Philip Portoghese, Ph.D.
Narrator

Dominique Tobbell, Ph.D.
Interviewer

ACADEMIC HEALTH CENTER
ORAL HISTORY PROJECT

UNIVERSITY OF MINNESOTA

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In 1970, the University of Minnesota's previously autonomous College of Pharmacy and School of Dentistry were reorganized, together with the Schools of Nursing, Medicine, and Public Health, and the University Hospitals, into a centrally organized and administered Academic Health Center (AHC). The university's College of Veterinary Medicine was also closely aligned with the AHC at this time, becoming formally incorporated into the AHC in 1985.

The development of the AHC made possible the coordination and integration of the education and training of the health care professions and was part of a national trend which saw academic health centers emerge as the dominant institution in American health care in the last third of the 20th century. AHCs became not only the primary sites of health care education, but also critical sites of health sciences research and health care delivery.

The University of Minnesota's Academic Health Center Oral History Project preserves the personal stories of key individuals who were involved with the formation of the university's Academic Health Center, served in leadership roles, or have specific insights into the institution's history. By bringing together a representative group of figures in the history of the University of Minnesota's AHC, this project provides compelling documentation of recent developments in the history of American health care education, practice, and policy.

Biographical Sketch

Philip Portoghese was born in Brooklyn, New York in 1931. He earned a bachelor's degree in pharmacy from Columbia University in 1953. After graduating, he pursued graduate work at the University of Maryland. Four months later, however, he was drafted. He served in the Army for two years during the Korean War from 1954 to 1956. Upon completion of his service, Portoghese completed a Master's degree at Columbia University in 1958. At the recommendation of his mentor, Portoghese pursued his Ph.D. at the University of Wisconsin. Though the University of Wisconsin awarded his degree, Portoghese completed his dissertation at the University of Kansas, having followed his advisor, Edward Smissman to Kansas. George Hagar recruited Dr. Portoghese to the Department of Medicinal Chemistry at the University of Minnesota in 1961. Dr. Portoghese was promoted to full professor in 1969. Dr. Portoghese arrived at the University with an NIH grant and has since been continuously funded through the NIH. Though his dissertation work was on anti-cancer research, Dr. Portoghese dedicated his career to research on analgesic receptors. His work on stereochemistry has led to paradigm shifting discoveries regarding multiple opioid receptor sites in the central nervous system. He has also designed highly selective opioid antagonists based on the message-address concept, many of which continue to be used as standard research tools. In addition to his research contributions, Dr. Portoghese also served as Director of Graduate Studies in Medicinal Chemistry from 1974 to 1986, as chair of the Department from 1974 to 1983, and as editor of the *Journal of Medicinal Chemistry* from 1972 to 2011.

Interview Abstract

Dr. Portoghese begins part one of his interview with a review of his education at Columbia University and then the University of Maryland. He briefly discusses his military service in the Korean War, his Master's work at Columbia, and then his move to the University of Wisconsin-Madison for doctoral work on cancer research. He then relates his recruitment to the Department of Medicinal Chemistry at the University of Minnesota in 1961 and his changing research interests in analgesic receptors. Dr. Portoghese then discusses his childhood interest in chemistry, relating several personal anecdotes, and how this led to his interest in pharmacy. He shares his recollections of the College of Pharmacy when he first arrived at the University in 1961, Lawrence Weaver's tenure as dean, changes in the field of medicinal chemistry, and changes in the structure of the Department of Medicinal Chemistry over the course of his career at the University.

In part two of his interview, Dr. Portoghese offers his impressions of the creation of the Academic Health Center and the College of Pharmacy's move to Weaver-Densford Hall. He discusses relations between the Department of Medicinal Chemistry and the Pharmacology Department, changes in concepts of intellectual property at the University, Dr. Robert Vince's development of Ziagen, his own research on analgesic receptors, his continuous funding by the NIH, corporate interest in biochemical mechanisms, his development of different compounds as research tools, and industry support for drug

research. He then discusses his time as chair of the Department of Medicinal Chemistry, administrative support for the Department, and his time as editor of the *Journal of Medicinal Chemistry.* He ends his interview with the major technological innovations that have revolutionized the way research in medicinal chemistry is performed.

Interview with Doctor Philip S. Portoghese, Part 1

Interviewed by Dominique Tobbell, Oral Historian

Interviewed for the Academic Health Center, University of Minnesota Oral History Project

Interviewed in Weaver-Densford Hall on the University of Minnesota Campus

Interviewed on June 14, 2012

Philip Portoghese - PP
Dominique Tobbell - DT

DT: This is Dominique Tobbell. I'm here with Doctor Philip Portoghese. It is June 14, 2012. We're in Doctor Portoghese's office in Weaver-Densford Hall.

To get us started can you tell me a bit about where you born and raised and your educational background?

PP: Oh, sure. I was born in Brooklyn, New York, and went to the public schools in New York City. Then, I attended Columbia University for a bachelor's degree in pharmacy. Today, it is a 6-year PharmD degree. When I graduated in 1953, we were in midst of the Korean War and my draft board was after me, but I decided to go to graduate school anyway. As many provincial New Yorkers in those days I wanted to stay on the east coast. .I was accepted into a pharmaceutical chemistry graduate program at the University of Maryland.

Sure enough, after four months in the graduate program I was drafted. I was in the Army for two years, from 1954 to 1956.

When I was discharged I decided not to return to the University of Maryland, but to continue my studies in New York City at Columbia University, and received my Master's degree in 1958. I wished to pursue a doctorate degree. When my major advisor asked me where I had applied to a graduate school, I told him, "Well, I applied to the University of Connecticut because they offered me a fellowship." Then he replied, "The University of Connecticut? Why do you want to go there? They don't have a good program." I responded, "It's close by." [laughter] Being a provincial New Yorker, I wanted to be within commuting distance of the City where all my relatives were living. By the way, presently most of my relatives scattered all over the country. He responded, "Look, there is a wonderful program at the University of Wisconsin. Why don't you apply there?" After thinking about his advice, I applied to the Wisconsin graduate program in

pharmaceutical chemistry. I received an immediate response and an offer of a fellowship. [chuckles] It's amazing how an offhand response by a mentor can change ones lifetime trajectory. I guess that really demonstrates the importance of a mentor steering you in the right direction. It didn't seem like a turning point at the time. My New York friends were saying, "Oh, you must be crazy to leave New York City."

Did you ever see these posters? Of a New Yorker's view of New York City?

DT: Yes.

PP: …with the Hudson River and, then, nothing beyond.

[laughter]

DT: I even have friends like that.

PP: Yes.

[laughter]

PP: That's the way it was.

Going to the University of Wisconsin, Madison, was a big eye opener in that I'd never been on a big campus like that. It was full of action. By comparison, the Columbia campus was very sedate. Moreover, I didn't spend much time on the Columbia campus because I was always commuting. At that time, I lived in Astoria, Queens. I thought later on, that if I had been an undergraduate on campus at the University of Wisconsin, with all the distractions I wouldn't have graduated.

[chuckles]

PP: They serve beer at the student union. They had a sailing club on Lake Mendota. As a matter of fact, I joined the sailing club and became a sailing instructor in my copious spare time.

DT: [laughter]

PP: I made a lot of friends. In fact, I met my wife [Christine Phillips] there. She was pursuing master's degree in library science. I met her in 1959, and we were married a year later.

Madison was a wonderful experience, and I did things that I would never have done in New York, like skiing and sailing. It was a different experience. I met a lot of good friends that I've been in touch with over the years.

I was nearly finished with my Ph.D. dissertation when my major advisor, Edward Smissman, accepted a position as head of the Department of Pharmaceutical Chemistry at the University of Kansas [Lawrence]. I followed Ed to Kansas, but my degree was awarded from the University of Wisconsin. While I could have stayed in Wisconsin to complete my dissertation, I thought, well, maybe I'm better off going with my advisor, particularly if I want him to recommend me a good academic position. [chuckles] So my wife and I moved to Lawrence, Kansas. I wasn't there that long. It must have been for, let's see, maybe six months or so.

I wanted to get back to the East Coast. There was a job advertized at the University of Rhode Island. I applied. They never even invited me to go down for an interview. If they had offered me a job, I probably would have accepted, because of its east coast location, even though it wasn't a first rate department.

At that time, my wife was pregnant with our first child. When I traveled to Madison for my final Ph.D. orals, my major Prof's wife took care of Christine at their house. [chuckles] That's the way it was in Kansas. I didn't know how Chris would fare because it was toward the end of her term. So I went to Madison, passed my orals and returned to Lawrence as a fresh Ph.D. A week later my first son, Stephen, was born.

Just about that time, my major Prof must have been talking to the dean, George Hager, of the College of Pharmacy, University of Minnesota. George Hager, incidentally, was my major advisor at the University of Maryland, so he knew me. Smissman learned that the College of Pharmacy at the University of Minnesota had an opening in the area of pharmaceutical chemistry and recommended me to Hager. Without my applying, I received an interview invitation for a faculty position. Smissman convinced me that it was an excellent opportunity. Without my applying, I received an invitation from Hager for an interview for a faculty position. I presented a lecture on my Ph.D. research to faculty from both pharmaceutical chemistry and organic chemistry departments. My recollection is that it went well.

I received an offer for a faculty position from the University of Minnesota in 1961 and accepted after Smissman mentioned it was a great opportunity. These days, job offers without search committees didn't happen. As I decided to hit the ground running upon joining the faculty at Minnesota, I prepared a NIH [National Institutes of Health] grant application, submitted it, and it was funded. I was able to join the faculty and start my research right away. They didn't have starter funds in those days. NIH funding was easier to get then than it is now. I've had NIH funding without any interruption ever since I joined the faculty.

The Twin Cities area grew on me. I had an opportunity to go back to the east coast for a job when I received an invitation from the University of Rhode Island. I visited the University just to look around, but I really wasn't interested. I thought it would be counterproductive for me to leave Minnesota after only a few years.

DT: [laughter]

My second and third sons [Stuart and Philip] were born [1963 and 1965] in Minnesota. In regard to outdoor sporting activities, that's something I never really did in the New York area. However, being closer to nature in Minnesota, I slowly became a Minnesotan.

[laughter]

PP: We went camping and canoeing, in the Boundary Water area, kayaking, and, of course, sailing. Right now, I still go sailing. I live in North Oaks on Pleasant Lake, where I have a sailboat. Sailing has always been very relaxing for me.

I was assistant professor for three years. In 1969, I was promoted to professor.

Actually, the department then was much different from the way it is today. There were three faculty when I joined. There was [Ole] Gisvold, [Taito O.] Soine, and [Frank] DiGangi. DiGangi really wasn't doing any research. The College had a low profile, which obviously is a big change from its high stature today. We're a high profile College in the Academic Health Center [AHC]. As a matter of fact, we're considered the cash cow because of royalties through patents. The department faculty generally were very supportive. Actually, the most supportive person was Tai Soine. He died prematurely in 1978. I got the seminar program going. It was in a shambles when I first arrived. I taught pharmaceutical biochemistry, which I had overhauled from a descriptive course to one that contained biochemical pathways with chemical structures.

I have to digress a bit to mention an important incident that affected my entire research career. When I was a Wisconsin graduate student, Smissman asked me give a seminar and suggested a topic which was quite different from my Ph.D. research in the anti-cancer area. The topic centered on analgesic receptors. I became interested in that area of research and have pursued it all these years.

It was a very intriguing area because of the receptor site that had been postulated. I completely switched my research area, and my first NIH application and nearly all thereafter were focused on analgesics. Smissman had a profound influenced on my research trajectory. I've often thought that it's amazing how presenting a single seminar can change your whole research effort for a lifetime.

Maybe you have some questions you want to ask me?

DT: Yes. How did you even get interested in pharmacy and in pharmaceutical chemistry?

PP: Oh! yes. It so happened that my father had pharmacy in New York. He was a pharmacist. I used to work in his pharmacy to help him out, but I really wasn't enthralled with the retail business.

I was talented in art and had a strong interest in pursuing it as a career. In fact, when I was living in New York, I used to go to the Art Students League [of New York] to paint. I always received the top grades in art. When I was a teenager, my father asked me, "Well, son, what do you want to do? What kind of career do you want?" I said, "Well, Dad, I think I'll become an artist." He said, "Son, do you what to starve?"

Oh, I forgot to mention was that I was also interested in chemistry, particularly explosives. I used to make firecrackers for the Fourth of July. The firecrackers were big ones.

[laughter]

PP: I thought seriously about my father's comment. I used to read chemistry books and created my own chemistry set. In a retail drugstore, a lot of different things are sold, like Rit dyes…I don't know if you've heard of Rit dyes? Well, I confiscated an empty Rit dye cabinet to make a chemistry set. It had little compartments that accommodated the chemicals that I obtained through my father's pharmacy. So I had created a *fantastic* chemistry set. You couldn't buy anything like that, because the chemicals were not available without ordering through the proper sources. I used to perform lots of experiments in my bedroom of our apartment a block away from the pharmacy. Oh, I was crazy. One day I mixed ammonia and iodine. What happens?

DT: Is it a bang? [chuckles]

PP: Well, not right away. You get a precipitate. That precipitate is nitrogen triiodide, *highly* explosive.

[chuckles]

PP: *Highly* explosive. When it's wet, it's okay. What I did was to filter it on filter paper. Then, I was gone for a while. When I returned to my room hours later, all I did was touch the filter paper, and it blew up.

DT: Ohhh [whispered].

PP: Nothing happened to me. The room was a haze of violet iodine vapor. The amount of precipitate was *tiny*, perhaps only ten milligrams. It shattered the Erlenmeyer flask and the glass funnel. My mother came running into the room and said, "Philip, what happened?" I said, "Oh, nothing, Mom…" [laughter] …in the midst of the violet haze. That was an experience I'll always remember.

So I was interested in chemistry. As a matter fact, when I was drafted into the Army after attending graduate school for four months, my reading material was the chemistry books that accompanied me. When I returned to graduate school after two years in the Army, my M.S. research in pharmaceutical chemistry at Columbia University was essentially related to the chemical synthesis of pharmaceuticals. Pardon the digression.

DT: That was a good digression.

DT: It's interesting that you stuck with pharmaceuticals and didn't just go into chemistry.

PP: Yes. What my father secretly desired was that I would decide to go into pharmacy and become a partner with him in his pharmacy, and eventually take it over. His argument was, "Hey, go into pharmacy. There's chemistry and biology there, and all sorts of things that you like. Then, if it doesn't work out, you always have a profession to fall back on." That was his argument. But I didn't have any intention of working in a pharmacy. [laughter] I wanted to really do something that I liked. I think that's very important. What I'm doing now is not a job. It's something I like doing. [chuckles] Otherwise, I would have retired a long time ago. So that's the answer to your question.

DT: What was the College of Pharmacy like when you arrived?

PP: Well, the total number of faculty in the college numbered only about a dozen. Look at it today. It's grown so much that I don't know some of the faculty. In the 1960s we met in a small conference room in Appleby Hall where the College was located at that time. We moved from Appleby Hall to Weaver-Densford Hall in 1980. Today, there are over 100 faculty in the College and this incudes about twenty in the Medicinal Chemistry department. We've come a long way since I joined the Department in 1961. In this regard, our departmental faculty dramatically increased after Prof. Gunda Georg became chair about ten years ago.

DT: In the 1960s, were you involved in teaching the pharmacy students?

PP: Yes. That was the course I mentioned earlier, pharmaceutical biochemistry.

DT: It seems like there were some changes to the pharmacy education in the 1960s. The college set up the master's in hospital pharmacy. Do you remember any of that process?

PP: I don't remember the details. Yes, there were changes. Actually, [Lawrence "Larry"] Weaver came in, maybe, 1967 and was instrumental in effecting those changes.

DT: Nineteen sixty-five.

PP: Nineteen sixty-five. Okay.

He started making a lot of changes. His interest was directed more to the professional end of pharmacy. Our department really didn't prosper under him in respect to hiring new faculty. That came after he left. He had big ideas, and I would say a lot of them were, in retrospect, good. At the time, the medicinal chemistry faculty didn't agree with all his policies. He pushed hard for a move to the Academic Health Center. As we were in Appleby Hall, our department at that time was more interested in being aligned with

the Chemistry Department, which was across the street [Smith Hall and Kolthoff Hall]. But times have changed, and Weaver rightly foresaw the importance of integrating the College of Pharmacy with the AHC by the move to Unit F, now Weaver-Densford Hall. He really lobbied hard with the State Legislature to get Unit F funded. After years of trying, he was successful. I agree with what he did now.

Times have changed. The name of my discipline, pharmaceutical chemistry, was changed to medicinal chemistry in the 1970s. In the 1960s, medicinal chemistry was more aligned with organic chemistry than any other discipline. Our Department didn't have a strong interface with the Medical School or any of the related biological sciences. But, now it's changed. It's really amazing. As a matter of fact the changes have spread even to chemistry departments, in that they are increasingly interfacing chemistry with biology. They now have faculty who carry out research in chemical biology. Don't ask me what the difference between medicinal chemistry and chemical biology is, because there is overlap, a tremendous overlap. Some of the research being done under the name of chemical biology is indistinguishable from medicinal chemistry. When I first arrived as a faculty member, the organic chemists looked down their noses at medicinal chemistry. "You're really not doing good chemistry. You're just applying the chemistry. We're exploring new chemistry." But, now, they're doing the same thing. That's how times have changed. Actually, there are many more challenges to using chemistry to explore biology than just exploring new chemistry. I've seen all these changes take place over the past fifty years.

Speaking of changes, when I was quasi-chair of the department for ten years when departments were eliminated by Dean Weaver, I tried to get one of the Chemistry Department members a joint appointment in our department. His name was Rick [Richard M.] Borch. My reason for pursuing his joint appointment was that he took a leave of absence, to obtain an M.D. degree, after which he returned to the Chemistry Department. I thought he would be a good fit for a joint appointment because of his background in chemistry and biology. You know what? He never did follow up on it. I believe it was pressure from his chemistry department chair at that time.

DT: [chuckles]

PP: I believe it was related to the way some people felt about medicinal chemistry in the Chemistry Department. They don't feel that way now, mind you. It's completely changed. Presently, we have several members of the organic chemistry component of the Chemistry Department who actually have appointments in our Department.

DT: What do you think changed the Chemistry Department's attitude and when did that change take place?

PP: Well, the field of chemical biology has become a big thing. An organic chemist, Stuart Schreiber, promoted the name because of opportunities for utilizing chemistry to explore biology. They didn't want to use an established term like medicinal chemistry because of the emphasis on drug design, so they coined a new term: chemical biology.

This was acceptable to chemists. Now, most chemistry departments have faculty members that are working at the interface of chemistry and biology under the umbrella of chemical biology.

I believe part of this change was related to NIH funding. NIH originally had funds for faculty in chemistry departments even though they weren't doing any biology. The argument there was they were exploring chemistry that could be used by others to make new drugs. Then, after a while, that argument wouldn't work anymore because the number of researchers being supported by the NIH had grown and funds became tighter.

Also, as I've mentioned previously, there seemed to be more challenges at the interface of chemistry and biology than pure chemistry. I think that's also a contributing factor in the creation of the new name, chemical biology. A lot of high profile chemists are now working in biology and chemistry. The old timers in chemistry are doing pure chemistry, but many newer faculty in the organic chemistry area interface with biology to a much greater degree than back in the old days.

DT: Are medicinal chemistry departments typically in schools of pharmacy or are they sometimes in departments of chemistry or parts of departments of chemistry?

PP: Not often. Typically, in departments of chemistry it's called chemical biology rather than medicinal chemistry.

DT: So that's not just Minnesota? It's elsewhere?

PP: Yes.

When all the pharmacy deans go to their meetings and get together to discuss pharmacy professional and graduate programs, perhaps ten years ago or more, there was a move to eliminate departments and just have single department named pharmaceutical sciences. This involved combining several departments in the college. Our dean was caught up in this and eliminated departments, but it never worked here. It was chaos.

DT: Which dean was this?

PP: Let me see. First it was Dean Weaver and later it was Dean [Marilyn] Speedie. They eliminated departments, but on both watches it lasted only for a few years. If you have a department, you have much greater visibility within the field, so we all felt very strongly that we were not as visible under that organization. Also there was a lack of organization and confusion. No one knew whom to report to. It was crazy.

In this connection, I should mention that a lot depends on the culture of the college. For example, the School of Pharmacy at the University of Wisconsin never has had a department of medicinal chemistry there, and they have no desire for one. In speaking to the dean [Jeanette Roberts] of the School of Pharmacy, who is a graduate of our department, I inquired about that. She mentioned that she tried to get them to agree to

organize as departments, but they weren't interested. [laughter] They could have so much more visibility as a group if they were departmentalized. It appeared they didn't want to answer to a department head.

DT: [chuckles]

PP: See what I mean?

DT: Yes.

PP: I don't know if I've answered any questions here. I got to rambling.

DT: This is great. This is perfect.

How are we on time?

PP: In a few minutes, I have to leave for a meeting.

DT: I'll ask this question then. The 1950s and 1960s were an exciting time in terms of the new drugs that were being developed. Did that influence you at all in the work that you were doing in why it was so appealing to do medicinal chemistry?

PP: It didn't have a strong influence. In those days, I was more enamored with the chemistry than with the biology.

DT: When the health sciences reorganized in the late 1960s and the College of Pharmacy became part of the health sciences, how did that influence things in the Department and in the College?

PP: Oh, I think it was a positive development. But it wasn't until 1980 when we physically moved to the Academic Health Center that it became generally recognized that it offered much more opportunity to collaborate with members of various departments in the AHC.

DT: I know you have to get to a meeting. Can we schedule to continue the conversation?

PP: Oh, sure. Let me see. [Doctor Portoghese consults his calendar]

Interview with Doctor Philip S. Portoghese, Part 2

Interviewed by Dominique Tobbell, Oral Historian

Interviewed for the Academic Health Center, University of Minnesota Oral History Project

Interviewed in Weaver-Densford Hall on the University of Minnesota Campus

Interviewed on July 24, 2012

Philip Portoghese - PP
Dominique Tobbell - DT

DT: I'm with Doctor Portoghese, again, and it is July 24, 2012.

Last time, we were talking about the 1960s. In 1970, the health sciences were reorganized. We talked about the College of Pharmacy moving over into the health sciences where they are now. What were relations like between the College of Pharmacy, the Medical School, Nursing, Dentistry before this reorganization? Was there much contact?

PP: All I can tell you is my impression.

DT: Sure.

PP: Are you referring to 1970 or 1980?

DT: Well, 1970… Right, physically you moved over…

PP: Here, in 1980.

DT: Right. But the health sciences were reorganized administratively in 1970.

PP: Actually, we had, in the early 1970s, virtually no contact with the AHC. We were in Appleby Hall. We felt more at home being across the street from the Chemistry Department than being in the AHC. The move to the AHC was promoted mainly by our dean at that time, Larry Weaver. He was a bulldog. Nothing would stop him. He wanted to be housed in the AHC complex, and he lobbied continuously for a new building with the State Legislature. Finally, by 1980, we moved to the AHC. But, by and large, I would say our…the Medicinal Chemistry faculty members, were not enamored with the

idea of leaving Appleby Hall. Of course, things were very different in those days in that there was more contact with chemistry. Also, we weren't doing as much biology as we're doing today. As a matter of fact, today most of my biological testing is done in my lab. So medicinal chemistry, over the years, has really changed immensely. I would say it was a good that we moved; although, at the time, we didn't think so. In the 1970s, there was some friction between Larry and physicians in the Academic Health Center. This was related to the PharmD program that Weaver was promoting. There was a group of physicians in the Medical School who didn't like the idea of a PharmD program, perhaps due to turf issues. Larry was a guy who just would not quit. Because of that, we're here today. Eventually, we would have come here, I'm sure, but I think he accelerated the move.

DT: Do you remember any specific faculty members in the Medical School who were resistant?

PP: [sigh] I used to know the names. Now, I've just forgotten them.

DT: Sure.

Was there any subsequent relationship with the Pharmacology Department between Medicinal Chemistry…?

PP: We had probably the closest relationship with Pharmacology. One of my key collaborators was in the Pharmacology Department, Aki [Akira] Takemori. In those days, my lab would design and synthesize the compounds, and his group would evaluate them for analgesic activity. It was based on testing concepts that I developed for explaining the relationship between chemical structure and biological activity. Do you know what I mean? We were not necessarily trying to find a better analgesic, although, we wouldn't ignore such a finding. The work was more focused on elucidating mechanisms. I had a long relationship with Takemori even before we moved to the Academic Health Center. In fact, we even had a training grant with the Pharmacology Department. I don't recall if it was before or after we moved to the AHC

DT: It seems like a natural kind of alliance between pharmacology and medicinal chemistry.

PP: Yes, I learned a lot of opioid pharmacology by interacting with Takemori. We used to go to meetings together. It was a good relationship.

DT: Was there ever much collaboration with physicians in what you were doing?

PP: No. Our work was more involved with basic pharmacology. We were making pharmacological tools. As a matter of fact, about a half a dozen of molecular tools developed in my lab are commercially available and widely used by researchers in the field. These help investigators sort out receptors. We made selective ligands, including

affinity labels, for all of the opioid receptors. All of the molecular tools were used for basic research. We have developed compounds that possess clinical potential.

Interestingly, early on when I started out, the AHC had only one patent attorney. I remember his name.

DT: [chuckles]

PP: [G.] Willard Fornell. He was the only patent attorney around, and he was half time. [laughter]

PP: Those were different times. Very few of us were thinking of intellectual property. No one was thinking of patenting anything. If we would see some good compounds, we would publish them without consideration for its value as intellectual property for the University. I remember someone from a pharmaceutical company saying, "Hey, you should patent those first." Today we would, but then, it was very, very different. Now, of course, with the OTC and Center for translational medicine, I think the AHC has invested a lot of money in trying to get the most out of what the University has to offer. We certainly weren't taking advantage of it way back then.

DT: When do you think that changed, that there was more attention from within the AHC toward intellectual property?

PP: Well, I'll tell you. Maybe the fact that one of our faculty members developed an anti-AIDS [Acquired Immune Deficiency Syndrome] drug may have something to do with it. Also, greater interest in intellectual property was also occurring at other universities as well.

DT: That's Bob [Robert] Vince?

PP: Yes. It raised the department's profile as a potential money generator. It's over $500 million dollars according to the University. Normally, patents don't bring in that much money. [laughter] But that's what happened. University administrators, must have started thinking that maybe we could do some more of that. I think that's what got them started, but the greater emphasis on intellectual property has happened at other universities as well.

DT: Did Bob Vince just decide individually that he would get a patent on the compound? He would have individually orchestrated that? It wasn't the University that was pressuring him to patent?

PP: I think he's the one. He was geared more toward developing a drug and patents. What happened was that his major prof became a research executive at Burroughs, Wellcome [& Company]. His research was not originally aimed at the development of compound for AIDS, but rather evolved out of an earlier project. It grew out of a project to develop adenosine deaminase inhibitors. Then, at the Southern Research Institute [in

Birmingham, Alabama], one of the biologists who performed the biological testing compounds for Vince tested it against HIV. That's when it was discovered that compounds were active against HIV. Vince then switched to that area of research and refined a series of compounds to obtain a compound suitable for clinical use.

DT: That's my sense of what happens in a lot of drug development.

PP: Yes.

DT: It's not what, maybe, the initial intention was or the intention wasn't to develop a drug for certain diseases. It's through that testing process.

PP: Now, Bob may tell you differently.

[laughter]

PP: But that's the way I remember it.

DT: Do you think the passage of the Bayh-Dole Act in 1980 had much influence on commercialization?

PP: Oh yes. No one could touch anything from NIH before then. Yes, that was important.

DT: Where were your research funds coming from for your work on analgesics?

PP: All from NIH. I always had funds from NIH… I must have told you last time… Did I?

DT: That you had the longest…

PP: I wrote my first grant while I was still in graduate school.

DT: And you still have NIH…?

PP: I still do, yes. The number is different but…

[laughter]

DT: That's fantastic.

PP: The National Institute on Drug Abuse wasn't even in existence then. I was going through a different institute, at that time. I've had it for over fifty years.

DT: That's incredible.

PP: You can't really rely on industry. Industry might support you for a while, and then the money goes away, but NIH is a very reliable source of research funding. They've been generous with me.

DT: Did drug companies ever get interested and approach you about supporting your work?

PP: Yes. A number of my compounds were licensed out but none of them ever developed into anything. One spinoff was for Type 2 diabetes. There's a company that it's licensed to. I don't know if that will get off the ground. I'm trying to get people interested in it here, but it's difficult to do. I don't know the Type 2 diabetes people the way I know the analgesic people.

DT: My understanding is that diabetes is a significant research focus in other units of the AHC.

PP: Yes. What intrigues me about this compound is it's an opioid antagonist. I'd like to know the mechanism. This company isn't even interested in the mechanism. All they want to do is market it. By determining the mechanism, maybe that might lead to the development of a new series of compounds.

At my age, I have so many things going on here that I'm now making lists of things I have to do. [laughter] That's not only because there are a lot of things to do, but my memory isn't as good as it used to be…

[laughter]

DT: I think it's impressive that you haven't had to use them before now, because I use lists.

PP: I never used lists, but I'm having to use lists now.

DT: With your experience with drug companies, have you met any drug company researchers or drug companies that are as interested in mechanism as you are? Or do you think that tends to be the domain of the academics?

PP: Well, I think drug companies would be if they had a good lead to a potential application.

For example, the type of compounds that I was telling you about that I have for Type 2 diabetes. A person who formerly worked at Eli Lilly & Company contacted me. He had a theory that wasn't based on mechanisms that opioid antagonists might be beneficial for treating his Type 2 diabetes. He never had an understanding of why that might be the case, but he was taking a compound developed in my lab to successfully lower his blood glucose levels. He had the idea that maybe a kappa opioid antagonist would be good. He asked me for some of my kappa opioid antagonist for self-testing, and I gave him a

microgram quantity. Since he was originally from Lilly and he had experience in glucose monitoring, he was able to monitor his glucose levels. He claimed that my compound lowered his blood glucose. On this basis, he created a startup company. The University licensed the compound to the company. I didn't think the company was going to go anywhere. He died and his friend, a venture capitalist, who doesn't have a scientific background, raised the money for pharmacologic evaluation. They have some use patents, and the University has a composition of matter patent for the compound.

DT: Yes.

PP: That's it. His company is paying the University to keep the license going with the University. They have spent millions of dollars in the biological evaluation of the compound by Covance.

DT: Was the Office of Technology Commercialization involved in that process of starting up the company?

PP: No. Tom Clemens started the company based on self-administration of the compound as mentioned earlier.

DT: What's his name?

PP: His name is Clemens, C-l-e-m-e-n-s. His nickname was Tom. He teamed up with a friend of his who was the venture capitalist. I guess he's looking for someone to buy him out. He must have spent a lot of money. I received some of the reports, and they did a lot of work. In fact, Covance tested the compounds on monkeys and conducted toxicity and pharmacokinetic studies. I'd really like to know how the compound works.

DT: In the history of medicine, you hear, in the early twentieth century, of people experimenting on themselves. They have a compound, and they try it out. Now, it still happens.

PP: It still happens, but not the way it used to happen.

DT: Yes.

PP: A lot of times, that was due to serendipity. You hardly see serendipity anymore. I think the last serendipitous discovery was Viagra.

[laughter]

PP: The way things are going today with high throughput screening and other drug discovery technology, God knows how much they're missing.

DT: It's a different approach to pursuing mechanisms if you're doing high throughput screening and just screening for activity versus the kind of more rational design.

PP: When they get a hit with high throughput, then they may go back, particularly if they want to develop the compound and find out what the mechanism is. The way it used to be was someone might pick up a compound off a shelf and fortuitously discover a useful activity. The benzodiazepines are a good example.

DT: Have you had much interaction with the FDA [Food and Drug Administration] then when you developed your tools, your pharmaceutical tools that you've developed?

PP: No, the FDA isn't really interested in that.

These are basic research tools for the study of drug mechanisms. Without the tools, one can't do very much. For instance, let's say you have an opioid antagonist that's selective for a specific opioid receptor. If one wanted to know which of the multiple receptors an analgesic is working on, selective antagonists would be able to sort that out. We have developed selective antagonists for different opioid receptors for that purpose. Different antagonists are used to determine which opioid receptor is antagonized. One of our opioid antagonists was employed to form a molecular complex with the mu opioid receptor for the determination of its x-ray crystal structure. The x-ray of crystal structures of all the opioid receptors were published just a few months ago, published in *Nature* [483, 383-383, March 21, 2012]. Two of those receptors [mu and delta] used antagonists that we developed. Crystallization of each of the receptors was dependent on the binding of a selective antagonist to the recognition site of the receptor. They wouldn't have been able to do it without a selective antagonist. I guess that's an example where the tools are not used in pharmacologic studies on animals. However, most of the use of our tools has been concerned with either cell-based studies or animal studies.

DT: I was a biochemistry major, and I spent a year working at AstraZeneca in the protein science department. Crystallography, that's all very familiar to me. So I wonder what's the difference then between biochemistry and medicinal chemistry. It seems there would be some overlap.

PP: In biochemistry, you're usually not designing small molecules and synthesizing them. I would say that's the main difference. Medicinal chemistry is at the interface of chemistry and biology. Biology could be any number of things. It could be biochemistry. It could be pharmacology and other biological areas as well.

DT: And as you say, the synthesis is unique.

PP: Yes. All members of our department know how to synthesize compounds—with the exception of an X-ray crystallographer…

DT: [laughter]

PP: …that we have in our department

DT: Okay.

[laughter]

DT: They probably have some specialized knowledge, too, that the rest of you don't.

PP: Yes. They know the techniques associated with growing crystals and the determination of their crystal structures. Also, they have computational skills that permit the design of new molecules that interact with the protein whose crystal structure has been determined.

DT: But not the organic.

PP: More physical chemistry. This is why x-ray crystallographers and medicinal chemists complement one another in developing biologically active molecules.

DT: Sure.

PP: That's the thread that goes through everyone's expertise in medicinal chemistry. It involves teamwork.

DT: You mentioned a little while ago about drug companies, that they might be interested in a project for a short time and, then, they'll go on to something else. Do you have a sense of what drug companies are interested in supporting? Do you have a sense of how they decide whether or not they're going to support a project or support the work that you're doing?

PP: Well, it has to have a payoff for the company, I would think. Of course today, for a lot of companies, the strategy has changed, particularly with well-known institutions on the West Coast, for example, where the company would give a research institute millions of dollars so that they would have access, first crack, at novel and profitable technology that's developed. I guess that's more recent, as that infrequently happened in the old days.

DT: Do you think when drug company funding is involved, does that kind of change the way the research is done? Does it influence the researcher?

PP: It all depends on what the contract reads.

[laughter]

PP: From what I've seen today, it may not. They have their own projects and the company is betting that maybe enough useful technology would come out of whatever

they're working on, that they would have a foothold in the development of that technology to produce a drug.

DT: That resonates with what I know historically. I've studied the pharmaceutical industry since the 1940s and particularly looked at Merck [& Company]. Sure, they had specific short-term projects that they would be interested in funding, test this drug or look at this, tell us about this. But it seemed that they were more interested in funding basic research and seeing where it would go and, then, as you say, being there to benefit. If it looks commercializable, then they can get in on that. They were also interested in just having connections with the leading researchers.

PP: Yes. But you can't really depend on that over a period greater than five years. One must have some assurance that funding will continue over a much longer period. This provides more time to do research without interruptions or deadlines. I've always felt that was important. For this reason, I never thought it necessary to consider working on a company contract unless the company that contacted me had a proposal that meshed with my research program and would advance my research. That has happened, but not frequently.

DT: I've noticed attitudes toward the pharmaceutical industry in the public have changed over the decades. Do you have any sense that there is any kind of reluctance on the part of faculty to take drug company funds, to be funded by them?

PP: I don't believe there is. I think if they need the funds, they'll get it wherever they have to get it. I think most of the members of our department would rather, if they had a choice, get it from NIH or some other funding agency. For instance, in the Pharmaceutics Department, there's more likelihood that they may be funded by industry. That's more in line with pharmacokinetics and related studies. A lot of the studies they are doing might be contracts, too. I think the Department of Pharmaceutics has many more contracts than in Medicinal Chemistry.

DT: That makes sense. You were chair of the Department of Medicinal Chemistry. I have it from 1974 to 1983.

PP: Yes.

DT: What did you think were the major issues that you dealt with when you were chair?

PP: [pause] Dealing with the dean.

[laughter]

PP: That's what I recall…dealing with Larry Weaver. [laughter]

DT: Of course, you were chair during that transition from Appleby Hall to Weaver-Densford.

PP: Yes.

Larry was more interested in professional aspects of pharmacy than in research. So it was always an uphill battle. [chuckles] It wasn't easy. He was a nice guy. I liked him. But if he had a bunch of money, I know who he would give it to—and it wasn't Med Chem [Medicinal Chemistry]. [laughter]

DT: Were you able to increase the faculty during your tenure?

PP: No. That was the thing. We were fortunate no one left. If someone would have left, Larry would have used the salary money for another department that he was trying to develop. He was building the clinical areas… Let me see now. Maybe, we did replace Soine, our department chair, after he died. He passed away in the 1974. We did get someone. I'm not sure, but perhaps it was Rodney Johnson. I don't think about this very often.

DT: It was a while ago. [chuckles]

PP: Yes.

DT: The Department of Pharmaceutics, how did they fare? Were they more on the kind of clinical side, or were they in the same boat that you…?

PP: It was clinical pharmacy that was really getting all of the attention. Clinical pharmacy was the dean's baby. It was important to him because of the Pharm.D. program that he was developing. All the resources were going to the clinical pharmacy program. We had to fight to keep what we had. [chuckles]

DT: That must have been particularly tough, I think, in the early eighties with all of the retrenchment that was happening. There was reduced state support, reduced federal funding. Was that a particularly difficult time?

PP: Yes. We were de-departmentalized for a while. I've forgotten when all of that happened, but we were de-departmentalized twice, once with Larry Weaver. When Gilbert Banker replaced Larry Weaver as dean, he returned us to departmental status. Banker allowed us to hire new faculty. When Marilyn [Speedie] became dean, she de-departmentalized us for a second time. I believe she was following the wishes of the new senior vice president, Brody, as there was a move to reduce the number of departments at the University.

It was a mess. No one knew who to report to. After two years we were re-departmentalized again. That's the way we are now. We were re-departmentalized by Marilyn Speedie because she realized that organization wasn't working well. The Pharmacognosy Department was integrated into the Medicinal Chemistry Department upon restoration of departments.

DT: So it was more the fact that the combination with Pharmacognosy didn't work, because of size?

PP: Pharmacognosy was combined with Medicinal Chemistry because of its small size. The combination has worked.

DT: Oh, okay.

PP: That was done when Brody was on board, and done to satisfy him. Everyone was doing their own thing. No one knew who to report to.

DT: It could be the greatest thing…freedom from…

PP: Yes.

DT: …or it could fall down.

PP: You bring up a good point about freedom. It depends on the culture. For instance, I went to the University of Wisconsin as a graduate student. Medicinal chemistry was not departmentalized, and they didn't want to be departmentalized. Because they didn't want to answer to anyone. [chuckles]

DT: Is their program as big as Minnesota's?

PP: No.

I think becoming a department gives you visibility that you wouldn't have otherwise. They had some very good people in in medicinal chemistry at Wisconsin, but they are not as visible as we are.

DT: You said Gilbert Banker was the one who really supported medicinal chemistry.

PP: Yes.

DT: Why was that?

PP: He came from Purdue [University]. They had a big tradition for research there. He was interested in getting us back to where we should be in research. This was in contrast to Weaver who exhibited some antagonism to research as Dean. He wasn't a friend of research.

DT: I saw that he previously worked in the research division of Pitman-Moore [Company].

PP: Yes.

DT: He was director of the R & D [research and development] lab.

PP: But his main interest at Minnesota was developing the clinical area.

DT: So when Banker arrived, did he deemphasize the clinical program or did he just maintain support for that?

PP: He maintained support for that, but he recognized that we'd better increase our basic science faculty. We hadn't hired faculty in many years in Med Chem during Weaver's tenure.

DT: During Weaver's tenure and, then, Banker's tenure was there any tension between the clinical faculty and the basic science faculty?

PP: Yes, from the standpoint that the clinical faculty were getting everything, and we were getting nothing, there was the tension during Weaver's tenure.

DT: Yes.

PP: The tension isn't there now.

DT: What about when Banker came in and increased the focus on the researchers? Did that antagonize the clinical faculty at all?

PP: I don't think he was ignoring the clinical area. He just had a more balanced approach. Weaver's approach was not balanced. That was the main thing.

DT: Do you know why Banker decided to resign in 1991?

PP: I'm trying to remember if he just retired.

DT: I think he went to [University of] Iowa afterwards.

DT: Then Bob [Robert] Cipolle served as acting dean for four years.

PP: Yes.

DT: What was he like as acting dean? Did he have a good balance for the clinical and the basic science?

PP: Well, there was still that bias. No one in the Medicinal Chemistry and Pharmaceutics Departments wanted someone from the clinical area to be a dean of the college. He wasn't that popular. I remember he was associate professor, at the time, and I recall he had to be promoted to professor to be considered for the deanship. He was voted down and that ended his being considered.

DT: I think he told me that. I interviewed him a few weeks ago, and I think he told me that.

PP: Yes. I think that's what happened. So the acting head of the Academic…

DT: Was it Cherie Perlmutter?

PP: Ummm… Or was it someone from the Medical School who was acting…?

DT: I think it was Shelley Chou, maybe?

PP: No. Was the dean also acting as…?

DT: Was it Frank Cerra?

PP: No, it wasn't Cerra. This was before all of that.

DT: I'm forgetting my chronology. There was Robert Anderson, who was only in the position for a year.

PP: Well, whoever it was felt that the faculty didn't have confidence in Cipolle.

DT: I can imagine with the prior experience that you had encountered with a clinically focused dean there was not a lot of interest in going back to a clinical dean.

PP: Yes, I think that was it. There were always budgetary problems connected with either hiring new faculty or how much funding the department was going to get.

DT: I guess until last year, from 1972 to 2011, you were editor of the *Journal of Medicinal Chemistry*.

PP: Yes. Forty years.

DT: Can you talk about what it was like serving as editor of the biggest journal in your field?

PP: I was appointed Editor-in-Chief [EIC] of the *Journal of Medicinal Chemistry* [JMC] in 1971 and officially started in 1972. I spoke to Dean Weaver about it, and it didn't impress him in the least. [laughter] That was Weaver, as he was focused on the clinical program. But the *Journal* then wasn't what it is today. I inherited the journal from it's founder, Prof. Alfred Burger, in the Department of Chemistry at the University of Virginia. The journal was about ten years old at that time. He had one assistant editor. As the second EIC, I decided that in order to increase the impact of the journal without ignoring my research, I needed some assistance. So I requested three associate editors and received permission from the American Chemical Society. This was long before

computers. I decided if I wanted to interact with these editors, they would have to be close by. So I appointed three faculty from my department as associate editors.

PP: We were in Appleby Hall when we opened the JMC office.

DT: Yes.

[telephone rings]

PP: Excuse me. [break in the interview]

PP: Now, where was I?

DT: Hiring three associate editors.

PP: Oh, yes. That was great, because one is able to interact with the editors. We would meet and talk about manuscripts and editorial policy. It was really terrific. Fast-forward to 2012, the journal has ten editors including the EIC. Over the years the journal grew slowly, but steadily. My aim was to give the journal a greater international flavor. So I appointed editors from Europe. Presently, there are three editors from Europe [Germany, Italy, and Denmark] and an editor from China. I've seen the journal grow from two inches to twelve inches of pages. You can't measure it now because it's all online.

DT: Sure.

PP: It has the highest impact factor of any journal in the area of medicinal chemistry. We went online a number of years ago. I must say, you lose a certain amount of collegiality with your associate editors when you're online. It's very nice to have them around.

DT: Yes.

[laughter]

PP: It was an interesting experience, I must say. I liked it from the standpoint of my interaction with all of the other editors of American Chemical Society [ACS] journals. Right now, they have about forty journals. The editors would meet every January in a warm place. All the editors would get together and talk about things related to their journals. The ACS staff also made presentations on improvements in store for the journals. La Jolla [California] was a key site for our meetings.

DT: That's not bad.

[laughter]

PP: That was a pleasant venue. I would say the Journal was good for the Department because its name was on the masthead. Over the forty years of my tenure, researchers in medicinal around the world recognized the Department as the home for the *Journal of Medicinal Chemistry*. When the ACS was looking for my replacement, I nominated my department head [Gunda Georg] as EIC in order to maintain the high visibility of our Department. Gunda was among the four finalists and was selected as a co-Editor-in-Chief [co-EIC].

DT: That's great.

PP: So it's still here!

[laughter]

DT: That's fantastic.

PP: Actually, Gunda's so busy, that she accepted on the condition that she would be a co-EIC. The other co-EIC [Prof. Shaomeng Wang] is at the University of Michigan. I also submitted his name. [chuckles]

DT: That's good. You were able to name your successors.

PP: Yes.

DT: Those first few years of being editor, you were also chair of the department. How were you able to balance your workload?

PP: That was why I appointed three associate editors at Minnesota. I wouldn't have been able to do it otherwise. Of course, as editor, you don't cross the t's and dot the i's. They have their own copy editors for that. The EIC's job is more for the science and knowing who to send the manuscripts to for review and to establish editorial policy. It's not as much work as you might think. I was assigning most of the manuscripts to the Associate Editors. When I first started as EIC, I handled a reasonable number of manuscripts, but over the years, I handled fewer and fewer myself. Manuscripts were assigned to editors based upon the content. Managing all the editors became a larger and larger job. I had nine editors. Also, I created some new publication categories. One of these was named "Perspectives." So I appointed a "Perspectives" editor. We used to have a book review editor, but we discontinued book reviews because publishers are printing far fewer books in medicinal chemistry.

Presently, the ACS journals division does not usually permit in-house associate editors. The ACS wants spread out geographically. Early on there was good reason to have in-house associate editors, but, with the development of the internet there is less reason to do so. Additionally, the ACS presently is attempting to reduce editorial costs by eliminating editorial assistants. In this regard, many of the new journals that are being

created don't even have editorial assistants. Everything is done online, and they have centrally located editorial assistants to assist the editors.

DT: How were you able to finance the growth of the Journal? Where were you getting the financing from?

PP: Oh, the Journals Department of the ACS.

DT: So it wasn't through increasing subscriptions? It wasn't through advertising or anything like that? It was from the ACS?

PP: It's from subscriptions, of course. The ACS has about forty journals that generate revenue through subscriptions. As a matter of fact, I think the *Journal of Medicinal Chemistry* is one of the biggest money-makers among the forty journals because it serves all of the pharmaceutical industry as well as academia. At one time, sixty percent of the papers were from the pharmaceutical industry, mainly from "big pharma." It's more like forty percent today because the pharmaceutical industry is publishing less, and there are more academic institutions that are involved in medicinal chemistry research. Industrial medicinal chemists are not publishing as many papers because they have less time to do so. It's apparent that the majority of publications are either from research institutes or from academia.

DT: It makes sense why the drug industry would be so invested in reading the journal, in addition to publishing. That's where they need to keep track of what's happening in academia and where the innovation is coming.

PP: Oh, sure.

The JMC has an editorial advisory board [EAB] of thirty to forty scientists. In order to assure balance, I appointed a representative number of medicinal chemists from industry and from academia.

In order to have EAB members representative of the cross section of published papers, I had formulas for the source and for gender. For example, of the European countries, Italy, submitted the greatest percentage of papers of any of the international contributors. Consequently, the greatest number of European EAB members were Italian.

[laughter]

Don't quote me on this, but the American Chemical Society has become much more corporate. They're competing with commercial publishers now. It used to be more of a society type of atmosphere. It's not that way anymore. It's more like, "We want to beat Elsevier [Publishing]."

[chuckles]

DT: You've alluded to some of this already, but what do you see as kind of the major changes in the science and technology of medicinal chemistry during your career?

PP: Oh, god! I'm doing things now that I never dreamed I'd be doing. I find this amazing. For instance, back when I started and as recent as twenty years ago, I never thought I would live to see the X-ray crystal structures or the opioid receptors, and here we are. All of the technology, the confluence of computers and biotechnology, has revolutionized medicinal chemistry. When I started, I was simply making molecules and sending them to someone else to have them tested. Then, thirty years ago I decided that I wanted more control over biological testing. I hired a lab tech who perform all of my biological assays. At that time it involved only animal testing. As the technology developed, we started to work with cultured cells, isolated tissue, and smooth muscle preparations that contain opioid receptors. With further advances in technology, we employed ninety-six well plates in a flipper apparatus and immunofluorescent imaging of receptors. That's one of the more recent technologies that I picked up.

That's what's so exciting about the field today, the enabling technology. I can simply carry a compound across the hall from the chemistry lab to the biology lab and have it tested in many different ways. When I started out, that wasn't possible. In this regard, it is enabling from the standpoint that you can create your own priority scale for testing. When you're depending on someone outside of your lab to test a compound, it may not always be that collaborator's highest priority.

[laughter]

PP: Right now, I have a couple of civil service research scientists dedicated to doing the biological testing. They're a very critical part of my research program.

Also, I have a consultant who got us started in immunofluorescent imaging of receptors. He works for R&D [Systems, Incorporated] in the Twin Cities. He was instrumental in training one of my civil service scientists to perform imaging experiments.

Technology has made a difference. We're doing so many things I didn't think were possible. It's a different world.

DT: It sounds it. I can just picture the kind of changes and how monumental they were.

PP: Oh, yes, and I've seen it all!

[laughter]

PP: The difference is like day and night. It's incredible. This is one of the reasons why I haven't retired yet. Well, also, as long as I have research money and my health, I think I'll keep going. I have four more years on this grant. Maybe I'll retire after that.

DT: Or maybe you'll just get another one.

PP: Possibly, the science very exciting.

[laughter]

DT: This has been really interesting and fascinating. Is there anything else that you want to share about the history?

PP: Oh, there probably are a lot of things, but I can't think of them right now.

DT: This has been fascinating. If you think of anything else, we can meet again.

PP: Yes. A lot of disjointed stuff. There is probably a lot of repetition.

DT: No, no.

PP: It was nice to discuss this with you.

DT: Great. Thanks.

[End of the Interview]

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