't defy the laws of physics, then we can't run the project. It is of no use for you to continue, and that's the end of the project."

So they all went back to the drawing board; they figured out a way to make it go faster. It was a crucial turning point, and they really were quite certain that it could not go faster than that.

Leonard Herzenberg: What also happened during that same period—I was on the Genetics Study Section, which is part of the NIH, which reviews grants, and I gave a talk to the people here at Stanford. They got into a sit-in then, which involved David Parks and others. I went off to the study section meeting in Bethesda. The sit-in went on, and out of this came continued work on the FACS self-sorter.

Leonore Herzenberg: It was a great deal of confusion. I know what Len's referring to. There was a long history in there that involves Steve Ela, who you probably remember. The sit-ins, again, were social events. People were sitting in in a building, but what did you do? All of your colleagues were there, so you also had discussions, and the discussions involved other people from other disciplines.

Leonard Herzenberg: And you put out newsletters.

Leonore Herzenberg: It was extraordinarily cross-disciplinarian. It was a very great ferment. But I think we should take a "funny break" for a second from all this history to just talk about the history in terms of sit-ins.

The physicist [William] Shockley was arguing that eugenics was correct. He had figured out how eugenics was correct. Lederberg was writing against Shockley. All the genetics department was saying, "Who is this guy? He doesn't know what he's talking about."

So we came to the sit-in. Len had a habit of opening the sit-in, coming to the front door, and then saying, "Sorry guys, I've got to go; I've got a study section."

This would happen again, and we said, "We know when the sit-ins are going to be. We just look at Len's study section dates."

Anyway, he got to the door of the sit-in—we never were in the vanguard of people. We were the chicken-soup brigade. We never were in the vanguard of anything that was being done in terms of civil violence, but we were coming to deliver a message to the president that we were going to have a meeting. We were formally inviting the president of Stanford to address this meeting or something, to which of course he was going to say, "Get lost."

But everybody came into the office, and it happened that Shockley was sitting there, and he saw an opportunity for an audience. He started talking about his genetic theory. Len came up and started debating him. Finally, Shockley found himself pushed further and further against a wall in a very gentle debate, but a debate.

Finally, he said, "I'm Shockley, and who are you? Who are you to argue this with me?" He said, "I'm Len Herzenberg. I'm a professor of genetics." It was a great time.

The students were all treated to this. This was part of being in a sit-in. The idea of sit-ins that people have is so different from the intellectual part of them that we had.

Leonard Herzenberg: They were called teach-ins by that time.

Leonore Herzenberg: There were teach-ins; there were sit-ins; there was everything. And a lot of great people.

Mario Roederer: During this time—and you mentioned Dave Parks and Dick Sweet—you maintained a laboratory and research group that was composed not only of biologists, but of engineers and physicists and electronics engineers. This is a mixture that you maintained for decades.

Leonore Herzenberg: Still do, still do.

Mario Roederer: In fact, you still have some of these people. What was it like to maintain a lab where you had to interdisciplinarily teach engineers and physicists how to do biology and the biologists how to do engineering? How did you get them to talk to each other?

Leonard Herzenberg: It was great. Dave Parks was working on light scattering, and he became a friend of ours. Wayne Moore is still with us, but at that time—

Leonore Herzenberg: Where did we meet Dave Parks?

Leonard Herzenberg: We met Dave Parks at the sit-in.

Leonore Herzenberg: He was a physics graduate student. His wife was doing her degree in biology, and he loved both biology and physics. He became a very close personal friend and political friend before he became involved in the actual flow cytometry stuff. He was hired in. He knew he wanted to do something in biology and we hired him to come back.

Mario Roederer: Arguably, Dave Parks knows more about flow cytometry than any person on the planet.

Leonard Herzenberg: I think that's correct.

Leonore Herzenberg: I think he would be flattered if *you* said that, Mario. Probably nobody else in the world. Since you have a camera here, if you're willing to take your camera up onto that wall and look at those two butterflies on the wall—can you do that?

Mario Roederer: Dave is quite the photographer.

Leonore Herzenberg: Those are David's pictures. He spends 6 months out of every year going out and doing naturalist photography. He's got traveling exhibits all over the country.

Mario Roederer: There's been an enormous amount of technology development in the laboratory, as well as science. You always manage to intertwine the two to recognize when the technology was needed to solve a problem in the biology and then, when you had a new technology solution, to apply it to the biology. The laboratory has been a fantastic mixture of technology, biology, and continued development. Is that a model that is something that you think is feasible in today's environment, with the privatization of patenting and all that?

Leonard Herzenberg: I think it is still viable. We have people who come from the technological side, and they come and work with us, and the FACS is a fantastic technology–biology interaction. There are complementary tools in immunobiology that I've published papers on.

Leonore Herzenberg: But Mario's right: It's a very interesting question because the funding for that, as we pointed out, was your OIG grants. I always had my biology grants alongside that, so we had funding to do it. I don't know (*a*) if there's anybody with the insight to do this in today's genomics world and (*b*) whether anybody has the funding to bring in the kinds of people that companies can afford to hire. The market hires them out into companies really quickly. Everybody's dreaming of being the next dot com.

Leonard Herzenberg: I think that they still do it. Mario, yourself, you are involved with companies and CRADAs, which are collaborative agreements between biologists and NIH biologists and companies—Becton Dickinson people. Mike Snyder, who is the chairman of the department, chairman of genomics, does have an interaction between the two. We got a lot of money, which we got from patent royalties, and we use that to support people in the laboratory who have different technologies behind them, including biological technologies.

Leonore Herzenberg: I just don't know the answer, Mario. I really don't. It happened only once, if we look across everything we know about that interaction between the engineers and the scientists in a first-rate biology laboratory.

Leonard Herzenberg: It's still happening. Dave Parks is still very much—

Mario Roederer: It's still ongoing.

Leonard Herzenberg: It's still ongoing.

Leonore Herzenberg: Wayne Moore, who's the other half of that, is still ongoing. We continue to support that these days out of our pocket because that's what it's going to have to be out of. But we continue to support that. If it was something that could easily happen again, I would think by now it would have happened again, and I can't think of anybody's lab where this is happening. There are a couple places here in Stanford where some people have done a little bit of it.

Mario Roederer: One of the reasons may be because of your philosophy that society or the government or the United States paid for your science, and therefore the science that you generate belongs to society and belongs to the people. Nowadays, there's this push to patent something and then take it to a company and try to make $100 million. As I recall, on the original FACS patent, you asked all the inventors to sign the royalties back over to the laboratory—

Leonard Herzenberg: Correct.

Mario Roederer: —and fund the laboratory. That's something that would probably never happen today.

Leonore Herzenberg: That's right.

Leonard Herzenberg: That's correct.

Mario Roederer: At that time, in the 1970s and 1980s, that was one of Stanford's most valuable patents, and it was very generous, obviously, to fund the laboratory and provide ongoing support in that way. I think that's something that sets apart the laboratory from many laboratories of today: The focus is on returning to society the benefits that were accrued by their investment.

Leonore Herzenberg: We should take a good look at patents and what's going on with patents today. What went on with patents before? There's some interesting history there. Bert [Bertram I.] Rowland was the guy who did the Cohen–Boyer patent.

Mario Roederer: Molecular biology patent.

Leonore Herzenberg: Molecular biology patent, the first really big biology patent. Around that time, Bernie Shoor and I were talking a lot about whether hybridomas should be patented, and we came to the conclusion that, no, they shouldn't be. There are some very, very strong arguments for why it is really wrong to patent hybridomas, the strongest of which is that when you patent a hybridoma to do a particular job, if somebody comes along who has a better hybridoma, they throw it in the garbage because the first one is patented, and if you've got one with 10 times the affinity, forget it. The companies don't pick them up. These days, the companies are a little better about that, but the whole concept of patenting something that was a piece of biological material, a DNA sequence expressed as an antibody, seemed wrong to Bernie, who was the head of BD. He said, "I don't think we have a problem commercially with selling reagents. People will buy reagents even though they can make their own. That's not going to stop them from making reagents."

Well, he lost. It cost BD $5 million a long time ago because he didn't believe in patenting things. It was really a very expensive lesson for everybody. Stanford pushes us to patent whatever we're supposed to patent. The government does. We have responsibilities with our grants. We're supposed to patent things. I still get this kind of feedback from Wayne: "Put it in the public domain; it will be okay." But it doesn't quite work that way, and it's a problem, so we do patent stuff. But I had a long running fight with Bert Rowland over that time about whether we should patent the monoclonal [antibodies]. I took the position, along with Bernie, that we shouldn't do it, and he took the position, as a patent person, that we should do it. Of course, he was much more in touch with the Stanford offices that eventually said we should patent this stuff.

I don't know that it's right that sequences where something better could do the job should be patentable as *the* thing that does the job. This went back to the whole issue of how CD antigens were named. I don't know if you know this: We were never a part of that group that named CD, and that was because César was still mad at me. As best as I could tell, he more or less ran who

was going to be invited to those meetings. I don't think it's cost us anything in our career, and I think that we might have had a much better notation system had we actually had that as an open discussion rather than the way they did it as a committee, but that's, again, yet another issue. They shouldn't have been named the way they were named.

Mario Roederer: To close up, maybe you can reflect a little bit. Your laboratory, as I said, has been this mixture of technology development and biology. You have enormous accomplishments on both sides, in terms of biotechnology advances, in terms of basic understandings of immunology, and so on. Where is your fondness? Do you more fondly remember the biological advances or the technology advances? What is it that you like to hang your hat on?

Leonard Herzenberg: All of it. I think I've had marvelous people who have come here, like you and like Vernon Oi, and like Garry Nolan and others, some of whom try to emulate what I've done or what Lee and I have done, or what Lee has done. I think that the mixture is really what makes it the witches' brew, if you will—stir, stir.

Leonore Herzenberg: "Bubble, bubble—"

Leonard Herzenberg: "Bubble, bubble, toil and trouble."

Leonore Herzenberg: It's the people. In the end, life is with people. It's the funness of all the people who were here. It's great to see that Nicole [Baumgarth] manages to get Peter [Katsikis] proposed for a job. All of this just keeps on going.

Leonard Herzenberg: I think your job was actually recommended by Garry Nolan, wasn't it?

Mario Roederer: Yes. We all look out for each other.

Leonard Herzenberg: We've had a number of social meetings that have gotten people from different parts of our life to be able to interact together—like Sam Black and some of these fellows you know the names of but maybe never met them. But you meet them because we have a birthday or we have an anniversary, and we have a meeting where people come together from different time periods.

Leonore Herzenberg: I think the purpose of all findings is to be overturned, no?

Mario Roederer: Right.

Leonore Herzenberg: You can have a fondness for the work. I'm particularly fond of the B cell lineage stuff, which I'm still working on; we're actually getting there. But it's the people, in the end, and the people who they connect to. Your real accomplishment in the world is in nurturing other people.

Leonard Herzenberg: Have you heard of the book called *Life Is with People*?

Mario Roederer: No.

Leonard Herzenberg: That's a book we give out to people. Margaret Mead wrote the introduction to it. During the last parts of World War II, what became the CIA wanted to know what was going on behind the Iron Curtain. They got people who could tell them, but they all turned out to be part of the same people. They were all Jewish, even though they came from different physical countries: Czechoslovakia, Poland, Romania, and Hungary. These people got together and had symposia and talked about their various backgrounds, and many of them turned out to be Jewish.

Leonore Herzenberg: What Margaret Mead said was that they had the experience of discovering a culture. They were anthropologists and they had no idea that there was this whole subculture that existed amongst the parents of their friends and amongst the newly emigrated Jewish refugees who were coming into the country. They were interviewing everybody who came from Poland. The vast majority were displaced Jews. They actually discovered the culture, but they named the book *Life Is with People* because when they actually described the Jewish shtetl—which is the cultural center, shtetl meaning "small town"—they actually described the whole culture, and it exists today with lots of the Jews of this country, and probably with you for having spent

10 years with us. It's this transmissible recognition that buildings don't mean anything, places don't mean anything, money doesn't mean anything, but interactions amongst people—those will stay forever.

Mario Roederer: That certainly is a tremendous nucleus that you have built here at the laboratory and all of the people who have come through that laboratory, trained in the laboratory—and certainly for me. It's been an honor and a joy to be part of your greater scientific family.

Leonard Herzenberg: Really nice to hear it from you.

Mario Roederer: Thank you again for this conversation.

DISCLOSURE STATEMENT

Neither the interviewer nor the interviewees are aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

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