Frank Taylor: We are at the Redfield Building in the Woods Hole Oceanographic Institution for our second session with Dr. John Stegeman. During the first session, we went over your early life, where you were from, education, working on your PhD. We had come up to the point where you were going to do a postdoctoral situation. You had an opportunity to go to one area, but then an opportunity to come to the Woods Hole Oceanographic Institution came up. Could we start there? How was it that The Woods Hole Oceanographic Institution chance came up?

John Stegeman: Well, I think I told you this the last time, but I'm not sure. It was while I was writing my thesis that I had been already engaged in a possibility for a postdoctoral fellowship at MD Anderson Tumor Institute in Houston, which would have been with a man named (Hez Shaw?) in the department of medical genetics at the MD Anderson Tumor Institute. While I was writing my thesis, I noticed a poster on the bulletin board in the biology department at Northwestern for postdoctoral fellowships at the Woods Hole Oceanographic Institution. Well, of course, I had heard of Woods Hole. Never had been there, here, and thought, "Well, this would be interesting." So, I called and asked the office, which was the education office at that time, about the fellowships, and that the deadline on the poster had indicated the deadline had passed. So, I asked if it was still possible to apply. They said yes. If I could get an application to them as soon as possible, then they would send me one. So, they sent me one, special delivery. I filled it out, sent it back, special delivery. And ten days later, had a telegram saying I was being offered a fellowship. Would I accept? Please let them know right away. So, in the space of two to three weeks, I went from not knowing anything about it, to having to decide, "Okay, now, do I go to Woods Hole or not?" I had obtained references from people in the biology department at Northwestern who were frequent researchers at MBL during the summers. They were familiar with – and knew well, I should say – the dean at that time. So, I think their references carried some weight. I talked with my wife about it and talked with the people in Houston. The man in Houston said, "Fine, we'll just postpone your fellowship for a year here. You go to Woods Hole. That would be a great opportunity." So, we came expecting to stay here for a year.

FT: I have a couple of questions around that. One of them is, as I review your whole career, I could really picture you as being at the Marine Biological Laboratory or involved with the National Institute of Health or something like that. What was the Oceanographic going to offer you in terms of your career development, where you were going to go with this, that made you make that decision to come for a year?

JS: What made it interesting to come?

FT: Yes.

JS: Right. So, one of the features of the process by which you find a suitable position after your PhD is how well it might serve some interest that you have, and you hope that whatever you have will serve the purposes and interests of the people or the lab or the institution to which you go. So, at the time that I was finishing my PhD work, I was looking at temperature as an influence on the activity of the enzymes that I had purified. Since these were enzymes from fish, this was a relevant thing to do. There were two people here at the institution who, at that time, were very much working on temperature as a variable affecting the activity of fish and processes

in fish. Those two people were John Teal and Frank Carey. They were working together. Teal is really an ecologist. However, he had a broad interest in things. Carey began as a biochemist, but he was really pursuing whole-animal physiology to a large degree. They had published a couple of papers at that time which were on temperature regulation in fishes. So, I was interested in that. It seemed like there might be something there that would further my abilities and give me some experience in areas that were, at that time, of interest to me. So, that's my side. It just so happened that, at that time, there had been a recommendation to the biology department here that they begin to hire people with backgrounds in biochemistry. My PhD was in biochemistry. Frank Carey, who had come earlier, was also a biochemist. He had worked with Phil Handler, in fact, who had co-authored one of the major textbooks in biochemistry, White, Handler, and Smith. Frank was here as a biochemist but moved to physiology. So, that, I think, was part of the reason that my application was viewed favorably by the committee that reviewed applications for postdoctoral fellows at that time.

FT: Now, you said you would never been to this area before. Can you give a little thumbnail of what your impressions were when you came here?

JS: Well, first of all, it was enchanting in a way. I mean, it was such a different visual impact from Illinois to see Little Harbor here. As those of you who know Woods Hole and Little Harbor, you'll understand, the first time you come down Woods Hole Road and drive along Little Harbor, and you look out and you see the harbor and the boats, and the island in the distance lights, it's truly enchanting. I mean, it was wonderful. That was one thing. As I recall, before we actually saw anything in the daylight, we had dinner with John Teal. My wife and I had dinner with John Teal and his wife at their house in North Falmouth at that time – Mildred Teal and John Teal. They later parted company, and John married someone else. But it was a very interesting experience having dinner with John Teal. I mean, we're from Colorado and Illinois. We were served, as I recall, pumpkin soup from a pumpkin, which was unusual at that time, and a stuffed beef heart. So, we were kind of impressed with the interesting aspect of a Woods Hole scientist that we saw in John Teal, which I maintain to this day. He's a very interesting character. So, as far as your mention of the MBL, certainly, I had known of Woods Hole from the time I was an undergraduate. It was largely because of the MBL, having taken invertebrate zoology and used a text by Libbie Henrietta Hyman, who did work for a period of time at the MBL, describing invertebrate critters of various kinds. Knowing also of the work of Albert Szent-Györgyi, who was here in Woods Hole at the MBL, I was familiar with the MBL. I was not familiar with the Oceanographic. I did not know much about it. I'm not an oceanographer. I didn't know much about the oceans. In fact, I could safely say I knew that the oceans were big –

FT: [laughter]

JS: – and that they were there. I hadn't really given much thought to anything about the oceans. I did hear John Teal a few years later give a lecture saying, "The most important thing you need to know about the oceans when you begin to think about them is that they are mostly water." That's actually a very important thing.

FT: Well, it is when you consider the fact that when the Oceanographic started and their mission was to be in the blue water zone, that average depth of the ocean, which does not have a heck of

a lot in it. So, it was the physicists, the chemists, the geologists. Biology back then was kind of on a backburner here in the institution.

JS: Well, yes and no. What happened in the early days of the Oceanographic, perhaps, but if – I like history a lot. So, the history of the two institutions became of interest to me. So, the fact that the Oceanographic is a daughter of the MBL, and that, I think, the intent originally was that the two institutions together now operate to address issues from one end of the spectrum to the other of marine science, if you will, from the use of marine organisms for fundamental research in biological processes, to understanding animals in the environment and the ecology, and understanding that environment, its physics and its chemistry and its motion and its role in the planet, you have one, seamless, full scope of marine science represented in the two institutions in Woods Hole. I think that was the original intent. To a large degree, that is the way it is. But because of things that took place during the 1950s with land acquisition, there was this rift that occurred between the two institutions that took about thirty years to heal. So, I don't think biology was on the backburner or on the sidelines. It was really an essential part of this spectrum of activity.

FT: So, in a sense then, your view is kind of as a whole organism down here, or that is the way it ought to be operating.

JS: I think that's absolutely right, yes.

FT: Now, this is an unfair question, but I am going to ask it anyway. Did you have that broader view when you first came here?

JS: Of course not.

FT: See, that is of interest to me. I know John Teal. You are right. I mean, he has multiple interests. I can recall one time he was letting a group of people who roleplay medieval warfare use his property to fire their ballistas to see if they were working correctly.

JS: [laughter]

FT: As you would suspect, he got very much involved in the whole thing.

JS: Oh, absolutely. That's right.

FT: When you had that first dinner with him and had a culinary surprise, I guess, is the way we can describe it.

JS: Great way to say it, yes.

FT: Did you get any feeling for how someone that was at the Oceanographic might operate, their world view, or did you discuss any of that kind of thing at all?

JS: Well, people who are in their mid-twenties often haven't got that perspective, even to think

about their worldview. I think it comes later. So, no, I was much more interested at that time in the kinds of things I might do. I was trying to figure out just what went on here and how I would do whatever I might do. So, at that first dinner, it was really getting acquainted. There wasn't really much discussion of the nature of the institutions, at least as I recall. My wife might have a different recollection.

FT: See, I asked that because one of the things I have found doing the oral histories over the past eight or nine years is that this institution is very, very unique, as I see it, in one respect. That is that people come here with an academic background, a discipline of a certain kind, and may end up doing something totally different. Yet, they do it at a world-class level. So, I just wondered whether coming from the straight academic experience where things are pretty punch-certain tickets, whether that started to come out and there was any difficulty, and kind of thinking how do you operate in a place like this. I see people that have academic backgrounds in biology, and they are engineers. I see people that have academic backgrounds in the physical sciences and they are working with Alexandrium or something like that and are noted experts in the field. I think that is a very unique thing here. It talks to the bringing in of people that have some pretty exceptional abilities. They can turn their hand to a lot of things.

JS: That certainly is true of the institution and the people in the biology department, many who have been here over the years. I'm not quite sure how that fits into the discussion that we were having.

FT: Well, anytime you come into a new situation – I can only do this from a very personal standpoint – you are kind of on your best behavior. You want to make a good impression. You want to try to find out some certain essential things that are going on, and kind of ease yourself into the society that you are going to be in in a place like this or in a school or any other kind of business that you might be involved in. That really kind of starts right from the get-go, that first meeting with someone. That is what I was trying to get you to talk a little bit about here. When you came in, how do you get yourself going in a field here, introduce yourself to the people?

JS: Well, they become aware of you. You talk about what you've done and whatnot. But really, it is the mentor, the advisor, the sponsor who has an enormous influence in leading you in a particular direction or pointing the direction in which you might go. So, at the outset, when I was here, after I came, I spent my time doing a couple of things. One was learning what was going on in the laboratory of the man who was my sponsor, who was John Teal. At that time, there were quite a number of things going on in his lab. I can talk about those in a bit, because they're important. But the other thing I did was to spend some time writing papers from my PhD work and finish that chapter. So, probably, for the first several months, I did spend a lot of the time working on getting those papers finished. Also, since this was anticipated to be a one-year stint, began to think about, "Well, where do I go after this?" Now, I did have the possibility of going back to MD Anderson. But I also was looking at the prospect of finding teaching jobs and academic jobs. So, you're sort of in a period of transition, and at the same time, hoping to and expected to be able to accomplish something in real research during this one-year period. So, learning about everything that goes on, learning the directions of work that might be possible for you to do, given the capabilities within the laboratory where you are – which I will say were quite different from those where I came from – and having to do all of the planning and thinking

about the next step, it's a fairly busy time. You have a lot of things to think about. So, we can set some of that aside, because, obviously, I'm here. Thinking about future positions and whatnot, that's not really relevant at this point. So, I looked at what was going on in the lab. In the laboratory, at that time, there was one graduate student whose name was Kathy Burns. She was the first woman graduate in the joint program. She was a student in John Teal's lab. There was another postdoc who later came onto the staff, Ken Smith. I'm not sure, but I think – or maybe Bob (Campano?) came later. He was another student of John Teal's. So, I looked at what was going on with Teal and his group, and with Frank Carey, who basically was by himself. Carey was doing studies with temperature regulation in tuna. Interesting. Kathy Burns was looking at hydrocarbons in the West Falmouth Harbor. Ken Smith was doing studies of ecosystem respiration. So, you put a bell jar on a patch of mud and see what the oxygen consumption is like, and look at respiration of mud, basically, and try to infer something about the activity of the community there. Teal was sort of doing a number of things, but principally working with the salt marsh. Now, that was his thesis area. When he got his degree, he did work in salt marshes. He had continued to work in salt marshes, and he was collaborating extensively at that time with Ivan Valiela, who was a faculty member in the Boston University Marine Program here in Woods Hole. I remember, now, I arrived first week in November. So, got settled and got things underway. In late November or early December, I remember going out into the salt marsh with Teal and Valiela to collect sediment cores. Now, I can't remember exactly what was to be done with those sediment cores, but one of the things that I had anticipated doing after discussions with Teal was to look at fiddler crabs. Now, this is already very, very foreign to me, but very interesting, because it was completely new. I didn't know what a salt marsh was. Never seen a fiddler crab. Never heard of a fiddler crab. But the idea of spending a very cold and rainy day wandering around in muck trying to get mud out, well, I was not particularly comfortable doing that. I didn't relish the physical part of collecting samples in the middle of cold, cold weather. I'm happy to go duck hunting if I can sit within a blind and be warm. But anyway, it was an experience. I thought about working with fiddler crabs and how they would burrow into sediments that had been contaminated or not contaminated with oil. So, here's the key thing now, oil. I arrived in [19]71, and it was a year or so after the West Falmouth oil spill when the barge *Florida* ran aground. spill had attracted the attention and shifted some research activities of people in the chemistry and the biology departments here. So, there were chemists who were looking at the hydrocarbons in the salt marsh. Teal also got interested in looking at the hydrocarbons in the salt marsh. So, Kathy Burns, his student, was looking at hydrocarbons in the salt marsh. So, there was a lot of analysis of hydrocarbons and identifying what they were based on gas chromatographic profiles. Now, two things – I had taken organic chemistry as an undergraduate, but not as a graduate student. So, I had to actually go back to the organic chemistry Bible, Morrison and Boyd, and start to look up what was a hydrocarbon, actually. I had never had experience with gas chromatography and couldn't figure out how they could look at this mass of peaks and sort out anything. Well, this is very interesting, and I think an important lesson. I wasn't particularly interested in those peaks. So, I started doing analysis of hydrocarbons. In the context of the experiments, which I'll describe in a minute, I became fascinated with gas chromatographic analysis and what it could show you. So, this was, I think, my first real conscious understanding that you can become fascinated in something that, at the first blush, seems to be pretty dull. I became very interested in the hydrocarbon chemistry and did experiments with oysters to determine how they took hydrocarbons up into their tissues, how much they took up, how long they held on to it, what happened to it – so, uptake and

accumulation, and also release or disposition of or depuration of hydrocarbons from oysters. Now, this was an important direction in oil pollution research at that time. How did animals become contaminated? How contaminated did they become? What happened to the hydrocarbons once they were in the animal? How did they get released? Where did they go? Now, we have hydrocarbons, which are contaminants in the environment. Features of their interaction with animals, coupled with the interest that I had gained in the environment from my graduate time and the Northwestern Students for a Better Environment, and in reading the literature about how hydrocarbons were eliminated from organisms, coming to understand that there was a very interesting and largely mysterious area of research involving the enzymes that acted upon hydrocarbons – so, with my interest in enzymes and interest in the environment, together with this new experience with hydrocarbons and how they got into and what happened to them when they were in animals, formed the basis for what then became the line of research that I have followed through various pathways from that time to this.

FT: You have described it absolutely beautifully. Because as I was sitting here listening to this, I am saying to myself, "I am seeing the seeds of his career start to form right at this particular point." I must admit, the thought hit me, that from something that was a disaster, the many thousands of gallons of No. 2 heating oil being dumped into the environment, that there was also some very positive sides of that, because Howard Sanders stood out there early and set up with – in many ways, is still the basis of how they investigate – from a biological standpoint, at least – the effects of an oil spill. Max Bloomer got involved and did the chromatography. You came along in this then and started to look at these bottom feeder types, and developed some enthusiasm and passions for things that were happening here that was new to you. There is some real positive things that came out of that.

JS: Right. Well, there were a lot of people who became interested in the contamination of the environment by oil and petroleum in the environment – as you say, Max Bloomer. But also, students of his, John Farrington, came about the same time I did. I can't remember whether he came slightly before or slightly after me, but I think slightly before, as a postdoc in the chemistry department with Max. So, he was involved in the West Falmouth oil spill studies with Max, and Howard Sanders and Fred (Grassley?) and Teal. Kathy Burns, when she did her PhD thesis, she was doing studies with the hydrocarbons, their accumulation by fiddler crabs and by fundulus heteroclitus, the little marsh minnow, the killifish. So, there were a number of students, postdocs, and faculty, all of whom became involved in studies of petroleum in the environment. The work that went on here was important in several reports and committee efforts at the National Research Council to deal with this question of how serious is petroleum in the environment. I was involved in some of those, as was Teal, as was Farrington, and others. So, there was a lot of research that came out of this. I think probably some of the foundations, as you say, of oil spill research and oil spill effect in the environment are an outgrowth of the kinds of things that went on. Of course, there were oil spills elsewhere. The *Torrey Canyon* and others at the time had been important in focusing the attention of scientists in those parts of the world on these questions of the biological and ecological effects of oil. But in my case, the –

FT: – quickly.

JS: Moved to wanting to understand how the oil was metabolized in the organism, what was

happening to it. I say that interest in how it was being metabolized really became part of my interest because of the literature on a family of enzymes – or I should say on an enzyme at that time, which was being identified as an enzyme that could metabolize or degrade or oxidize or otherwise become involved in pathways that would help eliminate hydrocarbons from an organism. That work was going on largely in medical schools, and in the National Cancer Institute, the NCI, part of the National Institutes of Health. As it happens, people who are looking at one thing often will see import or relevance of what they're doing in other areas. So, there was one investigator at the National Cancer Institute, Harry Gelboin, whose lab was very much involved in looking at the hydrocarbon metabolizing enzymes in mammals, who became familiar – and I'm not sure how he became familiar with what we were doing here, but I remember having been contacted by him with suggestions for possible collaborations involving enzymes that may become involved in hydrocarbon metabolism. I'm moving down at several years now. But let me step back to the first.

FT: Well, number one, here is something that happened right down the road. You did not have to go to Texas or up to Alaska or something like that. You had twenty, thirty minutes to get on, get right into the field, and to develop an interest in a procedure for analysis, the chromatography, and to really spark an interest in that little organic catalyst, the enzyme, that really was fundamental to a whole bunch of different ways you could go.

JS: Right. So, I just sort of put the enzyme into the picture a little sooner than it should have been. There are a couple of other important aspects of the early time here, during that first year. Now, I came in November of [19]71. A close friend of John Teals was in the chemistry department, a man named George Harvey, who was also using gas chromatography to look at another kind of chemical contaminant in the oceans, polychlorinated biphenyls or PCBs. This also is very important in the research that I've been doing over this whole period of time, as we can get into in a bit. So, there was a plan for a research cruise in the summer of 1972, and Teal said, "You should go on this cruise." I said, "Great, fine." So, it was a cruise on the *Chain*, RV *Chain*, which I thought was, in retrospect, wonderful, wonderful ship. After having been on several of the others, I appreciated how stable this ship was, like an oak floor in the ocean rather than a gimbal table. It was great, great fun. It was a cruise from Lisbon to Cork. Well, I'd never been to Europe, so this was also very exciting. If you go on a cruise, you have to have something to do. The cruise was largely biologists, although there were some geologists aboard as well, as I recall, and some chemists. The chief scientist was Dick Backus, who was, at that time, and for much of his career here, interested in midwater fishes and midwater trawling, and was the way you got these things. So, to enumerate them and determine their distribution, you had to get them up and see what was there. I was going to analyze hydrocarbons in surface waters and organisms that came up from various places – so, just kind of a look-see, what's out there. Flew to Lisbon, had a great time preparing for the cruise, traveling around Lisbon with others who were going to join the ship. Then when the ship came in, and we went down to the ship at the harbor in the Tagus River in Lisbon, man, that was really just so exciting. *The Rime of the Ancient Mariner* comes to mind. All of these nautical things, they're somewhat familiar, but not really very familiar to this kid from the farmland in Illinois. Well, Teal, by the way, was from Nebraska, which you probably know. So, going to sea was just absolutely thrilling that first time. I remember just being completely taken with it. Others on the cruise, besides Teal, I think Harvey was – I believe it may have been Alisdair Macdonald from Aberdeen on that

cruise. Maybe I'm thinking of a subsequent cruise, but we could find out. However, on the preceding leg of that cruise, there had been another postdoc, Richard Harbison, who was also given a postdoctoral fellowship at the same time I was in the biology department. Richard also had his degree in biochemistry. He became interested in the gelatinous zooplankton because of this enormous jellyfish that was collected in one of the trawls on that first leg of the cruise. So, there was a lot of talk about that. But going out, setting a trawl, watching the trawl come up with all of these fantastic creatures – some of which I had remembered well because of their odd shape and names from when I was an undergraduate in Minnesota, going through invertebrate zoology. One in particular was a ctenophore, Venus' girdle. I thought, "How fantastic to see this. They really do exist. They're not just in books. Fascinating." So, it was just wonderful to see these creatures come up. Then the midwater fishes, I had read William Beebe's descent in a bathyscaphe when I was probably twenty-one, twenty-two years old. So, I was fascinated with those fangtooth fishes that came up. So, this was 1972. During the course of the [19]70s, I went to sea a number of times, for various purposes which I can describe. But this first cruise was really, I think, most influential in cementing my interest in what was the ocean, what are the oceans, and what's in them. I thought, "How fascinating. Everyone on earth should have this opportunity, because then they would appreciate the planet a little better." It just was fascinating. My research project on the cruise was collecting organisms, extracting a lipid fraction, and preparing it for gas chromatography. I don't remember if we did it on the ship or did it on the shore when we got back. That's not really so important. But I do remember going through the steps, trying to get samples that would not be contaminated with the ship's hydrocarbon signature, one, and secondly, trying to get a sense of the ship's hydrocarbon signature so that if you did get material, you could distinguish what was ship from what was really ocean presence. So, I remember climbing up the stack – this was a diesel ship – and going with a beaker full of pentane or hexane – probably hexane – and a beaker full of water, and getting an exhaust sample from the stack, holding these beakers up there in the vicinity of the exhaust for a period of time, so that I could bring them back down and have that as one control – sampling off this side and that side and at the stern, in order to get what the ship was leaving in its wake, and then sampling with a bucket thrown in advance of the bow, and collecting it before the bow could touch the water – and doing all of this to get the control samples and then extracting.

FT: How many casts did you have to make before you mastered the technique?

JS: Of getting a bucketful in front of the ship?

FT: Yes.

JS: Not many, but I was surprised the first time to see how much drag there was and how it nearly pulled me in. [laughter] It was great fun going to sea.

FT: You have already answered one of my questions that I asked earlier. I had said I could see you at MBL. I could see you at NIH, and things like that. Correct me if I am wrong, but when I listen to you, I say to – the Woods Hole Oceanographic Institution does a lot of things. But one of the things it does is offer you opportunities to become part of something that can be very, very exciting. You have described this like, I can almost say, you write a book, *John Stegeman's*

Excellent Summer at – [laughter] – *the Woods Hole Oceanographic Institution*. There's this environment that breeds somehow this burst of enthusiasm with the new things. I mean, you had a PhD for heaven's sakes. To get that excited when you're discussing chromatography or being able to go to sea or something like that is kind of unique. It's very refreshing to hear you talk that way about what it's like to be here and how it starts to produce your career. So, I think I really understand now, from the way you've described this, why you've been here so many years rather than some other kind of institution.

JS: Well, there are a number of reasons why I've been here for so many years, and we can touch on it. One of them is students, which we'll touch on in another session perhaps. So, this was now this first year. I had done these experiments during the winter and spring with oysters – an experimental setup that was in a lab down at the MBL that had been rented.

FT: Were the oysters from the area or were they oysters that you brought in and introduced the hydrocarbons?

JS: The oysters were from the area, I think. This was during a period when another staff member, John Ryther, was looking at combining oyster culture with treatment of secondary sewage effluent – sewage effluent supporting culture phytoplankton, which would then be used to support oyster culture, so that you would clean the effluent and wind up with a marketable product at the end. It didn't work because of accumulation of things that you didn't want in the oysters – viruses, enteric viruses, and other things. So, coming from sewage isn't the best route. So, there was this research going on with oysters, and there were these questions about how things are accumulated. So, I had set up an experimental system with tanks and had devised a way to get fuel oil into the system in a pretty much dispersed and accurate concentration and had put oysters then in the stream and sampled them periodically to look at kinetics of uptake, amounts achieved, kinetics of release when you moved them out then into a clean system. One interesting feature was that some of the oysters had greater fat content, lipid content, than others did. There was about a fifty percent difference, and they sort of grouped into two. Well, what I found was that the fat content determined the amount – the concentration that hydrocarbons eventually achieved within the organism on an animal basis. Lipid basis, it was the same. More lipid, more hydrocarbon in the animal. So, that was an interesting finding. So, that was all done, and a paper written in the winter and spring of 1972. The paper was published in *Marine Biology*. It became an important paper for my career here, because it was on the basis of that that there was eventually an offer made for appointment as an assistant scientist.

FT: Now, it is an interesting point in your life, and it is a difficult point in your life in many ways. In many ways, you are a people person, I think. An academic career is a nice one, and you have lots of students that you interact with and guide. Then as a research career, and when I see the sparkle in your eye when you talk about this kind of thing, that is important too, but that tends to be more solitary. Was there any difficulty making up your mind as to which direction you wanted to go at that point?

JS: Yes, there was. I sort of wanted to be and envisioned myself as a faculty member in a tweed jacket with a pipe and a wood-paneled office at an undergraduate school, and fully immersed in that aspect of academia.

FT: Which is pretty neat.

JS: Which is pretty neat. It still has its appeal. When I get time, I may do that. I don't know. It still has appeal. But then there was this aspect of, "Well, this is an interesting place. It's an opportunity. Let's stay." My wife kept thinking, as I said, "Well, we won't be here long. We'll just be here for a few years." We stayed, of course.

FT: Can I trip into the decision-making on that?

JS: Sure.

FT: Because one of the issues in coming to the Woods Hole Oceanographic Institution is that a married couple – the husband, if he is the one that has become part of the Oceanographic as a career path that he is going to be working in. That leaves a situation for the wife as to what she is going to do in a place like this. That is something that has to be discussed. How did you guys work that out?

JS: Well, I guess I was fortunate, very fortunate, in having a wife who said, "Whatever you do, wherever you go, I will be there." She did very much want to go somewhere else, especially during that first year, because she didn't have a job. She didn't have any people that she knew here other than those we met when we arrived. She did have a friend from college who was teaching school in Charlestown, New Hampshire. So, she would go visit that friend periodically, as we both did. She did look for a job, but she was discouraged at the salaries she was being offered, all of which were less than she had been making as a librarian at Northwestern. Eventually she decided, "Well, this is what it is. So, I will look for something." So, she got a job working in Commonwealth Travel, a travel agency in Falmouth, which was owned and operated by a man named Charlie Bardelis. She is very talented and very intelligent. She had started in travel when she was sixteen years old at the Broadmoor Hotel in Colorado Springs, working in a travel office at the hotel itself. The travel agency was owned by a friend of her dad's. The hotel was a local family hotel, almost, at that time. So, she started in travel here, and she loved it and she was very good at it. For those who are younger and who are used to going on Expedia or Orbitz or something and booking their travel, well, at that time you couldn't do that. Schedules were published in a book about four inches thick called the *Official Airline Guide*, the OAG. A travel agent did all of their searching to satisfy your needs through this book. Well, she knew how to do this and do it well. She was an excellent travel agent. I probably would say the best on Cape Cod. People would gravitate to her, and she taught many people how to be travel agents, many of them in Falmouth, in fact. When we were on our way out to Woods Hole from Evanston, Illinois, I gave Betsy an article to read about Albert Szent-Györgyi, who was at the MBL. I said, "Betsy, you really need to read this, because this guy is a wonderful, fascinating guy." During the first year she was working at Commonwealth Travel, who should come into her office, but Albert Szent-Györgyi. This was a travel office with, I believe, four desks – one, two, three, four. So, she was the back on one side. Szent-Györgyi, we later learned, had a reputation as having an eye for young ladies. Betsy was a very attractive young blonde in the back of the room. Well, he came in, looked around, made a beeline for her desk. So, she became his travel agent. In the course of the next year and a half, two years or so,

I had need for some mice for some of the studies that we were doing, comparing fish to mice. I would go down to Szent-Györgyi's lab to get mice. So, I was, "Oh, yes, you are Betsy's husband." [laughter] Anyway, so she became much more comfortable after she got a job, developed friendships. But the first year was tough.

FT: That is the thing here. I do not mean to sound elitist, but people that are going to come to work here, for the most part, are married to people that need to have something, as far as they are concerned, meaningful to do. That is an issue. So, when you make that decision as to whether you are going to stay or go, and you are already conflicted a little bit with which direction you would like to pursue, that becomes a thing that you have to talk about. So, you did that. Tell me a little bit about the offer for assistant scientist here. How did that come about? Is it because of the work you have been doing for the year that you were here?

JS: I wish I could tell you in detail the process by which it occurred in those days, which is very different from the process by which it occurs now. It was more or less, as I recall, a question as to whether or not I would be interested. Then a proposal put forth by Teal, with endorsement, I assume, from others on the faculty, to the department chair, and then at what level and how much was discussed, what was the process at that time, by which this recommendation from Teal became acted on in a positive way, I really don't know. But I do know it must have been different from the way the practice is now, and certainly, I know that from having been department chair, that the practice now is not what went on then. But I gave a seminar. There was obviously some discussion within the department. Then an offer was made, and I said, "Sure."

FT: I always ask that about the interview, because I have had more different responses.

JS: I don't doubt.

FT: Everything from coming down and having lunch, and "Can you start tomorrow," to a librarian who came in, and face twelve inquisitors. They had medals from Russia and asked her to translate the Russian into English. It sounded like this horrendous experience. Of course, as you say, it has changed over the years, but it is always interesting how these appointments over the years came about.

JS: Right. I think there was the sense at that time, and not a bad one, that if there seems to be someone who seems to have what it takes, who has an interest, who has demonstrated some talent and capability, let's give him a chance to see what he can do, or her. I think that's not a bad way to do it.

FT: I can almost put on the logo for the institution, "Give them the opportunity," as a key sentence for this particular place. I will take that. You made a decision between the academic and the research in your own mind, or was this something you say, "Well, okay, I am going to take this," but you did not really have a feeling of permanence or –

JS: No, I don't think I had a feeling of permanence. As far as the academic or the research, well, I mean, this is an academic institution. The graduate program was in place at that time. So,

there were graduate students around. There weren't a great many, but there certainly were students, and the familiar environment of faculty and graduate students – although, the faculty were called assistant scientists, which, out in the world outside of these walls, assistant scientist doesn't sound like much of a position, whereas assistant professor sounds – well, it's –

FT: [laughter]

JS: But it had an academic flavor and a research flavor, and there were a lot of interesting things. I was becoming more and more impressed with the variety of things and the level of importance that the world, in my view, at that time, ought to attach to everything that was going on in the walls within this department and the chemistry department. At that time, the chemistry department and the biology department both were housed in this building, the Redfield building – chemistry on floor three, and biology on the second and first floors. As an aside, that led to a lot of interactions that were important, I think.

FT: Well, that is another thing this institution does offer, the ability to cross-check things – the environmental book, so to speak. I got a physicist over here. I can talk with him about this. I have got a geologist over here. I can talk with her about that.

JS: Yes, I think that is true. It was true then and it is still true. Although, having people located in proximity to one another tends to engender that more than if they're even two miles away, because you see them, and the idea comes to your mind when you see them. "What do you think about this and that and the other thing?" So, it was very important at that time to have, I think, this maelstrom of activity with all these different things going on. So, the possibility of doing things and learning things – I've never taken a course in oceanography and I'm not much of an oceanographer, but I've learned a few things along the way about the oceans and life in the oceans.

FT: You bring up a really interesting point, at least to me. Someone once described to me that he would sit in a meeting, and they would discuss and discuss and they were not getting anywhere. They would take a five-minute break and people would go out and walk to their cars to get some air and bump into this person and bump into that person. By the time everybody came back in, they were all set to make a decision. This ad hoc committee thing out in the hall that you run across, someone would say, "What do you think about this?" Really, it is an intellectual pleasure island that way. At least I have found that to be true. You took this appointment as an assistant scientist, and that lasted up until [19]76. Could you start to take me through your career during that particular period?

JS: So, one of the important features of the institution is that it's a soft-money institution and you need grant support. During that period of, let's say, fall of [19]72 until [19]76, [19]77, [19]78, [19]76, let's say, a number of things happened. One is that there was another – which I will mention, and then we'll move back to the main line. There was a colleague who was recruited, another colleague – who became a colleague, I should say, a man who was recruited from the Mallory Institute of Pathology and Boston – no, Tufts. I think he was at Tufts. His name was Dennis (Sebo?). He came as an assistant scientist. He had been an assistant professor in Boston with an interest in chemical effects and fish and whatnot. He didn't stay, but we worked together

for a while on various things. During this period, I developed this interest in the enzymes that I spoke of. These become important because they have been the fundamental thing that I've been – this family, it became a family of enzymes. Now, you recall when I talked about my interest in enzymes as an undergraduate and as a graduate student, I wanted to know how enzymes worked, what went on inside. I was interested in how they evolved and was interested as a graduate student in multiple forms of enzymes that seemingly did the same thing called isozymes. As I was now investigating hydrocarbons and how they got into animals and how they were eliminated from animals, it was then that I became familiar with or aware of an enzyme called hydrocarbon hydroxylase, which basically means it adds a hydroxyl group – an OH, an oxygen-hydrogen group – to a hydrocarbon, and that this was somehow an essential part of animals dealing with these chemicals that come in, these hydrocarbons. So, I did, through this period, had success in gaining a grant from the Sea Grant office at NOAA, the National Oceanic and Atmospheric Administration, to look at hydrocarbons and the activity of these enzymes – or this enzyme – in fishes from various marshes around New England. Now, the reason that this was of interest or relevance is twofold. One, that the enzyme at that time could have been proposed as participating in the protection of organisms from the hydrocarbons by helping the animal to eliminate them; secondly, that there was evidence that, in mammals, at least, such enzymes could be increased in the amount of activity or in the amount of the enzyme in an animal when that animal is exposed to the hydrocarbon substrate for the enzyme. So, the idea of looking at different marshes – one of them being the West Falmouth Wild Harbor Marsh where the oil from the barge *Florida* in the West Falmouth spill had gone, and other marshes around in New England, some in Rhode Island, and some others on Cape Cod – was that we might be able to see whether there was a correlation between or an association between the amount of hydrocarbon in the marsh from whatever source, and the amount of enzyme activity in the liver of the animal. It was thought that the liver was the predominant place, the principal place, and maybe the only place where this process of hydrocarbon metabolism aiding the elimination of the hydrocarbon took place. So, that was one part of it. The second part of it was to look at the histology of the animals to see if there was any relationship between the hydrocarbon exposure and the enzyme activity and any pathological condition, any histopathology, any tissue disease that might be evident in histological examination of the tissues. So, I formed a collaboration with a histopathologist who was working with fish at the University of Rhode Island. His name was Richard Wolke. He's long since retired, I think. Together, we had prepared this grant, and acquired funding from Sea Grant. This provided me then the grant foundation to continue on as an assistant scientist. During this period then, the issue of contaminants and their effects on marine organisms was growing. This question of how much effect was there was growing at the National Science Foundation. In the context of a program called the International Decade of Ocean Exploration, IDOE, that was the period of the [19]70s. So, there were large programs and grants that the National Science Foundation was providing – through competitive processes, of course – to researchers looking at chemical contaminants. The NSF funded a program called the Biological Effects Program, which had researchers from – I can't remember how many – half a dozen, a dozen universities who were sort of operating together with grants from NSF within the Biological Effects Program, looking at these large questions and using various organisms, various species of various types, various kinds of contaminants, and trying to come up with general conclusions about these kinds of questions. During this period, there was a meeting organized by the Biological Effects Program at Texas A&M University. I think it was in 1976. I went to that meeting. It was important to have done so. Because at that meeting, I became

familiar with others who were doing research in this area, including a man from NIH, a young staff scientist at the National Institute of Environmental Health Sciences. His name was Jack Bend, who was, by training, a pharmacologist, but was involved in studies of the enzymes just like I spoke of, looking at mammals and at fish. This could go on for about four hours.

FT: [laughter] I am sitting here with my jaw hanging down. Because as you were describing this, I am sitting here and saying to myself, "Did you, at the time that you were working on this, or starting to get yourself really into this, recognize in your own mind the huge ramifications that could come from studies like this?"

JS: Absolutely, I did. I think I did from the beginning. When I became familiar with these enzymes, there were two things that were important about it. One was the potential significance, and two was the enormity of the puzzle. So, just to take you back in time – I speak of this enzyme, and I have to, because it's been my career, my passion. The family of enzymes is called cytochrome P450. I'll say it again and again. I'll refer to it as P450. I'm a P450 junkie.

FT: [laughter]

JS: So, I became interested in this, and I became interested in it from the standpoint of the puzzle in entomology that it presented, and going from that, all the way to the environmental relevance of understanding these enzymes in animals in the sea. The reason it was clear that there could be importance was because of the connection between the puzzle, how they were discovered, this enzyme, or these enzymes, and this potential environmental relevance. So, from the middle, how they were discovered, it was in the mid-[19]50s when the enzymes were discovered. They were named in the early [19]60s by a man in Japan, Tsuneo Omura – wonderful man and a good friend these days. So, in 1963, he published a paper in *Journal of Biological Chemistry* that named them. There was a man in a group, I should say, in Pennsylvania who were studying an odd finding in liver and in adrenal membranes – in cellular membranes from adrenal and liver – others who were looking at oxygen metabolism, and then those who were studying chemical carcinogenesis and pharmacology. So, if you put all of these things together – oxygen metabolism, chemical carcinogenesis, pharmacology, environmental contaminants – and the relevance to the environment and how little we knew, it was like a world of opportunities for doing interesting and important things. These things all have, as one of the central connectors, the involvement of one or another of what we now know to be a large family of enzymes, all of which fall under the heading of cytochrome P450.

FT: I am almost speechless here. I really am. As a product of my generation, we first became aware of environmental problems when Rachel Carson published her book, and it was very, very popular. Then over the years, we started to hear more and more about these kinds of things. I mean, my heavens, when I think of what I was subjected to as a younger guy in terms of what was going on in the environment around me, and then to listen to you talk about how your initial interest came about, the things that excited you and the problem that you could see, and then when I sit back and look at the possible ramifications of what it is you are doing here – and even bringing a tour through this building this summer, and stopping downstairs at the little wet lab with all the little fish around there –

JS: The zebrafish.

FT: Yes. When there is a younger person there, I always try to give them the opportunity to talk rather than me saying, "Well, this is this." There was a young lady there, and I said, "Why do not you tell these folks what this is all about?" She talked about the fish from the New Bedford area and how they seem to have developed something that is resistant to – this was just a plain group of tourists that wanted to see what this institution was all about, or maybe even had nothing else to do down here. They have visited every T-shirt shop, and "Well, we will fill it out with this." But their jaws were kind of down thinking about, "Gee, that is really unique."

JS: So, there was another important thing that happened at this meeting in Texas. There were two important things. There were three important things. As I think about it, that was a very important – maybe a seminal meeting for me to have attended. Because as a result of that, and the conversation – I spent a long time talking with Jack Bend who knew well all of the people and what they were doing in the pharmacology and chemical carcinogenesis aspect of this – in other words, the human biomedical implication areas – and was familiar with because he was working with fish as well with some of the aspects of the metabolism of hydrocarbons by this P450 enzyme in fish. So, we sat, and he talked about these this project going on in the lab and that project. We talked about the people in the field who were the leading lights. Now, here I was, still wet behind the ears. As a P450 junkie, which I was developing into at that time, big time, I can now say that that these major players are friends of mine, and so the ones who have retired recently who are about to retire. So, I bootstrapped myself up to the position where I could bring the questions of environmental relevance and the role of these enzymes in aquatic species in the ocean in particular up to the level of interest where it would become visible to the rest of this large community. There are thousands of people in the world who work on this family of enzymes. But at that time, it was a situation where I thought, "Well, gee, Jack, you really don't leave any questions for the rest of us. You've done it all." Well, that is a naivete that I try to tell students. "Don't ever worry about somebody else doing something that you think you might have done and that there's nothing left to do, because it's never going to be the case." So, that was one important thing. Another was that through the interactions with the people there, I got a sense of a grant application that I could write, and an invitation, in fact, from NSF to, "Sure, send us an application." Thirdly, became familiar with a group of people who later put together a large program grant to the NSF that I was part of. Those three things were very, very important from that meeting. So, I did get a grant from the NSF. I wrote a grant to look at these enzymes in midwater fishes. Now, just think back, the fishes in the midwater that I became fascinated with in 1972 on that first cruise – I still have a fascination with it. Got a grant from the National Science Foundation in 1977 and did studies in [19]77, [19]78, and wrote a paper on the cytochrome P450 enzymes in midwater fishes – or I should say drafted a paper. Along the way, over the years, students came in. We did a little bit more, got a few more samples, did a little bit more, applied different approaches, got some collaborators involved. Finally, the draft of that paper, the first draft, which was written in 1977, if I recall – maybe [19]76, hazy times. Paper was finally published in 2001, twenty-five years later, on cytochrome P450 and potential chemical effects on fishes in remote regions of the world's ocean. I think it's one of my best papers. It started back then in the mid-[19]70s and progressed and was embellished and finally published twenty-five years later.

FT: Can we talk just a little bit about that process?

JS: Sure.

FT: Twenty-five years, that is a long time. It is a long time in a professional career in terms of the need to publish. How is it that it took so long? What were the strings that were coming into this that were just molding this product – they say the thing that was a big deal about Da Vinci's Mona Lisa was that he kept it with him. Over the years, he kept adding, subtracting, spending decades trying to come up with this perfect image. This is kind of reminding me of this in a certain way. When you are talking about the length of time you are talking about, you cannot see it, but I can. Now, you were talking about a work of art in your field.

JS: Yes, maybe. So, why did it take so long?

FT: Yes. What were the strings it developed it?

JS: What changed with it over time?

FT: Yes.

JS: Well, it took so long, in part, because I could recognize, as others would, too, that if you want to make your way, there are certain things that you have to accomplish. In this area, particularly, you can't be too slow. Well, I mean, twenty-five years is pretty slow. But looking at this question in midwater fishes, there was nobody else who was going to do it, not like we were going to do it. It was not of urgency to publish in order to beat someone else to the punch. The idea of being there first and possibly being scooped is not something that, at that time, was really common. It was not a common concern in oceanography. There wasn't this sense of somebody else doing the same kind of research and possibly getting to the same answer before you did. With these midwater fishes, I don't think that was the case. There were other areas in which we were trying to make our way and make some headway where there was that concern. Those were more urgent. We pursued those. This one, we could add to as we acquired new technology to address the same sort of question we had addressed with those samples in the 1970s. So, at that time, we could use some enzyme activity assays. Later, we developed antibodies to what turned out to be the protein of greatest interest – the P450 protein of greatest interest in environmental issues as an environmental indicator, and as the principal catalyst for hydrocarbon metabolism. So, we now had an antibody approach and we had additional enzyme activity assays. We had a collaborator who could take some of the tissue samples we had from those original collections, extract the chemicals from those tissues, apply them to cells and culture, and see if we got the same sort of response that would indicate it was those chemicals that could cause that at those levels in the fishes. We had immunohistochemistry looking at the tissues, and seeing what cells in the fish organs were expressing this protein. Where was this protein being made? So, it allowed a much fuller interpretation with the things that we were able to add over the years. Those things that we were able to add, we were pursuing vigorously in other questions where there was greater urgency. But this one, we had the luxury of being able to take our time. So, that's why it took so long for that one. I still think it's a very, very important paper, and there are very important questions raised in that paper. But it stems back

from this meeting in Texas A&M, in large part, because that's where the grant for that midwater fish study came from.

FT: A man that studies catalysts, and you just described to me the catalyst that put you on the road to this kind of thing.

JS: Right. So, that was the two. One was this conversation about the whole area, one was the grant to do this study, and one was becoming involved with a group of people who later were able to acquire a large multi-investigator grant from the National Science Foundation. It was called the PRIMA program, Pollutant Responses in Marine Animals. That was one of the large investigator programs that was funded within the context of IDOE, or as an immediate successor to IDOE. That program had six investigators. In addition to myself, there were Jerry Neff from Texas A&M University, (CS Guillaume?), who was a chemist at Texas A&M University, a man named Bud Tripp at the University of Delaware, myself, and later, a postdoc of Jerry Neff's, Peter Thomas, who's an endocrinologist who's now at the University of Texas, Port Aransas. A great friend, terrific scientist doing phenomenal work in comparative endocrinology, discovering important things. So, we got this grant, and it involved a set, a small selection of species that we would use as subjects, exposing them to a limited number of rationally selected chemical structures, and then analyzing a variety of endpoints.

FT: When you were saying, "A variety of," are you expanding beyond hydrocarbons now?

JS: Well, some were chlorinated hydrocarbons.

FT: Which you were looking at a little bit bigger picture?

JS: Right. So, PCBs, by the way, are chlorinated hydrocarbons. So, anyway, the chemicals had a structural relationship to one another except for slight differences. Chlorophenol is a phenol that has a chlorine on it. Benzo[a]pyrene was one of them, benzo[a]pyrene being the aromatic hydrocarbon that was the principal substrate used, and this hydrocarbon hydroxylase that was the enzyme activity that was important in eliminating hydrocarbons from mammals, and now, we know, certainly, of fish. So, we had a number of combined experiments we got together. We had worked with crustaceans, fishes, and mollusks. We had, I think, a very rational – and well ahead of its time – program integrating the various features that really are still important in understanding chemical effects in the ocean. The reason I say we were ahead of its time is basically the same reason that I'm glad we had the opportunity and the luxury of spending time in years, looking at these midwater fishes. Because we could do things that were much less ambiguous in interpretation and inference at the end, than we could in the 1970s or even in the early [19]80s. So, it was about at this period that there were two things that happened, I think. One is, now, this man, Harry Gelboin, at the National Cancer Institute, in whose lab, there were many of the important discoveries made about the hydrocarbons coming into an animal, causing an increase in the amount of this protein, this P450, that did the hydrocarbon hydroxylation, and that the hydrocarbon hydroxylation helped to eliminate these. Harry was involved in publishing a series of books called *Hydrocarbons and Cancer*. He called and asked if I would write a chapter for one of these books, the third volume in this three-volume series that he had edited.

FT: So, your reputation in the field was growing then. I know it is hard for you to say that, but when someone asks you to write a chapter – I always felt the greatest thing when you do your publishing or someone else does their publishing is you are referenced. That, to me, is the ultimate.

JS: Right. So, I did, and I wrote this chapter called – I can't remember the name of it, but I've got a copy of it around here somewhere. I think it was metabolism of hydrocarbons in the marine environment. I spent a long time. It was a good year I spent – over the course of a year, working on that chapter. I think it was, to me, a very important thing to have done. I think it was very well received, and I had, over the years, people who would come here and tell me how important that chapter was in helping them address questions and formulate questions. So, that now brings us to about 1980. That chapter was published in 1981.

FT: Then you were associated by this time?

JS: I think so, yes. By this time, I also have students in the lab. The first graduate student was Bob Binder, and the second was a man named Alan Klotz, both of whom did outstanding and important new studies on this whole issue of hydrocarbon metabolism, and particularly, the enzymes involved in fishes. Those two studies, the work of those two students, plus the work that I was doing myself with my own hands, pretty much set the stage for the next fifteen, almost twenty years of work. So, Binder's thesis involved looking at the enzyme involved in hydrocarbon metabolism in embryos of fishes, and the embryonic development of this whole capability. It is still a very important issue and relates to work ongoing in the laboratory today on developmental effects of chemicals in fishes. The human counterpart is chemicals and birth defects. The first studies on the developmental expression of these enzymes, Bob Binder. Alan came, and smart, smart guy, talented guy. He did what people ought to do when faced with a need to take a preliminary exam for his PhD with questions in oceanography. He didn't take oceanography courses. He sat down with oceanography books and read them all. He had a good memory, so he remembered them. That's important. Alan came and wanted to do some biochemical studies. Now, here we get back to purification of enzymes, an enzyme which I did for my PhD, and Alan did with these enzymes in fishes, these cytochrome P450 enzymes. He had the wisdom to seek a joint advisor. So, there were two of us, one in MIT and one myself – Christopher Walsh, who was, at that time, chair of the chemistry department at MIT, and myself. We co-advised Alan. That was helpful to have Chris involved. So, Alan worked about half time here, and half time in the lab at MIT, and purified a number of different cytochromes P450 enzymes. As an aside, by this time, this puzzle of P450 that I mentioned is really the ultimate isozyme puzzle, was beginning to be broken open.

FT: We are switching tapes. You were talking about the first couple of students that came in and started to work on the various projects.

JS: Right. So, Alan Klotz had purified a number of different P450 proteins from the liver of a local fish, scup, which, fortuitously, when I was casting around at some point for a species to work on – a lot of these questions, it didn't matter so much what species you use. If you're interested in finding out something about the enzymes themselves and how they occur in a class of organisms, you have to start somewhere. By that time, there were people working on these

enzymes in trout – a group at Oregon State, Don Buhler; a group at Gothenburg or Göteborg University, Lars Förlin; Jack Bend at NIEHS; (Jon Leach?) at the Medical College of Wisconsin, were the principal ones working on these enzymes and fishes as far as I recall. So, I was just about to say why this was such a great puzzle and where the intrigue was with sorting out this puzzle. So, if you recall back when I said that this P450 enzyme had a central role in chemical carcinogenesis and in pharmacology – and as it turns out, in steroid endocrinology, making and breaking down testosterone and estradiol, for example – and in oxygen metabolism, fixing molecular oxygen into an organic structure – people talk about nitrogen fixation. It means bringing nitrogen out of the atmosphere and putting it into an organic structure. Oxygen fixation occurs the same way. Oxygen comes out of the atmosphere and is put into a molecular structure. That's the catalytic – what's the word – commonality among all of the enzymes that are involved in all of these different things, and the environmental issues and the environmental impact and environmental import – and particularly, in the oceans, which is where we were focused. At the time, all of these features became apparent as involving P450. There was knowledge of only one enzyme, but knowledge that there could be hundreds, perhaps thousands, and as now we know, countless different chemical structures acted upon by this one enzyme.

FT: How did that work?

JS: There had to be more than one, but no one knew how many. There was evidence only for one, concrete evidence. Nobody knew how the enzyme was regulated. Nobody knew fully where it was expressed in the animal, how many different animals had it. There was a universe of questions, an unknown number of structures, as substrates acted upon by an unknown number of enzymes, regulated by unknown mechanisms. Well, that's a pretty good puzzle. So, in the early [19]80s, there was a lot of work – late [19]70s, early [19]80s, a lot of work going on in rats, mice, and rabbits, and in a few of our labs, in fishes, trying to get some leg up on these questions, this uncertainty. Allen did that. He resolved a number of different biochemical methods, was able to separate a number of different proteins that looked like they were different P450s, purified a couple, was able to see what kinds of catalytic activities they had, at least with a limited number of substrates, and make some antibodies in rabbits against these proteins. At that time, we also collaborated with Harry Gelboin at the National Cancer Institute to generate what's called a monoclonal antibody. In fact, a number of monoclonal antibodies against one of these proteins, which turned out to be the most important protein in environmental questions in fishes as well as in animals. So, now, we had the beginning of the reagent supply to be able to address questions more definitively in fishes, about this issue of how many substrates, what does it mean, how is the enzyme regulated. We worked on several of these proteins that had been purified initially by Alan Klotz, but principally, on this one that was involved in hydrocarbon metabolism. Later, and now, currently, we're working on all of them. There are eighty-nine different cytochrome P450 genes in zebrafish, and fifty-nine different cytochrome P450 genes in humans. But at that time, it was purified, see what's similar to what else, and see what you can learn by trying to characterize it however you could. Leading up to this, I also was involved in a collaboration which occurred as a result of stopping on the bridge to talk to someone, a summer investigator at the MBL, who was introduced to me by somebody else, who said he has an interest in this. He knew I was working on these enzymes. Collaborated with a group, published a number of papers on the characterization of these proteins using a technique called electron paramagnetic resonance, a group working at Bell Labs in New Jersey and Albert Einstein

Medical College. So, you get the sense that there is a biomedical relevance involved here. So, we saw ourselves situated ideally, working on a system in fishes with the potential biomedical relevance in enhancing understanding and a certain environmental relevance in understanding chemical effects in animals in the sea. This has continued on. We still see ourselves positioned in this way with a dual relevance. It's been important for our success in getting grants as well as in having the work recognized, I think.

FT: Well, it is also interesting to me, as I listen to you describe all this, how there is a certain amount of luck in certain things falling into place at certain times.

JS: Oh, no, question about that.

FT: I think when you talked about getting one of those initial grants, it is because that organization started to have an interest in that field and put money into that field. If the big organizations were not interested particularly in what you were doing at that time, there would not have been a heck of a lot of money for it out there. It was lucky that your interest and what they were willing to fund at that point.

JS: Right. So, there is a bigger question here. Is the agency's interest reflecting the field or is the field reflecting the agency interest? Well, it's a cycle. At some point, you jump in, and the agencies jump in.

FT: But I also think, further down the line, as you start to talk about multiples of multiples of multiples, it is a good thing computers came along.

JS: It certainly is. We would not be anywhere near where we are without them.

FT: I did not mean to be negative when I said this was a certain amount of luck. It is the happenstance of certain things happening.

JS: It is very much that happenstance. If, for example, we had not collaborated with Harry Gelboin in producing these monoclonal antibodies, the career would have been very different. Because for quite a number of years, we sat right at the forefront in our ability to ask and answer questions about these enzymes in fishes. So, you gain a position by what you're able to do, questions you ask, how you answer them, and the importance of the questions, and certainly, timeliness and serendipity, chance meetings, and an element of luck, maybe. But there also are those people who are speaking on your behalf sometimes when you don't know about it.

FT: That has taken on different degrees of importance over the years. Way back, the whole oceanographic area probably had a hundred practitioners running around. As some of the big organizations started to come into existence, you had people there that would speak for you and say, "Oh, yes, let us give him some money," and so forth. That has changed over the years. Then you get into what you were talking about with the other experts in the field. But not necessarily those that are going to distribute funds but are going to distribute the relevance of what you are doing and the expertise with which you are doing it. That helps you pick up stuff. When you have to write a grant – I just want to spend a couple of minutes on this. I hear such

conflicting opinions on grant writing. There are those that absolutely hate it, and those that say they like it because it gives them a chance to crystallize all their ideas, to put things together, see if they are heading in how is this whole process of grant writing for you? We talked about the importance of English, being able to write, to a scientist, which is not something the average person would think that would be of great importance to a researcher, but it is. What is that whole grant process like for you? Is it good, bad, indifferent, something you think, "My God, if I never see another one –" how does it work with you?

JS: The actual process is not that onerous, because I am one of those who finds that it does help you to really see what your questions are. How well are you asking your questions? What is the importance here? So, you have an opportunity to develop a theme in a way that you hope will be important. Sometimes, you have to do it quickly. Sometimes, you have more time to do it. Continuity of funding is very important, continuity of funding, because it allows you continuity of your activity in the laboratory. Without which, I know in my case, things would have been very different. I was very fortunate in being able to succeed with getting grant support, and support through the institution, or however, that allowed me to maintain an active laboratory that was continuous over a twenty-five, thirty-year period, thirty-five-year period. So, I was very fortunate in being able to have success in getting grants at various points in time. But I can tell you that the wolf was very close to the door. There were times when I felt sure that things were going to just crash in and end well. I don't have those thoughts anymore, because they never did. So, I don't think they will. Chance, I'm going to tell you just about chance and grant writing. So, I remember, at one point, this large program grant, the Pollutant Responses in Marine Animals, was a three-year grant with this multi-investigator group from the National Science Foundation. There was a second three-year competitive grant with pretty much the same group, although, one moved out and one moved in. When that was ending, that was in the early [19]80s, I was on the telephone one day with a colleague of mine at the University of California, Davis, who said he had to go because he was busy writing a grant application for NIH. I said, "Oh, what was that?" He said, "Well, didn't you know about it? There was this program announcement that is like a request for applications from the National Institute of Environmental Health Sciences for development of animal models for toxicology." Well, what I've been talking about is principally, toxicology, chemical effects in organisms. I thought, "Really?" He said, "Yes, you can find it online." So, I went online, and I found it. The deadline for that request for applications was eight days in the future. A grant application for NIH is twenty-five pages, single-spaced, carefully developed. I had, by that time, served on a grant review panel as a standing member at the National Institutes of Health, so I was reviewing grants in toxicology. Almost all had to do with rats, mice, and rabbits – in other words, all the people out in medical schools. So, I was working on fish. Well, they did get, periodically, grants with non-traditional species. They needed somebody on those grant review panels who they thought could do that. I would have been nominated for that position by this fellow, Jon Leach, at the Medical College of Wisconsin, who is another guy who was working on fish P450s. So, I was familiar with how to prepare it and what an NIH grant looked like, what it should look like, how it could succeed. I said, "I'm going to go for it." So, I marshalled all of the lab people. There were three or four students in the lab at that time and a technician or two. I said, "We're going to write this grant application and get it in." We did. We got it in. The deadline was eight days hence, but because it was a Saturday, it was actually due on a Monday. Monday was a holiday. It was actually due on Tuesday. So, I had an extra three days. Got the grant. So, if I hadn't talked to that guy on the

phone, that would not have initiated my entrée into the funding stream from NIH. Circumstances, happenstance, fortuitous events, chance, timing – then if those things work in your favor, then what you can do becomes important. I mean, your ability to write the grant, if you have the chance to do it, then you can do it. So, this is the mid-[19]80s. Now, we had a grant from the NIH to pursue studies of cytochrome P450 in fishes. To me, that was a big deal because this was something that put us now up at the level of the rest of the people funded by NIH to do biomedical research. So, now, we were really functioning at that interface between the biomedical and the environmental and oceanographic relevance of this kind of study.

FT: Nothing is more important today than this. I mean, the effects of what is around us –

JS: Right. So, now let me harken back. You said, "I can see you being at the MBL and at the medical and this and that." So, during those early years, in the 1970s, when I first got here – I'm going to take you back now to tell you what it was like to do this kind of work here. So, when I was a graduate student – I came from a biochemistry lab – you have a certain number of reagents. You have materials and supplies, and there's a glass pipette, long, slender pipette. You used a little rubber bulb on it called a Pasteur pipette. Well, in a biochemistry lab at that time, nobody uses them anymore because we've got micro and nano. But at that time, everything was done in milli. You'd use one, and you throw it away. You use another one, throw it away. Well, I came into the lab, and Kathy Burns was doing stuff with Pasteur pipettes. She had six of them that she had been using for six months, washing them. I thought, "Oh, my gosh. What am I in for?" The first time I ordered an ice bucket and keeping things on ice for biochemists is second nature. The procurement office here at the Oceanographic had called up and challenged my request for an ice bucket, "Well, what are you going to do? Cool champagne in it?"

[laughter]

Times were very much different, but that was the environment for biochemistry here when I first came. It was a non-environment for biochemistry. We persisted. There were people in the department here who would say, "Why are you here? Why are you doing this here? What does this biochemistry mean? What does this all mean? It's not oceanography." Without exception, all of those people today are doing molecular and biochemical research at one level or another, all of those who asked that question. I won't say any more about that.

FT: [laughter] Yes, I understand. Good. I think it is almost half past 12:00. We are going stop it here today. You were going pretty straight. Let me just make a quick note.

[end of transcript]