INTERVIEWEE: Dr. James Wyngaarden
INTERVIEWER: Jessica Roseberry
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PLACE: Duke University Medical Center Library, rm. 321

WYNGAARDEN INTERVIEW NO. 2

ROSEBERRY: This is Jessica Roseberry. It's March 21, 2005; and I'm here with Dr. James Wyngaarden. He is the Florence McAlister Professor of Medicine Emeritus. And we're here in the Medical Center Library in room 321. Thank you very much, Dr. Wyngaarden, for agreeing to be interviewed today. I appreciate that.

WYNGAARDEN: My pleasure.

ROSEBERRY: We're continuing an interview that Dr. Wyngaarden did with Dr. James Gifford. And that interview left off as Dr. Wyngaarden was chair of the Department of Medicine, and I wonder if we might begin again there by talking about some of the issues that were most important as you think back on your chairmanship. What were some of the things that stand out to you as being most important to you during that time?

WYNGAARDEN: I'll try to do that, Jessica, bearing in mind that I left that position in 1982, and we're now twenty-plus years later. (*Roseberry chuckles*) When I left in '82, I had been chairman at Duke for fifteen years, plus two years at the University of Pennsylvania. When I was first approached about being considered for the position at the NIH [National Institutes of Health], my thought was that I was very happy with what I was doing. But I didn't quite decline. I was asked to think about it a while, and I said I would do that. When the person called a second time about a week later, I said, I've been thinking about it, and if I was ever going to do anything else, the directorship of the NIH

appealed to me in many ways, but I wasn't really decided that I wanted to be considered. He said, "Would you at least send me your CV?" And I thought, Well, that's innocent enough, (*Roseberry laughs*) not realizing that as soon as I did that, I had formally applied for a position in government. (*laughter*) But at any rate, after a series of interviews and some little time, I was offered that position and took it. And it was a major change in the things that were on my mind. After fifteen years of working in and developing the Department of Medicine at Duke, I suddenly had to do things that were very different. And, although I kept in touch occasionally with friends at Duke and also made some visits here while director of NIH, I really wasn't very close to the scene. But now as I look back on those fifteen years at Duke, there are some things that stand out. First of all, as I indicated in my earlier interview, the Department of Medicine when I came and when I left was a superb clinical department of medicine, as good as any place I've ever been or seen. And clinical excellence in the Department of Medicine was a matter of enormous prestige, it attracted excellent residents and excellent students. There were standards here that were very, very high. The PDC was a great asset at Duke, and I presume it still is. It had a cadre of excellent physicians for whom the main job of the day was to take care of sick people and provide an outstanding referral service for this community and this part of the world. It did that then, it continues to do that now. The research side of the department was growing, as I indicated; when I first came to Duke in 1956, the NIH was just beginning to make substantial extramural awards, and we took maximum advantage of that in the growth of the medical center, particularly in the growth of the Department of Medicine. The kinds of science that NIH supported fit our portfolio very well. And we were able to acquire more space as time went on, and that

meant we could hire a lot more people. So it was an enormous growth period. And I set about, whenever we had a vacancy to fill, to find the very best person wherever he or she was. Clearly I looked within, but we also recruited from the outside very vigorously. As I look back on those days, that stretch of time, what stands out in my mind is the excellence of people that were brought in. In many ways the current reputation of Duke still rests on some of those very same people. Also as I looked over the list of people in the Department of Medicine during my tenure, at least thirty of those have gone on to become department chairmen somewhere. A number at Duke, but most of them elsewhere. So we did continue to produce important leaders of medicine. I took a personal interest of course in the Rheumatology Division, of which I was a part, and actually I was brought to Duke to help build that area. We had a series of excellent people that came through that department and made their own marks on the world, some here, some elsewhere. Bill [William] Kelley was probably the first major appointment I made, and Ed [Edward] Holmes was a fellow who grew into the department and became a full professor, then later was a chairman at Penn and later still a dean here and now vice chancellor or whatever his title is at San Diego. Nick [Nicholas] Kredich was one of those people. I recruited Dave [David] Pisetsky at one point, Mike [Michael] Hershfield at another. They both continue to work at Duke and to build its research reputation. They've become outstanding, widely recognized scientists. And Ralph Snyderman was one of the people I brought in. He had earlier been here as an intern and resident and then had gone to the NIH. I knew him there and visited him at the NIH a time or two and brought him back here, and he of course grew to become chancellor of the medical center. So that's a list of those in my own immediate division, but I also set out at one

point when [J. Lamar] Callaway retired to bring in a cadre of people in Dermatology. In one fell swoop, we brought in Sheldon Pinnell and Jerry [Gerald] Lazarus and Lowell Goldsmith, all of whom became department chairs in various institutions—in fact Lazarus and Goldsmith both also became deans, Lazarus at Penn and Goldsmith at [University of] Rochester [College of Medicine]. We revitalized the Neurology Department Division. Brought in Stanley Appel; he later moved to Houston as chairman, and then Allen Roses was promoted from within to head that division. And we started the new Division of Infectious Disease. Brought in David Durack to head that. And in Cardiology, we had some space coming available in one of the research buildings, Andrew Wallace, who was at that time the chief of Cardiology, persuaded me that we should devote more space to a different kind of cardiological research: more metabolic, more biochemical than the previous research which had largely been physiological and hemodynamic. So we brought in Bob [Robert] Lefkowitz and promoted Pat [Patrick] McKee to head two major laboratories there. Pat later moved as chairman to Oklahoma, where he had come from, and Bob is still here. And I think that if you look at Duke from the outside, look at the Department of Medicine in particular from the outside, probably the most visible person in the last ten or twenty years has been Bob Lefkowitz. And he continues to do world-class research that's widely recognized. Along the way we strengthened the divisions of Endocrinology, GI [Gastroenterology], Pulmonary, and so forth. But those were strengthened more from within than from external appointments. So those are, I think, the important aspects of my tenure here, or at least I look back on them with pleasure. But in the process of building the research division, I made sure we took nothing away from the clinical excellence of the department. It was understood that

everybody that I recruited into these predominantly science-based positions were also regular members of the Department of Medicine. They took their turns in teaching, in staffing the—what we then called the "public clinics." There's a better word for that now: the specialty clinics. And taking their turns rounding with students and house staff on the wards and also from time to time seeing some private patients, especially in consultation. I think the residency program became stronger not weaker by virtue of these expansions. We offered incoming residents many more opportunities for selection of subspecialty training if they would choose to go that route and particularly if they wanted to combine clinical medicine and investigative medicine, a whole lot of opportunities right here. We also made continued use of the NIH by sending people, many of whom spent two, three, four, or five years there and then came back to Duke after that. So those are the things I look back on with pleasure, and I think we maintained a very high standard of student teaching that had been established by Gene [Eugene] Stead.

Of course, Stead was around during all the time until I went to the NIH. And although many people were curious as to whether he could ever let go, he was a marvelous person to follow. He never, never interfered with anything I was doing. He never second-guessed. He got very busy in his own area of information science in the cardiovascular database and the PA [Physician's Assistant] Program. And although I saw him regularly in the corridors and elsewhere, socially as well—he never came to my office to give me advice. Except maybe once or twice a year, if that, he would say, "Jim, there's something you may not know about." And he would spend five minutes telling me what it was. Then he would say, "There. I've told you about it." (*Roseberry laughs*)

"I'm out of here. Blessings on you. Do whatever you want to do." He never once came back to ask me what I did about the problem that he had brought to my attention. Never once. I had colleagues who became chairs in the department in which they grew up and in which the retiring chairman stayed around and made their life miserable. I'm not going to name them, (*laughter*) put them on the record. But some of them could hardly appoint their own house staff. And I know of one situation where the former chairman essentially rode the new chairman out of town, because he didn't do things the way he wanted them to be done. I was very fortunate that way. I never had that experience, nothing even remotely like that. So that's my look back on the Department of Medicine, but I also realize that the change was good for me. After seventeen years—I've kind of jokingly said that when I first became a chairman, the most exciting day of the year was July 1 when the new interns arrived. And when I was thinking about, Should I consider the NIH or not?, I realized the day that I dreaded most of the year was July 1 when the new interns arrived. (*laughter*) I'm only kidding, half kidding about that, but it was a period of time that had its own stresses every year. Wonderful people would come in as house officers, but they entered a very demanding program, and some of them had trouble with the transition. We always had a few problems. Basically good problems for some of them to get adjusted and started, but after having done that seventeen times (*laughter*) I wasn't quite as anxious to deal with the eighteenth.

ROSEBERRY: Well, I thought I might ask you about—you had mentioned Dr. Snyderman and Dr. Lefkowitz. And they were both Howard Hughes Medical Investigators.

WYNGAARDEN: Yes, I did not mention that. That's right. Yes.

ROSEBERRY: I thought I would ask about your role in the Howard Hughes Medical investigation process, and then maybe bring in them as well.

WYNGAARDEN: Sure. The Hughes Medical Institute was started by Mr. Hughes himself in Miami, and his original plan was to build a research hospital in Miami. He was talked out of that, because Miami at that time was a backwater place medically. He was talked into supporting bright people who would be part of an extended institute that supported them for additional development and work in their own locations. There were originally three medical trustees of Hughes. George Thorn was the chairman. He was from the Peter Bent Brigham Hospital in Boston. The other two were [Charles] "Rollo" Park from Vanderbilt and Victor McKusick from Johns Hopkins—at least at the time that I joined the group. There had been some earlier people who had retired or died. But those schools were represented because Hughes had been under the care of physicians from those institutions over time and thought highly of them. When the funds permitted, the Hughes program expanded from three schools to five. That brought in Duke and the University of Washington in Seattle. I joined this group, and so did Hans Neurath, representing Seattle. Neurath had originally been here in biochemistry before [William] Perlzweig died and [Philip] Handler was appointed the chairman. So the five of us were on that board for a while, and gradually other schools were added. But the program that was promoted by the Hughes Institute was very different from what it is today. It was much more of a career development program than it was an extended decentralized research institute. There came a time when the Institute trustees realized that this was probably not exactly what Hughes had intended. They kept asking, What is our research program? There was the added stimulus of the IRS looking at the institute every year,

convinced that it was a tax dodge, which it was not. It was funded by after-tax profits from the Hughes Aircraft Company, which by Hughes's will, the institute actually owned. The aircraft company was located in California. The Howard Hughes medical Institute functioned on that pattern for a time. Eventually, we had to reorganize under pressure of the trustees to define our programs. Hughes investigators fell principally into three areas. One was immunology, another was genetics. And the third was called metabolic regulation. George Thorn was an endocrinologist, and he naturally was attracted to supporting many people doing endocrinological research. That area later came to be called cell biology. So these were our three major programs. After the Hughes Aircraft Company was sold, Hughes jumped from a rather modest program to hundreds of millions of dollars in expendable money.

ROSEBERRY: When was that sold, I'm sorry.

WYNGAARDEN: About 1980.

ROSEBERRY: Okay.

WYNGAARDEN: They sold the aircraft company for something like $5 billion. Hughes then continued these three themes but later added structural biology, which had to do with x-ray, crystallographic studies of protein structure, DNA structure, and then neuroscience. We had earlier supported a few people in neuroscience; in fact, Allen Roses had been supported before we had to concentrate on the other three areas and dropped neuroscience and many outliers like pulmonary research and cardiovascular work. The institute today still has those five programs: genetics, immunology, cell biology, structural biology, and neuroscience. Those are still the five programs. We were fortunate in being in on the Hughes program from the beginning. At one time or

another Allen Roses was a Hughes scholar, Ralph Snyderman was, Nick Kredich was, Bob Lefkowitz was and still is. Of course there have been many others since.

ROSEBERRY: Can you tell me when you first became involved with that selection?

WYNGAARDEN: With Hughes?

ROSEBERRY: Yes. If you don't mind.

WYNGAARDEN: It was about the time that I became chairman or very shortly after that, and that was 1967, so that might have been '67 or '69.

ROSEBERRY: Okay. And how did you first notice Dr. Snyderman?

WYNGAARDEN: Well, during those two years that I was at Pennsylvania, he was here on the house staff. About the time that I came back to Duke, he left to go the NIH where he spent three years in the dental institute [National Institute of Dental and Craniofacial Research] in a very, very good immunological research laboratory. And somewhere along the line I met him when I was at the NIH visiting. I dropped in to see him from time to time, so I got to know him a bit. And then I discovered that he was interested in leaving the NIH. Mort [Morton] Bogdonoff, who had been here, was at that time chairman of medicine in Chicago, and he was interested in bringing Ralph there, and I was interested in bringing Ralph here. I never knew what Mort had offered him, but Mort didn't have a school with the kind of reputation of Duke. And I think he had to pay people a premium to get them to move to Chicago. (*laughter*) So it turned out later (*laughing*) that I had offered Ralph about $10,000 less than Mort did, but I trusted his judgment; he came here. But he's made fun of that ever since. Ralph was a very, very effective investigator. He's also a *very* good speaker, on his feet and in prepared talks. He was regarded as a very fine teacher on the medical service. First of all, immunology

relates to every disease category. I'm not saying every disease is immulogical, but every medical subspecialty group has patients with conditions in which the immune system is disturbed. So his knowledge cut across every part of the department. Furthermore, he was interested in what he called *pharmacoimmunology* or *immunopharmacology,* which had to do with the interaction of drugs with the immune system. And so his area logically fit with everything going on in the hospital. He also gave *very* fine medical talks around the community on occasion. So he did very well. But he grew up here, and he eventually became chief of the Rheumatology Division when Kelley left. Then he left for two years, as you know, to go to Genentech in a high administrative position and was attracted back here as chancellor when Bill Anlyan retired.

ROSEBERRY: Was there a sense maybe of priming him for national leadership?

WYNGAARDEN: Well, no more than any others. I was even closer to Kelley and Holmes, because they were continuing to do research on the themes that I had worked on. I described this in the [James] Gifford interview. I became interested in purine metabolism in gout but also in the fundamental biochemical mechanisms that led to the production of nucleotides, purine nucleotides like adenylic and guanylic acids. And the regulatory mechanisms of the synthetic pathways. The three of us worked on the regulatory mechanisms; I started it, and Kelley took them over, and then Holmes took them over from Kelley. And so for fifteen, maybe twenty years, we were sometimes referred to as the "purine capitol of the world" because of our work on the regulatory mechanism in purine metabolism. And a number of foreign fellows came and spent a year or two here. From Australia and Israel, for example. And both Bill and Ed made enormous contributions to that theme over the years.

ROSEBERRY: So the Hughes investigatorship is not necessarily trying to bring out the national leaders and then maybe bringing them to Duke?

WYNGAARDEN: No. Not specifically. I suppose every school uses them as prestigious plumlike appointments, and we certainly did that. But, bear in mind that a school can only propose a candidate for a Hughes appointment. The Hughes Board makes the decision. I don't recall recruiting anybody to Duke with the lure of a Hughes investigatorship. We picked the best people here to propose, but bear in mind, that's back when it was more of a research career development award than a lifetime appointment as an investigator.

ROSEBERRY: Okay. Would it be safe to say that the concept of the physician-scientist has been an important one to you?

WYNGAARDEN: It was, and I talk about that in the original interview, too. I wavered as a student whether I would go into chemistry or medicine. I chose medicine, and then was delighted to find out that one could do both. (*Roseberry chuckles*) But you needed training for that, so I spent about five years in biochemical training before coming to Duke: a year in New York and almost four in the National Institutes of Health when it was just opening up. And naturally this was an interest that I tried to perpetuate, not only in what I did myself, but in the people that I brought in, the people I trained. So the people who worked in my group learned a lot of biochemistry. Most of them had taken a few years of solid, full-time biochemical work at the NIH or elsewhere before we brought them here. But we continued that, and then later we <u>as an institution</u> continued that. Yes, I was personally much more involved with the physician-scientist side than I was, let's say, in the medical practice side, although I made it a point early on especially to

maintain a moderately active practice, we were at that time rounding three days a week year round. And in addition to that, I had the rheumatology clinic one afternoon a week. Before we had any fellows, Grace Kerby and I were doing the consultations in Rheumatology on the non-private service. And I had a modest private practice for many years. Once I became chairman I just couldn't continue that practice.

ROSEBERRY: And I know that later on, on a national level, you became almost an advocate for the physician-scientist.

WYNGAARDEN: Well, I was elected president of the Association of American Physicians, and at the end of that year I had to give a presidential address. I was still at Duke at that time, before I went to NIH as director. I had been on a committee at the NIH that was designed to look at the need for additional personnel in science. The Nixon administration at one time tried to abolish all training grants, feeling that the government had no role in training, that it was an individual's own responsibility to secure training. It wasn't long before the countervailing forces became extremely active. And they managed to change Nixon's mind on the basis that we now had a national cancer program, we now had national goals in cancer, which could not possibly be met in the absence of a continuing supply of well-trained physician-scientists. So the Nixon administration brought these training programs back, but with a whole series of additional restrictions. One of these was that a national committee was to be set up to evaluate the need, field by field, for additional scientists. We knew the answer to that before we ever met: every field would have a continued need. (*laughter*) But we had to do this. And I was asked to serve on that committee. It was a committee of maybe ten people. Then I was also asked to serve, because of my RTP [Research Training Program]

experience, on the first committee to set up the MD/PhD program. I was a member of that original committee at the NIH, and later its second chair. When I was asked to give this presidential address, I could have chosen any topic, but I chose to speak on the need for a continuing supply of physician-scientists. I was aware from the data that had come before this NIH committee that the number of MDs applying for scientific training was dropping and that the percentage of research awards going to MD scientists was declining. So I gathered all the data then available and gave this talk and entitled it, "The Physician-Scientist as an Endangered Species." And that has become almost my middle name (*laughter*) since then. It is far and away the most-quoted paper I ever wrote. It's just leagues ahead of whatever's in second place. I'm still referred to as the person who spotted a trend twenty years before it became a crisis. And people still ask me where that insight came from. Well, it wasn't such a remarkable insight; it was not a bolt out of the blue. It came out of my work on that committee.

ROSEBERRY: Let me flip our tape over.

(*tape 1, side 1 ends; side 2 begins*)

ROSEBERRY: Do you feel that the role of the physician-scientist has maybe changed in current-day circumstances?

WYNGAARDEN: It has changed. It was changing at the time I gave this interview with Jim Gifford [April 9, 1982]. And I commented there that it was becoming more difficult to be a really competent physician and a really competent scientist. There are several reasons for that. Science is becoming more and more complex. We had long passed the day when we could see a patient on the ward in the morning and study that patient in the laboratory in the afternoon. There's still a little of that going on in the pulmonary lab and

the cardiovascular lab, but in endocrine and metabolic disease, and the genetic disease category, you had to have really well-trained biochemists to establish the mechanism of a disease. And so it became more difficult to do both. One of the things that changed early on was that we also had the advent of Medicare, which required very much more detailed attention by senior staff to patients or therapies in addition to that of the resident staff. Clinical responsibilities for the faculty greatly increased. A lot of that increase was not exactly taking care of the patient; it was taking care of the records. So the duties on the clinical side increased and led in one direction, and the complexities of the laboratory led in a different direction. And I always had the goal that the science coming out of the Department of Medicine had to be every bit as good as the science coming out of the basic science laboratories where people were doing it full time. And the only way we could maintain both of those goals was to add more people. And the roles did change, people migrated one direction clinically and the other direction in the laboratory. But I didn't want them to be such that the twain should never meet. So my position was always that the people doing primarily science continue to attend their subspecialty clinics, continue to participate in the ward rounds. I think fewer and fewer of them saw private patients.

ROSEBERRY: Can you talk maybe about the role of the generalist? Particularly at Duke, I guess.

WYNGAARDEN: (*speaking at same time*) Yes, although I was not very much involved in that, the medical school was. And there was, and I suspect still is, some uncertainty about how all of this will sort out. We had the traditional general practitioner, of whom there were now relatively few who were lightly trained in all areas of medicine. We had

the internists who were doing general medicine but frequently were doing subspecialty medicine in addition. And then there was the family practitioner. I didn't see that the Department of Medicine had any particular role in the family practice movement. We would continue to produce well-trained generalists in internal medicine and subspecialty people, predominantly with clinical interests; we would continue to produce physician-scientists and teachers, administrators, all these things. But it was really Harvey Estes' department that took on the role in the family practice programs.

ROSEBERRY: So not necessarily within the Department of Medicine, that was not a—?

WYNGAARDEN: No. I don't know how much interaction there is today. We did have some residents rotating at what was then—I guess it's still the county hospital, now it's Durham General, isn't it?

ROSEBERRY: Um-hm. Durham Regional.

WYNGAARDEN: Yes. So we had some residents that rotated over there until the end of my stay, but most of that change occurred after I left, so I didn't play much of a role in that.

ROSEBERRY: Okay. I wonder if maybe we could fast-forward a little bit and if I could get you to comment on the Bayh-Dole Act and the Technology Transfer Act—I don't know if I said that correctly—

WYNGAARDEN: Yes.

ROSEBERRY: —just how those maybe changed—

WYNGAARDEN: Well, the Bayh-Dole Act actually was passed a year or two before I went to the NIH. I think the date was about 1980. Maybe '79. And it reversed what had been federal policy up until then. Essentially it gave primary ownership of work done,

and discoveries made with government support, to the performing institution. And these institutions were also obligated to develop these discoveries for the good of the American people. If there had been a discovery that, for whatever reason, had not been patented and not been exploited and it should have been, the government had march-in rights. And at least in relation to the National Institutes of Health and the National Science Foundation, the government has never had to use those rights.

ROSEBERRY: Okay.

WYNGAARDEN: Not all institutions have revved up their technology transfer offices to the max. There are some even now that are just getting around to doing that. And there were some institutions where faculty members considered the academic-industrial link as an unholy alliance. I was later on a committee to visit Dartmouth where they had a problem because some of the faculty thought this development was inimical to education and the purposes of a university. They really resented it when somebody patented a discovery and then received royalties from it. Duke didn't have that problem; we (*laughing*) went after this money with a vengeance as we had from the very beginning. That was one of the happy consequences of the way Mr. [James B.] Duke set up the university: he built the buildings, but he didn't leave an endowment of the size where we could rest on our laurels. And Duke became extremely good at capturing every rolling dollar: government, private, whatever it was. (*Roseberry chuckles*)

ROSEBERRY: I'm wondering how much the scientist should be aware of things going on in Washington and kind of—you were saying that Duke has done very well in capturing dollars from the NIH and private funding.

WYNGAARDEN: Well, I think it's fair to say that no institution, whether of university or institute structure, has enough independent money that it can do much research without outside support. And the principal source of that outside support clearly is the US government, although there are certain foundations that support a good deal of it also; I'm a trustee of the Van Andel Research Institute in Grand Rapids, Michigan. Jay Van Andel was a grade-school classmate of mine. And he and Richard DeVos are the founders of the Amway Corporation. Jay just died a few months ago, but he set up this research institute—it's principally a cancer research institute—about six or eight years ago in Grand Rapids, which is where he lived and where the company was. Grand Rapids was not the most likely place for a research institute, because it does not have a strong base of medical education; it has good medical practice, but there's no university there. But it, too, can't survive with an annual trust. It is seeking outside funds whenever it possibly can. So that's true—that's universally true. And the NIH is the principal supporter of biomedical research in government; there are small amounts from other sources, but far and away it's the NIH that schools like Duke are dependant on.

ROSEBERRY: Have drug trials come in and maybe changed some of that dynamic, or—?

WYNGAARDEN: Well, yes. I view those as a mixed blessing.

ROSEBERRY: Okay.

WYNGAARDEN: Roy Vagelos, when he was president of Merck used to insist in testimony that pharmaceutical companies didn't do research, they did product development. We have enormous arguments about that. And I would still subscribe to Roy's statement. It is essentially testing a drug to see whether it's safe and efficacious.

There is no new idea that comes out of that activity at the fundamental level. Not that drug trials are not critically important. I'm not knocking it for one instant, but I bridle when I hear people talk about how much research is going on in the department and it turns out it's mostly product evaluation. I'm on the side of wanting universities to concentrate on fundamental knowledge.

ROSEBERRY: Okay, thank you. I wonder if we could talk about genetics, if that's all right. I know that you were, in the 1960s, on a committee to bring a department of genetics to the university. And I wonder if we could talk about—if you could outline for me how that—genetics at Duke, maybe.

WYNGAARDEN: Yes, we had a series of committees that were looking at the structure of the medical school. I can't recall exactly whether it was contemporaneous with our curriculum inquiries or separate, it was about the same time. I chaired a genetics committee, and someone else chaired a biophysics committee. Neither of these was a department. And I remember writing the report recommending that we set up a genetics department. From time to time in the history of science, a field emerges which achieves its own identity, and I thought genetics had done that. Biophysicists came to the other conclusion, that biophysics was so closely aligned with biochemistry that it should be subsumed by the biochemistry department. Well, it took quite a while before our recommendation was really acted on. We didn't have the resources to do a lot of department building, and I was aware that after I left, while I was at the NIH, there was a lot of further inquiry about genetics. But we didn't go the department route at that early time. I think there were chairs, who, at that time felt that a genetics department would take a lot away from what they viewed as their department's purview. And it didn't

happen. As a consequence, Duke made no important contribution to the genetics revolution. None. It is now making up for lost time. But it's very late in the game.

ROSEBERRY: Well, I wonder if you could talk about genomics under your directorship at the National Institutes of Health. Kind of how you view your involvement in that, the Human Genome Project.

WYNGAARDEN: The Human Genome Project, yes. Well, I've also written a chapter ["Jim Watson and the Human Genome Project"] on that. Do you have that book?

ROSEBERRY: I don't.

WYNGAARDEN: That history is laid out in great detail in a book [*Inspiring Science*] written for Jim Watson's seventieth birthday. I can loan you my copy, but I have only one copy.

ROSEBERRY: Okay. Maybe just—

WYNGAARDEN: And you can make a copy of that.

ROSEBERRY: Okay, thank you.

WYNGAARDEN: Briefly, I was extremely busy (*laughs*) as director of the NIH, and there are only so many things you can be devoting half your life to at one time. And I was aware that there were proposals about sequencing the human genome. They really emanated from a man named [Charles] DeLisi in the Department of Energy. I had asked Ruth Kirschstein, who was the director of the Institute of General Medical Sciences, to participate in those meetings and keep me informed. She did. I was in London for a meeting of the European Medical Research Council. The NIH is not a member of that, but the director is always invited as a courtesy to meet with them, and I was there for one of those annual meetings. Someone asked me what I thought of the announcement that

the Department of Energy had $2 billion to start a program to sequence the human genome. Well, I hadn't heard that. (*Roseberry chuckles*) It turned out not really to be quite correct. They had estimated the total cost of it to be that, not that they had the money, but that was what was represented to me. And my reaction was, "Not on my watch." If that is going to be done, the NIH is going to do it. And so I began to discuss this internally. There was not a single person at the NIH who wanted to go that route. First of all it was big science. And the NIH traditionally concentrated on supporting small projects of individual scientists, not organizing huge Los Alamos-like teams to bring in many people to do a single job. Ruth was rather neutral about it. But I decided that we were going to do it. If it was going to be done, we were going to do it. And I put a request in our budget. Our budget for the next year had already been submitted. At the end of the hearings, the chairman, Mr. [William] Natcher most often would find a little extra money beyond what we had been permitted to request and would ask me to prioritize. This year he asked me what I would do with, I think it was nearly a billion dollars extra in one hundred-million-dollar increments. I used the initial increments to satisfy most Institute Directors' major priorities. In about the fourth or fifth $100 million increment, I put in a request for money to start the Human Genome Project. We didn't get everything we asked for, but we had enough to start it. Then I was able to bring Jim Watson to the NIH to run it. And he did. He did it brilliantly. First of all, he got together immediately with the Department of Energy, so this became a collaborative project. We were not fighting each other. And they did more of the large group projects; we did more of the individual science initiatives, but even that distinction became blurred with time. Watson led this project very well, got us off to a very good start. He was an

extremely opinionated person; I guess he had the right to be. And eventually he rubbed Congress the wrong way. And he certainly rubbed my successor, Bernadine Healy, the wrong way. She made a change of directors after a while. But by then the Human Genome Institute was well launched, and eventually got the job done. Now, they didn't foresee Craig Venter's role in that. Craig was at the NIH when I was there. Craig was advocating sequencing cDNA fragments. Do you know what those are?

ROSEBERRY: I don't.

WYNGAARDEN: These are the complementary message segments of DNA rather than the full DNA strand itself. And that was rather contrary to what NIH was doing, so he went private. And in the end, the combination of the private sector doing cDNA sequences and the NIH doing direct genomic sequencing completed the full sequence in record time. It was estimated it would take twenty years and cost $2 billion. It was finished in about fifteen years or thereabouts, and the total cost was well under $2 billion.

ROSEBERRY: So how do you view your own role in that?

WYNGAARDEN: Well, as I look back on everything that I did in the eight years I was director of the NIH, initializing the Human Genome Sequencing Project stands out as the thing that I'm proudest of.

ROSEBERRY: Okay. Good. As you were director, were you aware of Genentech at all?

WYNGAARDEN: Oh, sure. In fact, I visited Genentech. David Martin was a Duke graduate and was for a time at Genentech. I visited him in the company; in fact when I left the NIH, I was offered a job at Genentech, the one that Ralph eventually took.

ROSEBERRY: Oh, wow. (*laughs*)

WYNGAARDEN: However, when I left the NIH, I went to the White House Science Office, where I chaired a committee on biotechnology policy, most of whom were Cabinet officers who didn't even know what biotechnology was. And we had Bob [Robert] Swanson come and talk to the committee. The White House became very concerned when he sold a major share of Genentech to Roche and wondered why he wouldn't have considered an American company. Well, the truth was, he had considered every American company; they hadn't considered him. And he had to make this decision because there was either enough money to develop products, which they were now ready to do, or to continue to do additional research, which they also wanted to do. But they couldn't do both without outside money. The Roche deal gave them the resources to do both. Roche of course was interested in the end of the line, the products that came from the fundamental research, but they wanted the pipeline to be continued also. So it worked out well for Genentech and Roche.

ROSEBERRY: Do you feel that Genentech affected what happened at the NIH at all, or—?

WYNGAARDEN: Genentech affected? I would not say directly, no. I would say indirectly it validated the kind of investment that the NIH was making. Because all those scientists who came into the Genentech organization were either trained at the NIH or supported by the NIH. It was part of a continuum. The NIH does not really develop products. That's not in our portfolio, which is to do the science on which products can be developed by the private sector.

ROSEBERRY: So the Duke connection with Genentech would be viewed as a positive thing, I would guess.

WYNGAARDEN: I certainly know nothing negative about it.

ROSEBERRY: Okay. Thank you. I wonder if we could talk maybe then about Duke as Dr. Snyderman is the chancellor.

WYNGAARDEN: Well, he presided over a period of substantial growth. And the acquisition of more buildings, more space, more resources. I think you'd have to say it was a very significant tenure.

ROSEBERRY: As far as his actions toward Dr. Greenfield, I wonder if you had any thoughts about that. Was that an appropriate—?

WYNGAARDEN: Well, I was not here for much of that. I don't know the details of that. I think there was, particularly in the clinical departments, a lot of friction between the departments and the chancellor's office. It was most noticeable with Greenfield. I know that I've thought Ralph was progressively strengthening his own office and weakening the chairs. I'll just let it go at that.

ROSEBERRY: Okay. As you returned to Duke from the NIH—I wonder if you could talk maybe about your role at that time at Duke.

WYNGAARDEN: I never really returned to Duke. When I left the NIH, I went directly to the White House Science Office. After some months I got inquiries about many things, one of which did interest me, and that was the foreign secretary position in the National Academy of Sciences. So I left the White House, ran for this position, and was elected to serve in it. And that was a half-time position. One of the reasons I decided to leave the White House was that I was getting so many inquiries about serving on industrial boards and other things, and I knew those opportunities wouldn't last forever if I turned them all down. And the NAS position appealed to me more than trying to come

back Duke where what I had done as chairman I never would have done again if they (*Roseberry laughs*) wanted me to. That was (*laughing*) not my role anymore. And they never asked me to do that. I'm just using that as an example. But it was, for me, a very good decision, to leave the White House after a year and get involved in these companies. That's what I'm still doing. Here I am, over eighty, and I'm not quite working full time, but I'm as busy as I want to be. I've served on five corporate boards, and I'm a trustee of two research institutes. I evaluate biotech companies for three venture capital firms. Small biotech companies are constantly looking for money, and firms are constantly looking for companies worth supporting. So I try to help make that match. And then I serve on an Academy [National Academy of Sciences] and an occasional IOM [Institute of Medicine] committee. It's just ongoing, one after another after another. I rotated off a couple of these boards recently, so I'm only on two of them at the moment. I'm still out of town almost every week somewhere.

ROSEBERRY: Well, is there—

WYNGAARDEN: It could be worse. (*laughter*)

ROSEBERRY: You're still staying very involved, it sounds like.

WYNGAARDEN: Yes. Yes, indeed.

ROSEBERRY: Well, is there anything else that I have left out that should be covered?

WYNGAARDEN: No. No, that's a wonderful summary, and I appreciate being able to get some of these things on the record.

(*end of interview*)