Yusuf Abul-Hajj, Ph.D.
Narrator

Dominique A. 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

Yusuf Abul-Hajj was born in Jerusalem, Palestine. He earned his bachelor's in 1962 and his master's in 1964, both from American University of Beirut. He moved to the United States and earned his Ph.D. from the University of Wisconsin's College of Pharmacy in 1968. He was recruited to the College of Pharmacy at the University of Minnesota by Dean Lawrence Weaver in 1968. His research has primarily concerned the relationships between estrogen and cancer. More specifically, he has investigated how tumors can transform cholesterol into estrogen, the development of alternative treatments for breast cancer, specifically aromatase inhibitors, and how estrogens are involved in carcinogenesis. He served as head of the Department of Medicinal Chemistry from 1984 to 2005. Dr. Abul-Hajj continues to serve as a professor in the College of Pharmacy.

Interview Abstract

Dr. Yusuf Abul-Hajj begins his interview by reflecting on his education, his choice to pursue medicinal chemistry at the University of Wisconsin, the difficulties of transition and travel between Palestine and the United States, and the Arab community in Minneapolis. Dr. Abul-Hajj then describes his early career in the College of Pharmacy at the University of Minnesota, with particular attention to the clinical pharmacy movement, the creation of the Pharm.D. program, and problems that consequently arose within the basic science, research-oriented departments of the College. He then discusses the following topics: collaboration between the Department of Medicinal Chemistry and the Chemistry Department; the revival of social and administrative pharmacy; relations between clinical and basic science faculty in the College; collaborations between faculty in Medicinal Chemistry and faculty in the Medical School; the appointment of Gilbert Banker and his tenure as dean of the College; collaboration between Medicinal Chemistry and the pharmaceutical industry; his own research on estrogen and cancer; drug development in academia; and the creation of the Center for Drug Design.

Interview with Doctor Yusuf Abul-Hajj

Interviewed by Dominique Tobbell

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

Interviewed in Diehl Hall, University of Minnesota Campus

Interviewed on August 6, 2012

Yusuf Abul-Hajj - YA
Dominique Tobbell - DT

DT: This is Dominique Tobbell. I'm here with Doctor Yusuf Abul-Hajj. It's August 6, 2012, and we're in my office in Diehl Hall.

Thank you for speaking with me today.

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

YA: I was born in Jerusalem, Palestine. I went to Saint George's School throughout my elementary school and high school and, then, went to the American University of Beirut [AUB], and I got my bachelor's and master's degrees in chemistry. That was from 1958 to 1964.

Then, I came to the University of Wisconsin where I spent four years at the College of Pharmacy in Madison. I graduated in 1968, and I accepted a position at the insistence of Dean [Lawrence] Weaver [from the University of Minnesota] to come and consider a position in Pharmacy. I never wanted to work in academia. My hope was, all along, to work in the pharmaceutical industry, but he came and talked to me in Madison and convinced me to come out for an interview. During that time when I came out for the interview, I met many of the faculty at the College, especially in Medicinal Chemistry. I was very impressed with the people, the quality of all the individuals, as well as the research. I decided, well, let's give it a try and see… I can always go to industry. So that's what happened. I've been here since 1968.

[chuckles]

DT: What led you to want to pursue chemistry and, then, medicinal chemistry?

YA: Actually, I always wanted to go into chemical engineering, but at the American University of Beirut, they didn't have chemical engineering at the time. So my other alternative was chemistry. I got into chemistry and did my master's in organic chemistry.

Then, I wanted to continue my graduate work. My professor at AUB suggested a professor at Georgetown University, and he was able to give me a research assistantship, and I agreed to come and join his lab. Then, my brother [Marwan Abul-Hajj], who was at the University of Wisconsin and who was in medicinal chemistry, said, "Why do you want to go Georgetown? Why don't you come to Wisconsin?" We were very close. Even though we are brothers, we are also friends. He was able to talk to one of the professors in Madison who said he was willing to give me an R.A. [research assistantship]. My brother convinced me to renege on the previous acceptance, and I joined Madison in this way. I always wanted to be in bioorganic, and Georgetown had a reasonably good bioorganic program. While being in pharmaceutical chemistry, medicinal chemistry, you bring in the interphase between chemistry and biology. At that time, it was more chemistry and less biology. But my interests were more biology, and I joined a professor that really did a lot in the area of biology, and that got me interested in this area of research.

DT: What was the professor's name?

YA: Charles Sih, a wonderful research scientist. I learned so much while I was in Madison.

DT: You grew up in Palestine. What were the educational opportunities like for you at that time and what options did you have for a university?

YJ: None in Palestine. There were no options for me there. The closest and best university in the region was the American University of Beirut, very difficult to get in at AUB, but I was a good student, so my credentials helped me get admitted. I could have gone to the University of Cairo, which is also one of the top universities in the region, but they use a lot of Arabic in their education and my Arabic was weak. Saint George's School is an Anglican school. I don't know when it was established in Jerusalem, but, at any rate, everything is taught in English, except the Arabic. So Arabic was taught as the Arabic language. So I grew up in a British school. Of course AUB teaches everything in English, so that was a good transition to go from Jerusalem to AUB.

DT: Did you always plan to eventually move to the States to continue your education?

YJ: No. I wanted to be a high school teacher. I got interested in chemistry because we had a British chemistry professor at Saint George's School. He is the one who really got me enthused about the topic of chemistry. That was what I really wanted to do. When I went to AUB, they did not have chemical engineering, so instead of that I got my

chemistry degree and, then, would back to Jerusalem and teach chemistry at my high school.

However, at the end of my junior year, I started thinking, do I really want to go back and teach in a high school? That was a turning point. I said, "No. I want to pursue my career a little bit more," so I enrolled for the master's program at AUB and continued on.

DT: What was the demographic of the British school that you went to? Is that where a majority of Palestinian kids in Jerusalem went to school?

YA: No, not the majority. Actually, we had public schools. We had Friends School in [Ramallah], which is a Quaker school; it's an American school. But there were some foreign schools there like a German school, a French school, and, of course, the British. School. Then, there were also public schools. These were all private schools. Public schools are really good; some of them are excellent schools. In retrospect, I think they have been very good training grounds for students. I've seen the graduates and what happened to some of their graduates as they grew and evolved and developed their careers. They have excelled now in their own bright careers.

Why I went there, I'm not sure…the rationale. My parents sent me to that school.

DT: My parents sent me to a private school, too, and I don't really know why. [laughter] They make those decisions.

Your brother who was at Madison, how much older was he than you?

YA: He was three years older. We were roommates at the American University of Beirut. We overlapped five years at the AUB and, then, he came… He did some work in nutrition at AUB and, then, went to Vanderbilt [University]. Although, the Vanderbilt's Nutrition Department was exceptional, he really didn't like the nutrition program as a discipline. So he decided to switch. He's a pharmacist by training, while I am not a pharmacist by training. But we ended up studying pharmaceutical chemistry at the University of Wisconsin in Madison.

[chuckles]

DT: That's really neat.

YA: When I came to Madison, we lived together. It was nice, because he already had paved the way for me, and I didn't have to have to start from scratch like other foreign students when they come to this country. They have to deal with a different culture, different foods, different things that you need to think of. I didn't have to do that because everything was already there.

[chuckles]

DT: Obviously, your brother helped with the transition as you said, but how welcoming did you find Madison not only to you being a foreign student but to other foreign students, as well?

YA: It was 1964 and that was the Vietnam Era and for me, it was a shocking experience when I came to Madison, because I had such an expectation of what American culture is, based on movies. I only think of Doris Day and Rock Hudson. Then, I come to Madison, Wisconsin. I see a lot of greasy hair and no shoes or sandals or what have you, torn pants, and lots of riots on campus. That's the second most liberal campus in the United States after [the University of California] Berkeley. There were bombings there in the Physics and the Math Departments. That was very close to the pharmacy school. We felt it at that time.

But, how was I welcomed by the community? Most graduate students, we felt welcome. It's a mixture of both American and foreign students, and it was fine. I'm not sure how it would have been if I came as an undergrad, at the time. But the University of Wisconsin is a very diverse school, and I think they had a lot of students from outside of Wisconsin, unlike Minnesota, at that time. There was an influx of a lot of easterners, because of the liberal way of thinking, so a lot of students came from New York, Philadelphia, and other East Coast cities. Both undergrad as well as graduate students came to Madison.

DT: When you were at Madison, did you think at any time that you might go back to Palestine once you'd gotten you degree or when did you decide that you might stay in the States?

YA: I decided in 1976. Yes, I always felt I wanted to go back, but the 1967 [Arab-Israeli] War broke out while we were still students, both my wife and I. When I graduated, I could not go back to Jerusalem, because I was married. If I was single, the Israelis would have allowed me to join my family. But they claimed that my immediate family is no longer my parents. My immediate family was my wife and our kids and, therefore, they did not allow me to enter Palestine or work even up until now. So I tried over the years to say, "Well, there's a temporary job for me here," because I had aspirations to go back to Palestine. It never materialized. In fact, my wife got very, very unhappy. That was her first time ever leaving Jerusalem. We got married in 1965. Then, we went on our honeymoon. Then, she came along with me, and she was enrolled in a school in Madison, Wisconsin, too. When she graduated, she thought that she was going to go back and see her family in 1968, but she couldn't. It was difficult times, after Weaver recruited me here. We didn't have internet at that time. My salary was quite low, and phones were quite expensive, overseas, but, still, she would call her family, and there was a big bill at the end of the month for me.

[chuckles]

YA: But we could not get a visa to enter Jerusalem. The Israelis were not allowing us. I had a Jordanian passport at the time. I talked to Dean Weaver. I said, "My wife's name is Fadia and she's very, very unhappy, and she's getting very antsy." Weaver took an

interest in both myself and my wife because we were the first foreign-born faculty to join the College of Pharmacy. Weaver liked foreign individuals as a whole, and he liked to travel, so he took us under his wing. He became like my surrogate father for maybe four or five years. At one point he saw me and said, "Oh, you look grim." I told him, "Well, I'm having a hard time with my wife. She's very unhappy. She hasn't seen her family since 1965." He asked me a few questions, and I said, "These are the issues. The problem is I cannot get a visa, and I cannot use my Jordanian passport to enter Israel. Once they stamp it, then I'm doomed. I cannot renew my Jordanian passport. That's one thing. Plus, I cannot enter then Jordan or any of the Arab countries." I talked to Lawrence Weaver, and he said, "Give me all the information about yourself." So I gave him all the information. Two months later, he came with an American laissez-passer [one-time travel document for humanitarian reasons only] a one-time trip. That allowed me to go to Jerusalem and come back. He helped us quite a bit in that regard. So my wife was very, very happy, at the time, seeing her family.

But I kept trying to figure out what I wanted to do with my career. Did I want to stay here? She's from Jerusalem. I felt that I wanted to have my family grow in our culture rather than in a different culture. I kept trying. The only offers that I was able to get from the Arab world were teaching. I had no interest in teaching. I had skills in pharmaceutical biotechnology, and I'm able to produce antibiotics from scratch using raw materials. I thought this is what my aspiration would be, to get started there by setting up some small company that can produce antibiotics, vitamins, and the like, because they didn't have any of those chemicals or drugs, except from buying it from overseas or buying raw materials like the active ingredient and the other excipients, that are, in say, a pill, and they just put them together, compact them, and you end up with a pill. Well, I just didn't feel that was exciting for me.

I tried working with essentially, over there, governmental institutions and tried to see if they were willing to set up companies and subsidize these companies, at least in the initial stages. We did some feasibility studies with an economist from the American University of Beirut, and he made a cost analysis of how much it would cost to produce, let's say, a kilogram of antibiotics using the manpower resources, other resources, raw material resources and so on. We would take these documents and present them to these individuals in authority. But they were so ignorant, most of them, although, some of them I knew when I was at AUB. Some of them became ministers of health at the time; I saw them in 1974. They say, "Why should we invest in starting something from scratch when the price for making the compound in Jordan versus the price if you are buying the compound ultimately from Italy or Poland or Spain or what have you were about the same? There is not really that much difference." But they didn't understand what it actually meant to do your own. It's not only your own pharmaceuticals. You are creating a bottling [packaging] industry, et cetera. You're creating a packaging [chemical] industry. You know, you have these concentric industries that surround this focal point of, let's say, the pharmaceutical industry and it could create new jobs for the population and also independence. They just didn't think that way.

Finally, I was able to get one guy from Saudi Arabia who was very rich. They got us

together through a common friend. This guy was interested to help out. He said, "I'm willing to pay a few million dollars, but I need to start getting interest on my money in three years. For that kind of industry, there's no way you're going to be able build the fermentation tanks—these are huge fermentation tanks, about 50,000 gallons—and then there are a lot of mechanical aspects of these fermentation tanks, plus marketing, and all that stuff. It's going to take a number of years before it can be profitable enough to give that person interest. He said, "He will wait only for a maximum of three years." I said, "There's no way it's going be doable." He said, "I'm sorry."

So, at that time—it was 1974, 1975—I was spending my sabbatical at the American University of Beirut. During that time, I got lots of teaching offers throughout the Arab world, but I just didn't want to teach. ~~plus~~ Research there was almost ~~null,~~ non-existent.

So I came back to the United States. I had two sons at the time. I didn't want to take my sons from one culture to another when they are teenagers. If I wanted to take them, I want to take them when they are still young enough so that when you shift them from one culture to the other, they adapt very easily, and they are not confused. So I came back. We decided that's it. We're going to raise our family in the US. We had a house, but we were not yet ready to buy what we wanted to buy, because it was all tentative. This was not the furniture that we wanted to buy, but we will buy whatever we can get by with during that period. Then, after we decided, we figured out, forget it. We're going to live here. I liked being here in Minneapolis, plus, I like the College as a whole, and my colleagues were nice to work with.

DT: Was there much of an Arab community at that time in Minneapolis?

YA: Not really. When we first came, there was no community. Most of the community that we got to know, a lot of them were professors mostly in the Medical School and some in Agriculture. They were more the educated individuals because the environment in the Twin Cities was not conducive for laborers and so on. So it was more clean industry. Most of the industry…you have Cargill. You have Honeywell. You have Univac. All these industries require individuals with, you know, degrees. At that time, it was only degree-holding individuals that could work here and mostly a master's level or higher and some medical doctors, as well, that we met.

The influx of the Arabs in the community started really after 1982, the Lebanese Invasion. That led many Palestinians to leave, some Lebanese left and settled here. But many of those that came here were not highly educated. They came in, and they worked as laborers, opened small stores, supermarkets, corner stores, and the like. Then, again, as the intifada, the first intifada, came about, that brought in an influx of Egyptians, Palestinians, and so on.

So, really, I would say, the build up of the Arab community maybe was after 1985, and you started to see a mass. Then there were no religious groups. There was no mosque at the time. There was a mosque built, I think, around that time, mid-1980s, the first

mosque, and that brought the Muslim community together, which, at that time, was donated by a Palestinian who had business in Saudi Arabia, and he was a very rich guy.

DT: Were you raised religious? Did you miss not having a mosque?

YA: I am a Muslim. Of course, so is my wife. I was not brought up very religiously. When we were here before we had kids, we didn't go to the mosque. I think the first time we went to the mosque probably was in the mid-1970s because we're talking about my kids. We wanted to give them some sort of training in Islam, and we would go, like, on Sunday and so on for a few years. They started growing up, the community started growing, and these kids started fighting there, and they weren't learning what they were supposed to be learning.

[laughter]

YA: Not being so religious, we didn't push any further.

DT: I can only imagine that it was a difficult time to be so far away from home. Have you been able to go back more freely than you were?

YA: Only after 1976, when I got the American passport. Then I could travel. But with that American passport, it was difficult because the Jordanians did not renew my passport because I had to renounce all other nationalities when I raised the hand.

[chuckles]

YA: In Israel, when I go there and they knew I am Palestinian, I tell them not to stamp my passport. Because if they stamp it, then I can't go to Jordan or Lebanon or Syria or any other countries. Sometimes they don't. They do all that transaction on a sheet of paper, a loose sheet of paper. Sometimes, at the borders or at the airport, they look at you, and they want to give you a hard time, and they stamp it. Then, for two, three years, I can't go there. We're still having problems. Right now when we go there, we try to tell them, "Please, don't stamp the passport." I would say sixty percent of the time, they don't; forty percent of the time, they do. It depends on if I am with my wife. My passport says, "Born in Jerusalem." Her passport says, "Born in Palestine." So when she goes to the airport and has the immigration officer look at it, they say, "What is this? Palestine? There's no such thing." My wife is a feisty woman and she says, "This is the land of Palestine." Of course, they get very offended, and they say, "Okay. You need to go to this person." They go and keep her in the interrogating room for two, three hours…earlier, like in the 1970s and early 1980s. Now, they're not so picky. But they will stamp the passports for her, and that's it. If they stamp her passport, then I can't travel, because I want to be with her. [chuckles]

DT: That sounds very difficult.

YA: Yes, it's difficult. Of course, we couldn't have two passports for many years. Around 1997, Congress allowed people to have dual passports if they were born in a different country, and they came and acquired an American passport. This was a new thing. Now, I have dual citizenship. If they stamp my passport in Israel, I still have the Jordanian passport, and I can travel to the Arab countries. Until such time when there is peace in that region and then different nations start accepting people from different countries, then all I need is one passport. I don't care, but right now, it's all good to travel with two passports.

DT: Can I ask how you had a Jordanian passport?

YA: After 1948, Palestine was split between Israel and Jordan. So Jordan took the eastern part of Palestine, and Israel took the western part. So any citizens that were in that region became Jordanians. So we became Jordanian citizens.

DT: That makes sense. I know a little bit of the history of the region, but not enough to place the role of Jordan, specifically. That just sounds like a very difficult time.

So your wife, obviously, accommodated to being here and being happy to be in the Twin Cities?

YA: Oh, yes. Now, no problem. It became difficult, of course, raising kids in this society here and the culture, especially the teenage years. Even for my American colleagues, the teenage years are difficult as is, let alone having a foreign kid of foreign ancestry grow up in this society here. We had certain moral values that we could not abandon, but my kids, of course, were under pressure to deal with these issues while they were growing up because all their friends were accepting these things and their families allowing these things and we weren't. So the struggle that we had to go through is like a push/pull thing and how do you draw the line between the two. If you are too tight and you're suffocating the kids, then you don't want them to run away from the house. So it was a difficult four years for us. But, luckily, we passed over that.

DT: [chuckles]

YA: The kids have done well.

DT: You mentioned that, even while most of the 1970s were particularly difficult in terms of trying to get back to Palestine, you really enjoyed being at the College. What was the College of Pharmacy like when you arrived in the late 1960s and those early 1970s?

YA: Dean Weaver was wonderful to me during the early years at the College. For others Dean Weaver, maybe a difficult person. He was especially good to me during the first five years, very nice to me and very helpful to me in the sense that I'm not a pharmacist by training, yet, I'm teaching in a college of pharmacy. I didn't know the discipline so well. We were on a nine-month appointment. During summers, I had to either work

outside the College for a living, because I needed to earn some money in the summer, or I had a grant to pay myself or do something. The first few years, it's hard to gear up to get the grant. The first year you write a grant, you're still adjusting and, then, to get out a research proposal… Unlike Doctor [Philip] Portoghese, he came with a grant. Dean Weaver told me, "Yusuf, most of the other faculty already have their pharmacy degree." I was the only one that didn't have it. He said to me, "I will support you for two months in the summer if you work and acquire pharmacy skills." Pharmacy skills—his thought was the beginning of clinical pharmacy—is to work in a hospital pharmacy, work in a drugstore, or work in a clinic. So I worked at University Hospital pharmacy for two months just learning the lingo. I didn't even know the lingo of what pharmacy is all about. I have a Ph.D. in chemistry.

[chuckles]

YA: That was, of course, like two different languages, especially when you start teaching the pharmacy students. So he paid my salary for three years: one year when I spent it in a drugstore, one year in a hospital pharmacy, and the third year… He wanted to institute the clinical pharmacy, and he said, "Why don't you go and work in a clinic?" So I worked in the Endocrine Department here for one month, and, then, I went to the V.A. [Veteran's Administration] Hospital. They had a very good endocrinologist, at the time. That was an area of interest for me, because I work in the area of steroids, so the endocrine and diabetes clinics were the right choices for me. I acquired a lot of knowledge being in these locations, not having had any experience in these areas. That helped me later on with my teaching and the influx of clinical pharmacy.

When we started the Pharm.D. program, we had six students. We didn't teach them pathophysiology. Our students were enrolled in the Medical School pathophysiology course. Every week, we had six faculty—three from clinical and three from basic sciences—that would meet with these six students for three hours, once a week. We discussed all sorts of topics, say endocrine and, then, you have the clinicians talk about, let's say, diabetes or adrenal disease or oral contraception or what have you. Then, you have…I'm the basic scientist, but I am from the field of chemistry. Then, we have people from physical pharmacy and, then, we have people from pharmacokinetics, drug distribution, and drug levels, and the relationship between the dosage and the drug's blood level and so on. We would be there as the basic scientist faculty, asking the students these questions.

So I acquired these skills early on. A lot of it had to do with Weaver's interest in me and pushing me to strengthen my pharmacy related background. And I, of course, was very supportive of him—in the early years…

[laughter]

YA: Yes, it was good.

DT: You mentioned the clinical pharmacy movement. It seems like that was such a strong priority of Weaver's.

YA: Very much so.

DT: What was that like for the basic scientists in the College?

YA: There was resentment. Initially, there were no funds for the expansion of the clinical program. Weaver tried to get funding for the program from the State Legislature to shift to the Pharm.D. or bring in the Pharm.D. program, hiring new faculty, and the like. The University and the legislators did not provide sufficient funds, so Weaver was using the College resources. The departments, at that time, did not have budgets. All the control of the money was in the dean's office. At that time, if a faculty member retires or leaves, the dean would take that salary and redirect it to other areas. The area that he was very supportive of and wanted to expand and establish was the clinical program. So we felt the impact of what Weaver was doing as we were losing resources.

Of course, later on, Weaver dissolved departments. When he dissolved departments, he took more authority over not just space, but budget and programmatic expansion. There was quite a bit of resentment from both Med Chem [Medicinal Chemistry] and Pharmacognosy, at the time, as well as Pharmaceutics to a certain extent. He was able to play with the faculty in Pharmaceutics. They were divided. Some were supportive of Weaver and some were not as supportive, while in Med Chem and Pharmacognosy, we were mostly not supportive. The reason is that we get NIH [National Institutes of Health] funding and with NIH grants you get indirect costs, and the only people that were bringing NIH dollars at the time was Medicinal Chemistry and Pharmacognosy, and Weaver kept all the ICR [Indirect Cost Recovery] funds, and he used them in any way he felt was appropriate. So he was a one-man show rather than a team effort. We were the players but he was the coach and he was saying, "Do this" and "Do that." There was resentment that we were not getting resources. We didn't get a lot of equipment support from the College. Small equipment, we can get ourselves, but a lot of pieces of equipment, we're talking about $50,000 at the time, a total of about $500,000 now, so it was very difficult for us to get these pieces of equipment. So we became very dependent on the Chemistry Department. Chemistry was across the street from Appleby Hall, so we can walk from our labs just across Fifteenth Avenue to Chemistry, and we could use their instruments for our needs. But we had to be secondary. So if we had chemistry students wanting to use it, they had priority over us. That was part of the friction that we had with Weaver.

DT: Was there any discussion among Pharmacognosy and Med Chem about protesting the way that Weaver was running the College? Was there any avenue for you to launch a complaint?

YA: Well, early on, there was not that much. As individuals got stronger they could speak out. I was assistant professor, so you just keep your mouth shut.

[laughter]

YA: That's why I say, I was very good friends with Weaver during the first five years. But beyond that, I would speak up, and I would say that this was not right and so on.

Then, he dissolved the department in 1974. So we became leaderless. We became like one unit, even though we had departments before, we didn't have budgets. But we still had a cohesive group that could sit together and talk and plan and, then, can go as a group and make requests to the dean. But once you dissolve the department, it becomes one on one. Whoever, it doesn't matter how big the person is, if you go in front of the dean, they'll break you, and they do what they can.

[chuckles]

YA: Yes, we didn't have it and, let's say, up to, maybe, 1977, 1978. But maybe around 1977, 1978, we started working collectively. Some of us actually went and talked to the vice president for academic affairs. I've been there several times complaining about the fact that the resources have been redirected, and there's no infusion of newer people—although, there has been newer people but all as it relates to the professional pharmacy program. The program has been shifting. Let's say, there was a demand that we start teaching immunology to our pharmacy students. It's not us that put the demand…the accreditation boards. So they say, "Students have to learn immunology in the pharmacy program." We didn't have an immunologist, so we have to go out and hire somebody who is capable of teaching micro [microbiology] and immunology. That's the approach at the time…the College was working. There was nothing planned for research. Research was individualized, or if we still were a department, then we think as a unit…but we didn't have resources to develop and expand the program.

DT: Were you taking any graduate students at that time in Medicinal Chemistry?

YA: Yes, oh, yes. Our first graduate student graduated in 1929. I have the list of all the graduates in the recently published book, *From Digitalis to Ziagen* [:*The University of Minnesota's Department of Medicinal Chemistry* by Yusuf J. Abul-Hajj and Richard Broderick, 2012].

[laughter]

YA: So some of these things are in the book.

DT: Sure.

YA: I tried to be not as, maybe, pointed in the book. I tried to be a little bit more politically benign.

[laughter]

DT: I'm glad that you're being forthcoming here.

Yes, I can imagine that that must have been difficult for the medicinal chemists in that way. So you were largely dependent, then, on NIH funding to build the research programs?

YA: That's it. We had to get funding. The thing is we were singled out as individuals or as a group of individuals by the dean to go out and get funding, yet, the other faculty in the other departments that could not get NIH funding were given some funds to do research from the dean. That became a point of friction, where, if I'm supporting my dean and there is, let's say, a critical vote at the faculty meeting, then I'm going to make sure that I'm going to be voting with the dean; otherwise, my resources are going to be cut. While, if I'm an independent researcher, I could express my opinion because the dean wanted the money and, at the same time, I already had tenure, so between the dean pushing us in Med Chem and Pharmacognosy to go get grants, because he is acquiring these ICR funds, and he's using them to run the College. Yes, we had some very tough meetings.

DT: When you went to the vice president for academic affairs in the late 1970s, was he supportive of your position? How did he react?

YA: You know how administrators are. They are always supportive of other administrators. I mean, don't…I have to be careful here.

[laughter]

YA: Maybe you can turn it off for a second.

[break in the interview]

YA: Weaver wanted to push the University to establish a Pharm.D. program in the early part of the 1980s. He went against the wishes of the University and even the Legislature. When the University said, "No," to having a Pharm.D. program, Weaver went up against the University and started publicizing that we had a Pharm.D. program, but he was using internal resources to redirect and establish the Pharm.D. program. That, of course, upset many of the administrators. The administrators' idea was, why decide to have only the Pharm.D. program? Why don't you allow the students the option of selecting a bachelor's degree in pharmacy or a Pharm.D. degree? That was the rationale at the time. I think he must have angered some of the top administrators. The claim is he has resigned but some of my colleagues say, "We think that maybe he was asked to resign."

DT: I was curious what happened, because I saw in the Archives this push to have the Pharm.D. only program. It looked like it was going to happen and, then, there was that pushback that you described. I'm glad that you filled in the gap there, because I was unclear on why there was pushback and who was supporting Pharm.D. only.

YA: We always, the basic science faculty, had questioned the role of Pharm.D. in pharmacy practice, because we weren't sure what the Pharm.D. graduates would be doing out in the real world. Yes, Pharm.D. was accepted, maybe in hospitals but mostly academic hospitals. But when you go out in the community, like in Ramsey or Hennepin County Hospital, early on, they would question whether these people are needed on the floors, and are they going to play a role in rounds and talking to nurses and medical residents, and the like? All we have done is we have been able to convince the medical community, especially in the teaching hospitals, that means, besides us here at the University, all the others like Ramsey and Hennepin County, Methodist, Abbott Northwestern, all of those that have sites have used these clinical pharmacists. And they found out that they actually play a role, that they could accommodate, and also they could rely on. But out in the community, some of the private hospitals were very reluctant to hire individuals like that.

But, then, in 2000, there was a mandate by AACP [American Association of Colleges of Pharmacy] that all colleges of pharmacy would have only the Pharm.D. degree. Now, that came from the top down, and the University had no say-so about it. But in the mid or early 1980s, when Weaver wanted to push, the University stepped in and said, "Let's have the two degrees and let the students decide."

DT: For the basic scientists then who were teaching the pharmacy students, how would that have changed your teaching responsibilities? Or what kind of teaching did you do in the Pharm.D. program and how was it different from the bachelor's program?

YA: Well, first of all, we had to dilute our curriculum. We had to eliminate certain things in our curriculum, like all the labs. We had labs in the basic science courses. We had to eliminate all those labs. They felt that we had too many credits in the basic sciences, and they wanted to decrease the number of hours. There's a lot of overlap between Med Chem and Pharmacology. And in fact, yes, there was overlap but also there was some redundancy. So we met as groups of faculty from Med Chem and Pharmacognosy and Pharmacology in the Medical School. Our Pharmacology faculty teaches a pharmacy course using Pharmacology Medical School faculty. I don't know how long this is going to last, but I think [Marilyn] Speedie would like to see maybe all the pharmacology courses taught by pharmacy faculty because a lot of the tuition dollars would shift from Pharmacology to Pharmacy. Administrators, this is how they think: how can they get more money to the college to run their programs?

At any rate, we decided then, all of us, to get together in Pharmacology, Med Chem, and Pharmacognosy and see how we can teach a unified course between three departments and decrease the duplication in the units and, then, sequence the lectures. Sometimes, I would be teaching steroids, let's say in the fall and, then, people in Pharmacology talk about, let's say, steroid pharmacology on prednisone or oral contraceptives, in the spring. What we decided is, well, if we're teaching the basic aspects of steroid chemistry and biochemistry, they'll come in right after I'm done with that section and talk about steroid pharmacology. We've done that throughout the sequence of what we teach in the Med Chem and Pharmacology. It's been going on since 1975.

Now, we're overhauling our curriculum, and we're using this as a model for what can we do to bring in some more clinical and maybe integrate some aspects of the clinical training in certain areas, like when we talk about insulin and talk about diabetes, and then, okay, treatment of diabetes. So they're trying to bring things as more of a package, as a unit, rather than separate entities. This is what we're doing right now in the curriculum division.

DT: That sounds like it would be a really productive change for the students. I guess having everything in sequence is easier to learn.

YA: It could be, but, sometimes, redundancy is not bad. The other thing that would happen is dilution of the material. I was telling one of my students, this year, as a matter of fact… I have a bank of questions, and I started teaching the endocrine unit the way that I have been teaching it since 1973. But I've lost a lot of time teaching it as I used to be teaching it, but, still, some aspects have carried over. I was looking at some of these test questions that I gave in the 1970s to see if I can use them. Believe it or not, some of these questions were hard for me to answer.

[laughter]

YA: There was much more rigorous basic science training in the mid 1970s and the 1980s. Right now, it's more clinical training, and we became more therapeutic even in as it relates to basic aspects of medicinal chemistry related drugs. It's become more clinically oriented, so we talk very little about research, about development, and so on.

DT: You mentioned, obviously, the Pharmacology Department. I'm curious…obviously you mentioned you have some collaboration in teaching, but I'm wondering whether there's been much research collaboration with the pharmacologists over your career.

YA: Yes, there has been. Phil Portoghese had a long-standing collaboration with Professor [Akira] Takemori for many, many years. Takemori left the University, and since that time, I think, Phil has decreased the collaboration. He started collaborating with Horace Low, who is the head of Pharmacology, now. They work in the opiates. I think, also, they're not working together as much right now. When you collaborate, personalities also have to click, even in science. You sit and communicate; you want to use your partner on an equal level rather than subordinate level. Sometimes, some people use their collaborators in a subordinate fashion. Some of them continue to work as such because they benefit from, maybe, a senior faculty that they're collaborating with is, in part, funding their research problem. But if they are equally funded, you see some breakups of some collaborations. We saw this with Phil Portoghese. I thought when Horace Low was hired, that we would see a lot more collaboration between Portoghese and Horace Low. It worked for only, maybe, four or five years.

DT: How about collaborations with the Chemistry Department? You mentioned obviously when the College of Pharmacy was in Appleby Hall, Med Chem was using

some of the Chemistry Department's equipment. How were intellectual relations between the chemists and the med chemists?

YA: Not very good. I think the chemists, for many years, looked down upon the medicinal chemists. Yes, we could use their instruments, but, for example, none of our faculty had a graduate faculty appointment in chemistry. Partly, it's cultural. The chemists felt that, well, we're doing an inferior kind of chemistry. Yes, our chemistry is not really the very basic chemistry. We're using the basic aspects of chemistry to apply it to drug-related topics and drug-related discovery. But we are using what they are using in many ways. I'm not going to be pushing arrows [electron pushing]. That's not what we are all about. You know? You've taken some chemistry?

DT: I was a biochemistry major.

DT: So you know when I say, pushing arrows you're getting two electrons going from the carbon to the oxygen and, then, that's the chemist, that's how it goes. Well, we use them in our research and in our training of students. When we're talking about why is this reaction working as it relates to the drug? We use that as it relates to the basic principles of organic chemistry. But they always look down upon us. Partly, it's cultural. They had very strong individuals in organic chemistry that did not accept us. We ate lunch with them at the Campus Club. We were friends with them, but never on an equal term. They always felt, "Ahhh, they are doing okay," but not to be part of the Chemistry Department. Once you become a graduate faculty, that means you're going to be training students in chemistry and getting a Ph.D. in chemistry while you are a medicinal chemist.

Now, later on, many years, I pushed for increased cooperation between Chemistry and us. We had a chemistry professor by the name of Wayne Gladfelter. He became chairman, and I was talking to him, "How can we increase the interaction between Chemistry and Medicinal Chemistry?" I suggested that maybe initially we have joint courses, the same course, but it has two different course numbers: one a Med Chem number and one a Chemistry number. Then, the students can take the course, but you'd have a mixture of Med Chem faculty and Chemistry faculty teaching that course—or Biochemistry [faculty]. The other thing that we said, "Let's start getting a graduate faculty appointed to Med Chem from Chemistry and vice versa. He told me, "Why don't you nominate one, and I'll nominate one." So I nominated Rick Wagner from our department, and he nominated Tom Hoye from theirs. That means they come present a seminar for the program and, then, the faculty welcome them. The same vice versa. Now, the old generation of chemists are gone. You have the younger generation, and I think, now, either four or five of our professors have graduate faculty appointments in Chemistry. That means we get more chemistry graduate students. Now we have a joint training grant between us and Chemistry.

DT: The tension then between Chemistry and Medicinal Chemistry here, was that specific to Minnesota or to do you think that was more broadly between the disciplines of chemistry and medicinal chemistry?

YA: I would say broadly. There are some programs at [University of] Michigan where the med chem and chemistry and biochemistry are much closer than we are.

DT: During the early 1970s, it looks like the Department of Social and Administrative Pharmacy was created. Do you have any insights on why that department was created and how that influenced the College more broadly?

YA: We always had something before that; it was called Pharmacy Administration. We've had this kind of training I think before I came even. I think they hired one professor by the name of Hugh Kabat. He came the same year as Philip Portoghese. Both came in 1961. Hugh Kabat came, essentially, to revive the Pharmacy Administration program. So it's been around. Then, after Hugh Kabat, they had Albert Wertheimer. He came in with a slightly modified form of training of students in Pharmacy Administration where they put more sociology, psychology, economics, whatever, a mishmash of courses they put together. I haven't followed it too much. I know a little bit about the politics in that program, but not really the content of the topics.

DT: Do you feel comfortable elaborating on the politics a little bit?

YA: Kabat was a very strong right hand of Dean Weaver. Essentially, he became like the associate dean for education. He was very supportive of the Clinical Pharmacy program. A lot of the ideas came from him about the Clinical Pharmacy program. Weaver was very supportive. But Weaver was never an academic, as you know. He came from industry, but Kabat was much more politically astute. Weaver doesn't negotiate—he said, "Well, this is it" and "this was it"—while Kabat is sort of the workhorse. So he worked with Weaver closely. When Weaver dissolved departments… I think Wertheimer came in… When did he come, do you know?

DT: I think 1972, the Department of Social and Administrative Pharmacy was retitled. I think it was 1972 that he came.

YA: Because in 1974, we dissolved departments.

DT: I have here that it was the early 1970s.

YA: It could be he came to build up another program. I can't remember what he did, more a research-based program and that had funding, a good amount of funding.

Albert was a very aggressive individual, and he's very ambitious. Dean Weaver and Hugh Kabat were very supportive of Albert, at the expense, again, of other priorities within the College. Albert and I worked together. When I became department head, I worked with him a lot because we were on the executive committee, and we had a lot of different opinions. He and I almost ninety percent of the time never agreed.

[chuckles]

YA: One time, we agreed, and he was surprised. He made the comment at one of our meetings, "Hey! I'm agreeing with Yusuf."

[laughter]

Maybe it was difficult for us to understand what they were doing, and I probably didn't take the time to find out more about them. I really didn't have the time to go and find out about another discipline. Maybe it's his failure, I think, right now in retrospect, in not educating us in what they are providing for our students. But he was able to get Weaver's ears and also [Gilbert] Banker's ears. But, eventually, he and Banker really had a fallout. This is when Banker decided to eliminate Social Pharmacy as an independent department and merge it with the Clinical Pharmacy program and they had, like, one department: Social and Clinical Pharmacy or something like that. Albert was very, very strongly against that. That's my recollection. Whether he left as a result of that, I'm not sure right now. I think he continued on as a member of the faculty for several years after that.

DT: Why did Banker merge those two departments?

YA: I asked him. Of all the deans, from my perspective, for Med Chem, Banker was the best dean. If you want to get to that, we can get to that. But, why? He could not deal with Wertheimer. And I told Gil, "Why are you doing that?" he said, "Well, I'm just going to cut his wings. I want to change leadership within that department," and he did. He forced it and combined them, and he put I think maybe Jim [James] Cloyd as department head. Two people that could give you a perspective on that era would be Jim Cloyd and/or [Robert] Cipolle. Have you talked to Jim Cloyd?

DT: No, he's on my list actually. Everyone I've spoken to so far has mentioned Cloyd.

We'll get back to Banker in a little bit, but before we do… Obviously, we've talked a lot about the tension between the kind of clinical mission of the College and the basic science. Given that, how did you find relationships with the clinical faculty?

YA: With some, I had very good relationships. The early faculty in Clinical Pharmacy, I had very good rapport with them, I would say, from 1972 through 1985. I could work with them. They had well developed programs for education and also started thinking of research, but mostly education. I could relate to them. In fact, in my endocrine course—I was teaching, let's say, before we joined Pharmacology or maybe even after that—I would always bring clinical faculty to come and talk about diabetes and give us a case study of a patient that had diabetes as well as other complications, like hypertension or kidney disease or something like that and, then, the drugs that these patients are on and how do they relate to the topics that I have been discussing in my unit. So I used to get, maybe, two or three clinical cases in my course. That was before we were Pharm.D., fully-fledged Pharm.D., back in the mid 1980s.

Later on, what happened is, the Clinical Pharmacy, you know, work as a team, as a research group, and they started playing the system. Some of these names… I don't know how you're going to eliminate them from my discussion.

[chuckles]

YA: Well, I can say that…like when they came up for promotion and tenure, we'd look at the publications, and we have, let's say, Professor X and, then, publications. Professor X plus eight other professors on the same publication, and they all are from the same department, and each one of these professors lists it as their work. The question is, who really is the PI [principal investigator] on this project, and who's responsible for what? That created a lot of friction within the College between the basic science and the clinical sciences. So in the mid-1980s to mid-1990s, lots of friction between basic science and clinical science. We had faculty meetings and, then, the faculty from basic sciences looked at the individual's CV [curriculum vitae], and they see twenty-five publications, but every single publication is multi-authored. The multi-authored are individuals from the same…the same individuals [from the same department]… and all of them list it. From basic science faculty, if somebody is coming up, at that time, for promotion from assistant to associate, they may have, maybe, seven to eight publications and they, the clinical faculty, say, "This guy hasn't done much research, but he may be a single author." Okay. On the other side, we look at it and say, "Well, who has done the work?" If you divide this publication… He has twenty publications, and you have eight people. Maybe it's only three publications total per person. That kind of friction at faculty meetings led to a lot of acrimonious accusations back and forth and very heated discussions. Some of these individuals are still around. They worked as a team—true—especially the Ramsey Group when they were at Region's Hospital [Saint Paul, Minnesota].

The guy that, of course, I liked the most of all the clinical faculty was Darwin Zaske. He was like the guru of Clinical Pharmacy at the University of Minnesota. He helped a lot of individuals like Cipolle, Jim Cloyd, John Rotschafer. All of these individuals were on Zaske's pubulication. Many years later, there was friction, after these individuals left Regions Hospital. They were appointed here as clinical faculty, but also their practice was at Regions. So their home base was Regions Hospital. Overtime, they were shifting these faculty from leaving their clinical site and moving them to the College as full-fledged faculty, so they lost their clinical site. I was very outspoken. And I was saying, "The reason we hired these individuals"—I was talking to maybe Dean Banker at the time—"The reason we hired these individuals is for them to play the role model for clinical pharmacy practice. They've had the training. They have the education and, now, you're taking them away from being that role model. We are sending our students to individuals that have no idea about clinical pharmacy. Yet, at the same time, these guys are becoming one hundred percent faculty members. They didn't have a research program. They didn't bring in any research dollars."

So what for? I think it was all for political reasons, all for strengthening of the clinical program at the College of Pharmacy. Well, in retrospect, looking at it right now, I'd say,

"Well, maybe they did the right thing" in the sense that, initially, they didn't have a strong research program at that time. That department has evolved and they have a strong research program right now, clinical research program. They have some good researchers in that department right now.

DT: You mentioned the Department of Pharmacology. Were there many collaborations that you saw between Medicinal Chemistry, and say, Nursing, the Dental School, or Public Health or were most of your collaborations with the pharmacologists?

YA: For us, it's either Pharmacology or Biochemistry, not much with Nursing or Dentistry. There may have been occasional small projects with a faculty member from another school, but not to speak of. We have a lot of collaboration with faculty in Medicine. Right now, almost every professor in Med Chem has a collaborator in the Medical School.

DT: Can you explain why there is so much collaboration with Medicine?

YA: Initially, we didn't want to be in the Academic Health Center [AHC] because we felt that we would lose our proximity to Chemistry, plus, we were in Chemistry even though we were not collaborating, but we attended their seminars and, being across the street, you know that helped a lot. I think on Thursdays, they have their regular seminars, weekly seminars, and most of us would attend them, and some in Chemistry attended our seminars. We felt that, well, we're going to see less interaction. But, later on, of course, we had no choice but to move here, because that was the dictum from the top levels.

We didn't have too much collaboration between us and the Medical School faculty at that time, prior to moving here. Now, once we moved here, then we started feeling, you know, talking to people, getting to know the people from Biochemistry more, Pharmacology, and some from Medicine. We seek some of them and, now, they're seeking us. In fact, they're the ones who initially establish the contacts. I remember when I was still department chair, they called me up and said, "We're people from the Medical School. We're working on this project, but we want somebody to help us work on this part the project. Who in Med Chem could help?" So, right now, they are feeling like this is the chemistry engine in the Academic Health Center, so who is doing what in Med Chem? As a result of that, I think we're seeing a greater collaboration, and it's been extremely beneficial because what we do in medicinal chemistry-is very relevant to what is being done in Medicine. Ultimately, these are drugs, and they have to be applied to a disease state. In turn, they have a disease state, and they want to cure their patients.

DT: [chuckles]

YA: I think it's mutual benefits that I see from this relationship now.

DT: When Lyle French was vice president of the health sciences, did you have any interaction with him or did you see him playing a role in fostering this collaboration?

YA: Well, Lyle French, I did not interact with him that much. I interacted with a number of vice presidents: [Robert] Anderson and, of course, Frank Cerra. [William] Brody, very little, I had two meetings with Bill Brody. I disagreed with him. He asked me to think about something, and I thought about it, and I gave him some suggestions. He said, "Fine, I'll think about it." But Frank Cerra, of course I worked with the most. I really liked working with Frank. I was very angry at Frank many times, but I always told Frank, "I go into your office so angry, and I leave your office happy, but I haven't gotten anything."

[laughter]

DT: The sign of a good administrator, maybe.

YA: He is a good administrator. He's so laid back and so knowledgeable. One thing about Frank is he just remembers so much in his head. Many, many topics, he can talk about, and he remembers details quite well.

So what were we talking about? Remined me of the question before we…

DT: I was curious about Lyle French…

YA: Okay.

DT: …but also more generally about the vice presidents, how much interaction…

YA: With Vice President Lyle French really, we had very little interaction as faculty, because he was just paving the way for the Academic Health Center, at that time, the health sciences, so he was working more with the administrators and so on. Weaver sort of pushed his way to be part of the health sciences, and Lyle French was supportive of Weaver. So that's the credit I would say I would give to Lyle French. He was supportive of bringing in everybody who is in the health sciences to work as a team and pushed this whole enterprise forward. But he didn't last too long.

Then, [Neal] Vanselow, I think. I worked a little bit with Vanselow. He was very receptive. My recollection of him is that he was receptive to listening and, also, receptive to new ideas. Do you recall when Vanselow was vice president?

DT: He was 1982 to I think maybe 1992…maybe 1983 to 1992.

YA: I see. So he is the one who hired Banker.

DT: Yes.

YA: Okay. Yes. I remember that's when I became department head, sort of interim department head, in 1984. I know I have interacted with Vanselow. Sometimes, he would come and meet with Banker, and Banker would have the executive committee

around the table, and we'd discuss issues and so on, but nothing so earth shaking, I would say. I think he was pushing the AHC as a community, and he was supportive of the deans and their roles as leaders of the college and pushing them to work as a team.

I don't know who set up the Dean's Council. I can't remember which of the vice presidents for the Academic Health Center pushed the Dean's Council.

DT: I think it was French.

YA: French?

DT: I think so. It was certainly in the early 1970s that the deans were all meeting regularly with Frank as a collective.

YA: Hmmm. That I didn't think—but I'm not sure. At least it did not filter down to the lower level. That role of the Dean's Council was very, very essential. Maybe it's more as it relates to figuring out what they can do with building up the infrastructure of the Academic Health Center. Vanselow initially was really the one who was pushing for the buildings and so on. Isn't that right?

DT: Well, the main buildings were under French's…

YA: The main buildings?

DT: Yes. I'm not so clear on what new buildings, apart from the new hospital, were established under Vanselow. I'm not sure.

YA: When we had the Pharmacy/Nursing building who was the vice president?

DT: That was still French.

YA: I have a picture of him in our book where he was digging the ground.

DT: Oh, yes!

YA: Oh, was it in that?

DT: Yes.

YA: Was it him?

DT: Yes [looking at photo].

YA: Okay. Yes.

DT: That's a good picture.

[chuckles]

DT: How long were you department head? Nineteen eighty-four until 2005?

YA: Two thousand five.

DT: That's a long time.

YA: I would say I hired almost everyone in the department with the exception of Portoghese, Pat [Patrick] Hanna, Bob [Robert] Vince, and Rodney Johnson. These are the four that I didn't hire. All the others, I hired later, up to Gunda Georg. We hired her. Beyond that, I was no longer involved with the hiring.

DT: You mentioned Gil Banker a number of times now, and you talked about Weaver's resignation as dean. Can you talk about the process by which Banker was appointed dean and how the College saw Weaver's replacement?

YA: Well, of course, there was an interim dean, Doctor [Mahmoud M.] Abdel-Monem, who came into a College that was so fractured, so unhappy. There were lots of people that wanted Weaver to continue and were very supportive and others were happy that he left.

We established a committee called the GTD Committee, Get-the-Dean Committee. This is the acronym for the committee, but he appointed the committee, Weaver. There were a lot of complaints about the organization within the College, that it was not functional…functioned very, very well. We felt as faculty that we wanted to go back to departmental structure. We just were not seeing growth. A department is like a family. We depend on each other. We help each other. We push each other. When we didn't have departments, it became an individual thing. You didn't see the growth, the natural growth of how things should evolve into strengthening a unit. We're not here just to do research. We're here to do some building, the building of programs, the training of students.

Wisconsin is a great institution, even in medicinal chemistry, but they have a very weak department. They have excellent individual scientists, but not too many students go to Wisconsin to get training there, because they don't really train graduate students.

I felt all along at Minnesota, as a whole, that we are here as an institution for training and graduating good scientists that are going to leave the institution and become leaders in the future throughout the nation, throughout the world.

So, actually, after complaining to Weaver for several years, he decided he would listen, and he would get the recommendation from a committee that he appointed to look at the organizational structure and come up with a recommendation. I was on the committee, one of the individuals. We recommended that we should go back to the departmental

structure, and he accepted that, I think in either 1983 or 1984. He started appointing department heads and all that stuff. A year later, after it was instituted, he left the University suddenly.

Cherie Perlmutter, I think, was assistant vice president or was the acting vice president for the Academic Health Center. Was she with Vanselow or was she…?

DT: I think she was acting vice president…

YA: With Lyle French maybe?

DT: She worked with French, and she worked with Vanselow, and I think she was acting vice president once Vanselow stepped down, which was the end of the 1980s, early 1990s.

YA: It must be in the 1980s, late 1980s. I know I requested some funds from her to support Doctor Portoghese because we almost lost him. He was leaving to go another university, and I didn't want to lose him, so we put a package together, and she gave us some money from AHC and we got money from the department, and the College of Pharmacy. Then, we said, "Look, this is our package. Why don't you stay here?"

So I think I worked with her. I remember while I was researching the book, looking at the files, I saw the correspondence that I had with Cherie. [chuckles] It was late 1980s, maybe 1987, 1988, something like that.

DT: That sounds about right.

YA: At any rate, after we made the recommendation to Weaver that we should reinstitute departments, he accepted it, and he announced it at a faculty meeting. He said, "We will have this reorganization, this departmentalization." The faculty were very happy about that.

But when Monem came, who was acting dean for one year essentially, between Weaver and Banker, he took a very…

[break in the interview]

YA: …fractured College. He was a good administrator, very thoughtful. He could team up with the devil, and he dealt with a lot of issues at the College, and he smoothed things down. During the last six months, he was dean or acting dean, the College was extremely serene and the faculty were very happy. The administration was happy with what was happening. I think a lot of people did. The dean of Nursing at the time said to Monem, "You should be applying for this position," because he'd done such a great job as an interim. But he did not formally apply for the position of dean of Pharmacy. Later, many years later, I asked him, "Why didn't you apply?" He could have been a good dean. He said, "Well, if they thought I was a good dean, maybe they should have appointed me as a

good dean." I said, "It doesn't work that way." He said, "I did not want to apply for it and, then, be turned down. Then, I will be very unhappy."

He said he had this experience with his mentor, Professor [Taito O.] Soine. He was a graduate student, this guy, from the University of Minnesota. Soine was a very renowned medicinal chemist. When Weaver was applying for the position of dean, Soine applied for it. Of course, the University selected Weaver. Soine became a very bitter professor. He always had conflicts with Weaver. The question was, is it really conflict because of his resentment of Weaver because he was not selected or actually a conflict based on real reasons for that resentment, besides his wish to have become dean. He [Mahmoud Abdel-Monem] said, "I did not want to be like that because I would feel very miserable. I've seen it work in my professor's lab and how he felt. But he went on to become dean at a different university [College of Pharmacy, Washington State University].

[chuckles]

DT: The appointment of Gilbert Banker… Do you know why he was offered the job in the end and what he brought to the position?

YA: To tell you the truth, I'm not exactly sure. I was on sabbatical that year, and I was outside the country. When they started thinking of Banker, to offer him the position, Abdel-Monem was acting dean. He used to be the chairman of Medicinal Chemistry. He became chair of Med Chem for one year after reestablishing the department. Then, he was appointed as acting dean. So they were looking for a replacement to become chairman. So he contacted me in the Netherlands. He said, "Yusuf, how about becoming chairman of the department?" I said, Monem, I am doing a sabbatical right now. I'm not going to think of being department head." [laughter] But he's a very convincing guy and I said, "Look, I'll consider it as an acting head position and not as a head position."

So when I came back, I found Banker here.

DT: You said he did well by Medicinal Chemistry.

YA: His philosophy of management is he meets with you. He believes strongly in having strong leadership for a unit, and he had high expectations of accomplishments for each of the units, but he provides the units with leeway and flexibility. Then, he has a strong accountability side. At the end of the year, he comes to you and he says, "Well, what have you accomplished, not personally, but for the unit?" In that regard, he allowed us to develop the things that we wanted to develop. The other thing that I liked about him is in order for us to develop and get stronger, the ICR funds that Weaver kept to himself… I talked to Banker and I said, "Look, I cannot accept being department head unless the financial system in the College changes." He said, "What do you want?" I was interim, and he offered me the position on a permanent basis. Then, I met with him and said, "Look, the budget in Med Chem has been in the red for the past five years." That's why I wanted to be interim. I wanted to find out what am I getting into. I'd never been an administrator and, you know, getting a faculty who is not administrator put him

in it…we are a tough group. Medicinal chemists in our College are extremely opinionated individuals, but a good heart for Medicinal Chemistry, and they would do anything to champion the cause of Med Chem. He said, "What do you want?" I said, "I would like to see the ICR funds, some of them, come back to the department. He said, "Are they offset funds?" I said, "If I paid thirty percent of my salary, Dean Weaver kept thirty percent of my salary. It never came back to the department." So I told Banker, "I'd like to see ICR and salary offset funds come back to the department." He said, "I'll think about it."

Now, Abdel-Monem was selected by Banker to become associate dean. I am close with Abdel-Monem. We were good friends. I told him, "Look, Monem, I'm not going to continue being department head unless you convince your dean to give up some of the ICR and salary offset." He said, "Don't worry." So he talked to Banker. They discussed it and, then, Banker came back, and he proposed to me that eighty percent of what the College receives from Central Administration in ICR funds would be distributed back to the departments. We were the only department that had NIH funding at that time, so all of a sudden, instead of being…start my fiscal year with, supposedly, it was $70,000 per year, but because we were $50,000 in the red, I started July 1 with $20,000 for the rest of the academic year. All of a sudden, I had $150,000. That made miracles for me.

DT: [chuckles]

YA: The department was in very bad shape in every respect, you know, equipment wise. We didn't have staff, a good staff. So we had to redevelop the department, the infrastructure for the department. I agreed with the faculty. I said, "I'm going to keep all ICR funds and the salary offset funds in the department's office. I'm going to use those funds to acquire whatever needs to be acquired, get new instrumentation, and so on." These requests were coming from the faculty. We discussed them at faculty meetings, and some would say, "We need this equipment replaced," and we'd discuss it and approve it. So I was using those funds to refurbish the entire department.

Now, after I did it for, I think, two or three years, I didn't need all that extra money in the department's budget. So I gave fifty percent of what I got back to the individual faculty that generated the ICR funds. Later on, I shifted to seventy-five percent. Ultimately, I gave every penny back to the individual professor, because the department doesn't need the resources. The professors need the money to hire technical people, buy instruments, chemical supplies, and so on to get their research programs running.

That's why I say Banker was very helpful to the department in this regard. He allowed us the ability to become somewhat independent and, then, actually grow. We had strategic plans under Weaver, but very benign type of strategic plans. With Banker, it was not him who pushed it. I think President [Kenneth] Keller, who put forth the "Commitment to Focus" plan. The "Commitment to Focus" was driving Dean Banker to do that. We had these strategic plans that we developed very well in Med Chem. We had this day retreat, just the deans and the department heads. Each of the department heads had to present their goals, objectives, and all that. When I presented mine, Banker stood up, and he

came and hugged me. You know he's a big fellow. He's almost as tall as this. I was coming up to his waist.

[laughter]

YA: He said, Yusuf, this is the kind of strategic plan that I like to see. It has substance, but it has a plan of how you're going to be accomplishing these [goals] over the next five years. That actually was because of his ability to give us these resources. Without these resources, really, we could not have accomplished any of these things. That's why I say Banker allowed the department heads to have the flexibility, not just department heads but the entire group through the department heads, because he deals with the department heads. He let them flourish and let them evolve. He is not a micromanager. But he's extremely critical at the end of the academic year. I had one year where he really crucified me. [chuckles] He said, "You had all that money and you didn't know what to do with it." But most other years, I think we have done very well under Banker.

DT: I'm curious, if you, individually during your research, or in the department more broadly, what relationships have been like with pharmaceutical companies.

YA: Within Medicinal Chemistry programs, we have very little interaction with pharmaceutical companies… Some of us are consultants. Some of us are on cases, you know, with lawyers and litigation and that type of thing. But funding for research, we get very little from the pharmaceutical industry.

The pharmaceutical industry's research is geared to a project. They say, "Okay, we want to give you"—let's say—"$200,000 for these two years. If you do this work, we will provide them with a report, and it's over. There is no continuity. So you shift from Project A and, then, all of a sudden, if you go to another company, you are working on an unrelated Project B. As a scientist, we thrive on our reputation, and the reputation evolves and develops over time, and it's not over a two-year period. Maybe over a fifteen-year period before other scientists recognize, "Oh, yes, Yusuf is doing and working in this area." NIH funding, on the other hand, you could have sustained NIH funding on the same project or topic for many, many years. That's how you develop this recognition and reputation. That's why we, in Med Chem, I would say get most of our research funding from NIH and NSF. Once in a while, we get somebody who contacts you and says, "Could you do this project for me?" I've had some contact for a year's project, but it would be a scanty thing I get either a technician or a first-year graduate student that works on it. But you don't want to rely on those.

DT: Can you talk a bit more your own research program, and how you became interested in estrogen and steroids and cancer, and how you built your program?

YA: Yes. Well, I worked on steroids when I was a graduate student but steroids as it relates to fermentation technology, the basic understanding of mechanisms of enzymatic dehydrogenations, enzymatic hydrogenations, and the like. I was looking more at the enzymological aspects as it deals with these types of transformations and looking also at

the stereochemistry of some of these reactions. So I was using both, a combination of chemistry as well as biochemistry in the early stages of my research.

Now, that kind of research program did not have a high priority at the NIH, so when I applied to NIH I did not get funding for my project. Around that time, President [Richard M.] Nixon signed the [National] Cancer Act [of 1971]. I said, "Well, maybe what I should do is instead of using microbial cells, I can use mammalian cells and cancer cells." I started using mammalian as well as cancer cells for looking at steroid biotransformations. So I applied for NIH funding. I got the grant and got started that way.

Then, I collaborated with a professor here in Medicine. His name is David Kiang. He would provide me with the mammary tumors. Then, I would do all the metabolic studies and looking at the relation between estrogen receptors and tumor dependency and independency. We had a theory at the time that independent tumors are capable of producing their own estrogens. Indeed, we went on to find out that both the dependent as well as the independent tumors are capable of taking cholesterol and transforming it all the way to estradiol. All the enzymology, all the enzymes that are capable of doing steroidogenesis are present in mammary tumors. It started with just a simple observation by a scientist, I think in Australia, where they were doing adrenalectomy in postmenopausal women. They were checking the urine of these individuals, and they found out that the urine of these individuals had estrogens. The question I was drawn to was, where are these estrogens coming from if the ovaries are not functioning and the adrenals, which is the source of DHEA [dehydroepiandrosterone], which ultimately goes to estrogen, is not there? What is left is cholesterol. Is the tumor capable of using cholesterol to go to pregnenolone to progestins and to androgens?

So we started that way, and we spent many years working with Dr. Kiang, maybe from 1973 to 1983, something like that. That's how I got started in the area essentially, and, then, we worked also with hepatomas but with a faculty member, not from here but at Georgetown University. That's why I say I work with animals. Those years were my animal years, actually from 1973 to 1983.

[chuckles]

DT: How do you spell Kiang?

YA: K-i-a-n-g. He's now retired. He was hired by Dr. B.J. Kennedy. You've heard of B.J. Kennedy?

DT: Yes.

Does your research then intersect at all with cancer genetics and the discovery of the BRCA1 and BRCA2 gene? Aren't they about estrogen receptors?

YA: Maybe, but I never went that far at that time. BRCA1 or BRCA2 were not discovered. By that time, I shifted my research away from looking at biochemistry and became interested more in therapeutic. I started looking at the development of drugs for the treatment of breast cancer, because at that time there was only Tamoxifen as a drug. And Tamoxifen had side effects. So we shifted toward more chemistry at that time.

DT: As I understand it, enzymology was really taking off in the 1960s and 1970s. Did you notice that there was a real interest in enzymology in terms of understanding drug research or basic research that eventually led to drug development? Do you think there was an increased attention on enzymology?

YA: Well, not in departments. When I came here, no one was doing any enzymology research. In fact, we needed a cold room. So I had to go out and get a cold room. I acquired some funds to set up a cold room. Once you set it up, then you start other individuals within the College that know a little bit about enzymology, that actually used the cold room. Over the years, of course, everybody saw the benefits of having a cold room and doing research on enzyme kinetics, the inhibition of enzyme systems, and so on. We, as medicinal chemists, of course, rely on two types of mechanisms…the inhibition enzymes or have to do with receptors. Everything that's biochemical, you have to know; otherwise you can't really move forward.

When I came—this is actually what Weaver wanted—he wanted a bioorganic chemist. In my training, I was one chemist who was doing bioorganic at the time as a graduate student. This is what he wanted to do. I had a very interesting discussion with Dean Weaver in Madison. He came to Madison and talked with the previous dean. He said, "I'm looking for Professor X. Do you have any graduate students with such a training?" Of course, at that time, nobody was doing post doc research. You could get into academia right away. He said, "We just had one guy who graduated in December, and he's still waiting for his wife to complete her education, but he's doing post doc with his mentor." So he said, "Who?" Then, he told him. He came to my lab and he said, "Can we go to a room?" He talked to me and I said, "I'm not interested in academia." He convinced me that maybe it's a good thing to consider, and I should just give it a chance. Give it a try. I wasn't interested. So he went back to Minnesota.

Then, a week later, he contacted me by phone. He said, "I think you still have a great opportunity if you will consider it." In the meantime, I talked to my professor, and he said, "What did Dean Weaver want from you?" I said, "He wanted to me to consider a faculty position. He wanted me to go out for an interview to Minnesota." My professor said, "Great! Why don't you do that?"

DT: [chuckles]

YA: I talked to him many times, and I've already had two offers in the pharmaceutical industry. But I told the industry, "I'm not going to come until my wife is done but I have not accepted their offers." One was at Pfizer in Groton, Connecticut and one [Upjohn Company] in Kalamazoo, Michigan. My professor said, "You should go even if you

don't want to. You'll have fun. You'll meet the scientists there. You're going to see them at national meetings. They'll take you out and dine you and wine you. That's it. If you don't want to go, don't, but why don't you explore it?"

Anyway, I said, "Okay, I will give it a try." Then, actually, I flew to Lincoln, Nebraska, because they were hiring the chairman of Pharmacognosy, John Staba, who was still at [University of] Nebraska. I interviewed him at the airport in Lincoln, and, then, I flew from Lincoln to Minneapolis, and I met with the faculty here, gave a seminar, talked with them. At the end of the day, I really liked the group. I liked the science that was happening in the department. I talked to my wife, and she said she didn't want to go to Connecticut or to Kalamazoo. [chuckles] She said, "If it was a big city like Hartford, Connecticut, okay," but Groton, Connecticut was too small for her. We'd been there, because my brother, who was a medicinal chemist, also a graduate from Wisconsin, actually had a job at Pfizer, so we visited him. We stayed with him a couple of days. We didn't like Groton, Connecticut. There's nothing there, essentially. So that was how we got started at Minnesota.

When I got here, I was very disappointed that they didn't have a cold room, because you can't do biochemical research if you don't have a cold room. So my first task was to go out and get a cold room for my research, essentially. But, of course, it became the cold room for the College of Pharmacy. Doctor Vince was very much interested in doing some enzyme inhibition. He's the only one for many years that was using it from my department. Then, later on, several others got started using the cold room.

DT: Do you remember trying to use the facilities in the Department of Biochemistry, or that would be too far away?

YA: You know with enzyme work, you are purifying enzymes. You go in and out of the cold room, sometimes you stay a half hour doing some manipulation, and it becomes very awkward. We could store some things maybe in the Biochemistry Department, but doing actual experiments, you need it there. Usually, cold rooms are not so big if you go to others, and I have explored it. I knew one guy in biochemistry from before, so I visited and you go there and it's cramped. All the desktops are taken, and they have all these columns. No, I didn't use the Biochemistry Department.

DT: As you talked about the cold room, I was flashing back on my experiences spending many, many hours in the cold room when I was doing biochemistry. It was cold being in the cold room. [chuckles]

YA: Sure.

DT: But how critical that was.

YA: Yes. For me, most of my work I could do outside the cold room. The maximum I stayed in the cold room was a half hour at one time.

DT: Was it Upjohn at Kalamazoo?

YA: Upjohn, yes.

DT: Why were you so interested in working for the pharmaceutical industry?

YA: Well, I got very much enthused about doing research. You're spending twelve hours a day in the lab working on research. A lot of my colleagues went to the pharmaceutical industry. My brother went to Pfizer. So, you know, that's how you think. I'd never been a teacher and didn't give it much of a thought. I knew you have to apply for NIH funding; although, at that time, it wasn't hard to get funds. Fiftieth percentile, you get a grant. On my first try, I got my grant. Now, for assistant professors, six, seven tries, and they still haven't had it. That was the basis, really. I liked research, and I liked to be involved in discovery and the like, rather than preparing lectures and correcting exams and that kind of thing.

DT: When you switched the focus of your research more to therapeutics and started looking more at drug discovery in treatments of breast cancer… Can you elaborate on that and what some of the main challenges have been or were to doing more drug development work?

YA: The two areas that I was looking at were steroidal type compounds that have antiestrogenic activity and the other area is aromatase inhibitors. Aromatase, if you remember, is the enzyme that takes androgens and transforms them to estrogens. At that time, there were no aromatase inhibitors on the market. There's one that inhibits, cytochrome P450, which is the 11 β-hydroxylase in the steroidogenic pathway in the adrenal gland. That was aminoglutethimide. It was used for convulsive therapy in the 1970s, and, then, later on, in, maybe, 1983. Then, they discovered that actually it has effects on inhibiting mammary tumors in animals. We found out, later—not me, but some other labs—that it inhibits the aromatase enzyme. But, it's not a selective inhibitor of cytochrome P450. It inhibits aromatase but it also inhibits also 11 β-hydroxylase as well as cholesterol side chain cleavage enzymes. So if a patient is on aminogluetethimide, then they start having a deficiency in cortisol, so they have to supplement the patient with corticosteroids, and, of course, that's not very good. That's how I got started with these aromatase inhibitors. There were no other aromatase inhibitors on the market, at the time.

It's a challenge for any scientist in academia to push drug development, because you can't compete with big Pharma. I knew there were maybe three or four pharmaceutical companies working in the area of aromatase. We were approximately eight scientists from academia working on aromatase inhibitors. Every five years, we meet, and we present our results. We had a few academicians presenting but none from industry. But the audience was mostly industrial people and taking notes. Now, they found out that this is a very good target based on the basic science studies that academics have done, and they felt that this would be a good target for development. So you had companies like in Italy, [CSO, Contract Sales Organization] Farmitalia got started, AstraZeneca,

before AstraZeneca was ICI [Imperial Chemical Industries] in England, they got started. Janssen Pharmaceutica in Belgium got started with developing specific inhibitors of aromatase cytochrome P450.

We, also, worked on aromatase inhibitors and I had two people in the lab who were doing a lot of work on this enzyme. We, finally, got a very good compound that was found to be effective in inhibiting mammary tumor growth in animals and has all the potential for being a good compound. We patented it and everything. The University said at the time, "You can't do it. Once you patent it, it belongs to the University." Okay. Then, they're supposed to be marketing it and contacting pharmaceutical industries. They are so slow, so ineffective. It took them maybe eight months before they started getting some interest. Of course, the University has to pay money to protect that patent. They are paying like $10,000 a year. Then, after three years, they told me, "We're not going to continue protecting it, because they can't see any potential prospects." So I had to go out and contact some individuals in these companies that I knew that are working in the area of aromatase inhibitors. I said, "Look, I have an excellent compound that has the potential of being an effective drug." But, in our facilities here, we cannot develop a drug. There's no way we can. We can go up to animal studies, which we have done. We induced mammary tumors in rats and, then, we give them the drug and look at the regression, so we've done all these studies. But that's the maximum we could do in academia. So you need somebody to take it on and see if they are interested.

AstraZeneca was working on non-steroidal aromatase inhibitors, and I knew one guy over there. I said to them, "Look, I have a good compound that is a steroidal compound." They agreed to take a look at it, and they signed an agreement with the University. They looked at it for one year, while at the same time looking at their own non-steroidal compound. They were moving parallel. Their non-steroidal compound was undergoing Phase 3 clinical trials, and ours was just beginning Phase 1 clinical trial. So by the time they looked at ours then, a year later, they contacted me and said, "We're dropping it." Then, their drug came on the market. So in 1995, one came on. In 1996, the other one came from a different company. In 1997 and, then, 2000…so we have four drugs right now on the market as aromatase inhibitors and mine is sitting still on the shelf.

[laughter]

YA: In academia, we're not really after a drug. When you read my book on the history of the Department of Medicinal Chemistry, I do bring the story of Ziagen. Most of us in academics are really more interested in identifying targets, looking for types of compounds, and actually increasing knowledge and concepts in medicinal chemistry. You have some individuals, like Robert Vince whose main interest was to develop a drug. He joined the University in 1966. Throughout my career at Minnesota, I said, "What do you want to do, Bob?" He said, "All I want is I want to have a drug. I want to develop a drug." This was his main objective. All his research was targeted…I want to develop. He got lucky, and we have a drug. That helped the department the College and the University tremendously. But the royalties are in their last year.

DT: You mentioned that when you patented your compound the University was slow. Was that the Office of Technology and Commercialization?

YA: Yes.

DT: Was this then in the early 1990s or was it in the 1980s?

YA: That was, I think, maybe around 1996 when I patented my compound. That whole office was not effective at that time. They did not have scientists, really. They didn't even have good chemists. If you talked with them, they didn't understand the chemistry. How can they go out and really push an idea forward? Now, it's different. I think they are much more aggressive now, and they have better individuals. When they revamped this whole group, they fired everybody and rehired some of them back, but they also had a new head of the program. It's a bit more aggressive, but we are still behind at the University compared to other universities about technology and making it more liberal for faculty to develop their own little industries or their own companies. We are way behind.

DT: It sounds like because of the limits of that office, it has to be the individual faculty member then who starts trying to build connections with drug companies. Rather than the office doing it, there's some sense that you have to do that?

YA: Well, the office does it. Individuals, most times, when the office as I said, "I've identified a number of industries. Why don't you contact these industries?" They do send them to some of these targets, but, sometimes, they go to individuals that are more in the business office, and they don't relate very, very well to the science. I think, sometimes, especially with personal contact, I find out that the ones I talk to are more familiar with this research. One guy, later on, as I said, at AstraZeneca dropped it. He said, "You should have talked to this guy at AstraZeneca." He was a lower level. But he pushed it. He just moved it forward. They did some Phase 1 studies on it. It was effective, but they don't… First of all, a lot of companies cringe from using steroids, because of potential side effects. Yes, it is a specific aromatase inhibitor, but it was an androgen structure. Okay? So potentially it may have androgen-like effects. We don't know because it was never tested, at least in our labs; although, we did some binding studies to androgen receptors and so on. It was not a good binder. We did as much as we could in our lab.

There is right now only one steroidal compound that is an aromatase inhibitor and that one is Pfizer's compound. But Pfizer actually inherited it from Farmitalia. Farmitalia was bought by Pharmacia and, then, Pharmacia bought Upjohn and later Pfizer bought the whole bunch of them.

[chuckles]

DT: My understanding is that the NIH, at least at this time that you're talking about, was not interested in funding any kind of drug development work among academics.

YA: Recent trends of actually using NIH funds, like we are right now using at the ITDD [Institute for Therapeutics Discovery and Development] and other centers in the United States started, maybe, I would say, around the year 2000. NIH has established these core areas. I think right now, there are five of them in the United States. We are one. Kansas has one, I think. Maybe Pittsburgh has one and somewhere in North Carolina. At any rate, no, they weren't pushing that, NIH. Now, of course, NIH set up their own drug discovery program using internal funds. Of course, many scientists are not happy about that.

DT: Yes. I've interviewed researchers, NIH researchers, who have supported, often, drug development for thalassaemia, and I've interviewed medicinal chemists who've done some of the early drug development work for finding oral iron chelators. I was interviewing these folks probably in the mid 2000s, 2006 and 2007, and that's when I think NIH was really starting its internal program, Pathway or whatever it's called [correctly Roadmap]. I've seen since [Barack] Obama has been president, some of his legislative efforts have been to increase funding for getting academic researchers across the Valley of Death, getting them from the animal studies to the clinical studies. There's now potentially more research money available for that. It seems to be a really recent innovation.

YA: Yes. But they also got distracted. I mean, [Dr. Elias] Zerhouni's program with all this Roadmap and all that. They took some money away from the RO1s [Research Project Grant] to fund these specific projects. The NIH is decreasing the amount of funding maybe for individual researchers, and it's getting harder for younger, newly starting assistant professors. I do sympathize with some of the assistant professors. We have one assistant professor that has tried so hard, and so far, he has not succeeded. He's an excellent scientist, and I feel bad about it because, ultimately, if he doesn't get funding, he's not getting promoted—but a very well trained individual.

DT: Yes. It just seems in the case of your compound that there's potentially a lot of compounds like yours that are sitting on the shelf, that aren't being picked up.

YA: Definitely. All these screening centers are screening hundreds of thousands of compounds. Many of them are compounds that have been on the shelves of somebody's lab, that have found some activity or partial activity. With some partial modification, these molecules have potentially higher activity. But there's some cases where compounds have been on the shelf, but never tested for this function. Just like AZT [azidothymidine].

DT: Yes.

YA: It was discovered in the 1960s or 1970s and sitting there until AIDS [Acquired Immune Deficiency Syndrome] came about. Yes?

DT: Yes.

Now your compound, has the patent expired on it?

YA: Oh, yes.

DT: So do you think that creates even less incentive for drug companies who might be looking…?

YA: Of course. Very much so. My wife was saying, "Why don't you try to see if some developing countries would like to develop that?" I said, "Developing countries don't have resources. They don't have the manpower. They don't have the facilities for doing clinical research and so on." I know, like in Jordan, they're starting to do some, but there's no way they can do full phase clinical research. They may go up to Phase 2. There's no way of going to Phase 3. It would be a waste of their time and the patient's time. I'm sure they won't accept because this probably would cost them about six to eight million dollars or more, but maybe over there it will cost a bit less. Now, some American companies are using Indian clinical research centers. The U.S. is accepting some with certain restrictions in certain institutions, I think. They're allowing that. It's cheaper.

DT: Good drug development is expensive.

YA: India is involved with a lot of these things, outsourcing a lot. But, they're not always the greatest compounds.

DT: Have you since been working on different compounds?

YA: Actually, I have been working on two parallel tracks. One of them is therapeutic, and that is, as I said, non-steroidal anti-estrogens and the aromatase inhibitors. Then, the other one is looking or trying to understand how estrogens may be involved in carcinogenesis. Lots of women that are taking estrogens, they say, "They increase the risk of cancer." The question that I want to answer, is it the estrogen itself that is doing the damage to the DNA [Deoxyribonucleic Acid] just like cigarette smoke or benzopyrene or does it just act as a growth promoter, because it binds with the estrogen receptor and helps with proliferation and growth of tumor cells. -We started this project in the mid 1980s. We kept it going until 2004. We found out, ultimately after many years of investigations that estrogens have a role in inducing cancer. It started with an observation in animals and in humans that estrogens increase the risk of developing cancer. With animal studies, you put certain species on an estrogen pellet and within x number of months, these animals develop cancer. Now take the example of the kidney Syrian hamster model. We collaborated with Jonathan Li who was here at the University and, then, he moved to the V.A. Hospital. In the kidney model if one places an estrogen you pellet, after three months, one hundred percent of the animals develop tumors. Now, if you put these animals on, say, cytochrome P450 inhibitors the incidence of tumor decreases significantly. Now, in *in vitro* studies we showed that activated estrogens lead to the formation of estrogen-nucleic acid adducts.

[break in the interview]

YA: Now that we knew exactly what needs to be done, we were able to get estrogen-nucleic acid adducts with every single nucleic acid: guanosine and, of course, adenosine, cytosine, and thymidine. Then, we began our studies with calf thymus DNA and looked at the effects of activated estrogens using the using electrochemical system we prformed in our *in vitro* studies. With the calf thymus, it formed reaction products, which we could cleave and analyze for the formation of estrogen adducts. We got both types of adducts: stable adducts and apurinic adducts. Are you familiar with that? Stable adducts means the compounds react with the nucleic acid, and it stays bound to the chain. Then, in order to find out which base is adducted, you have to cleave off the DNA chain and, then you can analyze for the adducts. Then, you have what we call apurinic adducts. That means the backbone chain of the nucleic acid chain stays connected, but one of the nucleic acids falls off. You get the apurinic adducts in the culture system and isolate, extract and purify the system. Then, you can do HPLC [high-performance liquid chromatography] and LCMS [liquid chromatography-mass spectrometry] and you can see the peaks and all that stuff. So, ultimately, we were able to isolate sixteen estrogen-nucleic acid adducts.

Once we did that, everybody in this area started work using our approach to look at the formation of estrogen-nucleic acid adducts. We were, like, maybe, six scientists working in this area, and they all started working in it. My best colleague, who was a professor at the University of Illinois, she's using Premarin instead of the natural hormone, because this is what women are using for hormone replacement therapy. Actually, she found out that these are very potent estrogens and very potent binders to the nucleic acids. So we've agreed now, the community of scientists, that estrogens act only as growth promoters. We think right now that estrogen acts first as an initiator as well as a promoter. So it's a full-fledged carcinogen as well as a promoter. But not everybody in the scientific community agrees with this. There are two camps. When we go to meetings, you should see the intense discussions that goes on this topic. One guy is an Italian hot-blooded professor at the University of Nebraska. If you ask him a question, then he starts attacking you personally. But he's in our camp, so I try not to bother him too much, but I'll listen. Then, there's another guy who is in the other camp where he thinks it's more genetic based rather than adduct based transformations. So that's what we have worked on for many years.

That was my last grant. I haven't had a grant for some time. I lost my grant. Well, I couldn't renew it because I shifted all my efforts from the year 2000 to maybe 2003. My time was entirely dedicated to Ziagen funds. Frank Cerra and Dean Speedie and the vice president for research met with us and said, "What are you going to do with your portion of the Ziagen funds?" You know, we are a small department. That was before the significant expansion of the department. They looked at us. We were eleven faculty members at the time. My budget for running the department, for salaries and everything else was, like, $2.6 million dollars. All of a sudden, every year my budget increased by an additional $6 to 7 million dollars. The University and AHC leadership started thinking about what can this small department use the additional royalty funds for.

Maybe they thought, let's take advantage of the situation and grab some of the funds. Each of the top administrators thought some of it might go their way. But we actually outsmarted them.

When Brody came as the v.p. for AHC he wanted to reengineer the academy. He hired Dean Marilyn Speedie and within a short time the departments were eliminated. However, we wanted to stay as a cohesive group. So we proposed to establish the Center for Drug Design. The faculty felt, well, if we can't call ourselves a department, let's call it a center that is really focused on medicinal chemistry research, just drug design. We wrote the proposal collectively using three subcommittees from within the department. We got together over a six-month period, and we wrote it. We presented it to Dean Speedie and Frank Cerra. They both were very, very impressed. That was in 1996, and they approved it. But Dean Speedie wanted to expand it to the Center for Drug Design and Development. The faculty in Med Chem didn't want development, because that meant if you have development, then you're going to have pharmaceutics and clinical pharmacy be part of the Center. The Center is going to be, in part, supported by the royalty funds in the event that this chemical compound becomes a drug. That's why we pushed Speedie so hard to re-departmentalize. If a drug gets approved and we don't have departments, all the royalty funds go to the dean and not to the department. We said to ouselves, "What's going to happen to us? We know what deans do with funds and she's been very stringent with Med Chem." She hadn't given us that much money since she came until I resigned. We pushed her, and she re-departmentalized and the drug was approved after we became a department, so we started getting the royalty funds.

So we met with these individuals, they said, "What are you going to do with your royalty money?" I said, "We're going to establish a Center for Drug Design."

Do you remember [University President] Mark Yudof? When we met with Mark Yudof, before we actually had litigation between us and Glaxo [Wellcome Incorporated], he listened to the story, our story from the department perspective. He had the internal lawyers from within the University, and we had a law firm from the outside that was looking at this whole thing. We had not yet established an adversarial relationship with Glaxo. After we met a couple of times with Mark Yudof, he said, "Let's sue the bastards." He approved using University funds to sue them. After nine months of litigation, Glaxo agreed to different terms for the royalty agreement.

As soon as we agreed, I met with Mark Yudof, and he said, "Yusuf, we're going to establish a drug center at this University. That was before my meeting with Frank Cerra and Dean Speedie and the v.p. for research, Christine Mazier. When these guys met, I showed them our proposal for CDD [Center for Drug Design], and Frank Cerra looked at me and he said, "I think this is familiar." I said, "Well, Frank, you approved it about four years ago."

[chuckles]

YA: He said, "Oh, yes, I remember." I said, "This is how we're going to use part of the royalty proceeds, to fund the Center, but we're going to use it for other things." So I spent actually almost a year with Frank Cerra negotiating how we were going to be using these royalty funds. The reason why we met with Frank Cerra was because he had authority over all of space in AHC, even though the royalty money are departmental funds, and Dean Speedie didn't have any space. I was negotiating with Doctor Cerra to give us space in the Academic Health Center, and he wouldn't budge until we agreed that we would, essentially, establish the Center, not under the College of Pharmacy umbrella, but under the AHC umbrella, and it would report directly to the v.p. for the AHC rather than to the dean of the College of Pharmacy. On that basis, he gave us space in the Phillips-Wangensteen [Building]. It has expanded. He gave us 3,000 square feet. Right now, it's like about 10,000 square feet.

We're using those funds. Then, I had to convince the departmental colleagues to use those royalty funds and not spend the principal, but rather establishing endowments. So we've set up four endowments: one for graduate student fellowships, one for infrastructure, one for the named professor that's the chair in Medicinal Chemistry, and, of course, the Center for Drug Design endowment. That's a $60 million endowment that is going to generate about, maybe 3.5 percent per year, annually, in perpetuity. That was, really, where I spent almost two years of my time. I remember I must have met with Frank Cerra about fourty times during one year.

DT: Wow [whispered].

YA: …every week. Sometimes, I met with him alone; sometimes, I met with him and with Bob Vince, because he had to agree to some things. He is the discoverer. But we had to also abide by the University policy, which is, the discoverer gets thirty-three percent. The department gets twenty-five percent. Who controls the money in the department? Is it the discoverer or the department? We had this friction between me, in particular as the spokesman of the department, and Doctor Vince. He felt that he had to have the bigger say about how those funds should be used. I said, "Absolutely not." He then agreed that anytime I wanted to use those funds, I'd have to ask him whether it's okay with him to use those funds. I said, "I can't do that, because if you say, 'No,' then essentially, you've vetoed the program. You've vetoed the entire department." And we'll say "You can't progress." Anyway, we've had some difficulty. We had to use Frank Cerra as mediator to listen to both Vince's argument and my argument. Frank said, "Yusuf is right. You can say whatever you want and the department will take it, and your colleagues will respect your opinion." But he didn't want that. So that was a tremendously stressful two years for me. That was it.

[chuckles]

YA: I still have some money to do research, but I have two small projects that I want to complete. I'm not taking on any research personnel.

DT: It sounds like quite an achievement to get the Center established and growing as much as it has.

YA: That's right. The Center, right now, has, I think, about thirty-five research scientists. They have some NIH funded research. It's doing reasonably well. But they are too, too narrow. My vision of the Center was different. I was offered to become the director of the Center by Doctor Vince. I said, "No way. I'm department head. I can't be director of the Center and department head. There is a conflict between these two entities. We're using the same pool of money. I have to fight for this pool." When we set up the Center, I submited a department budget to the dean and to Frank Cerra and the director of the Center submits a Center budget to Frank Cerra. Then, the four of us meet: Speedie, Vince, Cerra, and myself. I have to defend my budget, and he has to defend his budget. Then, we discuss it, and we come to an agreement as to what are the items that we are going to fund and which ones we're not going to fund. That worked reasonably well. But that was a very stressful situation for me.

DT: Do you think it has been beneficial for the Center to be within the AHC rather than the College?

YA: Ideally, if it's a Center like the Cancer Center, and it functions and operates like the Cancer Center, then it should be under the AHC. Right now, it is under AHC, but an extension of Doctor Vince's lab.

This was my idea for the Center… When I was the department head, I said, "Let's have a center," and that was my vision. It would bring in scientists from the entire University in and out, and it could be in any discipline and a source of increasing interaction and accessibility to the scientists, resources, equipment, or what have you at the Center. Just like I am a member of the Cancer Center, I can go and use some of the facilities over there like the tissue culture facilities, the animal facilities, and I have done so in the past.

But, right now, the Center is, unfortunately, too narrow. They're doing good research, no question there. But they are too, too narrow. It's really an extension of Doctor Vince's lab. So it's not open to the University community. In that sense, it could be a Center within the College of Pharmacy, because it almost operates like a one-person lab—but a big budget.

In the long run, the only concern I have for arguing with Doctor Frank Cerra about the CDD being in the AHC is if there's a change in leadership within the AHC… [Aaron] Friedman, right now, may look at it and say, "Well, we're going to get an M.D. to run the Center," so the focus of the Center may shift. Or Leo Furcht may have different ideas and plans. Leo Furcht has similar aspirations like in Med Chem. He has some faculty within his unit that are doing like what we are doing in Med Chem. He wouldn't mind seeing that this Center be, let's say, under his operation. If that happens, of course we will lose as a department.

But, at the time, I was thinking as, I wasn't thinking as a department, I was thinking as a research entity within the University of Minnesota. I wanted to stay at the University of Minnesota and the legacy of our department is, we would continually have research in the area of medicinal chemistry and drug design, whether it's going to be in the Med Chem Department or in AHC, who cares, as long as the research entity continues to go along.

The reason why I say that is we've seen, over the years, in the College of Pharmacy, we have been impacted negatively because of administrative decisions, because of legislative decisions, where funding from the Legislature can decrease the amount of resources to the College of Pharmacy. As individual faculty retire or leave, the dean may not replace them and that can shrink the program significantly and, ultimately, maybe, combine these departments, dissolve departments. Just like other Colleges on other campuses, it is possible that the entire College could be eliminated. Who knows? But we're the only College of Pharmacy, so maybe in the State of Minnesota, it would continue to exist.

My thinking at the time when I said, "Let's have it in the AHC," is it will stay forever and will continue to do this kind of research at the University of Minnesota. Ultimately, we should all thrive rather than being too parochial about *where* it's going to be. Right now, the way I see it, it's too parochial in its style of management and, also, in the involvement of other scientists. I love John Kersey. He's the kind of director I'd like to see at the CDD and how he helped transform the Cancer Center into the center that I hope, *I hope*, that the CDD would become but this is not happening uner current CDD leadership. Maybe new leadership would help in the future.

DT: We've covered a lot of ground. I wonder is there anything else that you can shed light on or if there's anything else that you think we should discuss about the College's history or the history of the AHC.

YA: I'll have to think a little bit about that after you transcribe this and after you read the book, because the book has a lot of some of the things that I have mentioned, but it has more detail and presented in a more logical fashion than jumping from here to there.

DT: Once I've read the book, and you've been able to review the transcript, if there's more follow up, we can do a second interview then.

YA: That would be fine.

DT: Excellent.

Thank you, Yusuf. This has been really enlightening.

YA: That's good. I'm sure you're learning so much about different aspects within AHC. These things will be placed as files?

DT: They'll be available in the Digital Conservancy, which is the online archival resource for the University. The digital recordings will be available to researchers who

go to the Archives if they want to listen to them. We anticipate most people will just use the transcripts. Then, the transcripts will be physically available in the Archives as well as in the Digital Conservancy and on the [University of Minnesota] Oral History website.

YA: Available only to the Minnesota community?

DT: No, to any researchers who might be interested. It can be outside the University, so anyone.

YA: There's accessibility to that digital site?

DT: Yes.

YA: I see.

DT: Anyone can access the Digital Conservancy from outside the University, and, also, the Oral History website where people can access it. Once the transcript has been approved, and we've finished processing it, we'll put it on the Oral History website and, then, anyone who searches your name will come across the interview.

YA: I see, yes.

DT: They should be able to find it, also, in the Digital Conservancy that way. The goal is to have it widely available to anyone who is interested.

YA: You're focusing only on the research and facilities? What about education?

DT: Yes, also on education and the curricula changes and the educational mission of the various units and the AHC as well…so trying to cover all bases as much as possible.

YA: Are you on a tenure track?

DT: Yes.

YA: Good.

DT: [chuckles]

YA: So Doctor [Leonard] Wilson is no longer around?

DT: No, he had retired by the time I arrived here. But he still comes to events. He's still around, but he's fully retired, at this point.

YA: I liked working with him. He's a gentleman.

DT: Yes.

YA: He chaired the committee that was a graduate school committee, but it was on clinical graduate education, especially as it related to the Medical School, and they're giving them Ph.D.s in clinical medicine. But the kind of programs that they were going through were not as rigorous as, I'd say, some of the basic sciences. It's a duplicative thing that they can use their clinical training as their thesis. He was questioning a lot. Of course, we had some medical personnel that were not in agreement. Very interesting meetings... I sat on it for three years.

[chuckles]

YA: A wonderful guy.

At any rate…

DT: Thank you so much!

[End of the interview]

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