Robert Wang

Interview conducted by

Mark Jones, PhD

October 21, 1997

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Source: Bloomberg Businessweek

THE SAN DIEGO TECHNOLOGY ARCHIVE

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JONES: Where are you from originally?

WANG: I'm originally from San Francisco.

JONES: How did you get interested in science?

WANG: When I was an undergrad at Berkeley during the Vietnam War era, I lived in the Haight- Ashbury district, and my local board could never fill its quota, so when I was at Berkeley, I got drafted, even though I was a full-time student. Through a series of events, I ended up not going into the military, and I had dropped out of school in the meantime, because I thought I was going to go into the military, but when I started back up, I couldn't go back directly to Berkeley because they were on a quarter system, I believe at the time. They had just switched and it was the middle of the quarter, so I started back up at the junior college in the state university, and took my first biological science course then. Before, I had always been in engineering, more of a family pressure thing. If you know Asian families, there's this big thing to become engineers or doctors, medical doctors. I certainly wasn't going to be a medical doctor. And I really enjoyed the organic chemistry courses I took, and the biology courses, and when I went back to Berkeley, I became a biochemistry major, so that's pretty much how I got into the sciences.

JONES: Were there any particular individuals at the time, teachers, who encouraged you?

WANG: Yeah, there actually was, not when I first went back into biochemistry. Berkeley's biochem department at the time, I don't know if it still is, was ranked number one in the nation based on faculty and their graduate students, and then

their alumni and what happened to them. My advisor at the time was Dan Koshland, who's a very well- known biochemist, and controversial also. His family was one of the, I don't know if they were founders, but big shareholders of Levi Strauss. His wife also taught at Berkeley, Miriam Koshland. Well, Dan Koshland called me into his office near the end of the winter quarter of my senior year, and asked me what I was going to do when I graduated, and I said I didn't know. And good old Koshland says, 'Well, how'd you like to go to graduate school.' And I said, 'Sounds good to me.' And he started naming off all of these schools. I recall Albert Einstein and Columbia, he said, 'I've got friends there,' and then I said, 'Well, I'd rather stay in California. I've been in California my whole life.' He ended up saying, 'Well, how about UC-Riverside.' I didn't really know where Riverside was at the time, but he said, 'I know the chairman of the department there.' I thought, 'UC, California, can't be all bad.' So, I went, 'Sure, that sounds good to me.' So he says, 'Well, I'll call him up.' So, about two or three weeks later, I got a letter of acceptance from the department of biochemistry at UC-Riverside, which turned out to be a very good department, for being a small UC campus, I think the school was ranked in the top 20 in the biochem departments in the nation. And I got into the department without ever taking the Graduate Record Exam or even applying, and I got accepted with a fellowship. They sent me a letter saying 'Congratulations, you're accepted dude, please respond.' And I sent a letter saying, 'I accept.' That was the extent of the communication until I got there. I was by no means a star student. I did well in my major courses, but my GPA was below 3.0 overall. I had a lot of fun in college.

JONES: Did your mentor have something to do with arranging all of this?

WANG: Well, I'm sure Koshland called them up, and Randy Wedding was the chairman of the department, to say, 'I've got an undergrad student who would be good in your graduate program.' I saw Koshland quite a few years later, more than ten years later, on an airplane flight we happened to be on, and I went up and introduced myself, and said, 'You probably don't remember me,' but he said, 'Naw, I do. I don't remember your name, but I remember you.' And I thought, 'I don't know, if he's just being courteous or what,' but I thanked him for it on the airplane, so.

JONES: Was Tom Adams there at Riverside at the time?

WANG: He finished just when I started. He was four years ahead of us. I was there with Dale Sevier. He lives up near Half Moon Bay now. He was with Toso, but he's

moved on from them for nearly a year now. He's doing some consulting work and some other things.

JONES: At Riverside, what kind of work did you do there?

WANG: I ended up, because I had come from Berkeley and taken all the biochem courses at Berkeley, my first year at Riverside was actually pretty easy. I got to go directly into my dissertation research. They considered all of my undergraduate biochem courses as fulfilling most of their course requirements, so I had an easy course load. And I ended up working in the laboratory of Brian Reed, and working on nucleic acid protein interactions and nucleic acid structure. So, I spent a few years doing that.

JONES: At this time, were you considering an academic career or were you thinking about industry?

WANG: Probably more academic at the time, that seemed, you know, up until then, in the '60s, probably the normal career path was get your graduate degree, do a postdoc, and go into academia. I was looking at a teaching position, I think. I didn't like the politics of the academic world. I think the politics of the academic world are much, much more significant than in industry, because in the academic world, you really don't have a person who has the final world. You have a chairman, but the chairmanship really, well at least at Riverside, it rotated, whereas in industry you've a board of directors and a CEO, and a guy pounds the table and that's it. But in academic, it's like, well, 'Wait until I'm chairman.' But I was looking at that, and interestingly enough, I was offered a post- doc by my dissertation advisor, Brian. He wanted me to stay on as a post-doc, but Riverside wasn't, you know, once I got to Riverside, it was in the fall, which was nice, but then, I did my first summer in Riverside, during smog season, and it was 'Whoa, I've got to get out of here in four years no matter what.' So, I ended up, Dale Sevier had left, he had joined, he had a master's degree when he entered the Ph.D. program in Riverside, which doesn't help you a whole lot other than making your course load a little easier, but he ended up doing a post-doc at Scripps with Ralph Reisfeld, and so, we became good, good friends in graduate school, and so, he suggested that maybe, you know, they had some openings at Scripps, and I might want to go down there. I had applied for a post-doc position at Joe Feldman's lab actually, and had an interview, and he was ready to offer me a position. It was the most interesting interview I've had. He called

me into his office and we're sitting there chatting away, and he says, 'How about a Coke?' and I said, 'sure,' and he was about ready to hand it to me, and I was real honest with him, and I told Dr. Feldman, I've got to let you know that I've had an interview in Ralph Reisfeld's lab, with Dr. Gary David, and I'm very interested in what they're doing with tumor associated antigens, and he says, 'Well, in that case, I don't need to talk to you.' And that was it for the interview.

JONES: So, you had been down to talk to Reisfeld?

WANG: Yeah, right, but mostly Gary David, though. I actually ended up working for him. I had very little interaction with Reisfeld. Reisfeld was more into histocompatibility antigens, and I worked totally on tumor associated antigens.

JONES: Do you remember meeting Gary David?

WANG: I don't remember the exact conversation, but we became good friends, and that friendship has lasted until now.

JONES: While you were there, this is when you developed the assay for screening monoclonals?

WANG: Yeah, we worked on actually carcinoembryonic antigen (CEA), and we developed, mostly Dale did the initial work, but we were a team, Gary David, Dale Sevier, and I, and I think having a basic trait of laziness, we didn't like the radioimmunoassays we were doing. It was pretty laborious and time-consuming. We ended up developing this faster solid-phase assay, so to speak, and when we all ended up at Hybritech, that's what we used for screening the antibodies at Hybritech, an adaptation of it.

JONES: Do you remember your thinking at the time, how you went about doing that, what problems you were trying to solve?

WANG: Yeah, I mean, doing radioimmunoassays, you rely on an immunoprecipitation reaction, and association to occur, and what happens is, sometimes if you don't add the second antibody right, or you've made a wrong dilution, you don't get a precipitation, you may get incomplete precipitation, you've got to centrifuge it hard, with a lot of G force to bring down the precipitate, because it's a fluffy precipitate. You've got to compact it at the bottom, and then you've got to wash it a few times, which means you've got to carefully decant off the supernatant,

and then you've got to put some buffer in, and re-suspend the pellet by agitating these little microfuge tubes and getting a good resuspension so it's not just a clump and only the outside of the precipitate gets washed. So, there's a lot of potential for variation in the assays. And therefore, we used to run them in triplicate, OK, because it was fairly common for one out of three replicates to give you a pretty far out result compared to the other two or the average, and so rather than run the whole assay, you relied on two of them being close, and just assuming the two close values were closest to the real value. So, we developed this semi-automated procedures and published a paper on it, actually, in some journal, using a cell harvester which we had gotten in at the time to do all of our cell assays. We had a technician who was complaining it was a lot of cell assays. And we applied it to solid-phase doing the assay with sepharose and then being a second antibody assay, or I don't remember, sandwich assay. They were first antibody, labeled second antibody, I think that was it, and being able to collect essentially your antigen on the solid phase, and then collecting the solid phase on these glass filter disks, or sheets, and then counting the sheets, the little disks where the solid phase collected. And it was very easy to just run several mils of buffer through the filter to wash the beads, and to wash away all the unbound labeled antigens. I think the other thing we had, too, was labeling the CEA. You had to radiolabel the CEA at the time, and as I recall, that was, you know, we had problems with that. Labeling an antibody is easier. I forget if we had a solid competition assay, or if we did a sandwich assay, but it's just a lot easier to work with solid phase assays rather than doing the conventional RIAs that DeLallo and Bursin originally developed.

JONES: Were sandwich assays being used a lot at that time?

WANG: No, early '70s, no, they were just starting to come in vogue. It was more the double antibody precipitation, DeLallo-Bursin type assays.

JONES: What precisely were the years you were at Scripps?

WANG: End of '73 through the middle of '75.

JONES: What was going on in '75.

WANG: I left before Gary David and Dale Sevier. Yeah, what happened was I got very interested in transfer factors, which were becoming, to me a very interesting field, being able to transfer memory or immunity from one organism, from one animal to

another. And we were writing a grant proposal, as I recall, at the time, and a big scandal broke out. I think it was a research reader at the Mayo Clinic or someplace who was working on transfer factor had published some of the more well-publicized papers on transfer factor, demonstrating the ability to transfer some immunity from one animal, from one hamster to another, to a naive animal. And what happened was, it turned out that this researcher who had won, I believe, a young researcher award, or something like that, had actually falsified the data, and he had colored the skin of some of the recipient animals with a marking pen or something, to show that they reacted, or something. I mean, it just blew the bottom out. It was kind of like the stock market crashing, stock in transfer factor just plummeted and no one was going to touch it because it was a real hot potato because the results were irreproducible and it was difficult to really demonstrate the added effect.

JONES: Because of differences between animals?

WANG: No one knew, I mean you're playing you're playing with such a complex system, you're just kind of grabbing something this gammish into another animal and lo and behold you see a response. You try it next time and you don't get a response -- which one do you believe? And so, I think, people are getting more interested in it again. I think that more recently, there's been some work in the past couple of years. But at the time, I was on a contract with NCI, and like I said,

JONES: Was this the same one that Gary David was on?

WANG: Yeah, we renewed it several times, I think, and like I said earlier, the whole thing with the politics, I mean, talk about politics at Scripps. Frank Dixon was in charge of the research foundation then, and Richard Lerner was on the rise. Joe Feldman still had some power in there. The Research Foundation reorganized at the time into separate departments, cellular immunology and molecular immunology, I believe, they all used to be experimental biology. You had the biochemistry and microbiology, and those two departments were more like poor step-sisters in the Research Foundation. There were a lot of politics among the senior investigators at Scripps, and you know, I'm sure it's still like that. It was a real Peyton Place, too. It was amazing how much the politics ruled in that place. They had a Doctor's Lunch, an M.D. lunchroom in the old Scripp's Clinic. PhDs weren't really allowed in there. This was a pretty nice lunch room. M.Ds could go there, and M.Ds are more highly regarded than PhDs in a research organization, which is just bizarre, and that was the

mentality, and it probably still is pretty much today. But I'd have to say a lot of medical doctors today are more qualified researchers because it's become more of a recognized area of specialty to be a research M.D. But back then, M.D.s learned by being put under fire and were not as qualified researchers as PhDs.

JONES: That must have something to do with the history of Scripps, evolving from the clinic.

WANG: Oh yeah, it's the way it was run. Obviously, they were an elite medical care facility. I remember sitting in a research meeting down at the old clinic one time, and there's John Wayne out there in a bathrobe, looking like an old man, which he was, you know, getting the physical exam. And everybody's, "Oh, look, there's John Wayne," So, it interrupts the research meeting and everybody looks out the window: "It is John Wayne." But now, they realize the economics, you know, they opened up the clinic to the masses, so to speak, and I think that was under the guy after, who came in, I forget his name, Sweeney, Keeney? Whoever came in and replaced him, came in and looked at establishing the satellite facilities. And the satellite facilities actually support the main facility in one way because the physicians have to pay a certain amount of their fees that they collect for seeing patients to the main clinic, and they sort of have a quota to reach, but more to Scripps, I should say, but the overhead is so great at the main clinic, an inordinate percentage of the income collected goes to the main clinic as opposed to the satellite clinics, but that was several years ago. Our physician used to be at Scripps in Rancho Bernardo, so I was talking to him about it, and it was phenomenal how much money the clinic was taking from the physicians to support the overhead. But, yeah, Scripps was an interesting experience, and that's what we really got me thinking about, OK, I'll go into industry, and I responded to this ad, kind of as a lark, for a start-up company, and ended up getting an interview, and accepting the position.

JONES: Was that IDT?

WANG: Yeah.

JONES: Tell me about that company.

WANG: They're up in Santa Clara, you know, and I always had, after we moved away from the Bay Area, we always thought about moving back to the Bay Area.

JONES: You were married by this time?

WANG: Yeah, I was married as an undergrad. I was married during the end of my junior year at Berkeley. So, we had two children at the time. Our two boys were born, and we moved back to San Jose, and it was a good learning experience for me, IDT. The company was eventually sold to Beohringer-Ingleheim. It was about less than a year after I was up there, though, being still very research oriented, I had found that the scientific basis by which they had based their assay system was all an artifact, and they didn't want to hear that. And the guy who was in charge of R&D at the time gave me a lot of crap for it, but we spent the next three months proving that what I told them was right, OK, and then developing a back-up system.

JONES: What exactly was the problem?

WANG: Well, they had gone through what they thought was a chemical immobilization of antibody on a solid phase, and as I recall, it was polymethylmethacrylate, a film that they were using. What is was, was a surface flourescence type measurement being made on a film, that's where you had your immunoreactions occurring. And so they took this polymethylmethacrylate and did a sulfuric acid etching of it, and then that roughened the surface, and increased surface area, and then they went through some cross link, assuming that they formed then some functional groups on the surface, they were able to graft or cross link some antibodies and then do a immunoreaction between labeled antigen and unlabeled antigen, a competitive reaction, and measure the amount of antigen in a specimen. Well, as it turned out, when I started running the right controls, it didn't matter whether or not I put antibody on the surface of the film. I said, 'We've got a problem here, boys.' And he says, 'No, you've done it wrong.' I said, 'No, I didn't. I repeated it several times. You don't need antibodies to run this assay, which tells me that you're looking at an artifact.' And it turned out that when you acid-edged the polymethylmethacrylate, you did create a lot more surface area with very good non-specific binding properties, and so you were binding stuff, and it was really a competitive binding between radio-labeled antigen and non-labeled antigen for non-specific binding to the surface, along with everything else which was competing with it. So, yeah, we ended up then doing, it was interesting, it worked out, but we used the surface as a non- specific adsorbent, actually, for binding antibody. I think what we did was put, do a solution phase reaction adsorb out antibody, which had bound labeled antigen.

JONES: So, you incorporated the problem in the solution.

WANG: Yeah, had to. There wasn't anything else at the time. We worked on a lot of surface modification things at the time trying to graft functional groups on and do chemical linkage of antibodies to surfaces, but at that point in time the plastics industry hadn't come up with the right substrates yet, and you couldn't, I'm sure that you probably got some specific binding and coupling and binding, but it was probably masked a lot by non-specific binding to the surface, and non-specific binding is always a big problem, especially the more sensitive your assay. But today the plastics industry has developed some good substrates for coupling, or chemically coupling proteins or macromolecules to the surface specifically.

JONES: This was a start-up company?

WANG: Yeah, I was like the fourth or fifth employee in the company, as it turned out.

JONES: And the customers they were targeting were clinical labs?

WANG: Yeah, all the reference laboratories.

JONES: Was part of your decision more money, to support your family?

WANG: Naw, I mean, I was in deeper debt when I moved up there, because housing was a lot more expensive. Sure, it was part of the consideration, you know, but it was, I think, more, I think the excitement of starting a new venture and being able to see it grow.

JONES: Do you perceive risk in doing that? Did you think what happens if this doesn't work, if this company…?

WANG: Cratered? I think at that time I was young enough that I wasn't too worried, I could always get another position. So, I thought I would take it. If you don't do it then, when are you going to do it? When you're sixty? I don't think so. The probability is a lot less, anyway, at sixty. At that time, I was twenty-seven, twenty-eight?

JONES: But going back to the Bay Area was important?

WANG: That's probably, I would think that that was one of the major considerations, because all of our families are up there. We're the only ones who moved away. So, I think that was a big consideration.

JONES: How long were you at IDT?

WANG: Four years. I left there in '79. I quit, found a job. The company had been sold to Beohringer-Ingleheim. They brought in a person who actually ended up in San Diego as director of R&D who had very minimal experience and qualifications, and yet had somehow been convincing enough to become director of R&D, and he lied to me. The guy lied to me, and I won't accept that. He did some things that I considered, I considered him to be, I don't recall now exactly what they were, but I felt that he discriminated against me, and I left, and I left without any job. I looked around in the Bay Area. I had the opportunity to possibly go to Genentech, or to, there was a small immunoreagent company called Pago, I think, in San Mateo, Burlingame, someplace, had offered me a job. I had interviewed at Bioscience Laboratories in Van Nuys. They had offered me a job. And I interviewed at Calbiochem, here in San Diego. They offered me a job. And I ended up taking the Calbiochem job because, one, it was San Diego, and we liked our time in San Diego before, and second, was that Heochst had bought Calbiochem and moved their immunodiagnostics business into calbiochem, and they needed a, they were starting a whole new group, so it was starting from scratch, and they wanted me to do that, so that's what I did, that's how I got back to San Diego.

JONES: And the notion was that you would starting something, even though Calbiochem was established?

WANG: Yeah, and it was new in the sense that Hoechst was now in charge, and so I did for exactly one year. And during the first year, actually, what happened was that Hybritech was going, and Gary David, I don't know if it was Gary or Dale or both, suggested to Ted Greene that he talk to me, because they needed people with industrial experience to help them develop products. That was later in '79. Probably, it was Gary more, because I think Dale started in August of '79 at Hybritech, and we started talking, I think, late '79, and I told them, 'Well, I've got a commitment that I made to Calbiochem, so I want to stay there for at least a year.' So, we kind of danced around for a while, and then I finally agreed and said I'd accept the position there, and left at the end of February 1980, and joined Hybritech.

JONES: Now, you had been aware of Hybritech from the beginning?

WANG: Yeah, because of Gary, and you know, Gary had been with Larson Diagnostics, that didn't go, and then he got involved in Hybritech. Through Gary, because we'd stayed in pretty close contact through the years, and I knew what was going on.

JONES: You had this commitment to Calbiochem that you wanted to honor, but you decided that Hybritech would be a place that you would like to go?

WANG: Yeah, it was a good situation. Again, the start-up aspect appealed to me, and I knew Gary and Dale well, and, yeah, it was a god opportunity, I thought, a good thing to do. The people I'd hired in at Calbiochem were established and had their feet on the ground and knew what was going on. One particular individual, Bill Gordon, who had actually gone to graduate school with Dale and myself, was fully capable of taking over and running the department, which he did.

JONES: You had been working in immunodiagnostics with IDT. Do you remember when you became aware of hybridoma technology?

WANG: It's when I was at IDT. It did make an impression on me because one of the big problems at the time with doing any kind of solid-phase immunoassay, you wanted to get as much specific antibody immobilized onto the surface as possible, onto the substrate, and at the time pretty much the standard procedure, you'd immunize an animal, collect the blood, and go through the purification of the antibody, you can make Ig fractions, so you get all the IgG basically, and then you got anywhere from 90 to 99.9% of the IgG was non- specific, or directed toward some other immunitive besides the one that you had used. So, it was pretty laborious, and inefficient to try to get specific antibody, so through the whole process, just by the nature of the processes that were available to get your antibodies at the time, you eliminated the higher affinity antibodies, and so, you're left with probably the lower affinity antibodies, and then you try to immobilize those if you want to increase the immunoreactivity of your solid phase, whereas if you use the monoclonal antibodies, you start out already with a very high percentage of immunoreactive antibody of interest for you, you don't have to go through as much of the inefficient and very laborious processes to clean them up. So, for solid-phase assays, which I was very interested in, yeah, that was a real thing. When I was at Calbiochem, I got my boss at the time, who was VP of R&D, to go over to Hybritech. We went over there actually,

and this became a little. It was interesting because this came up, too, in the litigation, the subsequent litigation, but we went over to talk to Hybritech about monoclonal antibodies and what they might be able to do for us, because we were trying to develop ELIZAs at the time. So, yeah, I mean, the potential was there.

JONES: How did Gary David represent to you what was going on at Hybritech?

WANG: I don't remember. My last day at Calbiochem, I think, was February 28th, 1980, and then I started March 1st at Hybritech. Part of that, too, was I had to repay Calbiochem all of my moving expenses if I didn't stay at least a year. Hybritech was willing to pick it up, but I thought it was so close, why should we? So, I joined Hybritech, and outside of Ted Greene, I was the only person in the company who had previous industrial experience at the time.

JONES: And what was your impression of the company and what they were doing?

WANG: It was a lot of fun. I mean, we really enjoyed it. In spite of the eventual personality conflicts, maybe the escalation of some differences of opinions in later years, the people at that time were pretty accepting of each other's differences, differences of opinion. There was a good atmosphere to present your ideas, technical ideas, and be challenged, and be able to deal with the challenges, differences, in constructive fashions. There was a real sense of camaraderie and teamwork at the time. Now you look back, and you look back to the group and you kind of wonder why, it was kind of really eclectic, that's probably being too mild when you look at the personalities.

JONES: Who do you have in mind?

WANG: I mean, Gary, Gary is different. Joanne Martinis, Richard Bartholomew, Walt Desmond, and they're nice people, but Joanne, in later years, became more of a thorn for people.

JONES: How come? It had to be her way?

WANG: Yeah, she's a pretty opinionated individual. You know, she was fine, I mean she was a key component in Hybritech being able to do what it did early on. There was, before I got there, what's his name, Curry, Russ, Russ Curry, he's another crazy guy. Someone was telling me a story one day about coming into the lab on a weekend and there was Russ Curry falling asleep on some table or someplace, because he had

too many beers the night before there while he was working. Bill Present was one of the technicians, who is now back in the Philadelphia area. He's pretty, at the time, he could be very abrasive. He's mellowed a lot. It was just a different group of people. All academic backgrounds, pretty much, except Dale Sevier, who had been at Bioscience Laboratories. I guess you could count that as industry, but really he was more in the research department, and they were a reference laboratory.

JONES: When you applied there, had he been there?

WANG: At Bioscience? Yeah, in fact, he had helped me get the interview. What had happened was, this is a pretty funny story. We were driving down to San Diego to look around for homes, and Dale was living in Valencia at the time, and we stopped by to say hello, and Dale was telling me, 'Hey, so and so, who was the director of R&D at Bioscience, was frantically looking for you. He called your house, no one was there. He was trying to get a hold of you, because he had called me and asked 'where's Bob,' I can't get a hold of him, and I want to make sure I don't lose him.' And I said, 'Well, you can tell him he's already lost me.' So, it was pretty funny, but Van Nuys was probably just as crowded then as it is now, or it seemed to be.

JONES: And that was a big part of your decision, even though Dale was there?

WANG: Yeah. Again, starting was more appealing than joining something which was already functioning.

JONES: And when you got to Hybritech, what kind of work did you start doing? How did you fit in with this group?

WANG: I was in charge of development, product development, so we started trying to develop, as I recall, the objective was that we needed to get our first immunoassay products out on the market, so IgE, that was the antibody that they had. I mean, talk about serendipity, I don't care what anyone says, you've got have luck, too, alright, in this, and it's got to come at the right time. So we start working on the assays and then about two months after I joined the company, Tom Adams was brought in, hired as the vice-president of R&D, and his sense was we didn't want to do any assays that required centrifugation, OK, that's how we came up, basically, the TANDEM system had been talked about, but we felt that, you know, that was experimental. We needed to work out some bugs, and what was the fastest, at the time, before Adams came, the objective was to get out as fast as we can. Well the fastest you can get out is using

more, using an assay system that required centrifugation, OK. When Adams came, he convinced, I think, Ted Greene, that 'No, you don't want to do that. Somehow, you've got be a little more patient, and you've got to come out with this other assay system that doesn't require the centrifugation.'

JONES: So speed in the assay was going to be….

WANG: Yes, simplicity, ease of use, and speed, OK. And that's where we had worked at the time. You know, working with these plastic beads or balls, that was new, and we were doing the different chemistries to it, and that's where I was real sensitive to non-specific binding, and sure enough, it made a difference whether or not you used antibody or didn't use antibody, but you still saw, you could still generate a lower quality standard curve, a much lower quality standard curve, by not putting any antibody in. OK, so there were issues with cross-specific binding that we had to resolve before we could really come out with that system. When Adams came, I think he bought us the time, and had the clout to say, 'OK, we're going to go with that system.' So we dropped all the work on the first system that we were working on, and devoted everything to the TANDEM system, and that's when I did all the experiments to generate the data for the TANDEM patent. And I remember pretty clearly, you know, coming in with the graphs and all the data and giving it to Adams, and then that going on to the attorneys, and that becoming the basis for the TANDEM patent. And we worked out, we had to scale up, oh, another thing was there were problems understanding how to scale up the modification process to the plastic beads that we were using, the styrene beads, and making sure we had all the sources, supply sources, for everything. So, that was a real challenge. But we worked all that out, developed the assay, and IgE was the first one. So, we were about ready to start our clinical studies, and we had this antibody to IgE, IEF-327, I think was the antibody, and we were testing it, and all of a sudden, one of the specimens that we collected, at the time, you know, it wasn't that sophisticated in regard to legal issues, and we were testing each other's blood, and I have allergies to a lot of different environmentals, and so, I tested my blood as one of the specimens, and I knew from testing with the Pharmacia kit, I had a fairly high IgE level. But, in our kit, my IgE level was below a hundred units per mil, and I knew it was closer to eight or nine hundred. So, that of course raised the red flag. We did some dilution studies and found out we had what is termed the high dose hook effect with my IgE, with my specimen. Now, we had tested other specimens which were a lot higher than my IgE level, and we did not see the high dose hook effect. So, there was something about the epitopes that those

antibodies were recognizing which ended up with a high dose effect in my specimen. What are the chances of that, you know? The guy in charge of developing the product, his specimen raises the red flag? And it was a mad scramble. We said, 'OK, let's go back and test all other positive clones that we had in different combinations. So we went through this thing and we found that IED-227, I think, was the final antibody which replaced the 327 antibody in combination with IEF-141. It's amazing how some of these numbers stick with you. So IEF-141 and IED-227 were the two antibodies that we ended up going with. But we were just about ready to go do clinical studies with the other antibody which turned out not to be a good antibody. So, we learned a lot about that process, and those were the two antibodies that we ended up going out on the market with as the first Hybritech product, TANDEM product. So, it was like, I mean, we were at the starting gate, ready to pull the trigger on this and set things rolling.

JONES: How far did that set you back, how much time?

WANG: I think a couple of months. I mean, it was a mad dash. But, fortunately, now, we had several other clones, and the reason IDE-227 was originally discarded was because the affinity was too low. But then, sure enough, when we ran our studies, we could show that our sensitivity with that antibody as the radio-labeled antibody was not as good as with the one that we were replacing. But, you didn't have the high dose hook effect, for whatever reason. Fortunately, in this particular product, we did not need, it wasn't an absolute necessity to have the sensitivity that we had with the other antibody.

JONES: This is IgE, the first?

WANG: Yeah, so that was, I mean, you know, we were close to having a major setback there, and we pulled the rabbit out of the hat. But you know, if we didn't have the additional clones, because if someone had discarded them, because they said, you know, 'We don't need them,' we would have been up the creek. But they had saved these old clones, and we went back and screened whichever ones were positive. I think there were about five or six of them that we were able to go back and look at.

JONES: Was there a whole library?

WANG: Yeah, well, the way the system was, was IE stood for, you knew it was an IgE. F was the fusion, so IEA, IEB, IEC, and so forth, each letter of the alphabet going down was the fusion. And what we said, OK, was, if you got to Z, and did twenty-six fusions, and you went back to A again, if A was unsuccessful and you didn't get any positive clones, you just used A again. If there were some IEA clones, then you would skip A and go to B, and go on, just recycle through that way because I mean, the vast majority of the fusions at the time were unsuccessful. You know, you had ten thousand clones to screen out of each fusion or so, you could have as many as ten thousand, depending on the selection process. And the first thing we did was screen to see if they were making any IgG, if they were making IgG, then we went and said, 'OK, is that IgG specific against the antigen of interest.'

JONES: Now you mentioned that when Tom Adams came, he bought time to work on the new assay…

WANG: Yeah, I think he saw that we needed to come out with something that was really different, that had significant marketing advantages, he convinced Ted Greene of that.

JONES: So, it was basically Ted Greene that he had to convince?

WANG: At the time? Yeah, you know, there's always the issue of having money. You know, we were running out of money at the end of '79.

JONES: Is this when the first….?

WANG: Hillman, Rockefeller, Stanford University, University of California, I think all their funds went in. As I recall, the company was looking to raise $7 or $8 million dollars, and they had $13 million of interest, which is good to have. Yeah, I remember at the time there were rampant rumors, because start-up companies? What are those? In '80? There were rampant rumors that Hybritech was running out of money and was going under.

JONES: Rumors within the company?

WANG: In the community. I would hear, you know, people would ask things like, 'Hey, what's happening to Hybritech? I hear that you guys are running out of money and are going to go under.' At the time, people didn't understand the process of venture capital. After Hybritech, people thought, 'Hey. It's a slam dunk. I'm going to

join a start-up and become very rich.' It's amazing, that mentality still exists today. People think that they're going to join a start-up company and more likely than not become very wealthy from the success of the company, which is just, unfortunately, dilutes the effort of a lot of employees.

JONES: Were a lot of people aware of Hybritech? Are you talking about the local research community?

WANG: Yeah, the research, the people at Scripps and Salk, Calbiochem was around at the time, you know, there was....I actually had someone from Calbiochem tell me that they heard the we were about ready to go under because we had run out of money.

JONES: But people were interested, they were watching what was going on?

WANG: I think enough, because it was something new, yeah. I mean, how many biotech did you really hear about back then? I mean, Genentech was still not...Amgen was struggling in the early '80s. Amgen almost went under, I think. It would be interesting to hear the Amgen story, because they struggled the first four of five years until they all of a sudden hit it.

JONES: Who were you working with on the new assay project? When you came in, in was to start something new, right?

WANG: Yeah, that was the start of new department. There was cell biology, there was research, immunochemistry, and then product development. And Bill Present shifted to work under me, as I recall. Bill Bermudas, and I hired Paula Van Hout. She got married and became called something else. She was somewhat spacey sometimes, she was on some kind of medication that made her spacey. I remember one time, walking into the lab at the old La Jolla Cancer location, and she was very consumed with what she was doing, and it's like, she was facing the door, there were shelves in the way, but you could see anyone come in. I walked in, came around, and said, 'Hi Paula,' and she jumped out of her seat, because she sitting there doing something, and it was like, I don't know where she was at, but it wasn't in San Diego at the time.

JONES: Was she a Ph.D.?

WANG: No, she had, she came to, I hired from Becton, I think. Yeah, I think she was up in Brea.

JONES: In putting together the product development team, were you bringing in PhDs to work on it?

WANG: Not at the time, no.

JONES: You recruited people from industry generally, rather than universities for this particular thing?

WANG: For product development, yeah, because the background and experience that you need in product development, if you brought from academia or a non-industrial position, you would have to teach them a lot, and we didn't have the time. The documentation, just all the different types of studies that you have to do, quality control, manufacturing, thinking about scale-up, and all that sort of stuff, isn't what you get when you're in a research position.

JONES: I talked to Jeanne Dunham, she was at Calbiochem when you were there…

WANG: What's her last name now?

JONES: Dunham. D-U-N-H-A-M.

WANG: That's her last name, now? She used to be Jeanne Van der [?] at the time. Yeah, she was in manufacturing, in fact, I think, I'm the one who put her together with Hybritech. I think Ted Greene asked me about who in manufacturing we might be able to get, and I think I suggested Jeanne.

JONES: Do you remember bringing in other people? How did your group grow?

WANG: Well, when Tom Adams came in, I didn't have to worry about it as much. I mean, he was responsible for managing all of R&D, and then after we got the money in 1980, I think the expanded, our product development group suddenly grew. Adams brought in Russ Saunders as Director. I ended up reporting to Russ Saunders. And our group, at some point in time, I don't remember when, it must have been late 1980, no, it must have been 1981, where we jumped from like ten people in product development to thirty, and it was very difficult to absorb that many people all at one. And we had a number of people transfer from cell biology and research, and we hired quite a few new people, Ph.D. level people, to be group leaders, and it was a real challenge to manage everything at the time. We ran into a few barriers. It was one of those phases. Start-up companies go through growth phases, and the dynamics of the

company change, and that was one of those times when the dynamics of the company really changed, I think.

JONES: What were the particular problems that you faced?

WANG: Well, you know, it's just communications, being able to work together, getting people to understand what the mechanism for getting things accomplished, the systems involved, making sure that, you know, for specific reasons, you evolve a certain system, like in screening antibodies, alright. Well, to make sure that people follow those systems and understand why you're doing what you're doing as opposed to just doing it, and then later on saying, 'Oh, it would be easier if we did this,' and then essentially negating the reason why you've developed this system, because you're trying to cover for say, non-specific binding, or some artifact that might occur. Things like that. I mean, eventually you lose a lot of that history and understanding, that knowledge base, when people move on, but at least to be able to disseminate as much as possible the logic behind the things that you're doing, and also maintaining the environment and culture that you've developed in the company. By then, probably, we started to, we were on the road to losing that real sense of camaraderie that we had originally. When we were at La Jolla Cancer, you know, we had those old trailers out in the parking lot, and when we put the first alarm system on those trailers, every time the jets flew over from Miramar, the vibrations would set off the alarms if they were on. That's how shaky they were. Dale will love this. It was a long walk from those trailers, for some people, over to the rest rooms at the main building, so out in back of the trailers was kind of a makeshift urinal. We had a lot of fun in those trailers. Some really funny things happened in there. Walt Desmond, have you talked to Walt yet? Walt is a great guy, OK, but he lives with what appears, to other people, to be disorganization. I mean, his desk would just be like, you'd look at it and you'd think that someone had rifled through all of his papers and just left a big mess, but that's just the way that he was. And one Halloween, I think it was Gary David went and got this fake cobweb and he taped it over his desk, and it looked great. It looked like no one had been there for hundreds of years, and all of these cobwebs were around. And Walt loved it so much that he left it up for a long period of time, weeks, months. And every time he wanted a paper, he would gingerly reach underneath the cobwebs and pull out this piece of paper that he wanted. We had some other funny things. I think this would be embarrassing, I wouldn't include it in any, OK, but Richard Bartholomew, you know, he has this birth defect, and so, you know, his clothes were all custom made by his wife at the time. You know, he didn't

have much money, he had a growing family. And, I guess he didn't wash his clothes as often as one might like, so he had a European aroma to him. So one day, Ted Greene comes into the trailer and says, 'Geez, what smells in here? It smells like a gymnasium.' And Walt and Gary and Dale and I are sitting there going 'Shhhh!' You know, Richard was down at the other end of the trailer, and we explained to him what the problem was, and Ted says, 'Well someone ought to talk to him about this.' And since Richard reported to Gary, it fell upon Gary's shoulders to talk to Richard. But that was one of the more humorous situations that existed there.

JONES: Can you think of any others that I might be able to use?

WANG: Oh yeah, there was one. It was in, when we were doing the financing in 1980, they had the investors come through and look at what we had. They were walking through the trailers.

JONES: These were the venture capitalists?

WANG: Yeah, yeah. Venture capitalists. This particular group happened to be Hillman's group, and we had a young lady as a secretary. I've forgotten her name, but she worked for Linda Halter. Now, Linda Halter was your more assertive type woman. She was divorced and had, I think, two sons, her older sons had given her some problems that she had to deal with, but Linda also was the type of woman where if someone put a hand on her and she didn't like it, she'd haul off and give you a fist to the face, probably. But this young secretary was working under her in the trailer. We had two trailers by that time, and they were in the trailer right across from ours. She was in the trailer, and apparently was bending over at the word processor, doing something, and I think it was Hillman's entourage of investment bankers came through and one of the guys pinched her in the butt, OK? And she didn't know what to do, and so she went to Linda Halter afterwards and said, 'Listen, this guy came through and he pinched me in the butt while I was bending over.' And Linda said, 'She did! I want to kick the guy in the balls!' So, that was one of the things that I recall.

JONES: When your department started growing and incorporating all of these new people coming in the door, did this correspond to new kits going out the door?

WANG: Yeah, I think that was late 1981. We finally got it approved. I remember when we submitted the 510K, all the studies and everything, we submitted it to the FDA.

The FDA was very cautious. Really, for them, for the FDA, it's safer not to approve anything. And if it wasn't for pressure from Congress, they probably wouldn't approve anything. We ended up having to go back there, giving seminars to them, and just educating as to what monoclonal antibodies were, and, I mean, today it would seem ridiculous, but they were afraid of some unforeseen problems arising by substituting polyclonal antibodies with monoclonal antibodies. So, they were very slow to approve our application.

JONES: This is for the first one?

WANG: For IgE, yeah. And we sent back, in fact, Ted Greene had the IgE FDA submission, the 510K, copied and bound for a number of people associate with the project. I still have it someplace.

JONES: Can I have a look at that?

WANG: Yeah, if I can find it. I have that one and PAP was done also. But we submitted a lot of scientific articles along with it. A lot of extra additional, this was a pretty long 510K submission. You know, 510Ks used to be pretty short. You could make them pretty short. Basically, you just had to show that you were equivalent to a product that was out on the market by doing a clinical study and showing that you measure the same levels in different people.

[Tape ends]

WANG: This guy Nino Hipolito. Here's another funny story. Ted Greene is real big on Ivy League graduates, OK, and Nino Hipolito was at the FDA at the time, and he was fairly high up, and I remember Tom Adams was telling Ted Greene, 'Oh, yeah. The guy there, Nino Hipolito, is in charge of this and this, and he's from Colombia.' And Ted goes, 'Oh, good! An Ivy League man!' Tom Adams looks at him kind of funny and says, 'No, Colombia, South America.' But that was Ted's mentality. Anyway, I remember I went to a cancer meeting up in Banff, Canada, a beautiful place, of course, and Nino was there and I spent an hour or so talking with him, and he was pretty favorable and Tom Adams had been back to meet him several times in Washington, so he helped us educate the FDA as to the advantages of monoclonal antibodies, and what potential pitfalls might arise, if any. And to show that the balance was in favor of replacing polyclonal antibodies with monoclonal antibodies. So, that submission finally got, I don't know, was it in June of 1981 that it got

approved, somewhere around that, I believe, and just before it got approved I think we may have submitted the PAP 510K also, but, yeah, Russ Saunders and I basically worked as a team, even though he was my boss. Russ is a great guy, originally from West Virginia, which we tease him about all the time, but we worked as a team, and we got the 510Ks, I mean, we did everything. We developed the original assay, developed the chemistries for preparing a lot of the reagents, scaling them up. Of course, development, a lot of the development stuff was just a team effort, from everybody, from cell biology and immunochemistry, but scaling up, we were really responsible for, and that was a real challenge, especially working with a lot of the concentrated acids that we were for preparing the solid phase substrate. And we set up all the clinicals, ran all the clinicals, collected all the data analyzed all the data, put together the 510K and submitted it, got the manufacturing processes all set up, I mean, we did everything. QA, QC. We had to set all that in place, and it was a lot of fun, but like I said, if we had gotten people from academia, it would have gotten done, but it would have taken a lot longer, and there would have been a lot more holes that we would have had to go and fill. But that was the first one, IgE. Not a great medical contribution, you know, but it certainly demonstrated, I think, the power of monoclonal antibodies and the TANDEM assay system. So, PAP was next. I was in charge of the PAP. In fact, I was in charge of all the, IgE, PAP, prolactin, PSH, and HCG, were the first five, and ferritin. Ferritin was the only one that I had very little to do with. I think we transferred that to Dennis Muriyama. HCG got transferred, I forget who got HCG. I did a lot of the early work on HCG. I had Irene Shimuzu working for me, who was very good, but kind of, personality-wise, in the mode of Joanne Martinis. The word begins with a B. Could be very bitchy, but very good at what she did. We hired her husband, too, Stan Shimuzu. We had Isaac Mizrahi, Lyle Rice, Jim Myrtle. I think by then, Dale had switched out of product development into the marketing group.

JONES: What was his role in product development?

WANG: Well, he had been associated with the IgE project and Tom Adams and him had some differences of opinion about things.

JONES: About the product?

WANG: No, about what Dale should be doing. And so, Dale had a real bug for computers. Tom Adams, even today, doesn't have much to do with computers, and

Tom viewed Dale's extra, the time he devoted to working with computers as being a waste, and then even if he did it in his off-time, he would rather have him put those extra hours into working in the laboratory, and Dale just didn't see it that way. So, he moved into technical services.

JONES: Do you recall putting together manufacturing QA and QC, having discussions with persons from different companies saying, 'Well, you know, at Calbiochem we did it this way, or…?'

WANG: What happened was, there was a guy who used to be at Calbiochem who was in charge of the QA, QC, and he left there, and he was a consultant. They hired him to come in and put together the original QC system, the documentation system, so he did a lot of that, putting together the documentation system. So, you kind of followed that, but obviously, the actual systems that were implemented and used were hybrids of the various experiences of the people who had been in industry. But there wasn't, or at least I can't recall anyway, that there were people who were insisting that things had to be done a certain way because this is how we had done it at Calbiochem, or this is the way we did it at Technicon. I mean, as long as it met the need, it was done, I think, if it seemed efficient.

JONES: But people are grabbing things…

WANG: Yeah, in some ways, and a lot of it was new, so this is the way we did it, but you know, when we had an FDA inspection we were fine.

JONES: What aspects of it were particularly new?

WANG: The whole manufacturing thing. You know, you develop a manufacturing process keeping in mind that it can be scaled, its economical, and then you have to write all the manufacturing documents in way that people can follow it, implement adequate controls for reproducibility lot to lot, but also not making it so cumbersome that it becomes uneconomical or that there are a lot of inefficiencies in it. That's a challenge, and when you're creating something, when you don't have a template to follow, then you know, you're kind of guessing along the way, and you have to do it somewhat empirically, and you know some of the things that you put in there, you find that, 'Oh, this isn't really necessary.' But it may not be necessary from a practical standpoint, but it may be necessary from a regulatory point of view. So, there's a lot of balancing that you go through. We had a lot of revisions of documents, plus the

process, you have to realize how fast we developed the overall processes. We basically, in a period of two or three months, worked out the bugs in processing the solid phase substrate and preparing it for coupling antibodies, and I always knew that there was, that we didn't put a real good effort into making it a robust system and as high-quality as we could, but we didn't have time to go back and improve the system. We built this whole system basically on the solid phase which Billy Present had put some work into on his own, but he was a bachelor's degree level person, and then two or three months of me being involved in saying, 'OK, we're going to do all of these different things.' And this is the foundation of the TANDEM system, and I mean even after I left Hybritech in 1986, I mean, they were still using that same chemistry, the same process that I developed from doing, like, ten to a hundred beads, to doing ten thousand to a hundred thousand beads. Now you can imagine, a hundred thousand beads may take up to a fifty to a hundred liter volume container, because there's a lot of void space in between each of the beads, right. And you had to dip this thing into concentrated sulfuric acid for a defined period of time, take it out, dip it into nitric acid for a defined period of time, then dip it into water, and then dip it into concentrated HCL stannous chloride solution, and you don't want to mix certain acids, number one, and number two, the weight of this thing, a hundred thousand beads, I mean, you're talking several hundred pounds that had to be lifted up. You're not going to have people doing it, because it's too dangerous, but then you had to figure it out, and then these are all concentrated acids, what are you going to use to hold several hundred pounds. You can't use metal. Even certain stainless steels, especially with hydrochloric acid, certain stainless steels still get eaten up. And there's an expense, too. You know, the containers are so large, how much does it cost to buy a stainless steel container like that? Then what do you do with the acids after you're done? We never figured out, can you reuse the acids? Eventually, in later years, I did some experiments to show that, yeah, by far and away, if you look at the mole equivalents that were being consumed, you know, by the chemical reactions that were going on, you could reuse the acids a lot of times. And we started reusing the acids two or three times, but people didn't want to take the chance of using them more often than that. We started to see some changes. So, we did start to reuse, but disposal of the acids afterwards was a real challenge. And Hybritech, one time, did have a leak of one of the acid drums. It got into the front page of the B section of the Union, I think.

JONES: Once you got this system sort of in place with the first kits, was it more or less a cookie cutter thing with the others?

WANG: In terms of the format of the assay, yeah. But each antigen that you're testing for, you've got different problems. You know, you're working with different antibodies. Some antibodies are affected by what you call serum effects, and there's something that interferes with the binding of the antigen to the antibody. You don't know what it is. Something may have a similar epitope that antibody recognizes. So, from the standpoint of the format, yeah, we tried to make everything the same because that was, again, a marketing issue, but there's probably a family of potential pitfalls that you have to look out for in developing any product, any immunoassay product, and you have to go through all of these things. Some antigens maybe are more apt to bind non-specifically to the solid phase than others, and some antibodies, also, so you have to deal with all of those sorts of things.

JONES: Russ Saunders came in because of his experience with radioisotopes?

WANG: Yeah, he was at Warner-Lambert, and he, again, still, I was the only one with real industrial experience, and Tom Adams felt that we needed more people with industrial experience. Russ was a good addition.

JONES: Did Tom Adams know him? Did you know him?

WANG: Tom knew him, I think from Hyland somehow. I didn't know Tom Adams, even though we had gone to the same graduate school. He left a month before I started at Riverside. I knew the name, but I never met him.

JONES: What was your impression of Tom Adams when he came?

WANG: Nothing stands out.

JONES: What about Russ Saunders?

WANG: A good ole boy. We pulled a lot of pranks on him, trying things. One of the things, I don't know, I never heard the outcome of it, it would be interesting. One time, when we were still in La Jolla Cancer, Howard Birndorf was kind of the butt of a lot of jokes because of his abrasiveness, and Howard's always on the phone, and he'd have to call you on the phone. I couldn't understand that. You know, why doesn't he walk over and be more personable? So, one time, I walked into his office when he

wasn't there, and I took the mouthpiece off, and I put a piece of tape between the contact and the mouthpiece, so you couldn't hear Howard, you know, but he'd be able to hear you, so whatever you said. I never knew what happened, he never said anything. He never complained and said, 'Who the hell did this?' You know, that would be Howard, but he never said anything. But that was one of the things. You ought to ask him if he remembers. Don't tell him who did it, just ask him if he remembers. But Russ is very personable, an easy-going guy, and I've hired Russ twice since then to work for me.

JONES: What happened at Hybritech after this period, putting out these kits in '82, '83?

WANG: I left the diagnostics part because Tom Adams called me into his office one day and said he had an offer for me that I couldn't refuse. And they needed help in the operations area to improve the product quality, improve the reproducibility of lots, improve the product transfer process, so I got transferred to operations under Ron Taylor. And basically, I was pretty independent. Ron Taylor just more or less let me do what I wanted. I was responsible for transferring new products in, from product development into manufacturing, making sure all the documentation gets done, that the processes are scaled up and reliable for use in the manufacturing environment. You're working with people who just follow a recipe in manufacturing, less so than say, in a circuit board, Qualcomm type situation, but still, if there's a problem, these people aren't supposed to think and say, 'Alright, this is how I'm going to fix it.' They're supposed to ask for advice. If it's a mechanical problem, then maybe they can fix it. So, I took over that, and basically they didn't have anybody doing that, so I had to build again a new entity, a process development and product transfer group. I hired two or three people in for that. I supported, anytime they had problems with QC, I helped them. Manufacturing, if they had a problem making a product, I had to figure it out. I tried to make all of the manufacturing processes more efficient to cut costs. Then, the famous ICON project came along, and that was a another team effort where Gunars Valkirs had this assay where he had a hand punch and a hammer and he was cutting out these disks, and he only needed a couple dozen, and we had to turn these things out by the millions. You know, how are we going to do this? So I worked out a scaled up process at Hybritech for the ICON. And, you know, when you needed all the little plastic holders, we needed to source out absorbing material, the film he was using, the whole processing. He used to string up the film in the laboratory, like on a clothesline, and he only had to make a few hundred of these

disks, so we're trying to figure out how we're going to make hundreds of thousands to millions of these things. And then we had to dry them and process them, and make sure they were uniform, cut out the disks, and then assemble everything. And a lot of the mechanical devices that were developed for the assembly part, I worked with the engineering department, and they figured all that out. But the chemistry part, and the scaling up of all the chemistry part, manufacturing, to get all of the components made for assembly, I had to work out. And we went, as I recall, from January, where this was a product concept, we had a little meeting with Cole, I think Dale was there, Gunars, myself, maybe Russ, a few other people, no one higher than the director level, and we said, 'Let's do it, let's push it,' to September, in pushing our first lot of product. And this was a completely new manufacturing process with a lot of parts that we didn't even know how we were going to make. And we got the first product shipped out September 30th, so, on the books, it got to count as product sold, and there was this thing, you know, you've got to make the end of quarter numbers look a certain way, and so, I guess, for accounting practices, if you shipped it by then, you can count it as sold.

JONES: Was a lot of this manufacturing done in Tijuana?

WANG: Not at that time. This was all done, we didn't have time set that up. I got the product like probably, to scale up, I had to figure out how to scale this thing up to make a hundred thousand of them. You can imagine going from a hundred to a hundred thousand, how to do this. I had maybe three months, three to four months to do this. You know, we got it done, though. It probably saved David Kabakoff's job.

JONES: Was he in trouble?

WANG: No products were coming out.

JONES: I've seen the ICONs, how were the earlier tests packaged? Were they just reagents?

WANG: Yeah, there was a box of reagents, and then a box of ICONs, and they were shrink-wrapped together.

JONES: I mean the earlier kits, the TANDEM kits, what did those things look like?

WANG: Oh, there was a bottle with beads in it. Everything went in one box, so you opened it up and there's a row of different size bottles, and one big bottle with beads

in it, and then people supplied their own other apparatus. One time, someone, I think from UCLA, someone had taken one of our TANDEM kits from the laboratory, the radioactive kits, not the ELISA ones, and determined that it wasn't worth anything or something, and just threw it out, disposed of it in a park in Santa Monica, and we got this call, something about Hybritech's radioactive products out there. And, of course, they had the Hazmat team out there and everything, and the regulation is you can't put more than 10 microcuries of radioactivity in these diagnostic kits. It's exempt if it's below that. It wasn't a hazard, but they didn't know, because it had the little radioactive symbol. Yeah, we had another incident with that, too, where Jim Frincke sent some, I think it was indium-labeled antibody back to Johns Hopkins. This is our near-genius, and along with his technician, who was Dean Tallam, who did not have a biology degree, the guy was not what you'd call one of our top technicians, told him to pack it and send it back there. Well, he packed it in a lead pig, which is a lead container, with some kit wipes, like Kleenex. And then he put this lead pig in a box and just packed paper around it. Well, this lead pig probably weighs about five pounds, right, in a box with paper, and he sent it out. Well, obviously, the lead pig rattled around and smashed the paper down, compressed, so it's loose in this box, and banging around, the glass tube which the indium-labeled antibody was in broke inside the lead pig and leaked out. By the time it got to JHU, it was wet on the outside. The RSO at JHU puts a monitor up to it, the thing just pegs the monitor, right. This thing is hot, whoa! Because this is part of the regulations for handling radioactive material. So, of course, she's required by DOT regulations to call FedEx, who shipped it. FedEx, then calls Hybritech, and the DOT. The DOT gets on our butts. The DOT threatens to fine us. Well, what they did, they had to go back and track, DOT had to track which delivery truck took it to JHU, what airplane flew it from Memphis to Baltimore, what truck carried it to this FedEx place in Memphis, and all the way back to where it was shipped from, Hybritech. And I heard a rumor that they had to close down one of the conveyor belts at the FedEx facility in Memphis, so that DOT people could monitor to see if it was contaminated. And, fortunately, I didn't hear that there was any other contamination, other than maybe at the end, maybe that was when the vial had broken, and the box was wet at Johns Hopkins. So, think of how money that cost. I don't think that Hybritech ever had to pay any money to cover the costs, but that was another incident that was pretty severe.

JONES: Taking the job in operations, that was moving ever farther away from the basic research that's going into this. Did you ever hesitate about doing that?

WANG: I probably hesitated at the time, but, naw, I'm more, product development and operations is probably more of a strength. Research, I'm OK, but I think the results of research, actual research, are too long term for my type of personality. I like to see something which is more tangible.

JONES: Whether working product development or operations, did you ever do stuff for the in vivo people?

WANG: I'm sure we helped them do some things, but nothing big.

JONES: Not a lot of interaction, this was like a separate part of the company?

WANG: It really was. It was one part making money and another part spending money.

JONES: Did that generate tensions, or friendly competition?

WANG: I don't think it generated any tension. I think people were still working together.

JONES: Well, Gary David was over on the other side, he was a good friend of yours.

WANG: Yeah, I think the tension was probably more with marketing. It's always between marketing and R&D. You know, marketing wants the products to be a panacea for every ill in the world. Marketing wants manufacturing to have perfect products made every time, and now, not late. Same old stuff.

WANG: The reality of it is, Ted Greene did not start Hybritech. He was brought in. And a lot of people contributed at the director level and below. You know, the vice-presidents got honored, you know, they made a contribution.

JONES: Are you referring to the Chamber of Commerce thing?

WANG: Yeah, but even subsequently, you know, they've all gone on to other things, but, oh yeah, you know, they really contributed to Hybritech. Well, I'm saying that they contributed, but I think that the people who really made were at the director level and below, working as a team, people put their egos aside for a period of time, it

didn't interfere with accomplishing what needed to be accomplished. I think the vice-presidents, had a lot of, there was a lot of in-fighting concerning who got credit for what. And you know, they went on to do other things, and they can list on their resumes that they were an integral part of Hybritech in helping it to become successful, but no more so, and probably less so, than a lot of other people who were at levels below them, in my opinion. And people made a lot of mistakes. I think a lot of the vice-presidents, you know, their mistakes are much more obvious, but we waded through them. But again, the team that we had to actually do the work, I think was the core.

END INTERVIEW

Recommended Citation:

Wang, Robert. Interview conducted by Mark Jones, October 21, 1997.
The San Diego Technology Archive (SDTA), UC San Diego Library, La Jolla, CA.

The San Diego Technology Archive (SDTA), an initiative of the UC San Diego Library, documents the history, formation, and evolution of the companies that formed the San Diego region's high-tech cluster, beginning in 1965. The SDTA captures the vision, strategic thinking, and recollections of key technology and business founders, entrepreneurs, academics, venture capitalists, early employees, and service providers, many of whom figured prominently in the development of San Diego's dynamic technology cluster. As these individuals articulate and comment on their contributions, innovations, and entrepreneurial trajectories, a rich living history emerges about the extraordinarily synergistic academic and commercial collaborations that distinguish the San Diego technology community.