Walter Desmond

Interview conducted by

Mark Jones, PhD

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Walter Desmond

After receiving his PhD in biochemistry from UCLA in 1979, Dr. Walter Desmond went to work for Hybritech for over twenty years, where he contributed to the development of TANDEM and ICON technologies and other important developments. He went on to work in the San Diego educational field with Lincoln High School and the Science/School-to-Career program, and as a board member with the San Diego Science Alliance.

INTERVIEWEE: **Walter Desmond**

INTERVIEWER: **Mark Jones, PhD**

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JONES: You were in Gordon Sato's lab at UCSD. Did you do anything with hybridomas there?

DESMOND: No.

JONES: So this was new?

DESMOND: This was new.

JONES: Had you paid attention to monoclonal antibodies?

DESMOND: I was aware of it. It was kind of a glamorous thing, and I was aware of it. P eople sort of talked about potential applications, but it was kind of exotic, a special branch of cell biology.

JONES: But when you were doing this at Hybritech, there was nothing particularly exotic about the technique?

DESMOND: Nothing. The reason I went there is I had a lot of experience in cell biology laboratory techniques. That's the sort of the basis. The basis of the cell biology part of monoclonals is just, the cell biology is 90% overlapped with other areas. Now, a big part is not

the cell biology, but the chemistry and the immunology. That was stuff that we were sort of developing.

JONES: Where do you get antigens? Was it common just to ring somebody up, or were these things that you could purchase?

DESMOND: There are a lot of sources. Many we would just buy.

JONES: Standardized?

DESMOND: Yes, standard stuff. And there were a lot of collaborations with people who were experts on a particular protein, so that would be another source - the people that were doing that work and who had particular expertise on characterizing and purifying those proteins. Some of them we would prepare ourselves. We had a chemistry department that did that.

JONES: At that time it was no problem transferring materials? These are people at UCSD, Scripps, or Salk?

DESMOND: You mean collaborators? Yes, mostly local at first, and then it sort of expanded to people all over the country. And typicallyit was a collaboration, I mean, we needed their antigens and they needed our antibodies.

JONES: So you would give them antibodies or they would purchase them?

DESMOND: Not in the early stages. The early stage was really mostly non-commercial. I think it's like the process everywhere. You start by making research products that you're making in the lab anyway. You bottle them and you sell them to people other than collaborators. So, for a couple of years, there were some products, but they were research products. Typically, they would be things that we had anyway and we'd be sharing them with a collaborator, and we

had it, so why not sell it to other people? But I don't think that commercial - I know that it wasn't the objective.

JONES: What about getting mice? Where did you get them? You needed a lot of mice. Did you have problems finding suppliers as it grew?

DESMOND: No, there are commercial suppliers where that's their business. I mean, that's always a thought that you had, when are mice going to be limiting? But there are also other uses out there for other things. There were suppliers that could easily expand to produce all of them, particularly early, even local ones. I would say that it was never a problem.

JONES: When you arrived in '79, '80, some of the publications typically use statements like, you know, Joanne Martinis came from Wistar, and the papers would refer to the "Gerhard technique," or others paper say, "essentially as described by Kohler and Milstein." So early on, you really used the published techniques?

DESMOND: You know, I used to say that the biggest secret was that there was no secret. I think that the main advantage that you have is in the antigen, the sort of data on the antigen and systems for deriving information. And another big, I can't say secret, another big requirement is efficient screening procedures, so that you're working with animals that have the cells that are going to be potentially productive without all the rest of them.

JONES: So for that you were using Gary David's assay for screening monoclonals?

DESMOND: Yeah, yeah.

JONES: And you used that throughout?

DESMOND: Well, I don't really think it was, I mean, he was responsible for the chemistry department, and he was responsible for putting the assays into place, but again, they were generally state-of-the-art procedures.

JONES: Well, he published something while he was at Scripps on a semi-automated radioimmunoassay. Were you using radioisotopes for this?

DESMOND: On some things.

JONES: Did you ever go to enzymes?

DESMOND: Sure.

JONES: For different purposes?

DESMOND: Yes. I'm trying to think. I think part of the strategy would be, a lot of times you're using assays in your development, or in research, or even in the cell biology-related part of the product that are related to the assays that are going to be the product. It makes sense for a lot of reasons. First of all, you'd be developing your research assays, and information gathered from that will help in the development of the product. And the other thing is if your assay is going to be an enzyme-linked, an ELISA assay, ultimately, you want to make that the antibody works optimally in that way right from the beginning. And ideally, you would be testing whatever you made in the final product format.

JONES: So you used a lot of different techniques?

DESMOND: Yes, mainly enzyme and radioimmunometric assays.

JONES: This is a long process from immunizing the mouse to finally having a useful antibody. What kind of time frame?

DESMOND: There's a range. At that time, I remember, there were difficult and easy antigens, I guess. I would say that it's one to two years for getting the clones. That probably sped up as we learned more. I think we used to say, one to two years for getting the clones you wanted. You would hope a year of product development, so two to three years for developing, from the beginning to the end, to having a product. Now, much faster than that if you're just making a research antibody. So, yeah, I'd say one to two years. Some of them probably took three years.

JONES: Did you have any problems once the techniques for fusing cells sort of became standardized, where you could rely on it, or did you run into problems with different antibodies, different cells?

DESMOND: I think overall that we were reasonably successful with the standard technique. There are lots of tricks for essentially for increasing the immunogenicity of the antigens. Those are tricks used in immunizing animals. The actual cell work, I would say, overall, would be pretty much the same. There were a lot of ideas for changing the basic cell biology, using different myeloma parents, there's always an interest, there continues to be an interest in making human antibodies using human parents. And a lot of that stuff now has sort of been obviated because of exotic genetic or chemical techniques. At that time, there was a lot of thought about different cell parents.

JONES: Were you going out and trying out different cell lines?

DESMOND: Yeah, we continually did that, against this background of the kind of standard technique. In probably every area of the hybridoma production process, fusion and so forth, there were always attempts to enhance those, particularly in the screening area. We had a substantial development process all the time going on, with people assigned to specific projects for looking at different myelomas, or looking at different fusion conditions. So there was a continual effort.

JONES: Do you remember particular improvements?

DESMOND: Well, we did make some human or human/mouse hybrid antibodies. There were a number of cells that had an improved myeloma parent that didn't make extraneous light chain, which was one issue. So there were, for sure, clones that were derived from those things.

JONES: When you made these changes, were these things that got published?

DESMOND: No.

JONES: Did you keep them as trade secrets?

DESMOND: I guess you would call them that. At that time, when we were really into the production of diagnostic products, we really didn't publish stuff, and I suppose it was primarily for trade reasons. You know, I'm sure that was the reason, and also we were really just focused on getting product out, and so there wasn't a lot at that time. We certainly didn't publish anything on technique improvements. That's for sure because it was proprietary information.

JONES: Early on, to purify the antibodies, you used precipitation techniques?

DESMOND: Yeah, but I wasn't really involved in that.

JONES: That was farther down the line?

DESMOND: That was just all the chemistry people. Essentially at that time it was Gary David and Dale Sevier's business. But we used standard techniques. Column and precipitation was one of the steps, and it was a standard one.

JONES: What was the division of labor then? Would you give them the clones?

DESMOND: Immunochemistry did things that worked on the chemistry of the immunizing antigens. There was quite a bit of effort there before immunizing. By the way, another area that I forgot that we really put a lot of effort into was in vitro immunization. I'm not sure that ever resulted in products, but it was certainly a big effort. Anyway, in the immunochemistry department, the other job was to take antibody that was produced in mice and purify it and characterize it. A third big job, one in between, was to develop screening techniques. So, they actually would do the screening of the cells that were still under development. So there was a kind of chemistry, and then was a screening process which is more of a chemistry aspect of it. I was involved in just the cell biology, the immunization, the cell culture stock, and antibody production in mice.

JONES: And then purifying that, the ascites...

DESMOND: Well, we just sent that stuff and they'd do the rest. They did it by precipitation and column chromatography.

JONES: When they needed antibodies for in vivo work, for imaging or whatever they were doing at the time, did you have to do certain things or special steps?

DESMOND: No. Well, yeah, actually a lot, in retrospect. A number of the antibodies that we used, particularly in the beginning, were existing diagnostic, in vitro diagnostic antibodies. I mean if they would recognize the antigen while they were on the plate, or on the ball, they would also recognize it a person. A number of those products were the same antibodies already developed. In vivo products have enormously different requirements for manufacturing, for production, and orders of magnitude more complex, expensive, and demanding requirements. Ideally, you start doing all of that stuff right from the very beginning in antibody production. And some antibodies were made specifically for the in vivo diagnostics, so those were the antigens that were cell antigens that we would be preparing. I

would say that as we got more and more into that, you would just realize that there are just more rigorous record-keeping demands, and maintenance of the archival cells, and so forth. I think I would say there are a number of reasons why: there's only a subset of antibodies that you would make that would work for in vitro diagnostics that would work in vivo, the immunigenicity of them when you would inject them, the stability, specificity, and selectivity are all much more critical. Essentially you would have to make a lot more clone cells.

JONES: Was there a lot of talk between cell biology and people using these antibodies down the line?

DESMOND: Yeah, there was certainly communication, and I think it was, you know, 'We have a whole array of antibodies, let's try them out.' We would hear that some of them would work really well, and some of them that worked really well in vivo that may not be a good choice for in vitro tests. There was a lot of interaction there in trying them out. In many cases, we went back and made more, did more immunizations and fusions in order to make better antibodies. In a lot of cases, you know, we had the antigens, say, colon cancer, there's an antigen that's used in in vitro assays a lot, CEA. That is one that makes sense, you can see it in the blood and also the cell surface. But there are other ones only on the cell surface, or other ones that are on the cell surface that aren't the most obvious one that you would be using in in vitro diagnostics. That would be like the second generation of antigens or cancer markers. So, that would be the other thing with the existing antibodies – continuing the campaign to replace them, or get other ones for the same cancer cells.

JONES: Do you remember when they stopped using T101, Ivor Royston's original antibody?

DESMOND: No, I don't. It would used for quite a while as an in vitro diagnostic, and I certainly don't remember. There were some ideas about in vivo use, but I don't know. That's a good

question. It was around for a long time. It was actually used, I believe, in some therapy trials, but that's a little hazy.

JONES: Now tell me if I have this right: in making bispecific, would you be using two fusion steps?

DESMOND: There are a number of ways. The easiest way is to just make them chemically.

JONES: Were you doing this initially?

DESMOND: Yeah, for sure, because that's most obvious way, you take and disassociate it and then you reassociate it.

JONES: But there are problems with that, denaturing the antibody?

DESMOND: Yeah, any kind of in vitro manipulation is not so good, particularly for, you know, those injectable uses. The other way would be to take a hybridoma and use it as a parent and fuse it with lymphocytes that are making the other antibody. The other way would be to fuse two hybridomas. Actually, that's the best way. I'm sure that we did all of these things. The good thing about using two hybridomas is that you already have the antibodies characterized. When fusing a hybridoma, you have one of the antibodies characterized. Then you're just hoping that among the lymphocytes, you're going find some that are making appropriate antibody. And then the other way would be genetically, I guess.

JONES: But this was later on.

DESMOND: Right. Yeah, so we certainly did those two things, hybridoma-hybridoma fusion, and hybridoma-lymphocyte fusions, and by that time, that was really kind of specialized. There were groups that were working on those and it actually wasn't me.

JONES: This was after you left cell biology?

DESMOND: Well, I was involved with those to some extent because we were making them. There was a while where I was involved in those through operations in cell biology-that would immunizations and antibody production.

JONES: With the bispecific antibodies, did any of those ever go into a product?

DESMOND: I think not, but I can't remember. One great idea was CK-MB, creatine kinase.

JONES: There were kits made for that?

DESMOND: Well, there were kits for sure. But, you can use a CK-M and a CK-B antibody-more exotic - but in some ways a more efficient way would be to have MB antibodies. I don't remember.

JONES: As time went on, people started coming up with different methods for fusing the cells, electrofusion, for example, did you ever try that?

DESMOND: I didn't, but there were people I remember doing that.

JONES: Did you ever use that for production?

DESMOND: Probably not.

JONES: And people were working on recombinant techniques, with bacteria spitting out antibodies?

DESMOND: Right. I didn't work on that at all, and I don't believe there were any products from that.

JONES: Did they set up an operation for making antibodies that way?

DESMOND: No, not large-scale, I'm sure.

JONES: They were just trying it out to see if it might work?

DESMOND: Yeah, I would say it was mainly a Gary David department. I would say mainly research and development into techniques that could be used for that. Again, I'm pretty certain there were no products. But there were also a lot of genetic manipulations which were sort of to address not the antibody specifically, but things like the label on the antibody, and so forth. In other words, getting genetic, you could envision making hybrid antibodies that already had the group that recognized it, instead of having to do chemical manipulations afterwards. So, there was a whole range of great genetic ideas to either replace chemical modifications or the biological modifications. I have to say, sadly, I wasn't really involved in that at all except just to be interested.

JONES: Well, you were involved in trying to scale up in vitro production.

DESMOND: Yeah, the early stages.

JONES: What were the deliberations surrounding that? Who was talking about it?

DESMOND: Well, I don't know who. Certainly, manufacturing people, regulatory people. You think about, 'Well, can you grow?' 'How big can your mouse colony be?' We had to start thinking about antibodies for injections where the production system had to be more controllable in some ways. There was also a huge technology in large-scale culture for all kinds of things like antibiotics and any other medical products. And we were, by that time, connected with Lilly which had enornous technology for doing that.

JONES: But up until Lilly bought the company, you were still using ascites fluid?

DESMOND: Oh, for sure.

JONES: Had you talked about switching over?

DESMOND: Oh yeah, but I can't remember exactly when, but we were certainly looking at in vitro production all along, from the very beginning. But, then, sometime around that time, and I can't remember exactly when, I did the first steps, which was a pilot scale, larger than normal scale, of so-called fermentation methods.

JONES: There were lots of different things to try, right, like hollow-fiber?

DESMOND: Originally, it was a so-called fermenter that stirs the cells the way they grow yeast and bacteria, and so forth, with some modifications for mammalian cells. And that was certainly the first, that was what we did first, and the first idea. The problem there is that your product is very dilute, your cells are very dilute. Mammalian cells would be much more dilute than bacterial cells, so therefore...

JONES: Is that because they need to have a different kind of medium?

DESMOND: Well, yeah, they just don't grow well at high density. That's their characteristic. In some ways, they don't grow in suspension. That's not the normal way for mammalian cells to grow. So that was always the debate. Although the mice may be smelly and inconvenient, they were also very efficient little producers. They had like a hundred fold higher concentrations. Concentration, of course, is the whole name of the game. Because the efficiency of operations, with a hundred times higher concentrations, you need a hundred times lower volume of materials, tanks, and media, and so forth. So along that line and along that time, people were thinking of ways to get the cells up to higher densities, so hollow fibers, encapsulated cells, and so forth. The whole idea of all of those was to get higher densities of cells that would still grow and produce, and therefore yield higher concentrations of antibody.

JONES: So, you were looking at all these things and did you try them out somehow?

DESMOND: Yes.

JONES: You brought in equipment?

DESMOND: Yeah, on small scale. And we talked to companies that did it large-scale. We actually had contracts with a number of places, including arrangements with Lilly, and outside contracts, to produce in vitro.

JONES: They would do the scale-up for you and would manufacture the antibodies?

DESMOND: Yeah. Certainly for a while, we didn't have the facilities there. Then when we were part of Lillyandit made a lot of sense to work with them. But eventually we ended up in the manufacturing department with in vitro production, reasonably small-scale, but still much larger than pilot scale. So, there were some antibodies produced at Hybritech. And then, I believe, right toward the end, they were back into the making. Most of that was in the stirred-tank.

JONES: Was that continuous or batch?

DESMOND: It was batch. Continuous is another real great idea. In fact, a lot of the hollow fibers and things like that are more or less continuous, it just keeps them going. It's not a very natural thing for cells. But at Hybritech it was basically batch. They stop making antibody or they die, and you would change the mixture. And right at the end, they did have some hollow fiber production.

JONES: So when the Lilly people came in, they had a lot of expertise in this area? Were there people at Hybritech who knew about it, or who had come from pharmaceutical companies?

DESMOND: Not very much. The reason I know that is because I went out and did a lot of the early leg-work. So, we really didn't have people at that time with experience with this with large-scale production.

JONES: And doing this with monoclonals was new?

DESMOND: Yeah, it was. I'm sure there were a lot of people that went through the same process - grow them in mice because it's fast and easy. That's the way you do it, but then you have to replace that. There were probably people who got a start later who would just start saying, 'There's no way we can use mice,' and they'd start with fermenters.

JONES: And when you were setting this up, you also had to think about how you were going to purify the antibody -- did it demand different kinds of techniques?

DESMOND: Yes. Well, the main thing is just because the concentration is lower, you've just got to concentrate the stuff. You'd just take your hundred liters and the first the thing you'd do, by standard techniques, concentrate it down to one liter so that you're at the same concentration that you are with established ascites anitbody.

JONES: But you have to worry about losing the anitbody?

DESMOND: Well, I guess you have to worry about loss, but not so much. You also have to worry about what else you have in the medium that you're concentrating. But that was pretty straightforward, so there wasn't too much of a fall-off.

JONES: So that's what you did, and you would just ship out that concentration to people down the line?

DESMOND: Well, yes, but I didn't do that so I can't really say. But I'm pretty sure that's what was done. The first step was just concentration and then purification.

JONES: OK, anything else I should know about that? Did you run into problems setting up in vitro production?

DESMOND: Yeah, I can't really say that. We sort of demonstrated the principle. About that time we got an in vitro production group going which went into the manufacturing department. Probably the big questions always are, you know, 'Should we change?' 'When should we change?' You know, there's this decision. It's going OK now, so where that became a big issue was with in vivo products, again mainly because of regulatory issues. But even there, in our products we used in clinical trials, they were mostly made in mice.

JONES: It was a question of purity then, worries about contamination?

DESMOND: Why you would use one or the other? I think the main question would be volume, projecting the scale. You know, you're going to need kilograms of these antibodies. I don't think it was really purity. You know, there are sort of trade-offs. On the other hand, you always think of the mice as being a less controllable environment, and maybe they are more messy. On the other hand, they do some things for you - they clean up infections.

JONES: You had to put stuff in the reactor, the fermenter, right?

DESMOND: Yeah, antibiotics, I guess. There are other problems, you know, in controlling pyrogens and things like that. So, overall, I think there's no question that the best system of production is this controllable in vitro one. But it's not trouble-free. When you have an in vivo thing going and it works, and as mouse production grows, there's always this major decision you have to make, 'We have to stop this.' And then we started getting data, clinical data, and it gets even more complicated to change things.

JONES: Did you ever have trouble getting money to do this? When you decided, 'We should do this now,' was it a battle to get it done?

DESMOND: I don't think so. I don't really recall that.

JONES: So, you were on your own, more or less, to determine the best way to do it?

DESMOND: No, they were actually policy decisions with our support to do this.

JONES: Did you feel confident that the money would be there?

DESMOND: I don't think we ever had those doubts. I guess the idea was always that if you had a way that is good, then probably there was an assumption of that.

JONES: ...This will be, more or less, 'the Hybritech story.' It's a good one.

DESMOND: And fairly unique. I mean it was just the right time and the right place, yeah.

JONES: You left cell biology shortly after. Is this the last thing you did in cell biology, and then you were on to other things at Hybritech?

DESMOND: No, I spent a lot of time after that in the R&D of the in vivo products, imaging and therapy.

JONES: What were you doing there, precisely?

DESMOND: Well, in the imaging projects, I was producing antibodies to be used in injectable products. That included regulatory and manufacturing, so I guess I was in that department because of my experience in cell biology but it was now more of a product realm.

JONES: When they were using chimeric antibodies, they would grow those in the mice, right? How would you manufacture the Fabs, the fragments?

DESMOND: One way to manufacture them was to do it chemically.

JONES: Was there a problem of getting enough of these things to shoot them into people? Was that the kind of stuff you were working on?

DESMOND: You know, that was not my area. There was a group that was doing antibody modifications and some beginning clinical trials. Mine was more the mainline, essentially, anti-CEA antibodies for in vitro use, so I wasn't really involved in that. And there were a lot of development projects like isotopes to be used for imaging and therapy, chelation chemistries to get those isotopes stuck on to the antibodies, fragments that you just mentioned, and so forth. That was handled by the Frincke group.

JONES: So, they would be making their own antibodies, essentially?

DESMOND: No, most of that was done with existing antibodies. They would do the chemistry on them. So that material would be produced by our manufacturing production department, and they would come up with the materials for those kinds of studies.

JONES: And they could get enough antibody?

DESMOND: Yeah, for those things, for the trials.

JONES: So, you were producing antibodies for looking at an in vivo product?

DESMOND: Yeah, specifically, essentially one antibody for an imaging product. So it was already an existing antibody - actually a couple of them - existing antibodies that we were now scaling up and thinking about the process, the regulatory process, and so on.

JONES: This was HybriCEAker?

DESMOND: Yeah, and eventually, we almost got it approved.

JONES: What did you do after that?

DESMOND: For two years, I just sort of took time out. I was still doing cell biology, but we had a big quality management program and I was heavily involved in that. It was sort of based on my experience as working as a manager.

JONES: So, this was a Lilly program?

DESMOND: No, no way.

JONES: It was something that you originated at Hybritech?

DESMOND: Yeah, and Lilly used it. Well, I can't really say that, but no, it was a Hybritech in-house drive. I'm sure that Lilly was very interested in, you know, cooperating with it.

JONES: Whose idea was that initially?

DESMOND: Don Grimm's.

JONES: So you were involved in designing that and implementing it?

DESMOND: Yeah, training, implementing. It was intense for a couple of years. During that time, that was probably the end of the time that I was working with the cell biology group. We had a lot of people, a lot of management by then so the transition into this product development/project management was natural.

JONES: What were some of the tasks that you had to do in order to do that?

DESMOND: Well, the major task was to continue the investigation into in vitro production. That was a major task. In fact, it became a separate product team.

JONES: So, was it a matter of just scaling it up larger and larger?

DESMOND: Yes. And then move into clinical trials and purification procedures, and regulatory requirements that go along with that as far as applications.

JONES: What were some of the problems that you had to solve there in terms of purity and regulatory demands?

DESMOND: No great problems stand out. It was sort of a philosophical problem. You have something that works, and you just have to demonstrate that this replacement is going to be the same. I mean, everybody thinks that it's going to be the same, or it seems to be the same. But you have to make this giant step in order to do this. So, there were no, I don't think there were any major issues.

JONES: But a big part of it was what the FDA wanted to see?

DESMOND: I guess you would say that. You've got to show equivalency. But you have to make these big product and marketing decisions. If you only had an in vitro product, you'd say, 'Hey, this is the greatest product. We'll just make it in vitro.' But wait a second, we also have this in vivo, mouse-produced product, so, I'm trying to think, actually, it's funny, short-term memory is a little different. Also, we were so involved in this, day by day, getting this stuff done, but probably, I mean, you could just look at it and say, "Well, these things work.' It's a real big change there, and you have a huge investment in clinical trials making a new product, and demonstration of equivalency is a real issue. Actually, the product went all the way through and was near approval.

JONES: Oh really, so all of the work that you did on the other was....?

DESMOND: Well, that was supposed to be like the next generation.

JONES: So, what was the fate of this product? It was almost approved and then...?

DESMOND: Yeah, well I would say that, just my own impression was that it was working well in the clinic. The doctors really liked it and they wanted more. They had patients that they were diagnosing with it, and so there was market interest.

JONES: The indication, was this for colon cancer, CEA is expressed by a lot of different cancers?

DESMOND: Right, but just colon cancer.

JONES: And this was better than anything that was on the market?

DESMOND: Well, that's a big question. That's very difficult to say, and you're talking about small percentage differences. I would just say that the doctors who used it really liked it, and probably liked it, certainly in preference to other techniques...

JONES: Was it less invasive?

DESMOND: No, well, I don't know. Other techniques would be like various radiologic techniques. I mean, I guess it's less invasive than going in with a scalpel. It's more invasive because you're injecting it into people. But certainly during those fairly extensive clinical trials, people said, 'Hey, this is really great. It really works better.' That's the rationale we presented to the FDA.

JONES: I'd like to request some documents about this product from the FDA.

DESMOND: The PLA should have everything in it. That's the thing they look at and approve. The PLA is the main thing, it's where all the, I mean, there's facility license stuff, too, but the main thing would be the PLA, it's got the manufacturing, the stability.

JONES: Did you leave when they closed the in vivo side of it?

DESMOND: I didn't. I stayed on for maybe one or two years. Probably one year, in Human Resources.

JONES: I guess at that point you were probably outprocessing a lot of people.

DESMOND: Yeah, I sure was. And I was involved in training and kind of general administrative management. The Magic Bulletin for a while was in my bailiwick. And personnel, a lot of training because of my background.

JONES: What was your impression about what happened to the company in the '90s? I guess around 1990 there was a big shift. Around 1990, everything is going great, we're going to have this product, and then in the next few years...what were you thinking about it?

DESMOND: Well, it's very hard to say. I mean, I have sort of personal impressions which aren't sort of expert impressions. I suppose that one problem is the problem of the front-runner, right? Part of it is real, and part of it is, you get going in something and there is probably a little bit of resistance to changing, to change, I mean, not tremendous. But then there are other things that are sort of associated with that - you have people there, and facilities, and processes. So I think part of it was other people with other technologies coming along. I think it probably, again, I probably should know more, and I probably did know more, but you could talk to other people who would know a lot more. For example, Russ Saunders. Because probably, and again, you know, we're talking about two things. The diagnostics, which is still a big part, and I know that instrumentation and packaging of instrumentation, and so forth, is a big thing. And so, there were some things that were tried with instrumentation which didn't work out. But, you know, other technologies come along, other formats. I guess the whole name of the game has got to be efficiency of manufacturing and efficiency of the use of it in the lab. So there were things that came up that were easier to use, that took less technician time, and you know, there was a lot of effort at Hybritech to improve those things. And I don't know

if there was that much of an expanding market in new markers and things. A pregnancy test is a pregnancy test, you know. Hybritech, I believe, at one time, had 50% of the laboratory pregnancy test market. But when there are fifteen other companies that make this stuff, there are bound to be people....and I don't know how natural or real the market is, either. And the in vivo side, first of all, it was just enormously expensive. You know, if you have a great product, which they had, one of the problems with the HybriCEAker was it was so damned expensive to make. I used to joke, you could send the customer a $500 bill and say, 'Please take this instead of the kit' -- don't put that down -- you know, it would cost you more to make. And there were all those ideas that you could improve efficiency and production. But other people would come along with products that were really more economical to make. In that game, you really get stuck when you have a $5 million clean room that's built to...

JONES: Is that a resaonable figure, or is that an exaggeration?

DESMOND: I'm not sure, but for an injectable product manufacturing facility, it's a huge investment. I don't know what it was. It was called E-bay. Ask somebody how much E-bay cost. That's one of the saddest things. I mean, here's this facility that's just a remarkable thing, but once you don't have that product, it is scrap. I remember that. So what happened? I guess it's mainly market. I can't really say that for sure, but that's my feeling. The other thing is I'm not sure, I mean, here we are, five, six years later, and there are not a whole lot of other products that are any better. Probably the other thing is that the technology didn't take off the way the simplest model projected: 'this is going to work and...' Because even today, I don't think others in antibody imaging and therapy, they're not five years further ahead than you what you would have predicted five years ago. And even if it wasn't our product, it would be somebody else's product.

JONES: Because of technical problems or because of the market? Or a combination?

DESMOND: I think it's because of the complexity of the human body. I mean, things just don't go there and shine and you get rid of them. It's far more complex. Hell, when I was learning all this cell biology, the complexity of cell biology, cell surfaces, control of cell death, all of these things, are just unbelievably complex, and all new.

JONES: So, tough problems.

DESMOND: Yeah, not as simple as you might have thought. Yeah, it's funny because, in many ways, there were lots of great things about that company. I think the way it operated, the employee quality, the money available, and the facilities, and this quality management thing.

JONES: It was a good company.

DESMOND: Yeah.

JONES: Well, employees. You got a lot of people from UCSD?

DESMOND: Originally.

JONES: When the company was expanding, at one point there were a thousand people working there. Didn't a lot of those of those people come from UCSD with bachelor's degrees?

DESMOND: Yeah, UCSD, Scripps, all local market, mostly. Some of the management people from Lilly, later on, a small number, and then from large pharmaceutical and diagnostics company.

JONES: At the upper levels, but the people that you were bringing to work in, say, cell biology?

DESMOND: Certainly, all local, and UCSD was a big source.

JONES: When did you decide to leave, and why?

DESMOND: I decided to leave when I was laid off.

JONES: Oh, OK, and this part of scaling down the operation?

DESMOND: Yeah, they were at also at that time trying to sell the company. I left before '96.

JONES: Well, you were out of a job, what were you thinking about?

DESMOND: Well, to be honest, I had been very interested in education, and I had done a lot of education outreach work, a lot. And when I went out looking for a job, I wasn't looking for a job in education but there were a lot and that was among the possibilities. I mean everybody, essentially, in biotechnology thinks about consulting, until they realize that consulting is a lot like looking for a job every day. And I had had this experience in quality management which I really loved, and human resources, and science, to some extent, so I looked at a lot of these jobs, and then, you know, this particular one came up, and it looked like quite a challenge, and quite unique. It was a unique situation. So, in some ways, it was quite a radical change. In other ways, I can't overemphasize the experience of being on a management team was really quite attractive with the particular training emphasis that we have. A huge effort I put in for part of those few years when I was working at Hybritech was on a Malcolm Baldrige award put out by the Commerce Department every one, two, or three years. Solar just got it this year. It's a huge self-examination, it takes a year and a massive company-wide effort looking at the company, describing it, making our recommendations and putting them in place. That was another very strong influence on me to see the science of management. I mean I didn't have any training in it.

JONES: You think of it as a science rather than an art.

DESMOND: Oh, yeah, sure, well, there's a lot of science to it, I guess there's art, too. Both. So, anyway, this particular job was mainly management, but technical, somewhat lower level

technical. My job was to be a liaison to various industry and medical organizations around the city. I had lots of contacts.

JONES: I was looking at the board out here, Scripps...

DESMOND: UCSD Medical Center.

JONES: Yeah, you've been involved in setting those things up. Were these not in place before?

DESMOND: Some of them had been set up, some of them. But now we're exploiting them more. Some of them I've set up. So, I've been using my technical background that way. The other thing that I do is a lot of grant writing, a lot of presentations on curriculum, particularly on collaborations, teachers working with outside organizations, and getting some of the things, modern science techniques and ideas from them into the school.

JONES: Do you have ample funding to do this kind of stuff?

DESMOND: We do. Let me just say that funding is not the limiting thing. The limiting factors are other.

JONES: For instance?

DESMOND: Well, you have this huge conflict between teaching the art and taking care of kids, personal problems and student educational problems, sort of like your quality control or quality assurance on your starting materials. And you know, that's the art of teaching - classroom management. That's a huge thing. The other thing is that, you know, schools, they're a very different kind of organization. They need to change. I mean, there are just unbelievable things, just unacceptable. The first thing is to have a three-month hiatus. Unbelievable. Name an organization of any kind that can afford to stop for three months. Why you would you take the most critical element by far, far more critical than in medical areas, and

stop it for three months? And the terrible thing about stopping for three months is that it's not just stopping for three months - it's stopping for five months. Because there's a month to wind down and month to start-up. The other terrible thing is that they've already figured out how to do it. They have year-round schools all over the place. I mean, it's not brilliant, but.... So, things like that. I always use that as an example, but it's just a very frustrating thing. You know, you stop ordering. How you could you have a company, or anything, that stops ordering in May? That's means that the window's closed for a month. So, those things I always have thought because they are so obvious as ways to improve. And there's a lot of influence outside that's very important to get into the schools, and I hope that I can help do that. I always talk to people, and I deal with this, 'If you see something that doesn't make sense, you have to tell us.' It doesn't make sense to write down messages at the telephone, to fold up a yellow piece of paper and give it to a kid, and it gets to the person the next day. There is voice mail. There are countless things like that which aren't trivial. More fundamental is students and where we are, and all of those things get in the way of delivering the wonderful science to kids.

JONES: Is it centered here at Lincoln, the program, at the magnet?

DESMOND: It's here.

JONES: And are you having success here? Are you preparing kids for going to UCSD and majoring in the sciences?

DESMOND: We're having success, but I don't know if you've gotten the point here.

JONES: Well, sure there could be improvements…

DESMOND: Right, but you can't sort of let yourself be deluded here. The idea is to make systemic changes, and that's still very frustrating. It's just, I mean, summer vacation is so

obvious, but there are other ones. You have people, you know, that for whatever reason, you leave behind, and so how could you logically get students caught up? There's only one way I know, and that is do more. Yet, nobody thinks of this. If you don't do more, the demand is always to do better, but in the same amount of time, same of teachers, same amount of resources, and class time, and so forth. It doesn't make sense. And the other thing I would say is, with students today, the demands in schools for personal services to students is just tremendous. Things that mom and dad used to do in Iowa at the farm. It's huge, and it's not at all addressed.

JONES: It could hardly be fully addressed. When you talk about systemic changes at the level, it goes far beyond the school.

DESMOND: Yeah, well, you can always say that, but the charge here is to do something with these students, at whatever stage. The responsibility is to say, 'Look, you've got three social workers and two nurses in order to educate kids,' and be so convincing that people start voting for it. Essentially, I think about that all day, I do a lot of work on that, and you do see successes. You know, I'll tell you a success. We just had nine students – juniors - who took a college biochemistry class at Point Loma Nazarene College. This is a college biochemistry class, And these are kids down in this poor old school with all these problems. But nine of them passed, and one of them got an A in a college class. To me, this is a very important thing and this is a sign that, probably another problem that we have is that our expectations for students are way too low. Even for students that are having problems. And all of this stuff is stuff that comes out of my experience at Hybritech. You see dramatic demonstrations of the power of teams, of the use of working together, the potential of people, and the effectiveness of challenging people, and what they can do when they're challenged. So, I apply that a lot.

JONES: Actually, we don't have time to get into it, a big topic, too, managing scientists at Hybritech….

DESMOND: Yeah, I mean, it was a fantastic group of people. It was a very high performing group of people.

JONES: How do you account for that? Just a lucky mix?

DESMOND: I don't think so. It was a challenging area, a glamorous field, with lots of people here - you know, right time, right place to some extent. And then the snowball effect with good people getting more good people. I don't know, a good mix, I guess. In fact, I can't say it's unique. There were probably lots of other places with that.

JONES: But this is different. And when you call management a science, yes, you learn techniques for setting up an organization in particular ways, but there are so many intangibles. Talk about the complexity of biology, the complexity of organizations...

DESMOND: Of human behavior. But I guess when I say science, I mean that there are questions that you can ask, and there are hypotheses that you can pose to answer those questions, and there is information that you can get out of it. You can see that it in little ways that are actually a lot easier to interpret and manage. I think that the talent of the people who are good in large scale management use data based things even if they don't think of it that way.

JONES: Well, it's empirical, it's based on experience rather than sort of the application. You develop rules of thumb, rather than formal principles, where I can take this, and plug…

DESMOND: Yeah, well, when you say empirical, that makes me think of science. You do this experiment and, yeah, the other part of science, formulating laws, I guess is a little bit

different. And part of the reason that I say this, as somebody who's a convert or something, I guess, is that I certainly never thought about any of this stuff when I was for twenty years of studying science and doing science in industry. Getting into the organization, and again, Hybritech was a wonderful experience because it was growing, it had lots of benefits. It was growing, it was successful, it had money. So I got to see this kind of organization in many phases, and also see some real experts come in and do things and see the results.

JONES: It was also new. When you talk about trying to make changes in the school system, you're talking about conventions and habits...

DESMOND: Yes, to have something there where there is sort of nothing to fall back on is a big advantage. It would be interesting if you ever got into it. My daughter-in-law just got her MBA from the University of Virginia, Darden, and I'm always trying to get her and her friends to get involved in education because the organizational dynamics and the way things go in education really are interesting. I'm sure you've seen just a little bit about what's going on in San Diego, and that's really interesting. And the thing that I say, again, one of the problems with education is that it's run by educators. I mean, the typical superintendent of schools, was a teacher forty years ago, and being a teacher is one of the most isolating professions in the whole world. I mean the door slams at 7:30 in the morning and opens again. In that time, that person only has to do with adolescents, and then they leave. They spend all of their time grading their papers and stuff. It is such an isolating profession. And those people, if they're good, it's the Peter Principle, they become vice-principals, then principals, then assistant superintendents, then superintendents. Basically they're fantastic teachers, and you know, they infuse management wisdom and so forth from inside, not outside. That's why I understand this guy who's an attorney general. Boy, is there a lot of clamor about that. I mean, one is not better than the other necessarily, but boy, it's really a hassle.

JONES: OK, good luck with it.

END INTERVIEW

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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.