CHEMICAL HERITAGE FOUNDATION

TUCKER COLLINS

The Pew Scholars Program in the Biomedical Sciences

Transcript of an Interview
Conducted by

Arnold Thackray and Frances Kohler

at

Le Meridien Hotel
Coronado, California

on

4 March 1991
(With Subsequent Corrections and Additions)

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TUCKER COLLINS

1952 Born in Lorain, Ohio on 3 November

Education

1975 B.A., Biology, Amherst College
1981 M.D./ Ph.D., Microbiology, University of Rochester

Professional Experience

Brigham and Women's Hospital, Boston, MA
1981-1986 Clinical/Research Fellow, Department of Pathology
1986-present Assistant Professor, Department of Pathology

Honors

1974 Oscar E. Schotte Prize in Biology, Amherst College
1980 Sherman Award, New York Branch, American Society for Microbiology
1986 American Association of Pathologist's Experimental Pathologist in Training Award
1987 Pew Scholar in the Biomedical Sciences Award

ABSTRACT

Tucker Collins grew up in a suburb of Cleveland, Ohio, one of three children. His father was a chemist at B.F. Goodrich, and his mother was a housewife, later she became a bank vice president. Collins spent summers with his grandparents on Long Island, New York. He was interested in science and medicine and attended the Program in Biochemistry (PIB) while in high school. He won the Westinghouse Science Talent Search and was accepted at Amherst College. At Amherst he worked with Edward Leadbetter and Walter Godchaux, two instructors from PIB. He also spent two summers at Marine Biological Laboratory (MBL) in Woods Hole, Massachusetts, where he attended Gerald Weissmann's physiology course. Collins went into University of Rochester's Medical Scientist Training Program (MSTP) program, obtaining both his MD and his PhD.

Collins began work on vascular endothelial cells while in Jordan Pober's pathology lab section at Brigham and Women's Hospital in Boston, Massachusetts, while finishing his residency in pathology. National Heart, Lung, and Blood Institute funded his research into platelet-derived growth factor (PDGF). He says PDGF is intrinsically interesting, but its implications for nerve regeneration make it more so. Collins set up his own lab with one of his numerous grants and began teaching at Harvard University. His lab continues investigations into cytokine adhesion and PDGF, hoping to discover how and why organisms form or malform.

Collins attributes his current ventures to his previous educational and lived experiences. He loves the excitement of practicing science. He discusses the balancing of career and home life. Collins would like one day to be chairman of a pathology department.

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INTERVIEWERS: **Arnold Thackray**
Frances Kohler

LOCATION: **Le Meridien Hotel**
Coronado, California

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THACKRAY: Tucker, could you begin by telling us a little bit about where you were born and the family you were born into?

COLLINS: I was the first child born in Lorain, Ohio, which is on the west side of Cleveland known for steel mills and burning rivers, actually, to an interesting woman and a chemical engineer.

My father grew up in New York in the city area in a reasonably affluent family, went to MIT and took a job with B.F. Goodrich, kind of doing chemical stuff, which brought him to a chemical plant in Avon Lake, Ohio.

My mother was much less fortunate. She went on full scholarship to Smith, was a very smart woman, and was working as a chemist with B.F. Goodrich, going to law school part time at night at Case [Western Reserve University] when she met my father. She's a very smart lady. I think nowadays she would have been a full-time [worker] throughout her life. She took time off to take care of us, and I'm not sure whether she actually lived up to all of her potential.

Anyway, I was in Lorain for a year and then basically in a bedroom community also on the west side of Cleveland called Avon Lake for a couple of years and then another community in Cleveland, where I started school. That community is called Bay Village. Those of you that know Cleveland know that the east side is the place to be—Shaker Heights, Cleveland Heights, University Heights. This is the west side which is, I don't think, nearly as interesting.

Okay, from there they left and went to New Jersey My father worked in and out of New York City, and at this time my mother was doing nothing but being a full-time housewife. Just parenthetically let me note that she was a full-time housewife basically from about the time I was small to about the time my brother went to college, at which point she went back into banking. She retired as a bank vice president and running a probate

department.

This was Summit, New Jersey, which is another bedroom community, known to some because it houses a big pharmaceutical and it's near Bell Labs. What can I tell you there? I was not the friendliest of people. I still am not the friendliest of people. My grandparents had a place out on Long Island. If you know Long Island at all, Nassau County is where the suburbs of New York are; Suffolk's where some of the nice places are located. Long Island splits into two parts, and they had a summer place, so I spent most of my summers (while we were in New Jersey) learning how to sail, and I've been kind of a life-long sailor.

Anyway, we went back and forth there—summers on Long Island, back to New Jersey for four or five years, and then went back to Cleveland, where I graduated from high school.

I would say the thing most important thing in terms of scientific development was the attendance as a junior in high school student in a program called the Program in Biochemistry, or PIB as we called it. This was an NSF-sponsored program (back when the NSF had funding), which basically allowed high school students to study what we would call molecular biology now—what was called biochemistry at that point. It's an interesting story actually. I remember my father—my father was basically a basketball fan, and being my size you really had to play, and he wanted nothing but to have me play basketball. My mother was the one who thought PIB was a great idea; I was very interested in science—should do this. They had a big fight. Anyway, she won—like most women, she eventually gets her way. [laughter] It's a good thing. I certainly remember her fondly for that because I had a great opportunity. It's interesting—you have in the Pew program a number of people that have benefited from PIB—Peter [R.] Arvan, for example, as well as a new first-year person, Stewart [H.] Shuman. We met then, twenty years ago, in this summer program for high school students.

THACKRAY: All three of you?

COLLINS: All three of us.

THACKRAY: In the same—

COLLINS: In the same group at the same time.

THACKRAY: Geographically in the same—

COLLINS: Oh, yes. This is the same program. The way the program ran was actually very interesting. They solicited juniors going to be seniors in high school, and basically took Lehninger's *Biochemistry*, which at the time was a standard college textbook of biochemistry and crammed it into six weeks. [1] There were assistants, or what were called "advanced students" and "instructors." Instructors were from the various colleges in the northeast, which was great because you got a chance to chit-chat with some of the folks from different institutions. Advanced students were seniors going into college.

The program was basically didactic sessions in the morning followed by afternoon experimental laboratories. You essentially were enrolled in a research environment—I basically have been doing science since I was fifteen, sixteen, something like that. Certainly by the time I went to this high school program was well enmeshed in what I would consider now to be post-graduate level research.

Anyway, yes, there are a number of people—I know Peter Arvan was there and I know Stewart Shuman was there because I taught both of them actually. I was involved with them. It would be interesting to check the files of the Pew against the files of the people that "played through" this program. It was a tremendous opportunity to experience different people from different institutions. The director of the program was from Amherst College and two of the instructors were from Amherst College. Based on our associations, that was the thing that led me to that particular choice of college. There were a number of people from Princeton and from MIT, and I just wasn't happy with the kind of general education; I could sense it from them, believe it or not.

After I graduated from high school, my parents moved again, to Ann Arbor, Michigan; so I basically have not been back to Cleveland since I left to go to college. I did go to Amherst College and was interested in English and in biochemistry, or in molecular biology and genetics. Amherst is a reasonable liberal arts education. You couldn't focus on one of those things. It was just kind of generic biology. In the subsequent four years, I would say I developed an interest in gainful employment, so I decided to go to medical school instead of graduate school, essentially to increase salary—still being a scientist for the most part.

THACKRAY: Your first interest in science—you said you were fifteen. How did that—

COLLINS: That was the first time I really decided to try and establish professional training.

[1] Albert L. Lehninger, *Biochemistry: The Molecular Basis of Cell Structure and Function* (New York: Worth Publishers, 1970).

I had been interested for a long time. I was alienated by religion very early in life and was interested in pre-biological synthesis mechanisms and organic chemistry. Until I went to Amherst I was interested in being an organic chemist, essentially. I remember trying to read chemistry books very early on, fourth grade, fifth grade. A lot of my relatives had leftover textbooks from one thing or another and I ended up with most of them, and I was rummaging around and kind of leafing through them. Because I lived in so many places I just kind of said the hell with everyone and spent a great deal of time looking at that kind of stuff.

In fact I should have mentioned, senior year in high school I was interested in a particular research project and submitted it to the Westinghouse people, and Westinghouse chose the project as what they called a National Westinghouse Scientist Award. Out of eighteen thousand or so people they chose a bunch of intermediate finalists and forty national finalists and we went to Washington for a week. We competed for scholarships, which, probably rightly so, I didn't receive one. It's interesting to see how the people in that top ten group did. Two of them are dead, interestingly enough, by suicides. Lots of mathematicians. The people in biology are still around, and are junior faculty in various institutions.

It was very interesting because I was the first person from the west side of Cleveland ever to win this award. They were astounded; the east side was absolutely flabbergasted. [laughter]

THACKRAY: You've described internal motivation, but was your school, was your mother, or what, from the outside?

COLLINS: No, they really weren't very helpful to be honest. The west side of Cleveland basically is kind of Big Ten in its mentality. It is an intellectual desert. You have to have a lot of self-motivation to survive. Most of the people I knew never got out of the Midwest. They may have moved on but they never survived. Certainly I'm the only one left in major academics.

THACKRAY: You must have got a pretty big boost out of winning that thing.

COLLINS: It was a blow to my father because he said, "You should be playing basketball, and basically you're out of your mind to do this—there's no chance in hell you're ever going to win it." It was great in terms of college applications because the only place that turned me down was the Naval Academy, interestingly enough. As I told you, another theme in my life is I was a sailor. I wanted to be a marine officer—I probably would have been in the Middle East, but I wanted my own ship. They said a) you're too tall, you'll hit your head

on a bulkhead, b) you can't see, so we can't put you in an airplane. But I could have gone anywhere else. In a sense, it's quite fortuitous that Amherst was interested. Once you win something like that, basically every place wants you. It's a question of how much money they want to give you.

THACKRAY: Can you just fill in a little bit about your brother and sister? They didn't go this route.

COLLINS: No, no. We are a very diverse family, actually. The politics is really not particularly good at all. My sister is the women's tennis coach at the University of Pennsylvania and is crippled by a debilitating disease, unfortunately. It's called scleroderma. I don't know whether you're familiar with it. It's an autoimmune connective tissue disorder that affects the respiratory system, the GI [gastrointestinal] system, and is potentially quite debilitating. Anyway, she's a great tennis player. Most of my family is good to world-class athletes. Many of the members of the family have played at Forest Hills in tennis. They're really good tennis players. Back when the U.S. Open was held, not in Flushing, but in the old tennis stadium in Queens they all played there. They never got very far, but basically they were good enough to get in. She probably could have been if she wasn't so damned debilitated by this disease.

Anyway, what can I tell you about her? She went to Rollins College in Florida on a tennis scholarship. She's married to a guy in Philadelphia who's a nice guy. She had one child. Shortly after the birth of her child, she lost her kidney function. We were all typed for transplants. I was mismatched at both HLA-haplotypes. My father gave her a kidney, and a year and a half later, unfortunately, he died of another incredibly awful disease called amyotrophic lateral sclerosis, or Lou Gehrig's disease. I guess he was fifty-nine. He was a guy who could beat me in tennis two years before his death. He was in excellent shape. Basically because of a chronic aggressive disorder that we really don't understand, he lost voluntary function of all his musculature and was eventually sitting in a chair unable to move and died of pneumonia.

THACKRAY: What does your brother do?

COLLINS: He was born in 1960, so he's eight years younger. We were just out of sync in the sense that we moved so many times we share nothing in terms of background. He graduated from high school in Michigan, went to a college in Ohio and is now doing environmental engineering. He basically did an undergraduate degree in geology and is now interested in pollution control. He's a fairly normal guy. Has one kid and lives outside of Boston.

THACKRAY: Back to Amherst if we may, you're coming in with Westinghouse.

COLLINS: Amherst College is an amazing place. There are a number of very, very smart people there. In terms of Amherst College, I didn't come from a prep school and I certainly did not have the level of sophistication that about half the class had, and it was certainly an aggressive place. I would say I was at best average, but it was a good experience. I think the people there are spectacular in terms of their breadth, their depth of interest, their writing skills. The quality of education is superb—and I certainly didn't take advantage of it—both because of the focus toward what turned out to be an eventual premedical interest, as well as my own cognitive function.

Anyway, it's a great place. I wish the English Department had taken me. It's a very interesting story. You have to apply to the English Department. My application—I remember the interview I had was with a very prestigious professor called Benjamin [H.] DeMott, who was a Shakespeare scholar. He won't remember me at all, but he picks up the essay, looks down, reads through it and then looks up at me, and his first comment was, "Mr. Collins, is there anything else you can do?" [laughter] "Mr. Collins, on a good day you'd be a mediocre journalist." So I knew my route to medical school was short, and my abilities to generate creative literature would be limited to scientific papers.

THACKRAY: Does Amherst keep up in molecular biology?

COLLINS: Amherst has the ability to fluctuate depending on the faculty members who are there, and I was fortunate enough to be there with a guy who did not get tenure, was eccentric as hell, but was the forerunner of what we would now call molecular biology, as well as the guy I had met at the Program in Biochemistry in the summer. His name was Ed [Edward R.] Leadbetter—he was a microbiologist. The other fellow's name was Walter Godchaux [III], and Walter was interested in initiation of translation *in vitro* and provided what I thought was an excellent education. In fact, graduate school in Rochester was worthless, to be honest. I got in and got out as fast as I could. The graduate program was pathetic. But we'll get into that in a minute. I learned most of what I needed in the time I was at Amherst.

THACKRAY: Were you doing research during that time?

COLLINS: In the summers I returned as an instructor to this Program in Biochemistry. Instead of being a student you're an instructor, so you taught. That's how I met people like Peter Arvan and Stewart Shuman. They were coming through as students. We were

interested in the metabolism of amines. These are compounds that are around us all the time, and the director of the program had a particular interest in these compounds, and he gave us each a different amine, and we were to understand the metabolism of the amine by microorganisms. It was a good experience.

That was freshman summer and sophomore summer. You'll notice I never went home. I was either in college or the program. Junior year I was fortunate in the sense that the biology department could nominate one person to go to the Marine Biological Laboratory in Woods Hole [Massachusetts]. That was the second of what I would consider to be four real breaks. We've already talked about one—that was the Westinghouse and getting into Amherst. This is the second.

The Marine Biological Laboratory [MBL] has a physiology course, so in 1974 I was in taking that course and that's where I met Gerald Weissmann, whom I would consider to be an important intellectual force. That's why I'm here basically. I mean, he helped. We'll talk about that. He knows who I am. He knows who many of us are, I think. He certainly pushes the advisory committee for folks when they don't look quite so good on paper.

The MBL course was fantastic. It broadened out what I would consider to be a reasonable education, but it filled in the gaps that Amherst College couldn't fill in, and it provided an access to a scientific/intellectual climate that was really spectacular. I don't know if you've ever been to Woods Hole in the summer. People descend from Boston and New Haven and set up housekeeping—there's an intellectual discourse there and a friendly environment that allows science to flourish.

But more importantly, Weissmann has an intellectual/cognitive function level which I hadn't run into before. Lots of folks there were good protein chemists, or they were good nucleotide chemists, but Gerry was the only one who could talk about impressionistic art or 19th-century British literature and protein chemistry in the same sentence. That kind of stimulation to get into intellectual life I found to be very powerful. Dr. Weissmann was kind enough to invite me back to work in his laboratory the next summer, so I went back for a second summer at the MBL, and I don't know whether you want to know about the scientific things going on at the same time. That's what's in the CV. You'll see two papers there that were very early, [19]75 and [19]76 or something like that, both due to Gerry. Gerry's very productive and converts things into printed text very quickly. One of the papers is actually still good, believe it or not. The one in *PNAS* [*Proceeding of the National Academy of Sciences*] by Weissmann *et al.* looking at immunoglobulin-coated liposomes, basically was a technique for transferring enzymes into cells deficient for that enzyme.

THACKRAY: How did you feel about getting into print?

COLLINS: Oh, it is always a spectacular feeling, but because that paper was cited in

Scientific American, I will never forget the day that it came out. People at Amherst College came up to me and said, "Did you know your name was in *Scientific American*?"

They have a kind of a commentary on science that was happening, sort of like the beginning of *Science* magazine, which has a "This Week in Science" column. *Scientific American* has "Science for the Common Citizen," or something, and they mentioned this paper. What we would call it now is gene therapy, and it got a lot of press. If this had been twenty years later, Gerry could have had a patent on this, and it could have been worth a fortune. We weren't thinking, "Oh, there's a transition that's going on." We just weren't thinking biotechnology in the mid-seventies. The idea of being able to put enzymes back into cells that are deficient in that particular enzyme is the basis for most of biotechnology now. For example, gene transfer using liposomes—Gerry has a whole company on liposomes now.

Actually I did write a thesis at Amherst College, I should tell you that—I don't think it's on the CV. It was basically having to do with the synthesis of opsin *in vitro*. Opsin is the major protein component of the visual pigment present in rods and cones. We were interested in this protein as a model for membrane protein assembly *in vitro*. This was a major interest of this guy, Walter Godchaux. We'd done a lot of *in vitro* protein synthesis.

So I graduated from Amherst College. I applied to medical schools and M.D./Ph.D. programs, and the only M.D./Ph.D. program that I got into was the University of Rochester Medical School. Reluctantly, I did get into some other medical schools, but the difference between an MSTP program and medical school is dramatic when it comes to funding. In one you go to school for free, because the tuition is covered for both graduate programs. The other you have to find private resources, and since I wasn't at the time really speaking to anybody in my family, I felt it was appropriate to cover my own expenses. So I packed up and survived six snowy winters in Rochester, New York.

THACKRAY: What's MSTP?

COLLINS: Medical Scientist Training Program. The NIH [National Institutes of Health] has, I think, fifteen institutions in the United States that fund these combined degree programs.

THACKRAY: Can you say a little bit more about motivations to get the M.D. and Ph.D.?

COLLINS: I'll be very honest since this is a frank interview. An M.D. is job security. It is a broad education. The problem with graduate education is it's very limiting. Medical school is a tremendous exposure to the human condition. You get things—psychiatry, pediatrics,

OB [obstetrics]—that you just would never encounter in graduate school. It's the best continuation of a Renaissance education that I can think of.

THACKRAY: Had you worked that out for yourself or was someone advising you?

COLLINS: Oh, no, no. No one advises me. I would say there are people who I talk to, but I'm responsible for the major decisions. There really wasn't—I'm trying to remember—there may have been some subtle thoughts. Most people at Amherst go to business school, law school, medical school, or into education programs. There are very few going to direct graduate school. But I think had I been interested in that I could have done that, but I just was more interested in continuing to broaden a bit, realizing that you could do both graduate programs, come up with at least a marketable degree, plus if you had any talent for professional research you could then continue.

THACKRAY: You said Rochester wasn't too good as an experience.

COLLINS: Well, personally, scientifically, I would say it was disastrous. Well, it wasn't a disaster—well, personally it was a disaster. [laughter] Scientifically I would say that the medical school is excellent, but it's a very traditional medical school in the sense that one does two full years of basic sciences with grades and so forth, and then one does the clinical years. It is a very pleasant place to do medical school. You're not going to get shot in Rochester. It's a lovely place to be entrenched because your life is very easy and there are no problems. It's a city dominated by Kodak, which is a very conservative company, and that tenor tends to reflect on all aspects of the city's life. Medical school is medical school and it's like doing plumbing. It's a trade school degree—they're pretty much the same anywhere.

The graduate education, I would say, was poor. Put it this way—I probably have more federal money now than my entire department did as a graduate student in micro. I was formally a graduate student in micro. After doing the first two years, I then went into a laboratory for two years and was working with a guy by the name of Jim [James M.] Wilhelm, who was formally in microbiology but was again what we would call a molecular biologist now. We were interested in the same kinds of things I was doing as an undergraduate, which greatly facilitated the rate at which I could get things done. Jim was a nice guy, but he had what I would consider to be a reasonably weak personality, and about the time I was leaving he didn't get tenure, and his marriage split up, and he ended up in Philadelphia [laughter] working for a company. It was clear to me that he was not a major scientific mind.

The nice thing about having worked with Weissmann is I knew where I had to go. I

knew what first-class science was, what first-class intellectual thinking was, and this wasn't it. So I tried to get through as fast as I could and get back to something else.

I came to Rochester single after having known an interesting woman in college—her name was Pat [Patricia] Gallaher. Pat was a very smart lady who went to Georgetown Law School, where she was a star and basically just missed being a Supreme Court clerk. Anyway, we were involved on and off again, and she was—so she thought—was interested enough in me to come to Rochester. She took a great job in one of the big law firms. After, I think it was the first two years, she had basically established herself in Rochester. And, I think, the following year, my third year in Rochester we, let's see, I have to remember exactly the dates—we were married for about a year, I would say. I was in my third year doing clerkships, and it turned out she was much more interested in some of the other, more powerful attorneys. She was an aggressive Democrat, an alternate at the Democratic National Convention and was very interested in politics and women's rights, and I was a medical student trying to survive. Basically we never saw one another, and my last year at Rochester we separated, and it was remarkable. She said her firm had a computer which could spit out separation agreements—and she said she separated us in about forty-five seconds. It was absolutely unbelievable.

[END OF AUDIO, FILE 1.1]

COLLINS: But in Patricia's defense, she was a smart lady who had established herself and basically had a reason to expect a bit more. I also at that point was convinced I could not stay in Rochester, and her legal situation was such that she really couldn't leave Rochester—she'd established herself. Anyway, we separated basically in May or June, and a year later I was out of Rochester. It turned out, she was an associate at that time. They did not promote her to partner, and then she went to work for some judicial court judge. I haven't actually spoken to her in almost ten years. She has subsequently remarried. I don't know whether she has any kids of her own at this point.

THACKRAY: You did get a couple of more publications in there somewhere.

COLLINS: Yes, but talk about making something out of nothing. Basically, I took something that I thought was "doable" and made something out of it so that I could fulfill the requirements for what they considered to be a Ph.D. I was underwhelmed. I think parenthetically when I got back to Boston and had a chance to work in some first-class laboratories, which we'll talk about, the difference between graduate education at Harvard and graduate education at Rochester is absolutely astounding. There is some truth to the fact

that where you get your degree does make a difference in graduate education.

THACKRAY: Can you talk a little about that?

COLLINS: I came to Boston in 1981 where I was a pathologist. I should actually tell you—that's an interesting story. I was very depressed when I left Rochester. I applied to one pathology residency—actually two, Yale [University] and the Brigham and Women's Hospital, which is a Harvard affiliate. I applied as a postdoc to Günter Blobel's laboratory at Rockefeller [University], and had all but accepted the postdoctoral position—I was going to get out of medicine altogether. I actually went to look at the gorgeous apartments on the Upper East Side. It's just amazing the lovely places Rockefeller has. Anyway, [Ramzi S.] Cotran, chairman of the department of pathology at Brigham, gave me a break and basically took me when no one else was really interested. And that's break number three.

So I came to be a pathologist having never done any pathology. I thought it was probably good for my science, but boy, was I rudely awakened. [laughter] Anyway, a year of pathology, and I basically could not handle that anymore and needed a break, and was fortunate enough to run across a guy by the name of Jordan [S.] Pober, who was a junior faculty person in pathology who had worked in Jack [L.] Strominger's laboratory. Jordan is brilliant; he's one of the smartest people I've ever met.

Jordan got me into Jack's lab, and that really was very helpful. Jack is a member of the National Academy of Sciences, and has two big labs in Boston, one in Biochemistry and Molecular Biology and the other over at the Dana-Farber Cancer Institute. Basically, I spent some time there, formally under the tutelage of Jordan but basically working in Jack's lab doing molecular biology. Jack is well known to lots of people. He's interested in major histocompatibility complex and basically the molecular basis of immune responses. Jordan was interested in vascular endothelial cells, and we just brought the two interests together. The next set of papers have to do with my experience with both Jordan and in Jack's place for the most part.

So I did that for three years and had a great time. It was at that point that I experienced the difference between the seven or eight years it takes to be a Harvard graduate, Ph.D. graduate, and the two years it takes to be a Rochester graduate, and the quality, the list of publications one needs for graduation. Basically I had a long postdoc to make up for the graduate experience that I didn't have.

Okay—three years of what I would consider to be sort of molecular biology. There's a transition in the CV. I went basically from cytokines and MHC [major histocompatibility complex] antigens on vascular cells to cloning growth factors. Basically, I didn't want to step on either Jack's toes or Jordan's toes, and made a transition into an area that I thought would be fundable, and it's proven to be so. That's this vascular expressed so-called

platelet-derived growth factor.

This is a mitogen that controls the behavior of smooth muscle cells, and the argument is very simple. If you take a blood vessel, the blood vessel's lined by endothelial cells—these are basically the gateway to the tissues. These cells interact with both the circulating blood elements, as well as surrounding smooth muscle cells. If you injure those cells, they produce substances which are chemotactic for circulating blood leukocytes as well as smooth muscle cells. Such injury, like hypertension or smoking, may damage the endothelial cell and cause it to release these growth factors and stimulate the proliferation of smooth muscle cells to form what you know as the atherosclerotic plaque. At that time the NIH Heart, Lung and Blood Institute (NHLBI) had very few molecular biologists, so I would consider my break number four was getting involved in the right place at the right time. I've had great luck with NIH funding. I have two R01's and part of a program project, which all have to do with this business of molecular biology of the vasculature. I think if you count the Pew I have six for six or something in terms of grants. I've been very fortunate.

Anyway, my third year as a postdoc I wrote the first of these R01's, and while that was off at study section and council, I went back to residency. My goal in life is to run a pathology department—I want to be a chairman. I'll state that straightaway, since most of my colleagues know it. To do that you have to be certified by the American Board of Pathology. The second year in anatomic path was designed to accomplish the credentials one needs to be board certified. So I did that, and promptly thereafter I was fortunate: I got a good priority score, I could immediately jump into a funded lab situation. All I had to do was find space, which was not trivial. Unfortunately, Boston has lots of people with money; lab space is an important commodity. Basically I had to elbow some people out of the way, some technicians who thought they were ruling the roost. I told the chair that "Look, I've got an R0l for heaven's sake, I'd like a little space to work on it." He said okay, so I got four hundred square feet or thereabouts where I am still now. I don't have a lot of space; in fact, my dollars per square foot are staggering. [laughter] Anyway, so I fulfilled the pathology criteria. I eventually passed the anatomic pathology boards, so I'm a card-carrying pathologist, and then basically have been doing research on these vascular topics.

THACKRAY: Can we go back and compare the graduate schools, the style of research? The differences—what really are they when you spell them all out?

COLLINS: Okay, I'll give you the feeling. Basically, the folks in Boston have more space. They have generally more people—usually fewer technicians and more graduate students and postdocs. If you go to Rochester on a weekend, you'll never find anyone in the laboratory. If you go there at night, you'll never find anyone there at night. I hope you're not from Rochester.

KOHLER: No, no. I just can't imagine a lab with nobody there at night.

COLLINS: It's the philosophy of the town. It's a very stable, home-oriented, traditional kind of family life. It's a job—it is not an obsession, and that's the difference. I'm obsessed. I work—I'm there before six and I'm there until eight every night. I go through spouses like other people go through cars. It is a level of intensity that is different. You have it in the Boston labs. People from all over the world have left their lives and have come to work. They work all hours of the day and night. A laboratory that works twenty-four hours a day is generally doing interesting things, in shifts. You have good ideas, and you have people pursuing those ideas, and that's what was missing in Rochester.

That was very clear to me, after having been at Woods Hole. Woods Hole—there's an intellectual fervor that's present in Boston that is not present at Rochester—at the time I was there in the areas that I was exposed to. I have to qualify that. At Harvard, MIT, either side of the river, it's there. It's there all the time. In my lab I have plenty of people that work till two in the morning—so there is a down time of only a few hours when someone's not around. Things are going (I think) on a seven-day calendar week. Maybe that's enough of that tirade. Intensity, I would say, to put it in a single word.

THACKRAY: Go back to mentors. Is Gerry Weissmann in here in this piece of the story?

COLLINS: Absolutely. At this point I think I am entrenched in Boston. I really didn't have much contact with Gerry. In fact, he only visited Rochester once to give a seminar, and that told me something. [laughter]

Gerry was someone who came at a time when I basically was impressionable, and he had a sense of how science should be done, how intellectual life should be pursued, and what he calls the "leisure of the theoried class," which I find a statement that's particularly good—how one spends one's time when one is in academics, that you have to learn. You can learn how to do science. You can learn how to write manuscripts. But to think about intellectual history is something that you need to live to some extent, and he's good at it. He's very smart. But I didn't have much contact with him at this point. I was developing the tools to be a professional scientist, a professional molecular person in Cambridge, and doing this pathology stuff to very pragmatic ends.

THACKRAY: Can you say a little more around the politics of that?

COLLINS: All right, let's do some politics, since you have people here that I'd love to talk

about. Let's talk about the politics in the vascular group of Boston, because there's a guy here that you interviewed last year who's involved in this.

Basically I came to Boston, did pathology, and then walked into the vascular group. Pathology at the Brigham, if I can be a bit boastful here, is probably the best pathology department in the United States. Ramzi Cotran, the chairman, wrote the textbook which all American students use. It's Cotran, somebody and somebody, *Pathological Basis of Disease*.[2] He is a very powerful guy. He has a long tradition of vascular biology.

Science is a very feudal system in Boston, and Ramzi's a king. The king hath princes; princes hath knights; knights hath squires; squires, and so forth, you know. Underneath Ramzi is Michael [A.] Gimbrone [Jr.]. Michael Gimbrone is one of the first people to culture endothelial cells, and Director of the Vascular Division. Jordan Pober was a junior faculty member in that division, and basically was the first person to treat endothelial cells, these vascular lining cells, with cytokines, specifically giving immune interferon. That observation was the stimulus which catalyzed Gimbrone's return to scientific credibility. His Harvard tenure decision was really hanging in the balance. Jordan wrote a series of manuscripts with Michael, on which Michael did basically nothing. I'm going to get myself in trouble since Gimbrone's nominated for the chief of Harvard pathology. Anyway, Michael was tenured. Jordan basically developed this technology of putting inflammatory mediators in endothelial cells and causing them to do things.

Enter another Pew Scholar, Mike [Michael P.] Bevilacqua. Michael was the first person to dump IL-l [interleukin-1] on endothelial cells and study leukocyte adhesion. I was basically peripherally involved, so I can kind of watch all of this stuff. Michael proceeded to observe that interleukin-1 has effects on endothelial cells, which are important in terms of the endothelial cells' ability to stimulate blood coagulation as well as to bind leukocytes. Why does anybody care? Everybody cares because major drug companies are interested in the anti-inflammatory drugs that could come out of the molecules that mediate these effects. Monoclonal antibodies were raised against cytokine-activated endothelial cells. One of those monoclonals was raised by a woman, Donna [L.] Mendrick, who was lost in all of this. Cotran, Gimbrone, Bevilacqua and Pober have all written many manuscripts and received multiple prizes for monoclonals made by Donna Mendrick. Anyway, this monoclonal basically defined the molecules that mediate leukocyte adhesion to endothelial cells.

That monoclonal was taken to Brian Seed's laboratory. Brian Seed is eccentric as hell. I could tell you Brian Seed stories that would absolutely snap your socks, but Brian is one of the world's best molecular biologists right now. He developed an expression cloning strategy which was used to clone the endothelial leukocyte adhesion molecule [ELAM-1].

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[2] Stanley Robbins, Razi S. Cotran, and Vinay Kumar, *Pathologic Basis of Disease*, 3rd edition (Philadelphia: Saunders, 1984). NOTE: earlier editions were authored by Robbins and Cotran only; since Collins here indicates three authors, we have cited the third edition.

At this point Pober wanted a piece of this action. Gimbrone and Bevilacqua were not going to provide it to him. Jordan was forced to move out of the division into his own separate little area. He has subsequently left Brigham and Women's. Vince [Vincent T.] Marchesi, former chair of pathology at Yale, has set up a so-called Institute of Molecular Medicine, and there will be a vascular division within that institute. Jordan's going to chair that as of July. He's basically leaving Boston because of this.

Okay—big splash in *Science*, a big article: molecular mechanisms of adhesions are defined. Lots of companies wanted in. One company came to Bevilacqua, offering him ten to twenty million dollars to start up a company. Gimbrone blocked the acquisition of those funds. Michael Bevilacqua and Michael Gimbrone then had a tremendous flare-up. Michael is now struggling to stay alive. He's had one NIH grant turned down and basically has not written another. He and I collaborate. You may notice there's one manuscript on there; he and I are reasonably good friends. I'm very interested in transcriptional regulatory mechanisms, of the ELAM-1 gene and what controls the restricted pattern of gene expression.

Anyway, Michael at the moment is definitely leaving the Brigham because of Gimbrone's political power. They can't seem to stand having one another in the same department. So Michael Gimbrone went from Pober to Bevilacqua and is now moving on trying to play another person, this guy Myron [I.] Cybulsky, who is another leukoctye adhesion person, into this whole thing. He's trying to show basically that Michael Bevilacqua's success was due to Gimbrone's architecture and creative thought processes, when in fact that's definitely not true.

Cybulsky's interested in "ATHERO-ELAM." It's another leukocyte adhesion molecule that mediates the attachment of circulating monocytes. The expression of ATHERO-ELAM may be the first step in atherosclerosis. Anyway, Myron's now at my lab cloning the molecule, kind of a resident cloner, which is nice, but you get into the politics. The sad part is Bevilacqua raised a monoclonal against another antigen which was called INCAM 110. That molecule turns out to be the same protein as this ATHERO-ELAM, so Myron and Bevilacqua are at odds with one another because they came across the same molecule, doing two different things.

Is that enough politics? [laughter]

THACKRAY: Was some sort of deal made with some other pharmaceutical company?

COLLINS: No, Michael was blocked from any kind of industrial fund acquisition by—I think it was Gimbrone, but I'm not—

THACKRAY: So this was an old-fashioned ethos of science or something was it, or what?

COLLINS: Well, Gimbrone wanted to set up his own "Vascular Institute." He didn't want to have a junior person, this guy Bevilacqua, running some sort of institute in the pathology department. There's really only room for one vascular institute, and he wanted to run it. Since that took place—this was all about a year ago—Gimbrone has gotten us together and we've tried to market our skills to various companies to recruit additional funds; Bevilacqua was excluded from these marketing schemes.

THACKRAY: Is it easy to get their attention, a company's attention?

COLLINS: Oh, in this business? Sure, because of the possibility of developing these potentially valuable drugs. For example, if one has a heart attack, one of the things that causes damage to the myocardium is acute reperfusion injury. Polymorphonuclear leukocytes [PMN] transverse the endothelial cell to the damaged tissue and basically engulf it. If one could block that process, one might diminish the infarct size. So there are several strategies that one could potentially employ, and the biotechnology companies are obviously very enthusiastic about developing these reagents. There are a number of companies that are well along the way in developing soluble forms of these molecules.

THACKRAY: Are these biotech companies or traditional pharmaceutical or what?

COLLINS: Biotech for the most part. When I mean a big company, I would say like Genentech for us would be a big company. We have dealt with Genetics Institute and Biogen for the most part. Most of the bigger companies can develop their own stuff in-house. The smaller companies generally have to recruit or buy vascular expertise—or at least that's Gimbrone's thought.

THACKRAY: Can we just push out on the biotech aspects for a while. How has that seen change?

COLLINS: Well, it's a tremendous transition. I would say ten years ago people who went into industry were viewed as second-class folks who couldn't do anything in academics. Now you've got great people out in companies. There's a lot of interplay. Many of us have submitted things to our technology transfer office for review for patents. Every time I clone something I call them and ask them is this something the hospital's interested in. If you have

something that's immediately or potentially marketable, then obviously they're much more excited.

I know I'm on one application—I may be on more, I don't know. Since we're so encumbered by Harvard, by the Brigham, we'll never see anything out of these. [laughter] It's almost another layer of bureaucracy these days we have to go through. The companies certainly are interested, because the hospital could transfer rights to some of these things to them, and it would save them a lot of developmental time. But no, we do battle with the companies in terms of scientific stuff all the time.

THACKRAY: Is all of this affecting people's research focus in any discernible way?

COLLINS: Well, not in my area per se, not in what I'm funded to do with endothelial growth factors. In contrast, in Bevilacqua's area they're blowing them out of the water. There's so much interest and resources that Mike can't hope to compete. My interests, really fortuitously, are not those that a company would be concerned about.

It's very interesting, though. We've recently stumbled across the fact that neurons have platelet-derived growth factor [PDGF], and the immediate interest for them is nerve regeneration. We went to the technology transfer office, and they, of course, were interested for a while, and they wanted us to demonstrate that in fact PDGF does stimulate neuron growth. In fact, it prolongs growth in culture and stimulates neurite outgrowth. The companies were certainly interested.

For the most part, what I do—growth factor research—the large companies now have their own growth factor divisions. Five years ago when we were the only ones with PDGF eDNA clones, they were still thinking that recombinant growth factors were really beyond them. I try to stay away from things I know companies are doing because you cannot compete with the kind of resources that they have. They're just very good. Similarly I don't try to do things that I know big molecular biology groups are doing, because you just cannot compete with forty postdocs, and a well-funded "army." They have too much talent, too many resources for me to be competitive.

THACKRAY: Who are they in your particular area? Where are they?

COLLINS: Oh, the sharks? My motto is, "If you swim with sharks, don't bleed." The sharks in molecular biology in Boston are pretty easy to find. In our building, Phil [Philip] Leder is definitely a powerful guy. He may be nominated for the deanship of Harvard Medical School. David Baltimore, over across the river has taken the presidency of Rockefeller. Phil [Philip A.] Sharp should have taken the presidency of MIT and did not,

and I don't know why. Harvey [F.] Lodish, one of the guys you know, Stuart [H.] Orkin, a Howard Hughes Investigator at Children's Hospital. These are people who have large labs, well funded, members of the National Academy, substantial resources. You really want to stay away from people who are at the peak of their career. Their intellectual skills are on, and you just have to be careful. You don't want to tread on their toes. It's like swimming with sharks. You don't want to make any mistakes because they could chew you up.

THACKRAY: How does that happen operationally?

COLLINS: Oh, it's easy; a single phone call—"Don't fund this grant." Or they get papers to review—"Don't publish this paper." Someone could finish my career in Boston with a couple of phone calls to the right people. These are very major players, that you really need to be very careful with. Yes, a certain amount of work is going to always overcome that, but politics being what it is in the feudal system, there's not much that a squire or a knight can do when the king says, "I want you out."

THACKRAY: Do you think everyone's very much aware of this? Are all the knights and squires aware of this?

COLLINS: If they want to survive. I've been there for ten years. You start as a resident and you end up almost an associate professor. To survive this is tough.

THACKRAY: What's the other side of the coin? You have to deliver things as well as avoid them.

COLLINS: Oh, you have to produce. If you don't produce, you're out; but you have to maintain political bonds—if you don't, you're out. The really gifted people are able to be incredibly productive, and if they can do so in a way that doesn't step on someone's toes, they do very well. Think about people who have been tenured at Harvard in six years or less, and there aren't very many. Those are the real stars. Doug (Douglas A.] Melton did it over in biochemistry and molecular biology. He's a world-class developmental biologist. He did something in a department where there is no one like him.

[END OF AUDIO, FILE 1.2]

COLLINS: The advantage to a clinical department is one's not quite under the same pressure for a tenured position which you are in the basic science departments.

THACKRAY: Can you run on indefinitely without tenure, or how does it work?

COLLINS: Well, no, not really. There's a lot more flexibility.

THACKRAY: Just more years.

COLLINS: Yes. Basically there's at least six years after they make you an associate professor, and that can take a while. So you can easily be unemployed at fifty. [laughter] I would like to hang out in Boston and either see what happens or take a departmental chair, and a tenured position at some time. The advantage, why do all that administrative stuff, the reason is the clinical revenues. The people with power these days have departments that generate clinical revenues. You can take those revenues, besides compensating people well, you can develop scientific programs and support junior people.

THACKRAY: You really would have with this chair a lot of discretion to generate some funds.

COLLINS: Under the current health payback situation, which of course is subject to change [laughter], but yes, some of those revenues come back to a department and the chair can allocate them as he sees fit. That's the difference, for example, between Cotran's position as the chair of pathology at the Brigham or the chair of pathology at MGH, for example, and the chair of pathology at Harvard—no clinical revenues. Yes, you have space, but you don't have the same kind of funds.

THACKRAY: Does that mean the Harvard department in fact gets less prestigious people or they're not just named to—

COLLINS: Well, no. There are people who, for example—well-established people who have turned down the chair of pathology at Harvard because of the revenue problem. They're better off being in a clinical context, or they don't want to move to Boston and deal with all the political migraines. It's interesting. The chair has been turned down several times. I'm trying to think whether any of them—I don't think anybody in the National

Academy, or the advisory board has turned them down. The current chair is Baruj Benacerraf, and he's resigned the position as chair of pathology and maintained the position as Director of Research at the Dana-Farber Cancer Institute.

THACKRAY: Let me go back inside your career if we may for a little while. '86: you're setting up your own lab, essentially. Is that right?

COLLINS: Right.

THACKRAY: How has that lab grown and changed over time? What is it now? What do you want it to be? Talk to me for a bit about the realities of running a lab.

COLLINS: Well, the reality—I had, as I mentioned, sort of elbowed the technicians out of there—the tenured technicians, basically, can be a pain in the ass. But I didn't get start-up funds because the chair knew that I had a big R01, and I could get anything I needed, so he didn't really give me much money. So I had to build it up: every wastebasket, every chair we had to purchase. It cost us a fair amount of time. We're still a very small group. Since there's no graduate program in pathology, I depend on residents to try and recruit. Current postdoc is Jochen [W.U.] Fries. He's an interesting story. He was basically fired from his first postdoc, which was in renal pathology. He went to the Harvard School of Public Health with Dr. Diane Worth, where he was also fired. He was on his way back to Germany—he's very loud and he's very aggressive. He's kind of manic depressive. When he's manic he's incredibly good. So I figured, well, he's better than nothing. And recruiting people is very difficult, but he's turned out to be quite good.

THACKRAY: Difficult how?

COLLINS: Well, it's difficult because why come to Boston to work with me when you can work with Phil Leder or David Baltimore or people who are more well-known, and the pathology department does not have a graduate program. The high-powered residents, the M.D./Ph.D.'s, who have been well trained, are candidates for the biggest labs in the city, so they wouldn't be interested in someone like me.

Now in contrast, if I were sitting in Rochester, I'd be mobbed. There are enough interesting things going on in the lab for people to join. It's just that in Boston you have such a wealth of such powerful people that the junior people can really struggle. I'd say that's my biggest complaint, or difficulty, is getting people into the lab. I've been dependent on Gimbrone, for example, to have folks available to help fill the lab and do interesting things.

Like this guy Myron Cybulsky, wanted to learn molecular biology, he's a good cell biologist and he's now cloning an interesting molecule.

THACKRAY: In terms of funding the lab—

COLLINS: Funding the lab, as I mentioned, has been reasonably good. I've been very lucky: wrote an R01 when I was a second- year resident which was funded, and basically it was used to start up the laboratory and fund a technician. I'm almost entirely—my salary is derived entirely from grant support, minus about 7 or 8 percent which I get from the autopsy service. If I don't stay funded, I'm out the door. They wouldn't keep me. That's why I don't really worry about a tenure decision, because they don't pay me anything anyway.

THACKRAY: Are there other people around Boston in an analogous position?

COLLINS: Oh, yes, absolutely. That's what, in a sense, makes it exciting. Even the more senior people are dependent on federal revenues for their salary support. They've gotten lazy in the sense that they've been very lucky in terms of grant support—they've usually been well funded. But times are changing, and even the more senior people are beginning to be a little cautious in their applications: applying early; making sure they have duplicate funding vehicles; trying to cut back and not waste, because the last few years have been very tough. Anyway, so I wrote one R01. Then, Mike Gimbrone's a powerful guy, has a three-million-dollar-a-year program project. I contributed a part of that program project. Then this winter I wrote another R0l, which, believe it or not, got a percentile score of 0.9. It was unbelievable: it was just a sky-high percentage—it was very good. So it was funded, but it was not funded at a level that I would have liked. Even though the study section approved it, there were mandatory fixed cuts of what they could provide. So even if you get through the scientific review process, the start date can be postponed, or counsel can change the funding amounts because of this or that. So that's where the Pew funds are so incredibly valuable. The Pew funds supported Fries, they paid his salary, a very valuable guy. And they support another individual, Parvez Sultan, who is an undergraduate in the laboratory who has been productive.

THACKRAY: Why did Harvard nominate you for the Pew?

COLLINS: That's another interesting story. Harvard didn't nominate me. Roger Brent was nominated by Harvard. Harvard, as you know, has a very interesting system, because they have these different schools. There's the Medical School, the School of Public Health and the School of Arts and Sciences. And each of those nominates two, and then there's a

Harvard-wide—some smoke-filled room somewhere, all of these big round-bottomed folks, great powerful types sit and choose someone. That year it was Roger Brent and somebody else, I think, and they're basically assured of any kind of junior faculty fellowship, whether it's Pew or Searle or this or that, it doesn't really matter. They generally get what they want. When the Pew changed—they went from I think forty institutions to eighty institutions. The Brigham receives an ungodly amount of NIH funds. The Brigham, this little hospital, receives more than most of the academic communities in the rest of the country. It's staggering, and Pathology has about ten million, and Medicine has about fifty million dollars, which is a lot. So the Brigham nominated some folks, and I was one of the Brigham nominees. I got canned by Harvard and then the Brigham people picked me up. [laughter]

The interesting story about this was my chair called me: he had forgot about the deadline. The application came back and sat on his desk. He called me Saturday at 3:00 saying, "I forgot your application has to be in New Haven by Monday at 5:00 p.m." So I drove in, slammed the whole thing together. I had to drive the thing down there, and my car broke down on the way back. [laughter] It was unbelievable! Unbelievable.

Anyway, it was very valuable: think about the total number of hours spent putting it together over the funds—given in terms of dollars per hour, it was a good deal. [laughter] I'm afraid I had to shoot my car, though. It never quite recovered.

THACKRAY: There must have been other possible candidates at Brigham. Why did they—

COLLINS: Who knows, who knows. That was the first year it had jumped from forty to eighty, and I get the feeling that the only reason I was nominated was that some of the folks knew who I was, and if the Brigham hadn't nominated someone because they fouled up logistically, they'd look bad, and I was available. Really, this was a last-minute deal. This was not a logical progression. This is not the kind of organized committee that they now have. It's a much bigger committee.

THACKRAY: How have you used those funds, in fact?

COLLINS: Okay. Odds and ends, equipment. I would say mostly salary support. The thing that I'm most desperate for is people. And I try and recruit. For example, this guy Fries wants a green card. The Pew funds will be used to support the green card. Let's see, mostly odds and ends, I think, things that—when we've run out of money on the R0l. I haven't used it in any logical way: it's mostly to fill in. I have about fifty thousand dollars left, which I'm going to use as "venture capital" to support novel ideas.

THACKRAY: Did your getting the Pew have a feedback effect on people's perception of you at the Brigham and around there?

COLLINS: No, not at the Brigham: there are too many good people. There are people that are just so far above you. As I said, I'm just a knight—maybe. I used to say I was a squire, maybe I'm getting a little old to be a squire, but there are people so far above me in academics, Nobel Laureates and members of the National Academy all over the place. There are so many folks getting these kinds of prizes and awards that no one pays much attention, to be honest. It's almost embarrassing if you don't get one. You live just the reverse, and that's probably unfortunate. For example, from the Brigham the Pew has selected me, Charlie [Charles N.] Serhan, Michael Bevilacqua and Jim [Paul J.] Anderson. There are people who are tenured full professors, for example—Louis Kunkel who is in his forties and elected to the National Academy of Sciences because of his elegant work with dystrophin and Duehenne muscular dystrophy. The Pew is nice. We appreciate it, but you just have to appreciate that there are a lot of very good people, all of whom will acquire this or that award. Even in our department we have two Pew people, Bevilacqua and myself. Bill [William A.] Muller, who was also in this same division, holds both a Pew and an RJR Nabisco. It's great. I come here, I see all my friends. It's fantastic. It's become a little incestuous, but they're good people.

THACKRAY: Can you talk a little bit about two different things: one is your research agenda, and the other is your career agenda.

COLLINS: My research agenda I would say could best be described as delineating endothelial transcriptional control methods.

We've been trying to define what makes an endothelial cell an endothelial cell. Are there lineage-specific gene products that determine a primitive cell to become an endothelial cell, the same way, for example, myoD determines that a muscle cell becomes a skeletal muscle cell?

We're also interested in the tissue-specific as well as ubiquitous factors involved in regulation of important endothelial genes, growth factor genes, cell surface adhesion molecule genes—understanding what role those factors play in pathological responses that the endothelial cell might be involved in. Basically apply the tools of molecular biology to endothelial cells. I could give you a more detailed summary, but that's pretty much it.

In terms of career agenda, I would say I would like to be productive, to do interesting things. There is a movement in the lab into developmental molecular biology. We began by looking at expression of growth factor genes in developing human embryos, and we're very interested in mechanisms by which developmental malformations occur. In fact, some of the

Pew funds are used to support these kinds of things. We're trying to understand why we have two arms and two legs, and what happens when we don't.

We're hoping that we can tie together growth factor gene expression and maybe transcriptional control of some the so-called helix-turn-helix, or helix-loop-helix DNA binding proteins. Put simply, these DNA binding proteins may tell a cell where it is, and the growth factor genes will tell it to move or to divide. And we're hoping that if we can understand that process, we'll have some idea why cells move anomalously and generate malformations. The nice thing about being on the autopsy service is you see a lot of dysmorphology—you see a lot of pathology in general. The Brigham does about ten thousand deliveries a year, and when things don't go right, we see a lot of dysmorphic events. We're in a unique situation to combine the tools of molecular biology to study normal as well as abnormal pathology. That's all unfunded. I don't think I can get it funded yet, but we're very excited by that. In fact, one of the guys coming to the lab, maybe he will pursue just that. And one of the guys, Ray Redline, who was writing a paper—I don't know whether it's on there [the C.V.], maybe at the very end—describing homeobox genes and Arturo [E.] Mendoza basically had an abstract describing expression of PDGF in human embryos. All of that is kind of an undercurrent. That's not what we're funded to do. That's not where our real strength is, but it's something I've been excited about.

Long term, as I said, I want to be chairman. I think it's possible. There are a couple of precedents where people can run departments, maintain good clinical services, and still run first- rate research labs.

THACKRAY: Why do you want to do all that stuff?

COLLINS: I enjoy it. There's nothing I like more than being involved with interesting ideas. It is an obsession. It is a level of intensity that I like, and as Cotran put it, he wants "residents who would rather write papers than go home and sleep with their wives." And that's generally my philosophy. He actually said that. [laughter] I couldn't believe it. But it basically sums up the philosophy: women come and go, but the ideas are always there.

Twenty years ago we were thinking about some of the same processes. It's really funny to look at some of these older folks—Harvey Lodish, for example, has been around a while. You read their textbooks, and you see how the field evolves. And that contribution is substantial and I think it's invaluable. If you're at the right place with the right training, you can make a major difference in terms of intellectual history. I find that compared to that everything else is secondary.

THACKRAY: The way you just formulated it, it sounds like a very masculine grouping.

COLLINS: Science is a very masculine kind of job. The big people are very aggressive. There are people who I could tell you stories about, but I think that I would be taking liberties that I really shouldn't take. That's not to say that there aren't good female scientists. There are. There are some in Boston who are really superb. Science is an equal opportunity business when you do it right. What I don't like is when it's not done right. I think women have a very difficult job today trying to maintain domestic harmony, trying to have a family. It is a tremendous burden. And the women that I know who are very smart, smarter than I am, are having a tough time trying to do both. I would say that is probably, one of the greatest challenges—to pull that off well—that I can think of.

THACKRAY: There are quite a number of female Pew scholars now. Are they running as strongly as the men?

COLLINS: Well, you ask yourself, how many people are world-class scientists? How many people have a national reputation? You can think of some. Everyone has their own prejudice. But you do have some women—Pamela [J.] Bjorkman, for example, is a nationally-known person. But everyone goes through ups and downs. This is a very difficult time for most people. They're trying to make decisions about their personal life. They're trying to make decisions about how they're going to balance their careers with their family life. Some of that I think depends on where you are and what is demanded of you by circumstances that are outside of your control. It's difficult. Another example is Mark [M.] Davis; he is recognized pretty much throughout the scientific community. Mike Bevilacqua is another individual who is well-established. I'm trying to think of people who I've read in the *Science Times*. That's my general rule. [laughter] If you're on the front page of the *Wall Street Journal* or in the *Science Times* you've made it. I think those guys classify. I'm trying to think of other people in the *London Times*, that's also important: if you've made it to the *London Times*, you're definitely doing well.

So I think that's really a point-by-point, or a case-by-case situation, and when a woman is not doing well, my first question is Why? Usually she's taken some time to have a family. And there's just no way! I mean, I've done pediatrics, there's just no way you can maintain the same kind of intensity and still take care of a kid. And my female colleagues who are successful are: a) very smart, and b) they have money. Usually they have live-in help, they have a spouse who is making a lot of money, and that kind of support, financial as well as just day-to-day handling of the kids, allows them to spend the time necessary to make it. But the people who try to do it alone—model moms trying to keep their kid in day care—it really just is tough, it's tough.

THACKRAY: You yourself are still putting in a very large number of hours.

COLLINS: Yeah, right. I'm crazy. [laughter] There's no question. Most people wouldn't do what I do. But it's pragmatic in a sense. I live on the South Shore of Boston in a very lovely seaport town. To beat the traffic I come in very early, and it gives me a couple of hours before the troops roll in. And I stay late, both pragmatically because they're there as well as to miss the traffic.

THACKRAY: Do you expect to still be crazy in ten years' time?

COLLINS: If the science is good.

THACKRAY: This is your second marriage?

COLLINS: This is the second marriage, which is marginal. There is a price one has to pay for all of this, and I would say that may be part of it. Plus I don't know about you, I tend to be much more productive when I am hungry, when I am less happy.

THACKRAY: Do you think what you're seeing in your own life really has its analogs pretty much in the other Pew Scholars?

COLLINS: No, we were actually talking about that. There are people who really are trying to maintain some sense of normalcy, especially the women. It's very clear that they are trying to balance their lives. You can sit back and look and know the signs well. That's fine. There has to be some moderation, I would say. As a department chairman, I have to be careful that I cannot let my own feelings—you have to encourage stability. The last thing you want is a bunch of people who aren't stable, and you have to be very supportive of family structures, because most people do very well with that kind of thing, and you need that to run the department. I think that's true here. Most people—but not all—most people tend to do better when you're supportive of their family life as a parent. But it is hard. They feel stressed because they see some of us who are still crazy, behaving like postdocs. The more senior people have all gotten beyond that, or they have had traditional marriages where they haven't had to worry about what the woman is going to do.

THACKRAY: Let's go to a different area, if we may. It's to do with the impact of technology, instrumentation, big science, all that sort of stuff. Is everything changing, or what?

COLLINS: Oh, yes, there's no question. The rich get richer, the big groups move faster. Companies are in areas where they are like armies. Once you get an army moving in the right direction, they'll just step over anything. The trick is to know where the army's going, and to get there before they do or stay out of their way. By armies, I mean big laboratories. Senior investigators for Hughes Institute [Howard Hughes Medical Institute], or members of the National Academy of Sciences. People with more than ten postdoctoral fellows or labs with budgets of millions of dollars a year. You don't want to compete with them. Because of their productivity, it's easier for them to get additional funds.

Okay, technology, I would say, has made our job, well, it's changed the level of the questions that we can ask, and it has certainly been important. I'm not someone who's dependent on instrumentation. I don't need a mass spectrometer, for example, I don't need a FACS analyzer to sort fluorescent-labelled cells. The kind of DNA sequence technology that's been developed, even since I was doing the business, has made it easier, but it's still not automated to the point where it negates the value of cloning genes. And that's kind of the next step. A lot of us will begin to—well, if the genome were sequenced, we'd be asking different questions than the questions that we're asking currently.

THACKRAY: Does that project make sense to you?

COLLINS: I'm a tremendous supporter of that. The sequencing information would be incredibly useful. However, I'd love to see the funds come from other sources besides NIH. You don't want to deprive people of one-on-one funds to support research. This is an industrial kind of an application, and it's a technology project which I think is proceeding more and more in directions to obtain a map, refine the map, and then, as the sequence technology develops, to do bits and pieces of that. I actually thought at one point about submitting an application to the Human Genome Project because of our interest in some of these developmental control genes, which are generally in gene clusters. Having published many tens of thousands of nucleotides, I'm obviously very supportive of the acquisition of sequence data, so I'm definitely a biased observer.

[END OF AUDIO, FILE 1.3]

THACKRAY: This question is from left field. Do you have any political interests?

COLLINS: Well, I'm kind of a hybrid person. Obviously, I'm dependent on the good

graces of the United States government, and when you think about it, I've been receiving federal funds since I was in my teens. Obviously, that is a Democratic leaning. I would say I have certain very strong convictions. I am pro-choice, which really removes you from the Republican camp in many respects, and I am not particularly religious. I would describe myself, I guess, as a fiscal Republican, in the sense I believe in the free sector economy and what it can do to support people, although I'm to some extent a supporter of the concerns of many Democrats. Which puts me an awkward political situation.

As a departmental chairman, I would say I'll have to be a Republican, since most of them are Republicans. So as you get older, you make more money, and you tend to become more conservative. But because you're in an academic environment, you're a Democrat, especially in Boston.

THACKRAY: Do you vote?

COLLINS: Yes. Issue by issue.

THACKRAY: What about religion? Your parents were religious and practicing, were they?

COLLINS: It's an interesting story actually. My father was Episcopalian, but my mother was actually part Jewish, and her father died very young. He was actually a foreign national and left Europe because of the rise of Nazi Germany. He was a very smart guy, but couldn't get an appropriate job. He died of pneumonia while working in a rubber factory. Since my father was tortured to death, and I have a sister who's basically dying a slow, agonizing death, I'm not very religious. I'm a scientist, and when you clone your first gene you realize there's not much to this business that you're not going to be able to understand.

That's a terrible thing to say, but when you build living things from inanimate molecules, e.g. assemble your first recombinant phage, you come to that realization. Yes, we're more complicated, but we're not—I'm not an atheist; I'd say I'm an agnostic, on a good day—usually I'm an atheist. [laughter]

THACKRAY: Talk about pet peeves about science. What would you change in the scientific scene if you could?

COLLINS: By and large I think the system is pretty good. The peer review system, since I've profited from it, has been very good for me and I think I tend to be a little biased. When you haven't had problems, you tend not to criticize the system. I know lots of folks who've

had difficulty getting grants through, for one reason or another, and that's usually the first thing out of people's lips. They'll say, "Well, we've got to fix that." Well, it's not a great system but it's the best one we've got, and I think it's reasonable.

Harvard has recently changed its position about the number of papers one needs for tenure. There are plenty of people, even in the Pew Scholars group, who have inordinate numbers of papers. I don't really concern myself with that because I'm a physician. The so-called "publish or perish" mentality is—what do I care? I'll go be a pathologist. A guy who left my lab is making one hundred sixty thousand dollars a year. To hell with this nonsense. He didn't want to have to have to deal with grant writing and a forty thousand dollars a year salary. That salary will double as he becomes more senior. He wanted real pathology. These days the money is still there. It's not as striking as it used to be, but it's still there. Anyway, so I'm less concerned by the traditional academic structure than perhaps I should be. Many people in the Pew group have straight Ph.D.'s. They are facing tenure decisions, and I think those can be arbitrary. I think they can be highly politically motivated. I've seen good people denied positions that I think they should likely have. On the other hand, it's the system, and the system basically is designed to protect people when they take positions that the institution doesn't support.

So, we need to come up with five good papers. Harvard needs five world-class papers, or they won't be interested in you at all. I think you resign yourself to say you're going to have leave at some point, and it's a question of when. How much can you get out of the institution.

THACKRAY: Do you think you'll leave?

COLLINS: Oh, yes, absolutely, absolutely. There are too many good people. The people who stay really are world-class people who have created the field and been involved in that field for a substantial period of time. Plus, as I mentioned, there's a lot of money in pathology department chairmanships. Most of the senior people at the Brigham—the director of the hospital makes about three hundred eighty thousand dollars a year. Many of the clinical chiefs make more than that. There's a none-too-trivial financial consideration, I would say. Unless you inherit money or you're incredibly sage with you investments, you're going to need some additional funds.

THACKRAY: How do you expect to time your exit?

COLLINS: Well, there's a truism—there are good jobs at bad places and bad jobs at good places. The trick is to find the job that's right for you at a time when you're ready to get out. Chairmanships come and go, but, for example, the Hopkins [Johns Hopkins University]

chair is open right now. It will be filled, I presume. That will not come open again in my lifetime. The Yale chair was just filled by a good friend of mine, Jon [S.] Morrow. That'll not come open again in my lifetime. To a certain extent you have to weigh the pros and cons of each position and make a decision. If it's a good department at a reasonable institution and they're willing to support you, then you're really obligated to them. Of course, there are all sort of conflicting problems. If you have a spouse who's never been out of Boston, then you may have to compromise. Or change spouses. [laughter] Which is a lot easier. Isn't that terrible. Like buses, there's always another one coming along. [laughter] That's sexist. See what happens when you go to an all-male school? Amherst was all male, and I was there the last year that was true.

THACKRAY: Couple of things—you talked about being a chairman of a department somewhere, in due course. Can you just say a little bit more about the sort of things you'd like to do if you do take that route?

COLLINS: Basically I would perceive myself as continuing to be a primary investigator with an NIH-sponsored laboratory directing the instruction of postdoctoral fellows as well as graduate students. I would like to see a strong graduate program in experimental biology. And I would like to be involved in training residents and establishing a training program for residents and fellows in anatomic pathology, providing the clinical services that pathology departments provide, mainly diagnostic information. I think it is possible to do all of that. There are a couple of people in the country who can do it.

What I need to develop is an ability to work with people. Chairmanships are successful because of someone's skills as a politician, and those skills have to be practiced. I don't think you just pick them up.

THACKRAY: Would you like to learn?

COLLINS: Well, yes, that's what this time period is for. I think I can do some science, at least enough to be in the pathology department, maybe not a world-class molecular genetics department, but I know enough to collaborate with people, to make things happen. To bring pathology out of the nineteenth century is a tremendous goal of mine, a resource that's being overlooked. The ability to create such a department, I think, and train people in twenty-first-century pathology—I think that would be fun.

THACKRAY: A much more mundane question that looks to our interests in documenting the careers of Pew Scholars. Do you routinely keep old correspondence, lab photographs, old research proposals?

COLLINS: Yes, I actually have two old notebooks, the type of thesis binders that come apart. Remember those, before the days of microfilming and fancy binders? I've basically kept all that's interesting and actually try and have people sign reprints that I think are important. I think that's important because there's a lot to science, and the catalog of publications is not what's most interesting.

THACKRAY: Well, you've given a very interesting interview.

COLLINS: Well, I hope I have. I hope I haven't done too much to embarrass myself.

[END OF AUDIO, FILE 1.4]

[END OF INTERVIEW]

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