Regional Oral History Office
The Bancroft Library

University of California
Berkeley, California

Program in Bioscience and Biotechnology Studies

RONALD E. CAPE, M.B.A., Ph. D.
BIOTECH PIONEER AND CO-FOUNDER OF CETUS

Interviews Conducted by
Sally Smith Hughes
in 2003

Since 1954 the Regional Oral History Office has been interviewing leading participants in or well-placed witnesses to major events in the development of northern California, the West, and the nation. Oral history is a method of collecting historical information through tape-recorded interviews between a narrator with firsthand knowledge of historically significant events and a well-informed interviewer, with the goal of preserving substantive additions to the historical record. The tape recording is transcribed, lightly edited for continuity and clarity, and reviewed by the interviewee. The corrected manuscript is indexed, bound with photographs and illustrative materials, and placed in The Bancroft Library at the University of California, Berkeley, and in other research collections for scholarly use. Because it is primary material, oral history is not intended to present the final, verified, or complete narrative of events. It is a spoken account, offered by the interviewee in response to questioning, and as such it is reflective, partisan, deeply involved, and irreplaceable.

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It is recommended that this oral history be cited as follows: Ronald Cape, “Biotech Pioneer and Co-Founder of Cetus,” an oral history conducted in 2004 by Sally Smith Hughes, Regional Oral History Office, The Bancroft Library, University of California, Berkeley, 2006.

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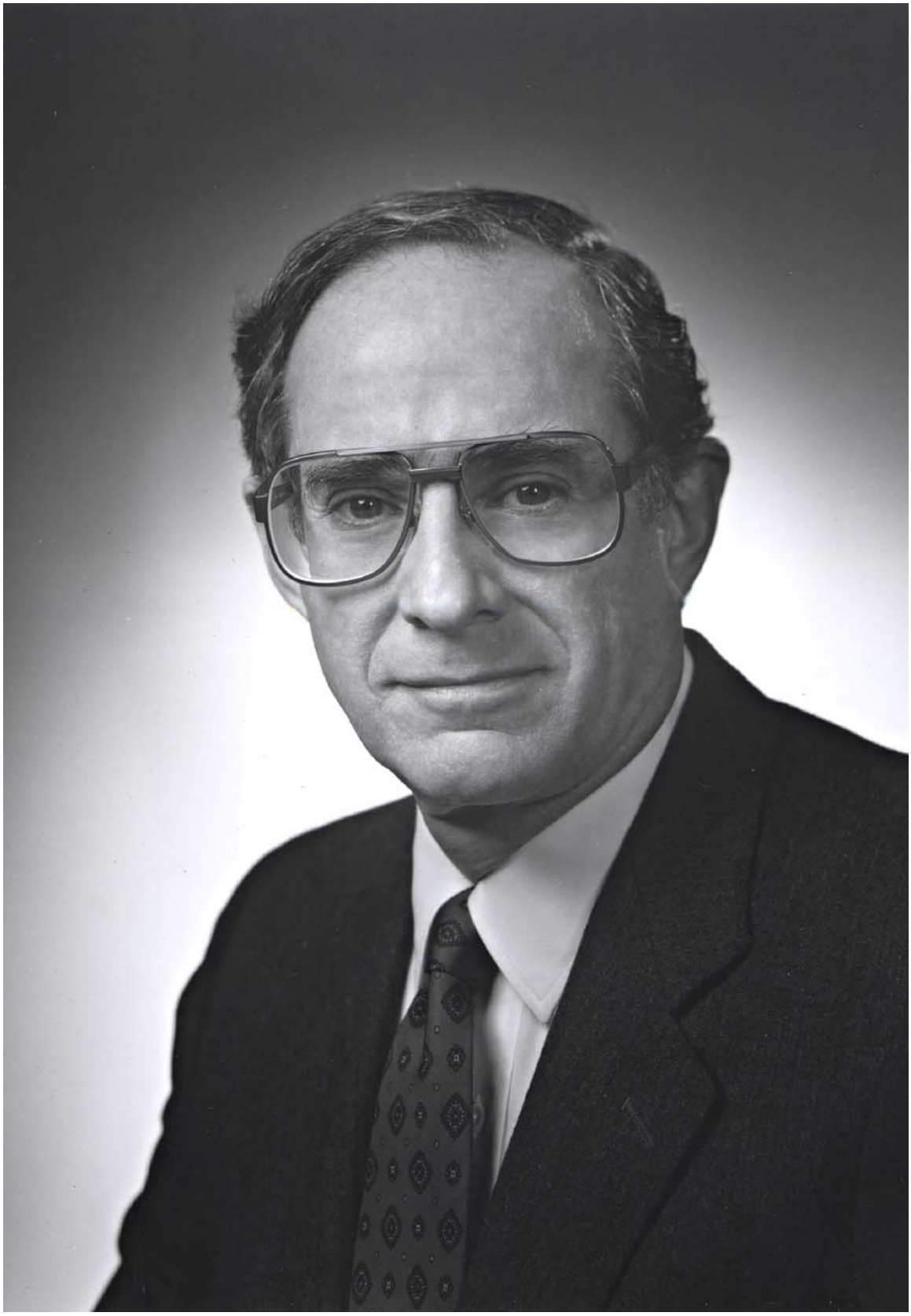

Ronald Cape, 1970s Photo: Karsh of Ottawa

Table Of Contents—Ronald Cape

Interview 5: October 28, 2003

Interview 6: December 18, 2003

Biotechnology Series History—Sally Smith Hughes, Ph.D.

Genesis of the Program in Bioscience and Biotechnology Studies

In 1996 The Bancroft Library launched the forerunner of the Program in Bioscience and Biotechnology Studies. The Bancroft has strong holdings in the history of the physical sciences--the papers of E.O. Lawrence, Luis Alvarez, Edwin McMillan, and other campus figures in physics and chemistry, as well as a number of related oral histories. Yet, although the university is located next to the greatest concentration of biotechnology companies in the world, the Bancroft had no coordinated program to document the industry or its origins in academic biology.

When Charles Faulhaber arrived in 1995 as the Library's new director, he agreed on the need to establish a Bancroft program to capture and preserve the collective memory and papers of university and corporate scientists who created the biotechnology industry. Documenting and preserving the history of a science and industry which influences virtually every field of the life sciences and generates constant public interest and controversy is vital for a proper understanding of science and business in the late twentieth and early twenty-first centuries.

The Bancroft Library is the ideal location to carry out this historical endeavor. It offers the combination of experienced oral history and archival personnel and technical resources to execute a coordinated oral history, archival, and Internet program. It has an established oral history series in the biological sciences, an archival division called the History of Science and Technology Program, and the expertise to develop comprehensive records management and to digitalize documents for presentation on the Web in the California Digital Library. It also has longstanding cooperative arrangements with UC San Francisco and Stanford University, the other research universities in the San Francisco Bay Area.

In April 1996, Daniel E. Koshland, Jr. provided seed money for a center at The Bancroft Library for historical research on the biological sciences and biotechnology. And then, in early 2001, the Program in Bioscience and Biotechnology Studies was given great impetus by Genentech’s major pledge to support documentation of the biotechnology industry. Thanks to these generous gifts, the Bancroft is building an integrated collection of research materials--oral history transcripts, personal papers, and archival collections--related to the history of the biological sciences and biotechnology in university and industry settings. A board composed of distinguished figures in academia and industry advises on the direction of the oral history and archival components. The Program's initial concentration is on the San Francisco Bay Area and northern California. But its ultimate aim is to document the growth of molecular biology as an independent field of the life sciences, and the subsequent revolution which established biotechnology as a key contribution of American science and industry.

Oral History Process

The oral history methodology used in this program is that of the Regional Oral History Office, founded in 1954 and producer of over 2,000 oral histories. The method consists of research in primary and secondary sources; systematic recorded interviews; transcription, light editing by the interviewer, and review and approval by the interviewee; library deposition of bound volumes of transcripts with table of contents, introduction, interview history, and index; cataloging in UC Berkeley and national online library networks; and, in most cases, digital presentation at http://bancroft.berkeley.edu/ROHO/projects/biosci.

Sally Smith Hughes, Ph.D.
Historian of Science
Program in Bioscience and Biotechnology Studies
The Bancroft Library
University of California, Berkeley
November 2005

ORAL HISTORIES ON BIOTECHNOLOGY

Program in Bioscience and Biotechnology Studies
Regional Oral History Office, The Bancroft Library
University of California, Berkeley

Paul Berg, Ph.D., *A Stanford Professor's Career in Biochemistry, Science Politics, and the Biotechnology Industry*, 2000

Mary Betlach, Ph.D., *Early Cloning and Recombinant DNA Technology at Herbert W. Boyer's UCSF Laboratory*, 2002

Brook Beyers, *Biotechnology Venture Capitalist, 1970-2006,* 2006

Herbert W. Boyer, Ph.D., *Recombinant DNA Science at UCSF and Its Commercialization at Genentech*, 2001

Ronald Cape, M.B.A., Ph.D., *Biotech Pioneer and Co-Founder of Cetus,* 2006

Roberto Crea, Ph.D., *DNA Chemistry at the Dawn of Commercial Biotechnology*, 2004

Donald Glaser, Ph.D., *The Bubble Chamber, Bioengineering, Business Consulting, and Neurobiology,* 2006

David V. Goeddel, Ph.D., *Scientist at Genentech*, CEO at Tularik, 2003

Herbert L. Heyneker, Ph.D., *Molecular Geneticist at UCSF and Genentech, Entrepreneur in Biotechnology*, 2004

Keiichi Itakura, *DNA Synthesis at City of Hope for Genentech*, 2006

Irving S. Johnson, Ph.D., *Eli Lilly & the Rise of Biotechnology*, 2006

Thomas J. Kiley, *Genentech Legal Counsel and Vice President, 1976-1988, and Entrepreneur*, 2002

Dennis G. Kleid, Ph.D., *Scientist and Patent Agent at Genentech*, 2002

Arthur Kornberg, M.D., *Biochemistry at Stanford, Biotechnology at DNAX*, 1998

Laurence Lasky, Ph.D., *Vaccine and Adhesion Molecule Research at Genentech*, 2005

Fred A. Middleton, *First Chief Financial Officer at Genentech, 1978-1984*, 2002

Diane Pennica, Ph.D., *t-PA and Other Research Contributions at Genentech*, 2003

Thomas J. Perkins, *Kleiner Perkins, Venture Capital, and the Chairmanship of Genentech*, *1976-1995,* 2002

G. Kirk Raab, *CEO at Genentech*, 1990-1995, 2003

George B. Rathmann, Ph.D., *Chairman, CEO, and President of Amgen, 1980–1988*, 2004

Regional Characteristics of Biotechnology in the United States: Perspectives of Three Industry Insiders (Hugh D'Andrade, David Holveck, and Edward Penhoet), 2001

Niels Reimers, *Stanford's Office of Technology Licensing and the Cohen/Boyer Cloning Patents*, 1998

Arthur D. Riggs, *City of Hope's Contribution to Early Genentech Research,* 2006

William J. Rutter, Ph.D., *The Department of Biochemistry and the Molecular Approach to Biomedicine at the University of California, San Francisco, volume I*, 1998

Richard Scheller, Ph.D., *Conducting Research in Academia, Directing Research at Genentech*, 2002

Robert A. Swanson, *Co-founder, CEO, and Chairman of Genentech, 1976-1996*, 2001

Axel Ullrich, Ph. D., *Molecular Biologist at UCSF and Genentech,* 2006

Daniel G. Yansura, *Senior Scientist at Genentech*, 2002

William Young, *Director of Manufacturing at Genentech*, 2006

Oral histories in process:

Stanley N. Cohen
James Gower
William Green
Daniel E. Koshland, Jr.
Arthur Levinson
William J. Rutter, volume II
Mickey Urdea
Pablo Valenzuela
Keith R. Yamamoto

Interview History—Ronald E. Cape

Ronald Cape was interviewed for the Bancroft Library oral history series on biotechnology primarily to capture the history of Cetus Corporation, of which he was co-founder and president, board chairman, and CEO for most of the company's lifetime (1971-1991). Cetus was among the first companies to commercialize discoveries in genetics and microbiology, before there was a biotechnology industry, and Cape with his long leadership position at the company is in a position to recount the significance of its history.

In these interviews, Cape describes the company's first project, the development and marketing of an instrument which Donald Glaser, Nobel laureate in physics, and his students had designed in his laboratory at the University of California, Berkeley to screen colonies of microorganisms for useful properties.[1] Cape and his business partner Peter Farley, with Glaser participating as a member of Cetus's illustrious scientific advisory board, convinced pharmaceutical corporation Schering-Plough to underwrite development and application of the machine. But the venture never became truly productive, let alone profit-making.

In the mid-1970s, Cetus had unparalleled expertise in recombinant DNA technology for engineering and copying genetic information. Stanley N. Cohen, the co-discoverer of recombinant DNA, served on the company's advisory board. But Cetus failed—for reasons Cape suggests— to exploit its first-mover advantage in commercializing recombinant DNA in a timely manner. Meanwhile, Genentech leaped ahead in the first successful industrial applications of recombinant DNA in 1977-1978.

This richly informative oral history of the earliest days of commercial biotechnology has much more to tell. Cape describes, for example, Cetus's vastly successful IPO, its partnerships with pharmaceutical companies, corporate realignment under a new CEO, development of the polymerase chain reaction technique, and the company's acquisition by Chiron in 1991 after a failure at the FDA drug-approval level. Because Cetus was eclipsed by its absorption into Chiron, and Chiron eclipsed this spring by its absorption into the Swiss pharmaceutical giant Novartis, Cape's personal account of Cetus history takes on added importance.

I conducted six interviews with Dr. Cape at the Bancroft Library, always preceded by conversation over lunch. He spoke freely and fully, visibly enjoying the interview process and his return to the campus where he had been a postdoctoral student. He later reviewed

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1. For details on Glaser's scanner and much more, see: *Donald Glaser: The Bubble Chamber, Bioengineering, Business Consulting, and Neurobiology*, an oral history conducted in 2004 by Eric Vettel, Regional Oral History Office, The Bancroft Library, University of California, Berkeley, 2006.

the interview transcripts, making a few minor changes and clarifications. We are grateful to Genentech for supporting these interviews and for partial support of those with Donald Glaser, in addition to the oral histories on its own corporate history which the company has underwritten.

The Regional Oral History Office, a division of the Bancroft Library, was established in 1954 to record the lives of individuals who have contributed significantly to the history of California and the West. We are pleased to have this oral history join the archive being assembled under the Program in Bioscience and Biotechnology Studies.

Sally Smith Hughes, Ph. D.
Historian of Science
Program in Bioscience and Biotechnology Studies
The Bancroft Library
University of California, Berkeley
August 2006

Interview 1, May 20, 2003

[Begin Tape 1, Side A##[1]

Hughes: Dr. Cape:, let's start back with your grandparents on both sides. Tell me where they came from and what they did.

Cape: Let me get there in one step. My mother, Fan Cape, was born in what she called Russia, which was Russia at the time, sometime around 1910. She came over to this country. As was common in those days– this is the wave of Jewish immigration from Eastern Europe, stimulated by the pogroms, I guess—members of a family frequently came one at a time. They had typically families of several children, and the father would sometimes come ahead and build up some kind of a nest egg, and then send, depending on how much of a nest egg he had built up, for his wife, children, one or more at a time. In the case of my mother, I believe, one year after her father [Menachem Mendel] came over, he sent for her to come to Montreal. She had four or five sisters and a couple of brothers, and they all (those who weren't born subsequently in Canada) came over together with their mother, my grandmother Sarah..

Hughes: Why Montreal?

Cape: One of the reasons, I think, for that great swelling of immigration was the combination of the pogroms and the development of the steamship. If you could make it to a port and a ship was going to Halifax, you went to Canada, and if the ship was going to New York, you went to the United States. I was never given a greater reason than that. But as it turned out, there were family members in Montreal prior to their arrival, so that may have been what led her father to choose there. So that family settled in Montreal, and that's where my mother grew up.

My father, Victor Capelovitch, was born in Montreal, but his family history wasn't all that different. Where my mother had a lot of sisters and a small number of brothers, he had a large number of brothers and only one sister, and in each case my parents were both the third in a rather large family of children. They both essentially grew up in Montreal. Each of them had a somewhat strange educational experience. My mother was very good in school but was yanked out of school after one year of high school, I believe, because she was needed to work to help

1. ## This symbol indicates that a tape segment has begun or ended.

support the family. My father never did speak of anything having to do with school, except for the fact that he didn't go to high school but he did go to university to get a degree in pharmacy. It was a source of pride in the family.

But you asked about my grandparents. I remember some details about them, but not very much. My mother's father died when I was one year old, so I don't remember him at all. My father's parents died when I was six, seven—one one year, and the other the next year.

Hughes: Do you know what they did?

Cape: Mother's father was a watchmaker. He was good with his hands, and that was considered a sort of mark of distinction. I don't know what my father's father did. My father started a small drugstore chain when he got out of pharmacy and gave his father and all his brothers jobs. And that's all I remember. Their professions were working in my father's drugstores.

Hughes: Do you want to tell the story of Neutrogena?

Cape: That was a fluke. It turned out that after World War II, my father was branching out and started a little business, which basically was importing stuff from the United States and reselling it in Canada to drugstores across the country. One of the lines that my father obtained was the Canadian rights to Neutrogena soap. I guess what you're referring to is that I subsequently joined the board of directors of Neutrogena Corporation in L.A. and spent about twelve years in the eighties and early nineties serving on that board. I forged a friendship with the family that ran the business, and in particular with the man who was the CEO of the business, Lloyd Cotsen, over a long period of time—when we first got the Neutrogena franchise for Canada and subsequently when we moved to California. As they say, that's another story, but when we moved to California, Lloyd Cotsen and his family were our first and best friends in California for a long time.

Hughes: Let's turn to you and your early and subsequent education.

Cape: I do realize that memory becomes more and more faulty. Sometimes you only find that out through depositions, and you could swear that it was this way, and when you're shown papers it was something else altogether. But what I do remember is that my father was relatively successful. My mother worked for him as a bookkeeper through the Depression.

Hughes: All the time for this chain of pharmacies?

Cape: Today we think of chains as hundreds or maybe thousands of stores. In those days it was a five-store chain. But there weren't any chains in Quebec, which has, like Louisiana, somewhat different laws. Even today pharmacy there is

considered an art and not a science. There was a lot of licensing fuss, and the bottom line was that it was very hard to develop a chain. That's changed enormously now, but in those days there weren't many big chains in Canada. His stores were Rexall stores, so they all had that similarity.

In any event, I went to regular schools. In '38, just before World War II broke out for Canada and Britain in 1939, we moved to a much nicer home from the duplex flat we'd been living in on a streetcar line to a place with a lawn and squirrels and trees and stuff like that. I must say that because my father was too old to serve, the war didn't impact our family very much directly. World War II coincided with my being seven when it started and almost thirteen when it ended. I was just becoming aware of the world, and following the war was – I don't mean to trivialize it—sort of like a hobby. You were becoming aware that things were happening by the news that you read every day in the papers. Class assignments were like that. Many of my classmates' fathers were soldiers. Having said all that, we lived somewhat of a charmed existence in an area that was a forest, which had started to become a housing development, but when the war came along, everything just stopped. So the woods and all which was eventually, and today is, housing, was our playground. I was thinking recently, no adult ever went in those woods. It was a different time with no safety concerns, and you basically owned those woods, and you lived and played your life in them.

I remember, you could travel all over the city, which had about a million people, on the public transportation system, from the age of eight. You knew where everything went; you went just to explore the world, and it didn't matter. Those are very good memories, and I'm still in touch with some of the kids that were in my classes. We're spread all over the place, and we remember those particular days during "the" war.

Hughes: Is it putting too much emphasis on the move to say that it was a move into the middle class or the upper middle class?

Cape: Well, I think that it was certainly exemplified by that move. I would be inclined to say that my parents had built up quite a nest egg in the drugstore business in the Depression. I remember that my mother had maids and nursemaids for my brother, Michael, and for me, so they must have been reasonably comfortable, even starting in the middle thirties. But quite clearly it was a step up in every kind of way. I can still smell the grass of the lawn and hear the noise of the sprinklers. They make fun now of the traditional suburban home—a suburban home that was ten minutes from downtown Montreal and still is. But it was sort of a protected existence in those woods.

Hughes: Say something about family life.

Cape: Family life was very uneventful. There are no traumas that I can remember. I did well in school. I can't remember having any great hassles with my folks. There is really not much drama there.

Hughes: What about siblings?

Cape: My brother came along a little bit later in my folks' life. They were beginning to travel a great deal, which sort of took over in the late forties and throughout the fifties. I think that he got not as good a deal as I did, where the war and the age and everything else was such that family life was really very conventional. Until I went away to high school, the big meal was at lunchtime, because the school was only three houses away. Then when I went to school in downtown Montreal, coming home for lunch was almost not something you could do, and in addition there was a very good cafeteria in the school. There was no such thing as eating dinner at night until I went away to high school. Went away—I didn't go away, but I went to school in the morning and didn't come home until late afternoon, so the big meal shifted to night. But my point is that we always had the same seats around the same table ninety-five percent of all days until I went away to college. And it was very conventional, and there weren't too many hassles.

Hughes: Was your mother in the kitchen or did she have help there as well?

Cape: Both. She had help but she cooked. I had all my favorite meals. There was even a rhythm to that. I think I could count maybe ten typical meals she would make and rotate, mainly on her whim, but sometimes according to some expressed wish—why don't we have that again, lamb chops, whatever it was. And she was very good at baking, so there were a number of cakes, pies and cookies that I remember. The usual, really humdrum but great stuff, about whenever she'd make the chocolate icing for the chocolate cake, there was that yellow bowl with the white inside that still is sold in stores. And she'd have the rubber policeman [spatula], and then when she was finished with the cake I could take the rubber policeman and finish off the bowl and eat the chocolate icing. It was really very sweet.

I was doing very well in school, such that in my senior year of high school, recruiters from Princeton came around. It's important to note that in Canada—and in Montreal, certainly—going away out of your home city for college was almost unheard of. To give you an example, in my class of 750 entering freshman at Princeton in 1949, there were six Canadians all together. I mean, it was practically not done. And because of the way the Canadian educational system was then, I was sixteen when I entered Princeton and twenty when I graduated. So you sure got a head start on things.

Hughes: Had you skipped a grade?

Cape: No. By-the-by, my Princeton roommate David Saunders, for four years was also in my class in my high school in Montreal, and he's still a good friend of mine. He lives in Seattle and was the head of gastroenterology at the University of Washington for many years, and he's now retired.

Hughes: Your high school was on the route for the Princeton recruiters?

Cape: No, I can't tell you if they got wind of me. I wasn't all that famous. The culmination of high school in the English-speaking schools in Quebec was a series of grueling exams in late May and early June in your last year of high school, which in those days was eleventh grade. The French and English, then and still now, to some extent, were very much two separate communities. I could have been first in the province, and by a mistake in simple arithmetic I was second in the province in those exams. So they knew they had a good student on their hands.

When I entered Princeton and I had an interview with a counselor, there was some kind of, you'd call it mentoring today, but there was a series of appointments you had in your freshman and sophomore years. And I remember vividly being told that I was doing very nicely, thank you very much, and was doing more or less what they expected, maybe a little bit better. They had a funny grading system but, to make a long story short, they thought I'd be a high-B student. As it turned out I led my class every year and cumulatively as well. So that surprised them. I don't think they saw that coming. It was a surprise even to me. I do believe, and it's true today, you build up a certain momentum, and you become a self-fulfilling prophecy. It's like going to a game and expecting Barry Bonds to hit home runs. And if you can help it along, you would, because that's what you came to see. The teachers, I would say, get behind the students who are on a roll.

But your question had to do with—I think it was a highly unusual thing and probably prompted by some alumni who lived in Toronto or Montreal, and it just occurred to them that maybe they should get some Canadians into Princeton, the same as into Harvard and Yale. It was the beginning of a new way of thinking. You asked me if there was any drama in my home life: coming home one day and announcing to my parents, hey, you thought I was going to go to McGill like everyone else, but I'm not; I'm going to Princeton. They didn't give me a hard time.

Hughes: Now were you headed in any particular direction in terms of your intellectual interests at that stage?

Cape: No. There is always the dealing with, are you going to follow in your father's footsteps or not. My father was in a strange kind of profession that represents itself to some extent as being a science, and today we'd say, hey, it's a marketing operation. There's certainly some professionalism about it, and there are schools

of pharmacy, even at UCSF. I majored in chemistry in college, to some extent to placate. But I think I was genuinely interested in it too. And then I remember one time at Princeton, beginning of my senior year, I guess, my father came down for a visit, and I told him, I'm going to Harvard Business School. Not that I'm going to business school, I'm going to Harvard Business School. And he said, "Well, I hadn't anticipated that. But sure, why not?" I think at the time, and I certainly think in retrospect, it was like many people who decide they don't know what they want to do so they go to law school, to sort of give themselves another three years to think it over. Not that any of them would like to be lawyers, and many of them would not like to be lawyers. But the point is always made that all the congressmen are lawyers and a lot of people in industry. It enables you to do anything.

Hughes: Had you at one point toyed with the idea of being a hands-on chemist?

Cape: Well, I can tell you the extent to which I diddled with it. I took a job in between my two years at Harvard Business School [1953-1955] and worked for American Cyanamid in Stamford, Connecticut. So I did industrial chemistry there.

Hughes: And what did you think of that?

Cape: It was fine, but it's not a way I wanted to spend my life, with smelly chemicals, many of which, with people keeling over all the time, had to be toxic; they couldn't be good for you. You didn't need to decide what your political affiliation was to know that this is bad stuff.

Hughes: Was anybody making anything of that, or did it come along with the job?

Cape: It's sort of like with soldiers today: there's a certain macho element where you announce that you decided to get into this line of work, and it has its hazards, and unless it's a total turnoff, which it probably isn't, it shows, like a marine, you're tough. My son-in-law got his degree in chemical engineering here [at Berkeley], and I have a lot of nostalgia looking at the corner where my building used to be. I did my post-doc at Berkeley [1967-1970].

The way I played with my father's profession was to work two summers as a clerk in his store, which was mind-numbing. I never really hassled him about this, but thought to myself, this is crazy!

Hughes: Do you think he wanted to you to go into business with him?

Cape: Oh sure, that comes out later. I was confronted with the fact that he was building up a fair asset in a business, which in retrospect was not very much at the time, but it seemed like big stuff. My friends would say, "Your dad has a soda fountain? You can go down and have a sundae anytime you want? Eat all those

candy bars? You're the luckiest guy in the world." I laughed about it at the time, yes, it's good. On a scale from zero to ten, it's a two, nothing wrong with that. I didn't like working in the drugstore, but I did realize that because of the law then, if I didn't have a pharmacy degree, I could not own a drugstore. That was the way it was.

It turned out that—I'm making a long story short here—to get a pharmacy degree you had to have a Quebec pharmacy degree. It's a long political story, but that was the bottom line. My father obviously knew a lot of people in the pharmacy business, both the manufacturers, the retailers, and the academics. The summer that I worked in Stamford, my father and I went together to see the dean of pharmacy at the University of Montreal, the French Catholic university, and said, "Could you spell out what Ron has to do to enter pharmacy school and get a degree?" And the guy was very, very nice, except that it was a very, very memorable interview for me, because he said, "In Quebec, pharmacy is an art and not a science. Therefore we have certain prerequisites, and with all the stuff that you've done at Princeton and the stuff you're doing at Harvard, you never took Latin. You've got to take Latin." So, go with the flow. I said, "I'll tell you what, I can take Latin at Harvard. I've got a whole year there again, and I'm pretty good at school, and I can do my Latin at Harvard." "Not acceptable. The Latin we need is Latin from Loyola University in Montreal. That's the only Latin we'll recognize."

Hughes: You're kidding.

Cape: Honest to God. And I said to myself, then, I'm out of here. I didn't confront my father with that directly or immediately. I said to myself, I don't want to live my life in this kind of a circumstance with this kind of thinking and adhering to those kind of rules. P.S., my brother, years later, who now has that business—it's his entirely, the one that my father started, because I'm here—did, in fact, get a chemical engineering degree at McGill and followed it up with a pharmacy degree at the University of Montreal. But they sold off all the drugstores, so it turned out to be a moot point.

At that point I made the decision, which was, I think, psychologically determined by a trip that my family took. My mother, my father, some adult friends, and my brother and I took a long trip in the summer of '55 after I graduated from Harvard Business School and my brother graduated from high school. We went to Banff and Lake Louise and Vancouver and Seattle and San Francisco and Los Angeles. I am sure that subliminally, or subconsciously, on that trip I said, I'm going to settle in California someday. I don't know how and I don't know when, but I am getting to California. But I didn't act on it immediately. The next time I went to California was to negotiate the Neutrogena thing.

Hughes: What was the attraction to California?

Cape: Freedom, climate, scenery—everything. I haven't changed my mind about any of that to this day. But fast forward for a second: in 1967, I completed a Ph.D. at McGill and came to the Virus Lab, the molecular biology department at Berkeley, to do a post-doc. Everybody I know that came to the United States to study came on a student visa. Just as an indication that I obviously was doing more than just very deep subconscious thinking about it, when I applied for papers in January or February of my final year working on my Ph.D., I got permanent immigrant visas for all four of us, my wife and two children. And when we arrived at the place we rented in Kensington, the green cards were in the mailbox. I obviously wired that one. They all asked me, why did you do that? Well, it's just as easy. I mean, you have to get a full TB X-ray. It's all a matter of paperwork. Why should you have to leave the USA when you're done? As a matter of fact, that became extremely important when I finished my post-doc at Berkeley; I didn't have to leave.

Hughes: Let's go back to the M.B.A., which comes after Princeton.

Cape: You can't do that anymore, go directly to business school without some work experience. In fact, there was a period where they strongly encouraged you to go out and get some real work experience before you go to business school. I think that's become rigidified in most business schools; they will not allow you to go directly from college into business school. Whereas in my class at Harvard, there were roughly fifty people from my class in Princeton who went direct.

Hughes: Why did you want an M.B.A.?

Cape: It was a place holder. I knew I wanted to run something.

[End Tape 1, Side A] ##
[Begin Tape 1, Side B.]

Cape: I think one of my significant missing pieces is I never really had a mentor or a role model. I'm not saying I suffered from this, or that I had anything against it. But one of the things that I think would have stimulated me to go into academics would have been if there had been a professor who had taken me under his or her wing or who had been such a remarkable object of hero worship that I would have gravitated in that direction. But that simply never happened to me. There's one thing I did notice a little bit later as I got claustrophobia in the family business. Making Neutrogena, which was a real kick for about six months, stopped being such a kick, and selling, which was a kick for even less than six months, really became a drag.

Watson-Crick and DNA and all that hit the papers in the years that I was starting a family. Watson-Crick was 1953, the year I graduated from Princeton, and they got the Nobel Prize in 1962 after I'd been in the family business for several years. I had the distinct feeling that the train was leaving, and I'm not on it. And

with a little bit of a push from my wife's brother and his then-wife, I figured, what the hell, I'll go back and take some courses. But I had a wife and two kids and a split-level and two cars—very conventional kind of thing, except for the fact that I had been good in school and I had a chemistry background. What I'm leading up to is that for the next almost ten years, first auditing some courses, then taking some courses for credit and then –

Hughes: Now this is at McGill?

Cape: McGill, yes. After Harvard I went to Montreal, worked for a year for Merck and Company in a trivial job, and then joined the family business. And it was as if I was bouncing back and forth between two worlds. If I was getting a Ph.D., I was back in academics. On the other hand, I was running a business at the same time. Next to the diploma, which I finally got from McGill in 1967 before I came to Berkeley, the most important piece of paper I got from them was a parking permit. It permitted me to get up early in the morning, go to the office, see what's what, do what I had to do, look at my schedule, time to go down to McGill, park in the snow, go to a lecture, second lecture, go to the lab, go back to the office. I was doing this juggling for a number of years and it was lucky for me that my brother was ready to come into the business. So the last two years that I was working in the lab and a lot with my thesis, going back to the office became a less and less and less important thing because he was sort of taking the slack.

Hughes: And that was fine with you?

Cape: In retrospect they sound like clear-cut decisions, but they were fuzzy at the time. I won't say you drift – sometimes you drift – but most of the time it's just the fact that there isn't entire clarity as to what you *want* to do. There's no question in my mind that a certain point of clarity came when I realized that the logical thing you do after you get your Ph.D. is to do a post-doc. I applied to NIH, Harvard, Caltech, and Berkeley, and that was it. So I was getting out of there.

Hughes: Well, let me hear a little bit about McGill. Was there anything formative that happened there?

Cape: Well, I got a lot of encouragement. I was sort of mentored by the professors who saw this guy coming in as a retread, at the age of twenty-nine or thirty, and he's doing pretty well. What is he doing with his life? Let's see if we can push him in the proper direction. Two professors in particular did push me to put my nose to the grindstone and get a Ph.D. and leave the minor leagues and go to the major leagues and get a post-doc someplace. So with that encouragement, I realized, I'm sure, this is the way out.

I should mention in passing that I got to Berkeley on a research fellowship from the Medical Research Council of Canada, and I'm sure they expected me to

come back to Canada, and I didn't. And as a consequence of that, whenever Canadians ask me to do anything, I'm a sucker for it.

Hughes: What years were you at McGill?

Cape: '62 to '67.

Hughes: '62 to '67. So molecular biology was really beginning to spread out at that point.

Cape: There are two things I can remember that really indicate the story. One is there were no textbooks; things were happening too fast. A series of paperbacks started to get published, because you could get to press faster. All of this seems rather archaic with the internet and everything today, but it was a problem. You had to either read the original papers or get involved with the people who were at the vanguard of the revolution. And I became very friendly with some of the authors of some of those paperbacks back in the early '60s—Prentice Hall paperbacks. One in particular was a developmental biologist at Stanford called Clifford Grobstein, who became the first dean of UC San Diego's medical school, and he wasn't even an MD. He was like a Gregory Peck, a gangling guy with a great intellect. He was at Okinawa or Iwo Jima, and that was the closest thing I ever had to a role model, but he came along very late in my life. But I'm digressing.

The other thing that illustrated the turmoil at the time was the turf wars that erupted in universities when molecular biologists demanded their own departments, and the biochemists were furious. And when you really probed it, and that came out a little bit then but a lot subsequently, it was money. You're going to take our grants. You guys are winning all the Nobel prizes, and we're going to be pushed off front and center stage. And it was very bitter.

Hughes: You found that again when you came here to Berkeley.

Cape: I sure did find that out when I came here, because I got into the major leagues and I discovered that the biochemists were "bad guys". In point of fact, the two [disciplines] worked together in x-ray crystallography and everything else, but I'm telling you, the generalization I came to after spending three years in the major leagues at Berkeley was, business, academe, it's all the same thing. They're human beings; they're all playing I want to be the king of the castle. It's nice that I'm in an exciting field, discovering the truths of life, but the viciousness and the ethics, not terribly different in the two realms.

Hughes: What was your dissertation about?

Cape: Oh, my dissertation was very trivial. It was on the early forerunner of sequencing DNA. It was called cluster analysis. It had, in its heyday in the late '60s been started by a guy named Erwin Chargaff, who was a crusty old

biochemist who hated the molecular biologists and was widely quoted with great one-liners, and for his bitterness. He thought he should have had a piece of the Watson-Crick Nobel Prize, because he is the one who discovered the base pairing. Except for the fact that nowhere was Einstein's statement about genius better than in describing why Chargaff didn't deserve the Nobel Prize. Einstein said, "Genius is looking at things that everybody else is looking at and seeing something that nobody else sees." Well, Chargaff didn't see it. And he decided to take it out by beating up on the characters of Watson and Crick, which is a separate subject.

Hughes: As a student, was this all unrolling before your eyes?

Cape: Yes. Much more so as I started the postdoc. If I am going to go back to school, what should I do? Well, my God, the greatest secrets of life are being uncovered. There's no question as to what to do. So alone in the biochemistry department at McGill, I worked on DNA. And it was lucky that my professor, John Spencer, had just taken a job at McGill, having postdoc-ed for Chargaff. So it was a slam dunk as to what I'd be doing. But the significance of it is close to nothin'.

Hughes: Was your professor one of the few that was working with DNA at McGill at this point?

Cape: That's right; that's why I went there. And he was a very, very sweet guy, very nice to me. Became a very good friend.

Hughes: Why the decision to go on?

Cape: Why did I pick Berkeley?

Hughes: Yes, why did you?

Cape: I think I picked Berkeley because that's where the action was. I worked with Gunther Stent. I worked in the Virus Laboratory where there were already two Nobel Prize winners and several more later. None of the labs that I applied to were anything other than tops, with the people absolutely on a first-name basis with Jim Watson and Francis Crick and all. There were a lot of silly practical questions. But the most important thing, I'm sure, was, Mario Savio was here. And that's where things were happening, and why not?

Hughes: What were the years of your postdoc?

Cape: '67 to '70. I got a two-year fellowship, and I extended it for one year. And by absolute fluke, where did I choose? The center of venture capital of the world. I mean, that was not planned.

Hughes: Well, let's hear about the Virus Lab in those years?

Cape: It was a great place. The professors were wonderful. They interacted splendidly with the students, not as equals—you can never be that—but as friends. I remember Howard Schachman at tea one day, saying, "If you put the Bill of Rights in front of a thousand Americans and asked them to sign it, nine hundred and ninety-five would not sign it." Those kinds of conversations; I'll never forget them. The level of the science was very good, and the variety of the people you met, and the bold individualism that I saw here was everything that I'd always dreamed about.

I forgot to mention: my parents sent me to two summer camps, one for five years, from '39 to '44, in Quebec, and then from '45 to '49 in the Adirondacks. The first, Canadian one was like hell and the second one, the American one, was heaven. Those counselors in that New York camp – they were all from the New York school system. They were so wonderful, I can't tell you. My brother and I both remember, they were like gods. They were role models, too. We had such a good time at the camp. It was my very first exposure to the United States of America. And I *loved* it. And I'm sure way back then [I decided] it was the place to be.

Hughes: So you were very aware at that young age that there was a difference between Canadian attitudes and American?

Cape: Yes. There's a good joke about that. What's the difference between Canadians and Americans? An American will say, "I don't know." And a Canadian will go through the roof! He'll hold your attention – he would like to, anyway – for a long time, telling you the difference.

Hughes: You were in Gunther Stent's lab. Doing what?

Cape: Doing phage genetics.

Hughes: Which he was doing.

Cape: Which he was doing, but he'd gotten out of it. As a matter of fact, that's another role model of a kind, in the way that Carl Djerassi has turned into a poet and a playwright and the way that Gunther Stent at that time broke away and became the university lecturer. He gave four lectures [that] he put into the book that he called *The End of the Golden Age.*

Hughes: Oh, yes.

Cape: Real dilettantish stuff. But the point is, he stopped working at the bench, and he started literary stuff. It's not a matter of right or wrong; it's a matter of the can-do attitude in this country. I'm going to change myself if I want. Or I'm not going to change myself if I don't want. The point is that it's possible, and in

Canada it's not admired, let's put it that way. So there were role models for me in the academic world, and there were role models for me in the venture capitalists.

Hughes: At this point had the biochemists decamped to Barker Hall?

Cape: Yes, and one of my postdoc opportunities was Bruce Ames. But he was still at NIH when I was ready to come to Berkeley, and he wasn't going to come here until seven or eight months after I was ready to come here. It struck me as too disruptive. I'd rather get settled someplace, although I got along with Bruce and Giovanna very well, and I would have liked to have joined him.

Hughes: Did Gunther have the name then that he has now?

Cape: Yes, I think he was –

Hughes: Member of the phage group and all of that?

Cape: Well, I read that book that was basically a series of autobiographies inside Wendell Stanley's department. It was called *Phage and [the Origins of] Molecular Biology* or *Viruses and the Meaning of Life* or something like that, but it was basically what Hans Fraenkel-Conrat was doing, and what Gunther Stent was doing, and what Wendell Stanley was doing. They each wrote a chapter in very down-to-earth language.

Hughes: Before you came?

Cape: Oh, no. I came here specifically to interview Stent because I wanted to work in his lab because there was something about the data, and the same thing was true at Stanford. I wanted to work for Paul Berg or one other guy who were working directly with DNA, except Paul Berg just that year was going off to do a sabbatical at the Salk Institute, and the other guy was going to Harvard.

Hughes: Who was the other guy?

Cape: I can't remember, but he was working directly with DNA, with the molecule; he wasn't working with concepts. I mean the concepts were there. But it was still at the time where you were trying to say, how can the molecule do this job, and it's very well to speculate that that molecule seems to be implicated, but unless you can explain exactly what's going on…. Well, there were all kinds of people at Oregon and Harvard doing different kinds of experiments, all of which amounted to this. This guy at Stanford, whose name eludes me, was sizing DNA in different ways.

Hughes: Was he in the biochemistry department?

Cape: He was in the same department as Paul.

Hughes: That's biochemistry.

Cape: In the medical school.

Hughes: Grobstein was in biology, which is on the other campus.

Cape: Right. The people I came to know later in my biotechnology years were mainly at the medical school, and I got to know that part pretty well.

Hughes: That's interesting in itself, because those are the people—I don't know if I'm right in this—who seemed to be more entrepreneurial.

Cape: I don't know. Many generalizations, if you want to look for what proves the rule and what disputes the rule, you find examples of all. For example, and this is just an example, there was a period when we were first starting companies that Paul Berg, Yanofsky, and Ron Davis took a very holier-than-thou point of view, saying that this commercialization is corrupting, and blah, blah, blah, blah, blah. And within two years they hard started a company which they sold to Syntex. It reminded me of a classmate of mine who was the chairman of Kidder Peabody.

Hughes: You're talking about DNAX?

Cape: DNAX, that's right.

Hughes: It wasn't sold to Syntex.

Cape: No, it was Schering-Plough. You're right. See, that's an example, and you're going to hear many other examples.

Hughes: Not to worry.

Cape: Hey, this has to do with aging.

Hughes: Oh, I don't know anything about that. [laughter]

Cape: It's really bad, but it also tends to be self-serving, too, and you've got to watch out for that. The point is, you'd say, well, the bastion of anti-entrepreneurial activity was temporarily Stanford, then suddenly, bingo. As I was saying, a classmate of mine was the chairman of Kidder Peabody, and during the period when we were all networking in Wall Street, I visited him and we were talking about various financings that we would do at Cetus. At that point, there was one particular model, research partnerships, I think it was—it might have been something else—and he said, "That is morally wrong; I won't do it; we'll never do it. I don't care how many people on Wall Street do it." Well, you know the B.S. Six months later they were right in there doing it with everybody else. So it blows in all directions.

I think the Bay Area as a whole, was the hotbed, still is the hotbed, of that kind of thing. You could pick a moment in time in which the Berkeley campus wouldn't be doing so well. Bruce Ames was certainly highly entrepreneurial for the last ten or fifteen years. There were times when Stanford seemed to be where all the action was. If you reflect on it, it's possible that UCSF has done more for biotechnology that any other university campus in the world. But it didn't seem that way at that time. A snapshot wouldn't have given you that impression.

Hughes: Except that you could have said, could you not, circa early the 1970s, that Berkeley was *not* the center. Would that have been a safe thing to say?

Cape: Well, there were a couple of reasons. The Cohen-Boyer experiments, which you documented a lot, I guess—Stan thinks very highly of you—illustrates the point that the Berkeley patent department was basically in charge of UC. And they were telling scientists, "Stop bothering us." In fact, even Niels Reimers had to twist Stan Cohen's arm at Stanford. So I guess being MDs who can do anything they want, maybe there was some tendency at UCSF and Stanford to do more of that than here. But I don't know, I think over the years there's been a lot of stuff at the Berkeley campus. But you're right—there was the assumption that because Don Glaser, the founder of Cetus, was at Berkeley, there was a hotbed of something here—and I don't think so, I think he was more entrepreneurial than most.

Hughes: Did he get static for his commercial endeavors at the time? Circa 1971?

Cape: I don't know. I certainly didn't go there, as they say now, in conversations with him. I would imagine a little bit.

Hughes: It probably depended on what department the individual was in. After all, the chemists and the physicists have had associations with industry for ages.

Cape: Well, I used to make that point a lot. In the Vietnam War street [protest] scene, it was largely true that biologists tended to be in the streets, and chemical engineers and physicists tended not to be. I'm sure sociologists have made a big deal of that. And certainly in our department, people were running around in bare feet, which is certainly bad procedure. The place was full of hippies and free love and everything else.

Hughes: You had finished your postdoc. So what were you thinking?

Cape: I want to stay in the Bay Area, that's what I'm thinking. I used to say later that not enough stress is laid on where the entrepreneurial scientist with the blockbuster idea happens to live at the time. We were very fortunate to have three great universities and a great deal of entrepreneurial encouragement. And those guys know where their Japanese restaurants are, where their Chinese

restaurants are, and they have their homes, and what the hell's the point of going anywhere else? And your question was?

Hughes: What you were planning to do.

Cape: I wanted to stay here.

Hughes: But to do what?

Cape: I wasn't sure. I told you I had two mentors at McGill. One turned out to be the head of a department at the Medical College of Ohio in Toledo. I went there and gave some lectures, and he offered me a job as an assistant professor. But my heart wasn't in it. It didn't seem the kind of life I would want to have.

Hughes: It was that in addition to the region?

Cape: Oh, no, there's one other thing. I was very much aware after being here for three years that the time off, i.e., the years between ages twenty-one and thirty, when I was largely in business, were the years when I would have been the most scientifically productive and could learn best. And here I was thirty-six, and you know what? I mean if it were a mathematician talking, your career is over. The fact is, I looked around and I said, these guys are so smart, I can't get over it. Plus when I was bouncing back and forth between business and academe, I was being told, somewhat impolitely, by people in each, that, obviously I didn't know what I wanted to do, number one. Number two, that other world is basically not good, and why are your wasting your time there? There was in fact no biotechnology industry. Notwithstanding the fact that a lot of chemical and chemical engineering and physical and electronic developments had turned into companies, that hadn't happened yet in biology. It was like maybe a dam waiting to burst or an egg waiting to hatch, but the fact is, there were a lot of Nobel Prizes in molecular biology, but no practical applications.

Hughes: Syntex would fall into the chemistry category?

Cape: Yes. It's a tragedy to think back on Syntex, the greatest center of steroid chemistry knowledge in the world. Part of my routine in Montreal when I was running the family business was to check the patents that had been issued each week. I would say that the names Carl Djerassi and George Rosenkranz—well, they were weird names—but they jumped off the page every week; they were patenting everything in sight. But it was just in chemistry. It was a conventional drug business, but steroid chemistry was their bag, and they did a great job.

Hughes: But it wasn't biology.

Cape: Well, let's face it, the whole idea of Watson and Crick was to combine the insights of chemistry in terms of their significance in biology. Woody Allen used

to have a comic strip, whether he drew it or somebody else drew it – but he was talking about the secrets of life. He had one panel in which he said, "It's all chemistry." Which it is.

Hughes: And of course, Crick came out of the physical sciences.

[End Tape 1, Side B] ##
[Begin Tape 2, Side A]

Cape: On the one hand, the people in academe and the people in business were both giving me a hard time: "Make up your mind. You're trying to do both and that's ridiculous." I remember Gunther Stent mentioned one guy who did a *great* experiment. So I said, so what became of him? He says, he's an insurance salesman now. So not everybody ends up continuing in academia. But the point is that I discovered in my early contacts with the venture capital community, hey, you've got it wrong: you're a hybrid. And that's what we're looking for. This is before education came in and made hybrids. There weren't too many hybrids that just happened by force of luck and circumstance.

Hughes: Some of that was due to the cultural context. Particularly for the academic side, you weren't supposed to put feet in both camps.

Cape: That's right, notwithstanding very famous chemists who did, and became very rich in doing it.

Hughes: Yes, but not in biology.

Cape: Exactly right.

Hughes: It wasn't necessarily that biologists are more high-brow than people in other scientific disciplines. Where were the commercial opportunities?

Cape: Well, that's the point I wanted to make. Until monoclonal antibodies and recombinant DNA came along, there really was no way to manipulate the stuff of life in a new way. The drug companies were built on fermentation technology as well as chemistry, and although there were some genetic insights, which then and still today they should have been using—and that's how Cetus started out—in terms of finding better production organisms, better discovery organisms or situations. In fact, that now is very much the rage. There are *Newsweek* and *Time* covers about all the new antibiotics and what's going on. The point is that unfortunately the drug companies were doing very well, thank you very much, and were convinced also that infectious disease was licked. Therefore the insights that could have informed their future research were really not welcomed by them, generally speaking. But when recombinant DNA and monoclonal antibodies came along, I'd say in hindsight you'd have to be an *idiot* not to recognize that suddenly an enormous universe of new possibilities opened up.

Where prior to that, the Nobel Prizes that had been awarded might as well have been awarded in astronomy. You can look at the stars all you want; you can't move them around. They're doing their thing, right. And that to a large extent was true of biology—you couldn't impact it the way you could impact chemistry or nuclear physics. Remember it used to be called gene manipulation? That was the name of Stan Cohen's first *Scientific American* article. Manipulation is what it's all about. You can get your hands on it, literally. And that's what started the revolution.

Hughes: What would you do then with the connections between academics and the pharmaceutical industry? Why isn't that in the same category as what happened when recombinant DNA and monoclonal antibodies became so applicable?

Cape: It didn't happen so fast then, either, and there's a reason for that, I think. First of all, we all know about the timelines in the drug industry. No sensible person, if you really spell it out in brutal terms, would be as patient as to wait ten years between an invention and marketing that invention. The drug companies have something good going for them, because they've got a cash cow going, and that can support a certain amount of research. A biotech company is very exposed because it doesn't have, unless its name is Amgen, too many cash cows. Consequently, it's a totally different business model, okay? Now comes my point: If you're a 45- to 55-year-old decision maker in a drug company, and you see a new technology that's going to revolutionize your business, you have everything to lose and nothing to gain by making a decision.

Hughes: A decision to take it on.

Cape: Yes. If you are wrong in moving with this new technology—there are exceptions—you're going to suffer for it; your family's going to suffer for it; your career's going to suffer for it. If you were right, you will have retired by the time it becomes clear that you were right, okay? So you've got everything to lose and nothing to gain. The entrepreneur, on the other hand, in the new biotech field has everything to gain and nothing to lose. He's living in a culture that says, so you failed; start over again! Right? And for more or less thirty years the capital was there to support that. And that's the main reason. It isn't that those guys [at the drug companies] weren't smart. They're extremely smart. But at some level they're doing the right thing in terms of their own personal lives.

Hughes: When did you finally flow towards one side rather than the other?

Cape: Well, I didn't have to do that. The very lucky thing of the early 1970s was to be in the right place at the right time—the right time with respect to a lot of things, but most particularly with respect to the explosion of unbelievably transforming science in the universities, and also an increasing awareness on the part of the universities that this is a legitimate thing to be industrialized, and a realization

on the part of universities and Congress in the 1980s that we'd better streamline some aspects of the way the country is run.

Hughes: Yes, but that latter was a decade after you began thinking about Cetus.

Cape: Oh, yes, but the point is that the typical entrepreneur doesn't worry about stuff like that. They see the future in some way or another. Some will represent to you, and maybe it's true, that they see it with great clarity. But the point is that the future lies ahead. As Gunther used to say, the future lies ahead. [laughter] The point is that you do the art of the possible, and you try to move towards the art of the outrageously seemingly impossible but maybe possible. If you find that you can finance this, there's no shortage of people, particularly in California then, as contrasted with the East. If somebody has done something once that you thought couldn't be done, like run the mile in four minutes, or break the sound barrier, then there will be a lot of people who will do it afterwards. They didn't do it because it couldn't be done. Why waste your time with it?

I think the stories convey it better than anything. Herb Boyer was speaking to a great international congress of microbiology in Munich. And they had just announced the somatostatin success. Somebody gets up after he's given his talk and asks the question, "Dr. Boyer, do you realize that not only for somatostatin, but the principles that you've just enunciated, could be used for a whole host of other proteins, like insulin and stuff?" And Herb said, deadpan, "The thought has never entered my mind." [laughter] I thought that was one of the great comebacks

Hughes: So that must have been 1977?

Cape: '78.

Hughes: Takes a while to get around, the word out. All right. So what were you hanging your hat on? In 1971, sure, Berg and the Stanford group were recombining DNA, which is different than what came to be known as recombinant DNA.

Cape: Well, I think the reason Paul got the Nobel Prize, in addition to the fact that he deserves it for a whole pile of stuff, but the reason he is mentioned as being a recombinant DNA guy in the citation is that he was in fact showing you can attach different pieces together and get functionality out of them.

Cape: I think you really had to be a prepared mind to grasp the significance of the research. What Cohen-Boyer did, you didn't have to be really smart to realize, oh my God!

Hughes: Two things spring to mind in relationship to what Paul was doing. First of all, he wasn't cloning, and secondly, the technique itself was really complicated.

Cape: Well, the guys who got the enzymes did get the Nobel Prize. Ham[ilton] Smith got the Nobel Prize. It's the same thing as the polio story. It was [John F.] Enders who got the Nobel Prize for growing the virus. That was the big problem. The development of the vaccines was perceived at that time as a slam dunk after you learn how to grow the virus. But if you can't grow the virus, you can't stimulate the immunity.

Hughes: Well, what I'm trying to get around to is, presumably, around about the early '70s, you were beginning to look at these possibilities in biology. But what were you actually seeing? Because of course it's a couple of years before monoclonal antibodies and recombinant DNA.

Cape: If I fish around in a trunk, I can find our original financing proposal.

Hughes: I'd love to see that.

Cape: But I can paraphrase it for you. You know that story about the little boy and the birthday present?

Hughes: I don't think so.

Cape: It goes something like this. A little boy has been looking forward to his tenth birthday. So has his father. His father figures he's got to teach this kid some reality, that the world isn't such a great place and you have to face disappointment. So he presents the kid with a barn full of horse manure as his tenth birthday present. And the kid goes wild. He's so excited! And his father says, "I don't understand you. What are you so excited about?" He says, "With all that horseshit, there's got to be a pony in there someplace!"

Okay. This is basically the way our company started. There were specifics—you can't get away with that. But the point was, look, the secrets of life, to some extent, have already been uncovered. (They use words very loosely in journalism. They talked about DNA being decoded in 1999 or 2000. Sure, human DNA was *sequenced* in 2000, but it was decoded by Marshall Nirenberg and Ghobind Khorana in 1962, okay?) So DNA had already been illustrated to be *the* thing. The genetic code had been decoded. All kinds of Nobel Prizes had already been awarded. The field was preparing for something. I mean, it hadn't been exploited *at all*. And we presented ourselves as there's got to be a pony in there someplace. We dealt with a financial community that had just gone through the go-go years of the first computer companies, and was looking for the next big thing. And they decided the next big thing was going to be, first of all they called it medicine, and then they focused in on molecular biology.

Hughes: They had that mindset before you came along?

Cape: It was interactive. I don't think they had thought it through that clearly. I remember having a breakfast with Tom Perkins and [Eu]gene Kleiner. I remember that they were considering financing Genentech, and they wanted to know, did I think that recombinant DNA really could make proteins? I remember just telling them, "Darn tootin'. Of course I think that." And there was a lot of excitement. People were incredulous. Oh my God, is it possible?

Hughes: Was Stan Cohen an advisor at that point?

Cape: We started Cetus in '71; we got Stan Cohen in '75.

Hughes: Right. But if Perkins and Kleiner were thinking about Genentech, that's got to be no earlier than 1975.

Cape: That was 1975 or 1976.

Hughes: But you've got Stan on board by then as a consultant to Cetus?

Cape: I don't remember the exact dates. Let's assume as one possibility that we had Stan Cohen already, and I believed the commercial future of recombinant DNA to be true. So these guys asked me to breakfast and asked me, do I believe it to be true. I might have told them—I cannot remember telling them—because they were also small investors in Cetus, that we believed in this, and we believe it will happen, not knowing that they were going to start a competitive company, right? I do know that they asked me did I believe in this, and I do know that I told them that I did. And that's really what they wanted to hear, I think.

Hughes: Let's go back to 1971, or is that where you're headed?

Cape: Oh, I'll go back to 1971. The point is, we were able to put together a business plan which promised to build as a first, but by no means the last, illustration that there's great stuff going on in universities that could be commercialized: Don had built a flying-spot scanner to measure the shapes, in a computer-friendly way, of bacterial colonies on a Petri dish, which we thought could be translated to an improvement of sensitivity testing, which is a way of finding out what antibiotic is going to work for you when you come down ill with something.

Hughes: How does it work?

Cape: Well, Don's thing was a big thing run by minicomputers, as they were called in those days, made by Digital Equipment, that had a laser going back and forth and back and forth and back and forth and building up a topological map of the shape of these colonies. And we were obviously trying to develop some clinical instrument of a very much simpler nature, but using the same principles, to make it possible for clinical labs to get that important information to a doctor in a hurry.

Hughes: So you could diagnose by the shape of the colony?

Cape: That was the hope.

Hughes: But it turned out not?

Cape: Well, it turned out that as a business model, it was superseded by something else within six months. If I can presumptuously compare it to what the generals didn't do in Vietnam: if you find out that you should change your plan, change your plan—don't just stick to it. And this was a better model. Schering-Plough was interested in improving their production strains for Gentamicin. We convinced ourselves and them that we could do that for them, and they basically financed our next five years. And I would have to say that in retrospect—and hindsight is lovely—that project with Schering-Plough probably slowed our getting off the dime on recombinant DNA, because ultimately, within interleukin 2 and beta interferon, we had candidates, and ultimately with Kary Mullis we got a Nobel Prize. But we were, first of all, very nicely financed for five years with Schering-Plough for what they wanted to do. After the Arab oil boycott, all the oil companies decided that genetic engineering is the next big thing. So if oil's going to turn rotten on us, let's get into that, and Chevron and Shell financed a whole bunch of stuff that we were doing.

Hughes: Well, we're skipping ahead too fast.

Cape: I just wanted to explain why we dropped Don's idea.

Hughes: Right. Why you weren't first off the block in terms of recombinant DNA is what you're also saying.

Cape: And I'd also say that Genentech's scientists were superb. And there was an obsession—I would say that of all the genetic engineering companies, some of which worth billions today, have changed their business plans a dozen times, sometimes five times in two years. Genentech has not varied from their initial statement of objective to this day almost.

Hughes: And what would you say that is due to?

Cape: Well, it's partly willpower; it's partly great intelligence; it's partly luck. I don't know—it's a combination of a lot of things.

Hughes: Genentech from the start has based its business on recombinant DNA, and of course there were other things that came in. But that was the focus. Cetus from the start has not done that.

Cape: No. One of the fights that I had with my father when I was in business with him was the fact that there are many different ways to run a business, and there are

many business models that work. Amgen's is the best by far: get two blockbusters right in a row. Right? The business model that they had has possibly been executed by them, and it no longer is a business model that anyone would care to justify. Try to build a new pharmaceutical company from scratch, vertically integrated right from the bench to sales, everything? Companies many times their size are saying, we're too small; we're going to merge, partly possibly out of egos of the CEOs. But nonetheless, Amgen is unique.

Anyway, I don't think we did anything wrong. I do think, just like Chiron, over the last ten years, we didn't come up with any blockbusters. And that's also a major thing: the two molecules which we bet on never turned into anything major. They happen to be today major molecules for Chiron.

Hughes: Cetus got them almost there, wouldn't you say?

Cape: Yes. But the point is that if you want to take the years 1975 to 1985, I'd say Genentech scores ten and Cetus scores zero in terms of really great accomplishments.

Hughes: What is that about? Genentech had some top-notch scientists, there's not doubt about it. But Cetus did too.

Cape: Yes. And we won a Nobel Prize.

Hughes: Well, and more than that. I mean, it was more that Kary Mullis.

Cape: No, no, no, I'm just using the symbolism of the story. No, I – you've got to recognize the score as it was. I think we were diversifying at a time when it was not generally applauded. Other people diversified later, and it was applauded. You can't play a popularity contest. I think what we were doing was anchoring a certain amount of conservatism in the work we were doing for the big companies. If I had to do it over again, having seen where that led, I'd say that's not very smart. On the other hand, the stock market thought pretty well of it in 1981.

Hughes: In the late '70s, at the time they were beginning to think about their IPO, Genentech was heading towards diversification, too. Do you remember the venture they took into veterinary medicine?

Cape: And also Genencor and a lot of other things. But it's all timing and if you're riding the crest of the wave or not. But I think it would be a very bad mistake to do anything other than recognize the fact that they had, and are still having, and it's in the papers today, a great run. They've done so many things so well and so right. George Rathmann used to actually use that in promoting Amgen. "My role model is Genentech, and if I can be half as good as them, I'll be very happy."

Hughes: Did he really?

Cape: Words to that effect. He may have said, “I’ll try to improve on their …” It’s easy for number two to just model on number one. But they were great. They were greatly [inaudible.]

Hughes: Well, listen, I think we should stop for today

[End of Interview.]

Interview 2, July 21, 2003

[Begin Tape 3, Side A] ##

Hughes: We talked some about Cetus last time, but I thought we should go back this time and go through systematically. Systematically in my mind is starting at the beginning, when, as I understand it, the company was pretty much you and Peter Farley in a Volkswagen?

Cape: Well, a magazine piece might read that way, but I don't think that's the way it was. I mean, that was one element of it. The company sort of revolved around Don Glaser in many ways. I was a postdoc in the Virus Laboratory. My lab supervisor was Gunther Stent and Don Glaser was one of his colleagues, another professor in the department. But, most importantly, in addition to being one of the several Nobel Prize winners up there, he was inclined to think along the lines of venture capital financing of ideas that might originate in the university laboratory.

Don Glaser had had previous relationships and a friendship with Moshe Alafi, a venture capitalist. I had chatted with Don about this because he was in the same building, without anything like the idea of we would associate with each other. I also sort of knew his most brilliant student at the time, who was Calvin Ward. Because I was looking for ways to stay in the Bay Area, it had occurred to me that maybe my background in business and science was not, as many people represented it be, a make-up-your-mind kind of situation. But it could come together, if in fact there was a business to be seen in the kind of biology that I and others I knew had studied. As one of the steps in that direction, I had been introduced to some venture capitalists in San Francisco, most particularly to Sandy Robertson. And it was in Sandy Robertson's office that I met Pete Farley. In any event, the five people who started Cetus, when it got started, were Don Glaser, Moshe Alafi, Cal[vin] Ward, Pete, and me.

Hughes: Had Pete Farley come to Sandy Robertson's office hoping that

maybe there would be—

Cape: He was totally independent. We were both in the office at the same time. He was, if you like, a forerunner of something which

became sort of trendy twenty years later: he had an M.D. and he was in the M.B.A. program, so he was going to end up with an M.D. and an M.B.A, which was unheard of at the time. The last piece of the puzzle is that the venture capital community had decided pretty well informally, but nonetheless a consensus had developed, the next big thing was going to be in the medical field. Therefore, Pete's credentials were attractive to Sandy and other venture capitalists, and my credentials, while not an M.D., I had a Ph.D. in molecular biology. Actually, it was in biochemistry. And an M.B.A. and some business experience. My postdoc here was in molecular biology. So everybody was trying a little of this, a little of that. How do you put them together? What kind of combinations might work? There was no such thing as a biotechnology industry. The term wasn't even really used until ten years later.

Hughes: Were you at that stage thinking more widely than Don Glaser's microbial screen device?

Cape: We all were. Yes and no is the best answer, and not exclusively myself. But everybody that was involved, as well as people who had it on rather soon, like Carl Djerassi, were of the feeling that as we even stated informally in our first business plan, there have been so many Nobel Prize winners in this field since the end of World War II, and unlike other fields like physics and chemistry, there had been no specific, exploited, commercially harnessable discovery. But nonetheless the background of so much information and understanding had to sooner or later, result in an explosion of applications. Whereas we started with something with something which was at hand, which was a development or, you might say, a derivative of the kind of stuff that Don [Glaser] was doing in his lab. We decided within months of launching on the basis of a rather clever small-scale version of that that Cal Ward had developed, which we could possibly use in the clinical laboratory setting, as opposed to Don's enormous and multi-computer-controlled device at Berkeley. We scrubbed it as a way to go within six months and went in a somewhat related direction, which was using genetics to help industrial problems.

Hughes: Oh, I see.

Cape: Rather than say, we have this thing; let's shove it down the throats of whatever market we can find. We found that there was a market in industry that had certain needs, and since we thought that we had a way of addressing those needs, it was a much easier sell than trying to create the need in the first place, in the minds of whoever provided the money.

Cape: What was your question?

Hughes: I wanted you to describe how the apparatus worked.

Cape: Oh, well, what Don had, and it was run by one or more what are called minicomputers, I think they were called. They were made by Digital Equipment. There were PDP 6s and PDP 12s and other things. But they were very large things. They looked like refrigerators—a lot smaller than an IBM mainframe but a lot larger than what we now know when we think of computers. And it ran and took readings after running what was called a flyspot scanner, which was basically using a laser or some other kind of light that – like you see the scanning lines on a television picture tube until they discovered ways of making it not visible. You scan very quickly and then repeat the scan, and the computer is also moving the scanner across a tray which contains bacterial colonies. The intention is to relate these computer-generated shapes, or the analysis of these shapes, to be able to tell what kind of a colony it is, and, in our particular application, what would kill that colony most effectively. In other words, screening for antibiotic sensitivity, which is something that is done, and most people are familiar with this when they show up with maybe pneumonia, and the doctor wants to find out if it is pneumonia, what antibiotic to use. There has to be a certain amount of, at that time slow, and now rather quick experimentation done on the bug that's isolated from the patient, matched up against various antibiotics, and see which are effective and which are not, and asking a lot of other questions.

Anyway, Don was for the first time developing a computer and electronics—lasers and things like that—to make much more sophisticated what had been going on in clinical laboratories for some years, which is called sensitivity testing. A simple case would be where the swab is placed on a petri dish, and it's spread out in such a way that only one cell is in each location, and then they grow up into little colonies, presumably each exactly like the first cell, so they're pure colonies. Then you hit them with antibiotics and see, by a zone of inhibition, when you stop the growth of a colony with an antibiotic. Depending on the strength of the antibiotic against the bug, it will clear a larger or a smaller zone by killing bugs. So that was basically an analog and non-computerized technique that was standard at the time. The vision was to convert it to a sophisticated technique, which doesn't even require a technician to measure the zones. It's all done by the scanner and written down and statistically analyzed and so forth.

Hughes: Now had Glaser thought of this particular application?

Cape: You'd have to ask him. I don't really remember. I think probably the answer is yes. I do recall that his main purpose was to see if you could recognize different kinds of bacteria by the shapes of their colonies. I mean, does it look like a little Mount Vesuvius or does it look more like a Mount Diablo, that kind of thing, as the cells pile up on top of each other.

Hughes: Was there anything in the literature that implied that indeed you could diagnose by colony shape?

Cape: I don't know. I think Don would know that, that he would remember that very well. But in terms of the literature that related to sensitivity testing, it is one of those funny and enjoyable coincidences that the guy who was writing papers describing what the state of the art was and what the weaknesses of it were—and those weaknesses were even simple things like the technician measures the zone and writes it down wrong—was Professor Tom Merigan from Stanford. He later became one of the scientific advisors to Cetus on totally unrelated grounds; it had nothing to do with sensitivity tests. And we laugh about it. I see him frequently at the opera now, or at Hayes Street Grill before going to the opera, and we remember those early days in 1971. We were talking to him about sensitivity testing, and it was not why he joined our scientific board, and five years later we weren't doing anything with it.

Hughes: Well, we've left you and Farley in Robertson's office. What actually happened there?

Cape: We actually liked each other very much and decided to form a company, which was called Cape-Farley—it didn't take much brains to figure that out. It was to be a vehicle that we would use to evaluate businesses, particularly start-ups, and possibly provide consulting advice to them, possibly invest in them—who knows?

Hughes: In biology?

Cape: In biology and medicine. Even today it's hard to know where one stops and the other begins.

Hughes: But you weren't particularly thinking of molecular biology?

Cape: We were, among other things. As it turned out, for a number of years after we founded Cetus, molecular biology was not manipulatable. We talked last time about Stan Cohen's article on recombinant DNA being called, "The Manipulation of Genes." If you couldn't manipulate it, well, what good does it do you? Whereas in a very closely related field, genetics, where a lot of information had been inferred about genes before it was even known what genes were made of, and even after it was determined by a series of brilliant experiments and a number of Nobel Prizes, the genes were made of DNA and that the codes were such and such and so forth, unfortunately an industrialist might still ask, *so what*? Tell us what we can do with that information, except regarding it with awe and amazement and wonder and delight. *What can we do with it?* [Pounds on table.] What intellectual property can we build around it? How can we do what we do better with it? That had to wait until recombinant DNA and monoclonal antibodies, and that had to wait even a few years again, until it could be demonstrated what scientists believed certainly to be true. "Yeah, sure," was the reaction from most industrialists until Genentech actually

proved it, either with somatostatin or certainly with human insulin that, hey, this is real.

Hughes: But we're talking now sometime in 1971 when Cape-Farley was operating.

Cape: Right, for three or four years.

Hughes: So what companies were you looking at? What was out there to look at?

Cape: Well, as I think I mentioned to you, one of the ways that turned out to be relatively easy in looking at deals was, if no money would change hands, and you were willing to share your perceptions with venture capitalists, they would let you look at their deals. It's quid pro quo. Certainly at the time it worked, and very much later on as we were selling pieces of our company, first private and then public. There was a great hunger for something new, and it was never really a major problem. Certainly compared to today where it is a major problem, in those days it wasn't.

Hughes: What kinds of companies in those—

Cape: Little startups. Largely in our case it was a device or a machine, and we got off of that one. There were other things that were non-invasive tests for blood glucose, a wide variety of things. Sexing in veterinary situations, so that you could separate male sperm from female sperm, I mean ones that had an X instead of a Y chromosome. They were all over the lot. Not too many were in molecular biology because at first there was no consensus that there was anything yet available, certainly in intellectual property, that would give you a leg up on anybody else.

Hughes: Were you in any way interested in Syntex, or were your dismissing Syntex as just a chemistry-based company?

Cape: In no way were we ever dismissing Syntex, for a number of reasons. It seems to me that the imagination that Syntex exemplified would produce people that would be excited by any new biological idea, and indeed, two of our major investors in the first round, when we went outside our founding group, were Carl Djerassi and Alex Zaffaroni. Unfortunately, for a complicated series of reasons, we never made a deal with Syntex on anything, and that includes even non-commercial things, like getting them to join what is now BIO [Biotechnology Industry Organization], at the time, the Industrial Biotechnology Association. It's complicated and beside the point at this point in the story, but notwithstanding all of the really imaginative thinking and the enormous amount of brain power at Syntex, we struck out in repeated attempts to do things for them and with them.

Hughes: I wish you'd give me an inkling of what some of those strikeouts were based on.

Cape: Well, let me select one where we learned a lesson. This is, remember, to be conditioned on the fact that my memory is far from perfect. I wasn't there. It's partly hearsay, and so forth. We—and this is one of the things I hope I'll find in my trunk—made a proposal to Syntex in the middle '70s that consisted of more than forty things that we could do with recombinant DNA, and all they had to do was take the pick of the litter. Choose two or three or four, and let's go. And I believe—I was told, anyway—well, they turned us down. I was told that we made the mistake of presenting too many things. In addition, we were told, and I don't know this to be true or not—I never asked Paul Berg about it; I never asked anybody at Syntex—but this is the feedback we got, and I don't even remember from where—that it's all pie in the sky. It was of no satisfaction at all that about ten years or fifteen years later, I thought back to that failure on our part to convince Syntex to place a bet on us, and those pie in the sky things, more than three-quarters of them, had already been accomplished. And that in fact is the story of the first twenty-five years of biotechnology. A lot of the accomplishments that were spoken about as just pipe dreams, turned out to happen a lot sooner than anybody had imagined. We think about cloning today, and everybody says we've got lots of time, and yet things are happening.

Hughes: Well, a theme that one gets from the very earliest publications is that the science itself is going to take a long time to commercialize. Stan Cohen, I believe, was saying that early on.

Cape: But Bob Swanson is not. If you'll check your records, I think you'll find that Bob Swanson is more bullish than anybody: it's going to happen sooner, and damn it, we're going to do it. And I'd have to give him a hundred percent for prognostication and a hundred percent for doing it.

Hughes: Well, I'm thinking you have to give Herb Boyer some credit.

Cape: I told you this story already. I thought it was fantastic. I was attending an international conference of biochemistry in Munich, and someone said, hey, this would work for a lot of important proteins, and Boyer said, "The thought has never crossed my mind."

Hughes: Well, the thought had occurred to him before he ever met Swanson.

Cape: Of course! What he was saying was, "You idiot! Here we show you what we are able to accomplish, and you think that we of all people need you to point this out"? That kind of laid-back response is the best. And it's the same thing as that famous sentence, which is being mentioned in paper after article after everything this year, that Watson and Crick put in, "It has not escaped our attention…" One of the key criteria of the structure they were looking for is that it had to be obvious to an idiot how it could replicate.

Hughes: Yes. But on the other hand, I think the parallel with recombinant DNA is not quite accurate in the sense that when Boyer and Cohen were first doing this work, they were thinking of a basic science technique. They each wanted to further their respective basic science interests. Who knows when the light bulb went on that this technology had applications far beyond basic science.

Cape: In fact, you're right. It's a rather gruesome memory, but Stan Cohen was at that meeting, too, and we went to Dachau together for a day. And I remember the conversation on the train, when he was explaining that his lab was either in the midst of proving or had already just proved or was going to prove that the mammalian enzyme works in the bacteria. That's very important. And his experiment was very clever, but industrially absolutely beside the point, but that wasn't the point. He was using tetrahydrofolic reductase and dihydrofolic reductase because you can distinguish between them, although they both do essentially the same thing, reduce folic acid. One is a mammalian enzyme, and one is a bacterial enzyme, and they are inhibited by different things. If he can get his bugs to be resistant to the things that disable the bacterial enzyme, there's no other conclusion but that the mammalian enzyme must have gotten in there. And so that was the sort of things that was driving them. But you're right. In its own way, it led to the biotech industry.

Hughes: What year was that?

Cape: That was '78. I remember it because I remember the year that I took my kids on a trip that ended up at that meeting.

Hughes: 1976 was the year that Genentech was founded.

Cape: Well, Herb Boyer had just announced this. I think that Bob Swanson was still operating out of an office at Embarcadero Center. They had no lab. They used the City of Hope.

Hughes: Yeah, um, which reminds me of a quote from Ron Cape:, or it could have been Pete Farley. One or the other said that Cetus would *never* do contract research. I took that as kind of a slam at Genentech.

Cape: I think we made a lot of inappropriate slams to Genentech, but I don't think that was one of them.

Hughes: Well, I'll try to find the quote. But pursuing it a bit further, what choice did a Genentech have at that point?

Cape: Well, I think—

Hughes: [Interrupts.] I should have said, it was research in a university laboratory. I'm sorry.

Cape: I told you I could list hundreds of mistakes we made.

Hughes: Right. I won't ask you to do that.

Cape: Okay. One of the mistakes we made was not to realize the enormous leverage that you get from using a university laboratory. The fact that it is enormously cost-effective—you're using laboratories and other goodies that are already *there*; you don't have to raise money and spend the money to establish them. We at the time thought that if you don't control—We were in a way making the same mistake that drug companies had, becoming a control freak and not realizing that there's a better way to go faster and cheaper. In addition, it's also worth mentioning that now, many years later, there's been a substantial number of millions of dollars, like hundreds of millions of dollars, paid by Genentech to UCSF.

Hughes: Well, also remember the circumstances. It certainly was not a given that it was okay for a company to pay people in an academic lab.

Cape: Still isn't a given. A lot of people say one thing and do another. I'm not pointing fingers; I don't even know the facts in each case. I only know that Genentech got more bang for the buck by doing that, and it is without question that their scientific accomplishment was spectacular. But it is true that if I recast that question in slightly different terms, as you've just done, yes, we were making the point that hey, they're contracting out this [research] to be done at City of Hope, and this to be done at UC San Francisco, and so on and so on and so forth. We would never do that. Yes, we were saying things like that. It wasn't just PR. We felt that this [in-house research] was a better way to go if you had enough money to go that way. And I think that they beat us because of the excellence of their scientists in cloning, getting human insulin and getting—

Hughes: Well, that doesn't seem adequate to me, because you had excellent scientists, too.

Cape: Well, somebody's got to win and somebody's got to lose. And there is utterly no point in denying that by 1982, the score was three to zero and then suddenly became four to one and then five to two or something. They were doing a great job.

Hughes: But another thing is, they were focusing; they were selling themselves as a recombinant DNA company. Cetus was going out of its way to say it was *not* just a recombinant DNA company, that it was an antibody company, it was an industrial enzyme company, and so on.

Cape: By the way, Genentech went in all those places later.

Hughes: True.

Cape: It's all a question of what you can sell to the analysts and to the press and to your investors as being a good idea at the time.

[End Tape 3, Side A] ##
[Begin Tape 3, Side B]

Cape: Mind you, they were going to do it with recombinant DNA, but so were we at the time. Genentech's first big monoclonal antibody, Herceptin, is a monoclonal antibody. Their timing of their many things, their Hoffmann-La Roche deal, the way things played out after the Hoffmann-La Roche deal—they did very well at everything they did, and they're still brilliant. To mention their mistakes is like talking about Barry Bond's strikeouts. So what?

Hughes: Let's go back to Cetus at the earliest stage. So you've got some interest from the investment world. You've got a general plan, which is to look at startup biology-based companies and see if they're worth an investment, and you've got Glaser's microbial screener. So what happens? Where's your lab, and where are your people?

Cape: Well, our first lab was in the marina at the foot of Bancroft Way. We had labs from the very beginning. We had people working in the labs from the very beginning. I say from the very beginning, six months after raising our own first money.

Hughes: Where did you get money?

Cape: That is something I wanted to say: we had no trouble getting money *ever,* up to the debacle at the FDA in 1990 or whenever it was.

Hughes: Yes, 1990.

Cape: We had no trouble raising our initial money from ourselves. We had no trouble raising more money from a partnership which included Carl Djerassi and a couple of investment bankers to join us. We had no trouble raising money from the drug companies. We had no trouble raising money from the public market over and over and over again. We never had any trouble raising money. We never worried about a payroll. That was never a problem. We worked hard in each case. We didn't wing it. But the fact is that the frustrating thing that we've seen in the last five years simply didn't exist.

You asked earlier about hiring scientists. We were hiring scientists from all over the place: university labs, Lockheed, all kinds of people. The people we were hiring from industry were really worried about security. Why should we go with a little company that might be failing in six months, when we're working for Lockheed. Then all of a sudden Lockheed lays off tens and tens of thousands of people, including their buddies. It's pretty paradoxical.

Hughes: What was it that was capturing people's imaginations, or was it many things?

Cape: It was many things. But primarily it was a combination of two things, the unbelievable nature of the discoveries which were being harnessed and the accomplishments that were being made, and the very easy extrapolation: there had to be more, there had to be more, there had to be more. There was relatively little emphasis on the things that we know about now, for example, the diabolical way in which cancer resists any rational attack on it. And the second thing was to invest in health pushes a different button in everybody than to invest in anything else. This has been demonstrated repeatedly, because there have been love-hate relationship oscillations between the financial community and biotech from the very beginning. I remember David Padwa's company, Agragenetics, came within two or three weeks of getting their next slice of money in 1983, and the deal fell through, and Agragenetics disappeared.

I miss David Padwa. He retired to Santa Fe, I guess, and he's just a charming, brilliant executive. He first got the idea of pulling together seed companies when nobody else knew what he was talking about, and look at Monsanto now, Pioneer Hybrid, Cargill, and so on. And look at the huge worldwide fight about Frankenfoods and all of that stuff. My only point here is, and I got off the subject, even after being burnt three years ago, the investing market was back again—repeatedly, over and over. Have these people got no memories? No. They're in love with the idea of curing cancer or finding some super-huge opportunity. There are super-huge opportunities before us today.

Hughes: As early as 1983, there is a raft of these little companies being formed, these biotech startups.

Cape: Have you got a count of how many?

Hughes: I've seen tables. Do you know the book by [Martin] Kenney? He has a table listing foundation dates for early biotech companies.[2]

Cape: It must be on a semi-log scale, because when we formed the Industrial Biotechnology Association, which was probably in 1981, we could find only seven companies to found it. Everybody else was so small. There was Amgen; there was Genentech—no Genentech refused to come at first; they eventually came—

Hughes: Genex.

Cape: There was Genex. There was Cetus.

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2. Martin Kenney, *Biotechnology: The University-Industry Complex,* New Haven: Yale University Press, 1986, p. 140.

Hughes: Hybritech?

Cape: No, Hybritech formed after Genentech. They were very tiny.

Hughes: Well, it begs the question, how do you define a biotech company?

Cape: That's true. Oh, you'll run into a little bit of argument if you talk to people like Ori Friedman at Collaborative Research or David Schwartz at Bio-Rad who claim, hey, we were there ten years earlier. Okay, good for you; you started it. I mean, who *cares*?

Hughes: Unfortunately a lot of people do care. Anyway, my point is that by say the mid 1980s, there are a lot of companies to which investors interested in putting money into biomedicine could go, and yet so many of them go to Cetus. You've just said that you never had trouble raising money.

Cape: I know that Amgen went through a very bad time before they finally found themselves. Genentech I don't think ever really had any trouble.

Hughes: They always made a profit. Swanson was very proud of that. Sometimes borderline.

Cape: But in any event, the supply exceeded the demand. I remember there was a time when I said there haven't been any big failures. Well, that's not true anymore. Or you get companies that are absolutely spectacular scientifically. Take David Martin's Eos, which gets sold [in 2003] for less value than Cetus had in 1975. And so the rules have changed; the world has become very cynical. As a matter of fact, when I was trying to raise money for Darwin [Molecular Corporation]—very difficult. I'd use the argument, "Look, you're being given the opportunity to come in at the ground floor, and Bill Gates and Paul Allen have paid their price. Okay?" That wasn't good enough for a lot of the people who were my personal friends. The attitude was, they've got lots of money, what do they care?

Hughes: Did that come as a real surprise after your experience with Cetus?

Cape: Yes. And that was for much lesser amounts of money.

Hughes: It seems to me that biotech and the average investor's philosophy are in total disarray.

Cape: You've got me here, let me tell you my version. When I was raising money for Darwin, I said, "Look, you're my friends. I've got to tell you the truth. You're talking about a business which, unlike Japanese watches or Intel chips, has a turnaround time of ten years between the discovery and when you're going to get some money from putting your product on the market. A large amount of

that is regulatory, but nobody disagrees with the fact that the consumer protection component of that is extremely important.

But let me just cite to you the success story. The success story is Amgen, and it involves a cash flow of negative half a billion dollars before you turn around, and probably another three or four years after that before you break through and net net you're in positive territory. And anybody who goes, "*What"?* I say, "You know what, you shouldn't invest in biotech. It is sort of insane compared to the rest of the world." Maybe I turned off a lot of people with that story. But that is the truth. And a lot of people know that if they discover that the cancer cell is incredibly clever, but also they suddenly wake up to the fact that people with a whole half a billion dollars, maybe [inaudible] larger now. Small wonder the model now, which it wasn't then, is you've got to be in partnership with a drug company. Now again, I think anybody who would have been in insulin would have said, you've got to do a deal with Eli Lilly or maybe the Danes, but you've got to do a deal. There's no point in trying to set up an infrastructure to try to fight it out in the market with them. And Genentech, fortunately, got a deal with Eli Lilly, so human insulin had an easy entry to the market.

Hughes: What difference, if any, did it make that you were in the Bay Area, rather than almost any other place in the world, where there was a history of investment in high technology companies? There was in a sense an economic infrastructure there in the form of the venture capital industry and all that goes along with it.

Cape: Well, there are a number of obvious things that I'm going to say. I was not in any way special in California. I was an immigrant to California. The population of people in California, in particular in the Bay Area, consists of a self-selected group of people who are willing to turn their back on the past, on tradition, on what you might call normal things, including cost-benefit analysis of risk. It may be a lousy comparison, but in the East the concept of failure in itself is a self-fulfilling prophecy. Nobody wants to take a risk because they think that their reputation will be ruined forever. In the West, people fall on their face over and over and over again.

What used to be the West was Illinois. Abraham Lincoln lost nine of his first eleven elections. You'd think he'd get the message that people didn't want him? No, he bounced back. Which reminds me of my one conversation with Donald Rumsfeld, who was once the CEO of Searle, which came up with Equal and the birth control pill. And I was teasing him—it was a cocktail party—about the fact that he was on the board of a company called Gilead, which, by the way, is now worth billions, and they seemed to be changing the game plan every six months. And he said, "That's not what's important. What's important is that the CEO bounces up off the floor after every defeat. He comes up with something new. He's charging ahead." That really is something that might be acceptable in California. It's not acceptable in Boston. I think things have changed in these

generalizations. But by and large, that's the way it was in 1970, and what you were asking about was 1970.

I think one of the biggest ingredients of it all isn't all that, though it's important. It's the concentration of universities in this area. Boston has that. There's nothing like a role model, or, as Don Glaser would say, the existence principle. Those guys said, "Show me it can be done. Damn it, we can do it just as well as they can!" And that's, I think, what overcomes the reticence by the investors and by the entrepreneurs.

Hughes: Do you want to tell the story of naming the company?

Cape: Yes. I also want to tell you the story about the logo of the company.

Hughes: Okay.

Cape: The name of the company: everybody's suggestions were thrown on the table, and they involved a lot of conventional things, which, at the time, I thought were meaningless. Now I have the feeling they are intentionally meaningless: Applied Biological Laboratories, Inc., Advanced Concepts in Medicine, Inc. The kinds of things that are generic, and after you've heard about a hundred of them, you can't tell one from the other. Well, that kind of anonymity can be useful. Amgen stands for American Microbiological Genetics, or something like that. Who remembers that? They remember Amgen.

Hughes: Well, Genentech is Genetic Engineering Technology.

Cape: That doesn't sound like any name that you've ever heard before. Other people were trying all kinds of little word pieces. And we had a number of those. We also had a number of words for 'first', whether they were in Japanese or in Hebrew or whatever, trying to be a little bit exotic. And we were going around in circles. We had nothing we really liked. Don Glaser and Moshe Alafi had had a company called Berkeley Scientific Laboratories. That's what in my prejudiced mind I was trying to stay away from. I wanted a *name*.

Well, one day, Calvin Ward, who spent a lot of time diving for abalone, was bitten by something which, at the time, we thought might have been a killer whale. Suddenly, "Whale, hmm, not bad. Cetus." It is a constellation; that's also good. We had been thinking, among other names, Andromeda—the location of a nebula. A lot of companies name themselves after stars or constellations. Well, it turned out, too bad, it was a great white shark. They proved it by the number of bites and the size of the teeth. But somehow the word Cetus caught on. We liked it. We didn't like it when in their brilliance, the journalists were starting to talk about Cetus being a beached whale. I guess anything you choose makes you a target if somebody wants to be clever. But we liked the idea, and as it turned out it was very convenient because all of these whale logos and symbols are

available super cheap. I used to get gifts; that was the downside. What are we going to send Ron? Send him a whale of some sort. I have a large collection of whales. When Cetus ceased to exist, I put them all in my office, and it was first come, first served. You could take one thing and out you go. And they all disappeared. They were really great.

But anyway, we liked the name Cetus, and we started out with Cetus Scientific Labs. After a while that "Scientific Labs" had some of the feeling of the old generic names, and we changed it to Cetus Corporation. Doesn't mean anything. A nice thought that appeared in the story was, here is a company that deals with the smallest elements of life, and they've chosen the largest living animal as the logo.

Hughes: But you didn't think of that when you were choosing the name?.

Cape: No, we thought of the constellation. Now as to the logo, we hired a design firm, whose name I've forgotten, to come up with representations. They were all labored. None of them caught my attention. I remember sitting in my home watching the World Series, flipping through magazines, and it occurred to me that what I would do would be when I saw a 'C' I liked, I'd cut it out. And when I saw an 'E' I liked, I'd cut it out. And it turned out there was a type style, which is what Cetus is, which is represented—and this is another paradox or irony—in Chevron and Standard Oil. The 'C' is from Chevron, the 'E' is from Chevron, the 'T' is from Standard, the 'U', well, it must have been the 'N' upside down, and then the 'S' again from Standard. And then the last stroke of genius is that, since we're talking about a marine animal, the 'E' could very nicely be replaced by a trident. That's the logo. Later on, when Chevron invested in the company, I told them. They had no problem with it.

Hughes: You say, "Who's interested in first?" Nonetheless, I'm going to ask you. Is Cetus the first biotech company?

Cape: Yes and no. The question is what constitutes the New Biology. The New Biology can be defined in a number of different ways. Genentech defined it in a way their self-concept found agreeable, and I think that's an acceptable way, and they would be the first company.

Hughes: Meaning—

Cape: The things that have been invented just about now. As opposed to our attitude being, anything that derives from the new insights into the secrets of life that started right after World War II, in fact, a couple of experiments preceded World War II or were used in World War II. Demonstrations that DNA is the genetic principle was [Oswald T.] Avery, [Colin M.] MacLeod, and [Maclyn] McCarty, and I think they published in '44. Anything that is based on that is the New Biology. Since Collaborative Research, Ori Friedman's company, was selling

tools to do that biology, they could be the first company. A connection that I found nobody ever makes is that Marshall Nirenberg really did what was claimed was done two years ago: he deciphered a genetic code, using Millipore filters. Therefore maybe Millipore is the first biotech company. Or I'm sure that some of Dave Schwartz's columns for separations were used in some of the key experiments.

Hughes: Well, I'm sure there are others too, if you're going to use an instrument as a link.

Cape: But it would be nice to be the first.

Hughes: Well, you can define it so that you are. [laughs]

Cape: That's right. That's what I'm saying. Isn't that transparent?

Hughes: Yes. A prospectus that Cetus circulated to prospective investors—and I don't have the date, unfortunately—said, "We are proposing to create an entire new industry, with the ambitious aim of manufacturing a vast and important spectrum of wholly new microbial products using industrial microorganisms."

Cape: That could have been as early as '72. And we did. As a matter of fact, our custom work for Schering, which kept us alive for five years, did produce new bugs for them to make their antibiotics. And we were using certain principles of genetics ,which I don't remember at the moment.

Hughes: And Glaser's microbial device?

Cape: Oh, no, no, we scrapped that after six months. I remember a board meeting at which we said to the board, "This is going to be a hard sell. We're not sure we've got the technology in a way in which can really do everything we've told ourselves we're going to promise." And here is Schering that would like to pay us handsomely to give them a hand in improving the human antibiotic strain.

Hughes: Well, how were you going to do that?

Cape: By selection of the best mutants by other means than Don Glaser's flying spot scanner or any variation of it. It seemed to us one of the things that's long been known has been that the behavior of a bug on a jelly, usually a nutrient gel where you spot things like he was doing, simply does not correspond to its behavior in a vat, when it's in a solution, growing, like making beer. And damn it, that's that way antibiotics are made. So why select on the basis of how it does sitting on a surface, when in point of fact it's not something that's going to function in industrial production. So we created basically our version of mini-wells, and inspected the mini-wells. What we discovered was, most important, an absolutely low background-noise situation. We built incubators that didn't vary one-tenth of a degree from one side to the other, from the top to the bottom, and

we discovered that doing so removed the large part of background noise. You can actually see differences that you couldn't see normally because there is so much variability from one test tube to another. And it worked.

Hughes: So this was a selection process rather than a mutation.

Cape: A mutation and selection.

Hughes: How were the mutations being created?

Cape: Oh, I believe we tried a lot of different things. Mutagens, radiation, I don't really remember. But we created the mutants. Schering didn't supply us with the mutants. And we had a lot of geneticists of great standing.

Hughes: On your board.

Cape: Yes.

Hughes: You're thinking of [Joshua] Lederberg and [Stanley N.] Cohen.

Cape: Well, Cohen was more specifically for recombinant DNA. That methodology was so discontinuously brilliant. The people I'm thinking of in terms of bacterial genetics are definitely Josh Lederberg, definitely Sir David Hopwood.

[End Tape 3, Side B] ##
[Begin Tape 4, Side A]

Cape: He's as knowledgeable as anybody on earth about all matters relating to genetics, of actinomycetes, which made penicillin and cephalosporin particularly microorganisms. Sir David Hopwood, who wasn't Sir in those days, was one of our very early consultants, as was Arny Demain, who had been a microbiologist at Merck for many years, who wanted to bring the industrial input and the scientific-academic input and mix them all together. Those guys got along very well with each other and helped us a lot.

Hughes: By whatever means, you did come up with strains that were more productive than whatever Schering had originally?

Cape: Yes. And they paid.

Hughes: Did they pay on the basis of producing them?

Cape: My memory is fuzzy on this point. I know that they paid in terms of the amount of work we put in, which was priced in such a way that we were sure to be profitable. And I believe they paid us if they used what we came up with.

Hughes: I see. How was the relationship with Schering established?

Cape: Well, we were going around talking to whatever other drug companies would talk to us. The chief microbiologist at Schering, Marvin Weinstein, was convinced that we were right, and he made a gamble on us, and he convinced his superiors, and they continued to feel that this was a good decision, and they kept it up for more than five years.

Hughes: There's a quote that I've seen several times from [Peter] Farley – something to the effect of being thrown out of pharmaceutical offices. Was that in regard to recombinant DNA?

Cape: No, but that happened with recombinant DNA as well. It's fairest to say only that the majority of drug companies considered us as self-serving promoters with very little to offer them. I could be less generous in characterizing their opinions because a lot of them would not take chances, and I will come back to that in a minute. But the fact is that from the very beginning, those who didn't accept what we were trying to sell exhibited various versions of hostility, and in the extreme cases, we would basically be shown the door, and that's what Pete was referring to. I'm sure that Genentech and other people have made this point, that it was a blessing to find Hoffmann-LaRoche and Eli Lilly, because the vast majority of those companies didn't want to talk about proteins at all. They didn't see that this [recombinant technology] had anything to help them. And their reactions varied.

And now it's an opportunity to make a point about Syntex. Syntex was in that hostile camp for no reason whatsoever. Maybe they were against proteins. But they characterized us as a bunch of promoters, and nothing much more. And when we asked them to join the Industrial Biotechnology Association– this was a trade association with political and public relations and many other things, and big companies like Monsanto and Eli Lilly were joining—and they kept characterizing us to our face as a bunch of promoters, and they didn't want to be associated with us.

Hughes: But Carl Djerassi was on your board.

Cape: Didn't help. So when Pete made that remark, there's a certain amount of attention-getting in the words he used. But we were treated very badly. I remember one guy, he didn't throw us out the door—they even served us lunch—but he said, "If you ask me, and name a good price, you can have my wife, but you can *not* have my bugs!"

And now comes my pop psychology. If you take a look at two populations of people, people in the existing pharmaceutical industry who've grown up in it, and people in biotech, they do come across as establishment on the one hand and promoters on the other. A man looking at his career in the traditional business

has everything to lose and nothing to gain by betting on your new idea, because it will never pay off when he's still rising in the organization. If he's right, somebody might mention that, but he's long since retired, it didn't do him any good. If he's wrong, and somebody decides that they're wasting their money, his career is severely crippled, his family is hurt, there's nothing for him to gain.

In the biotech camp—we're talking about the Genentechs and the Amgens and people like that. They've got everything to gain and nothing to lose. That's the kind of business they're in. They're funded by venture capitalists. They're looking for an enormous swing up, and the culture is such is that if they fail, fine, try again. You're good guys; you've given your best shot.

Hughes: Why would a pharmaceutical company contract with a small company, such as Cetus, as opposed to adopting the technology, creating a group, and all that would be entailed in bringing a technology in house?

Cape: There are two phenomena going on. Everyone knows it. There's what they call the NIH syndrome, Not Invented Here. If you've got an enormous investment in your research staff and in the buildings they occupy and everything else, you're going to lean, for that reason alone, towards using them and considering them to be very smart and having them do this work instead of contracting it out. I think that there's also the question of letting your secrets out. But on the other hand, there's a make-or-buy duality that's also characteristic of big business. The automobile companies do it; the airplane manufacturers do it. Those are solid fundamental industries. Sometimes it pays to go outside. The same make-or-buy decision by Genentech and Cetus that we were talking about earlier.

Fortunately for the biotech industry, fortunately for us, in specific terms, a number of companies decided that if they weren't in there at the forefront, like Merck is in research, it's going to take years to catch up. Why not just jump on one of these bandwagons and see where it leads you? Schering did that with Biogen for interferon. The contract was a pick of the litter. Look, we don't know where you guys are going, and we don't even know if we're going to want one of your products, but we want the first three picks. Okay? I'm speaking very, very generally about a contract I've never seen. But that sort of thing is a good way to split the difference from year to year. There's no question that for a number of reasons, the whole relationship between drug companies and biotech companies has drifted in the direction of relationships at the research level. The drug companies still want to be sure they're not betting on some crazy idea that has yet to be proved, but once they're convinced, they repeatedly show that they will jump in and form partnerships. And it's good for the biotech companies too, because they don't have to think of investing enormous amounts at fixed costs in regulatory, market, all that kind of stuff that the drug companies already have in place.

Another thing is the fact that increasingly big companies are realizing that research is a *huge* fixed cost. If they can make it a variable cost, it's something to think about carefully, and some of them have gone in that direction. Let's assume that you want to cut your research budget. What are you going to do, fire five thousand employees, shut four different locations down? If you decide that your research isn't going well, you fire off a letter to the biotech company that's working for you and say, "We're invoking the sixty-day clause in our contract. We're done." And suddenly, with no effort at all, no firing is necessary. It's somebody else's problem. And that has a certain attraction to drug companies.

Hughes: There was a contract with Rouseel-Uclaff. My notes say it was to produce vitamin B12. That was another use of this microbial selection method?

Cape: I believe so.

Hughes: The contract was signed in January '81.

Cape: I don't have any vivid recollection of that.

Hughes: Is there a story to be told about the interaction, or lack thereof, between the executive board and the scientific board?

Cape: I don't think there was ever any great interaction between them. The purpose of getting the scientific board together was to help these scientists. At the same time, there were a couple of members of the board who would attend the scientific board retreats—talk. There was never any attempt to keep them apart. To say that Carl Djerassi wouldn't be talking to Stan Cohen and Josh Lederberg is crazy. First of all, obviously you'd be encouraging them to do so, and second of all, he would hesitate to tell the board what he thought after those conversations. There was never in my mind, or brought to my attention, any sense of an isolation of the one versus the other.

I'd be inclined to say that every biotech company should be aware of the fact that the scientific board has an evolving relationship with the company. It's incredibly important in the early years. In later years, however, you run into the problem that the scientists, if you picked excellent ones, are up to their ears in their work, think about it all the time. As an example, I was on the ski lift once at a scientific meeting, and I happened to be sitting beside a woman who was a waitress at a Mexican restaurant there, and she said, "You guys are crazy. You talk science until midnight! I mean, most people who come here, when they're starting to drink beer, they start talking about what everybody else talks about—sports, women, whatever. You guys talk science all the time."

I really think that as time goes on, the working scientists get not possessive of their work, but they tend to resent people, just because they're famous or very smart, trying to pull rank on them, if I can put it that way. The best relationships

with scientific advisors are one on one—the guys who come in, visit the lab, sit down, chat with the scientists at great length. They *love* that. And the more brilliant and famous the guy is, the more they love it. But the scientific board acting as a board, if you like, a court of star chamber, they increasingly resent it, because they feel the guys haven't done their homework; they don't even know the details of the experiments, and they're making pronouncements.

Hughes: Cetus did not have an exceptionally large scientific board, at least by biotech standards, but it was an exceptionally prestigious board as well. How many Nobel Prize winners?

Cape: Six. There weren't at that time that many in all of Canada.

Hughes: Was that a good idea?

Cape: Yes. I saw that as my present to the guys, and it worked out that way for, I'd say, about ten years. To have the opportunity to see Francis Crick attempt to convey some new insight without the use of a projector and without even the use of a board, just with his hands, is like going to see Michael Tilson Thomas compose in front of you. And the opportunity to hobnob with those guys for two or three days in a retreat once a year—they seemed to love it.

Hughes: [Interrupts.] "They" being your scientists. What about the Nobel Prize winners?

Cape: Oh, well, they liked coming to things, I have no doubt of that. It is, however, true that I did constantly have to remind them that their job was not to sit at a table with each other. That we don't need! They can do that on their own time. But we want them to be spread around so that everyone can enjoy them.

Hughes: Why were they willing to serve?

Cape: The concept of real-world benefits from their insights I think was genuinely intriguing to them. They enjoyed it. Scientists enjoyed mixing with other scientists. And those meetings had lots of stories come out of them, and lots of interactions come out of them. As Frank Sinatra would say, they were a real gas. I remember once, in a feat of embarrassing manipulation, I wanted to keep those guys working as long as possible, so I put Francis Crick on at eleven o'clock at night. In retrospect, it was a dreadful thing to do. But they all grooved on that. Kary Mullis gave presentations year after year after year. He was hooted down and nobody realized how great he was. I give ourselves some pat on the back for continuing to fund it. PCR [polymerase chain reaction] wasn't reinforced until late on by anybody. Everybody thought he was nuts.

Hughes: Including your prestigous Nobel Laureates?

Cape: No, not so much. Kary enjoyed the audience. He enjoys audiences, generally. But the point was, the retreat was definitely a recreation. It was partly to move the company's scientific policy forward. But at some level you can't just force things out of people. It was also semi-recreational. That's what guys in that field liked to do. Something good is going to come of it.

Hughes: When did the retreats begin and where were they held?

Cape: I don't remember when they began. My guess is that they began in the late '70s, maybe even in the middle '70s, and they continued up to the late '80s. They occurred – let me just name the places: Asilomar—the Holiday Inn at Seaside, near Monterey, right on the beach, as it was then; then changed its name, then changed its name again, but it was all the same hotel, the same logistics and everything; the Holiday Inn at Napa; the convention center in Monterey. The last one was just during the merger with Chiron—Pajaro Dunes. But the usual local places you would go to get away but not quite.

Hughes: Both the scientists and the scientific board made presentations?

Cape: Yes.

Hughes: The retreat was a series of presentations and discussions?

Cape: That is correct. And there were also breakout sessions about specific interests, which instead of having 200 or 300 people in a room would be 40 people in a room.

Hughes: And it was stimulating?

Cape: I think so. But you've got to ask the people who went what they thought.

Hughes: I've read in several places about E.F. Hutton's conference on biotechnology in the fall of 1979, which some people bill as the first conference on biotech. Apparently, somebody from Cetus went. Was it you?

Cape: No. Because all I remember are negative things about E.F. Hutton. Their chairman presumed, without contacting us at all, to be describing us and suggesting what we were worth. I'm not sure of any of this because I wasn't there. And because of legal and other reasons, we were advised not to get into an argument with him—just don't talk to him. And I never did. But it seemed pretty nervy to be representing yourself as knowledgeable about people that you've never had conversations with.

Hughes: The name that I associate is something like Schneider.

Cape: [Snaps fingers.] Nelson Schneider? He was the chief of their biology practice. That's a different matter. I interacted with him a lot.

Hughes: Now was he at E.F. Hutton?

Cape: He may have been. And as a matter of fact, I think he claimed that he invented the term "biotechnology" and tried to copyright it. What a silly thing to do. I attended numerous meetings with Nelson there, and he was a very intelligent guy.

Hughes: What came out of it, anything?

Cape: No. We never had a relationship.

Hughes: Here's a quote from Ronald Cape:, and I don't have a date. "We're not a recombinant DNA company per se, we're not a hybridoma company per se, we're not a mass screening company per se, and we're not an industrialization and fermentation technology company. We're all of those."[3]

Cape: I think that's good thinking. I hope I said it. It turns out that it was the wrong thing to say at the wrong time. Only Genentech has ever said we're purely a recombinant DNA company, and they made it happen, and they made it happen with bells on. But with all these developments in their just starting phase, why should you define yourself out of just going where your common sense tells you to go as opportunities show up? Seemed reasonable then. Still seems reasonable.

Hughes: There's also something I've read along the lines of Cetus insisting on a large market. It is contrasted with Genentech policy which *supposedly* made market less important. Do you buy that?

Cape: No. But they might have said so. It might be inferred by some self-appointed expert. They went after somatostatin, which has a small market if any; that's a zero market. They went after it to demonstrate a point. They demonstrated it brilliantly, leading to that question in Munich. But their first new product was human insulin. That's not exactly a small market.

I went to a famous meeting at the National Academy of Sciences where Jeremy Rifkin was making the Nazi salute and taking over, as happened in those days. Activist after activist assumed the podium and was putting down human insulin as a plot of big business, and what's wrong with pork insulin, and this and that. They came from a doctrinaire position: my mind is made up and don't confuse me with the facts kind of thing. I remember that vividly.

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3. Sharon McAuliffe and Kathleen McCauliffe, *Life for Sale*, NewYork: Coward, McCann & Geoghegan, 1981, p. 38

There's been a lot written about UCSF's Mission Bay project. The *San Francisco Weekly* or the *San Francisco Bay Guardian* had a big article on it, and the theme was the establishment guys, rich guys, are behind this, so it's gotta be bad. And we don't know how yet, but we'll find out. I spoke with Bill Rutter about that. I think he said the thinking behind that was, UC is under enormous constraints by virtue of being a public institution and even more so by being a state institution. It was felt at that time that if they could somehow, in some ways, privatize the Mission Bay project, they could go a lot faster and get done what they needed to get done. Anyway, I'm just saying that what people—including the biotech people—say about these various markets, and what they say about Frankenfoods—they've got an agenda, and you can almost predict what they're going to say.

Hughes: The annual report of 1981 stated, "Cetus is not merely a recombinant DNA company," which of course it wasn't. But I also wondered what part of that, if any, was to distinguish Cetus in the public mind from Genentech.

Cape: Partly true. I'm making this up in retrospect. I don't remember, but it would make sense. In our prospectus—we went public in March of '81—some of the nicest pictures were recombinant DNA pictures. And it's also true that we were operating under the perception that Genentech left a lot of money on the table. They were far more famous than we were. They were so famous that they became a household word—Johnny Carson's program and places like that. Their stock took a huge jump on opening day, and I remember the headlines, big block letters in the *Chronicle,* "Genentech Rocks Wall Street," or something like that. But we raised I think three times as much money as they did. We wanted the image, I think, to be that the pie is even bigger than it has been represented so far. When we grossed a hundred and twenty million dollars, except for Comsat which was a government corporation, we were the largest IPO in history.

Hughes: Well, let's go to the IPO, and again a quote. This one came from the *Wall Street Journal*. Pete Farley was quoted as saying in August of 1980—

Cape: That was before Genentech went public.

Hughes: Just before the Genentech IPO in October.

Cape: I bet you're going to say he said we're not going public.

Hughes: That's about what I was going to say—that Cetus would not go public until the mid-1980s.[4]

Cape: We changed our mind.

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4. "Cetus is second firm in genetics filed planning to go public," *Wall Street Journal*, December 3, 1980, 20.

Hughes: The question is, why did you change your mind?

Cape: Because we could. It was demonstrated by Genentech's success. I'm making this up again. There may have been ten reasons. The one that's obvious now—Monday morning quarterbacking—was since Genentech demonstrated that there was this great hunger out there—and everybody is aware of the maxim in finance, particularly in biotech finance: the time to take the hors d'oeuvres is when they're passing them around—suddenly we saw that we were the only other visible game in town, and it would be silly to pass up the opportunity; that would be very bad business planning.

Hughes: Plus, you know, building on what you had said, just a statement or two before, Genentech had left stuff on the table. I mean, it would—

Cape: [Interrupts. Inaudible.]

Hughes: What did you have to do? That meant moving fast, didn't it?

Well, yes and no. The investment banking industry is a remarkable engine. You say moving fast. Genentech went public—was it in October?Cape:

Hughes: Yes.

Cape: We didn't go public until March. We were pretty busy.

[End Tape 4, Side A] ##
[Begin Tape 4, Side B]

Cape: When you realize that suddenly an opportunity presents itself, you gear up as quickly as possible and take advantage of it. There was a one-hundred-million-dollar fundraising that we got done in three weeks, two or three years later. Part of the reason was the entire team, the people who'd done it before, were in the same job to do the same thing. So it was, okay, DO IT!—all the elements of it, including careful marketing and legal things involved in the prospectus involving the road show: where do you go and how do you do it, and how much time is it taking, how large is the team? They're all logistic questions. It doesn't take a rocket scientist, as they say. But somebody's got to know what they are.

Hughes: Those are not things you had learned in business school?

Cape: No. I mean, you learn about it, but that's not the same thing as knowing who the people are.

Hughes: To whom did you go?

Cape: They came to us. After Genentech's success, Wall Street woke up to the fact that here's an enormous opportunity, and suddenly we were besieged with investment bankers asking us to let them take us public.

Hughes: Who eventually did?

Cape: We eventually chose two, Lehman Brothers and a company that doesn't exist anymore, L.F. Rothschild-Unterberg Tobin.

Hughes: Why those two?

Cape: Well, the guy who did those things at that time at Lehman Brothers was Fred Frank, who was then, and may still now be—although we're all getting on in years, so I don't really know if that's true today—the most knowledgeable, the most personable, and therefore most attractive person to be our number one contact. And we wanted one other company who'd done a lot of high-tech deals, and Unterberg Tobin, which had recently merged with L.F. Rothschild, was such a company. We liked Tommy Unterberg very much, so we told the two of them to work together, and they did.

Hughes: And it was a smooth sail to the March opening?

Cape: Apparently so, although we didn't have a first day like Genentech had. The stock sat there for a long time, and that's not a good outcome.

Hughes: Why was that?

Cape: Maybe we asked too high a price, maybe we sold too many shares. I don't know to this day why. The stock didn't move up quickly, at least in a dramatic way like Genentech did, not that this was very good, because that means a lot of people sell the stock. So suddenly you're dealing with a whole new population of buyers. We took satisfaction that we had the money, and we had it in the bank. And with the interest rates in 1981, we could sit there forever. The interest rates were twenty percent.

Hughes: Did people make money on the IPO?

Cape: I don't know. And from what I read in the last two or three years about what goes on on Wall Street, I now know how much I didn't know, and I still don't.

Hughes: What difference did it make to the day-to-day operations, or in any way, that now Cetus was a public company?

Cape: Not anywhere near as much as people like to think. I was on the board of another company recently. They carried on at such length about the difference. The differences have very largely to do with relationships with the public—the legal

obligations as well as responsibilities, communications—that's also been in the papers a lot. I'd say a large amount of that is absolutely necessary. But a large amount is stuff you have to go through is paperwork, paperwork, paperwork, which almost gets you thinking it's make-work. I don't want to overstate the case. All I'm saying is that the extent to which it changes your life doesn't very much affect the creative engine that is your science, that is your value. We tried as much as possible to shield those people from it. They were perfectly happy, I think, to be shielded from it, except to the extent that it's necessary and to the extent that you have to point out to them that they may or may not be insiders. But if they come up with some sensational discovery in the lab, they are the ultimate insider, and they'd better not trade the stock under those circumstances. We had very little trouble with that sort of thing.

We had one run-in after our disaster with the FDA where the strike[?] lawyer firm in San Diego sued us because the implication is if your stock drops dramatically, you knew something that the other people didn't. You make that assertion to the court, and then you settle for what the insurance will cover. In those first eighteen years of being public, I can't remember any significant problems except the enormous additional overhead it takes to be a public company, and the fact that you have to look at your price every day. In some places they try to pretend that nobody cares, which is sort of ridiculous. I think Genentech—again, I don't know this—but I believe they posted the price of the stock on a bulletin board every day. Why not?

Hughes: When I was doing research in Corporate Communications, which was maybe ten years ago, there were monitors with the stock price visible.

What was Cetus's early policy about stock options?

Cape: Oh, we tried to be as liberal as possible, as generous as possible, and price them at as attractive a price to the employee as the lawyers would tell us is okay. Just to make a contrast: since I'm originally Canadian and serve on a number of Canadian boards, I've been astonished at the reaction that shareholders in Canada have that they don't realize is counterproductive. I think in fact the game may be over with these recent changes in how options are handled. Although to companies that are losing money, I don't know how all of these things apply. But the shareholders seem to begrudge the prices at which stock can legally be optioned to employees, considering this inappropriate dilution. I understand where they're coming from. It's a legitimate point. But it's overwhelmed by the fact that if the government has policies that permit you to use non-cash incentives, and cash is so hard to come by sometimes, and this enables you to hire people away from university labs and big drug companies at will, why not do it? I think all of the biotech companies had the same philosophy—for God's sake do it! We can't do better than to get the best people you can get. And one of the best ways to get them is to give them a lot of stock options and price them as low as possible. And I don't ever remember any shareholder objecting.

Hughes: Interesting.

Cape: Yes

Hughes: Well, let's stop.

[End of interview.]

Interview 3, August 21, 2003
[Begin Tape 5, Side A.]

Hughes: We are talking more systematically about Cetus, and I have some questions today roughly categorized as on the business aspects. My first question is, when you were founding Cetus, did you and Farley, and I include Farley because you both have MBAs, have a specific business model in mind?

Cape: No, we were aware that we were in uncharted territory. The field [biotechnology] didn't yet have a name. That was ten years in the happening, right? The one thing that we did know was that we'd have to make it up as we went along. First of all, I think one of the things both life and business school teach you is that there are a lot of different successful ways to run a business, and, that to a large extent, any business is a manifestation of the personalities of the founders and of the creators and of the CEOs. Sometimes that's all the same person, particularly in a science- based start-up. But that we'd have to take it one step at a time and just see what happened. I think some of our investors had their experience in larger companies, both investment banks as well as more established companies of the '60s, where you made a product, you sold the product, and it was much more conventional. Here we were talking about biology, which, until the early or middle '70s, was never even harnessed. Certainly *modern* biology hadn't been harnessed. Quite clearly the drug companies growing up various biological products—vaccines and later antibiotics—had businesses. But I'm thinking of those inventions for which Nobel Prizes were awarded between 1945 and 1972. Harnessing just hadn't happened, and that's why the startups just started in the '70s. I think we basically dealt with the specific alternatives that presented themselves.

One thing that does come to mind was—and I think I've mentioned this before: somewhat of a truism that turned out to be a straw man or a red herring was that—the proposal was to harness brilliant biology and brilliant biologists into an industrial setting. There were numerous observers, both within science and the press and in the investment fields, who thought that this was going to be a difficult thing to accomplish. As a matter of fact, it was *not* a particularly difficult thing to accomplish. Though I've seen situations where, in fact, a collection of prima donnas might be a problem in focusing on a goal, the ones that come to mind are all relatively recent. There

really weren't, to my memory now, any significant examples of where that was difficult. Well, it's like an opera company. Sure, it's full of prima donnas, but everybody knows that with the proper handling and management, and that varies with the manager, it can be worked out, and wonderful things can be created as a result of collaborations of this sort. That was our experience, that certainly was the experience at Genentech and others. I think these various companies were probably managed differently.

Hughes: And was it the prima dona possibility that came to mind with the traditionalists, or were there other things as well?

Cape: I don't know if it was that as much as the fact that, in the early years certainly, there was a lot of talk about the fact that industrial objectives were going to fit the classic anti-establishment mode of being run in a crass manner for crass objectives, and that any scientist worth his or her mettle wouldn't be caught dead in a place like that. Well, I don't want to philosophize, but I can just tell you that none of the early biotech companies had trouble hiring the greatest people they could possibly think of from universities and from established drug companies, and those people made it happen.

Hughes: Why did they come?

Cape: They came because, and I think Genentech is the best-known example of this, they were free to do the most remarkable things and to set objectives that nobody dreamt would have been achieved maybe ten or fifteen years hence, but certainly not soon, and to make them happen pretty quickly. And to publish and to talk freely about them. I know I experienced, and I'm sure they did, when going to scientific meetings, that people in the drug companies thought we were a different breed, that we weren't playing everything close to the vest, that a lot of the things we said were, in their opinion, injudicious and should be kept secret.

I think all of the companies were aware of the fact that one of the appeals of being in a biotech company instead of a pharmaceutical company is your freedom to disseminate your ideas and to exchange ideas at scientific meetings with other scientists in other places. It was of a different order of magnitude in a biotech company than it would have been and, for some of the people we hired, had been in the drug company, where they were under very tight scrutiny and subject to very, very restrictive rules. So much so that in one of the meetings I remember vividly, the people from the drug companies were told specifically not to talk to us. And this is anathema to a scientist where communication is everything. I don't know if you've read recently all these stories about Isaac Newton. James Glick just wrote a book about him, and one of the things that he mentions over and over again is that Isaac Newton was not a very communicative guy. As a matter of fact, he never published anything; he never told anybody anything. I'm exaggerating a little bit, but certainly in the 1960s

and ‘70s, today’s model is the more communication the better. The example is in Cetus where one of our scientists won a Nobel Prize, and certainly it was in the face of all kinds of sharing of his information, and being ridiculed by his colleagues, and persevering, nonetheless sticking to it and prevailing.

Hughes: Did you anticipate, as you were thinking about this new type of company, that you would be adopting some of the appurtenances that are more closely associated with academic life? You mentioned publishing, and along with that goes presentations and all of that. Did you think at those very early stages about how exactly scientists would be operating in industry?

Cape: We didn’t formulate rules, although there were some implicit things. It’s hard to remember that back in those days there were debates as to whether patents were of any use. I think it was Wally Gilbert’s stated belief for a while after Biogen was founded that patents weren’t terribly important. Even Genentech, which probably had as open a sharing of information situation as anybody, you had to not be deemed to have published it by blathering about it until you filed your patent application. I’m sure that they were aware of this and that there was some common sense control. But it wasn’t overly tight. Compared to the prevailing behavior in the drug business; it was comparatively free. We hear a lot about freedom nowadays—it really meant something to people to be in a free environment.

And yes, we were saying at that time that when you come to Cetus—and I’m sure it was true of the other biotechs as we call them now, but they weren’t called that in those days – you won’t really be able to tell much difference between your freedom of activity every day and what you enjoyed in the university. We all know that at some university labs you’re like a slave in a factory, and at other university labs, you’re very much on your own. So the same spectrum exists in biotech companies. But we try to make you happy that you’re here, and that you’re fulfilling yourself as a scientist. One of the things we used to mention in recruiting and successfully, that we had a few occasions of a few well-known people—and Genentech also has examples of this—who left their academic positions to take full-time jobs with a biotech company, and then two or three or five years later, went back to an equally prestigious job in some academic institution. They, in other words, were able to keep their reputation growing and keep contributing and growing as people in the biotech companies. And since we could point to specific examples, and there’s nothing like role models, it made recruiting easy.

Hughes: Did you have these things, such as the publishing and the relative freedom of exchange, because you knew you had to in order to entice academic scientists to come, or was it a more deeply-grounded philosophy that science works through communication, if we’re going to have a science-based company, we’ve got to have scientists talking not only to themselves internally, but to their colleagues elsewhere?

Cape: I think it tended to be more of the latter, though there was some of the former, too. I mean, if you've got it, you flaunt it. If you happen to feel very much like an academic scientist, you don't keep it a secret when you're recruiting or when you're managing. Your response to people who are iconoclastic isn't to slam them down for not knowing their place, but to applaud them for independent thinking. And I'm sure that was true in other companies.

Hughes: Roughly, what kind percentage turned you down and what percentage was eager to come?

Cape: The percentage of success was so high—it was like fishing where there was an overabundance of fish—that I can't remember losing a hot prospect to another company. Occasionally, perhaps, we'd lose another prospect to Harvard. But I think Genentech and Biogen and Amgen and ourselves didn't step on each other's toes very much in hiring people. I think it was just a matter of fact that friends knew friends and vouched for them, and that's how you built up your staff. I just don't remember any difficulty, and that went on for years. Occasionally it happened with an advisor. You'd go after some world luminary and discover that one of your competitors had signed him up. But even so, there were more than enough of them.

Hughes: The way you're putting it, it doesn't sound as though you were losing people in either category because of the response, "How dare you ask me to join a company or advise for a company? I'm an academic!"

Cape: There were a few such individuals at the beginning who reiterated the fact that they thought the development of these companies was a disgrace and was a very bad reflection on the scientific merit of the people who made that decision. But I think the accumulation of accomplishments in the biotech industry, everything from Genentech's first successes with somatostatin and human growth hormone to our Nobel Prize (that came in 1993, but the work was done in the early '80s), made manifest to everyone that we weren't lying: the quality of the work, the ground-breaking nature, the fact that we were lucky enough to be in the vanguard of a mushrooming field of actual accomplishment, and harnessing of all these discoveries for better products, better medicines, and so forth. The evidence was overwhelming. And even some of the early objectors actually formed their own companies.

Hughes: Cetus was formed in 1971. Genentech was formed in 1976. In 1977 Genentech cloned somatostatin. So there were about six years in which biotech as we know it today hadn't proved itself commercially. So it's in those years when you were building Cetus from nothing to something that I would think the hard argument came. What is it in those years that's drawing scientists? Cetus hasn't really done much yet. You've tried Glaser's scanner, and that's not been a terrific success.

Cape: We killed it before we tried it. It was a business decision.

Hughes: You told me you had a contract with Schering-Plough.

Cape: Oh, yes, but that was not using that technology at all, just the concept of being able to marshal what was known about genetics. One of our consultants was David Hopwood, now Sir David Hopwood, from England, who was an expert in streptomyces genetics. And it was streptomyces that produced a lot of the antibiotics. And Josh, of course, Dr. Lederberg, was a Nobel laureate in the genetics of microorganisms.

Hughes: And is that why he came to Cetus?

Cape: Well, what they all saw was potential. We helped organize an ACS meeting in Virginia in the late '70s that had as its title, "Biology: Poised for Growth." Or something like that. It was the fact that we were positioned and were prepared to pay salaries and give options to people to come be with us to start a revolution. So the fact that there weren't any visible accomplishments, except for the fact that we were delivering improved strains to a drug company, no one doubted that it would happen. The most dramatic thing that happened, although monoclonal antibodies had been discovered just about the same time as recombinant DNA, was recombinant DNA. And it was the fact that Genentech showed that it could be done. A rising tide raises all yachts. It worked to everybody's advantage.

Hughes: But before Genentech had shown the potential of recombinant DNA as a commercial methodology, it was the revolution in biology that attracted people of the caliber of Lederberg?

Cape: Well, Josh was of the opinion that finally some real-world products of his insights—and his insights go way back. I mean he was writing about the kinds of things that are frightening us today, like SARS and the next flu epidemic and the fact that the drug companies were saying infectious disease was finished, and how ridiculous that was. So to find a group of people industrially focused but able to talk his language made it very easy for me to persuade him to join our team. It was a really enjoyable thing for him to do.

Hughes: Did you go after him?

Cape: Yes. I met him on the Berkeley campus. He was here to give a talk, and I sort of ambushed him but not really. I got to him right after the talk and talked to him. And we started to talk more and more.

Hughes: And he came in 1975?

Cape: Before that. I'd say '74, '73, I think.

Hughes: In what manner did Stan Cohen come as an advisor?

Cape: I phoned him, went to see him, we chatted, and we liked each other.

Hughes: Did you get the impression that he and Lederberg had been talking before that?

Cape: I don't remember. They knew each other. It's funny, considering how far the world has come in this respect since then, that they were both interested in the use of computers. I think if you ask each of them what they were doing in those days, computers had something to do with it. I think each of them headed the Stanford program in that at some point in time.

Hughes: You're certainly right about Stan. I don't know about Lederberg. Stan had an appointment in the department of medicine, and I believe it was there that he was setting up a computerized program on drug interactions, something along those lines.

Cape: Yes, he was a pharmacologist, as I now remember. I like to think that I was very successful in approaching and getting six Nobel Prize winners [as Cetus advisors]. But in terms of something in hard copy that will blow you away, get hold of Ariad's first prospectus when they went public, or maybe it was a financial memorandum before they went public. I believe they had four or five pages of scientific advisors. It was an overwhelming list, starting with David Baltimore.

Hughes: Isn't this a huge expense for a young company?

Cape: Yes and no. Remember that was in a period when you could think of exponential increase in the value of your company, and the Silicon Valley philosophy of being able to issue [stock] options, which are not a cash drain and not any kind of a drain, even if you worried about it being charged against your income—yes, you were losing money anyway. At least in those days it was easy. Once you intrigued top scientists with the idea of people who are doing top science in an industrial setting and not in any way controlling their thoughts, and have them shared with our scientists, that was relatively easy to accomplish.

Hughes: Tell me about attracting Francis Crick.

Cape: Well, that is the same sort of thing as Josh Lederberg. I quaked; it's sort of like the feeling you might think of approaching Gregory Peck or somebody like that. The point is that he was considered to be unapproachable. Maybe Laurence Olivier or Richard Burton would be a better example—somebody who would just flick you off. Who are you to be talking to Francis Crick? What have you discovered lately?

Actually, I had met him before I went to Berkeley. The summer before I went to Berkeley I went to a molecular biology school on a Greek island, and Francis was a teacher and Jim Watson was a teacher and Alexander Rich was a teacher, and just about anybody in the world in molecular biology was a teacher at that course. And so I'd met them all. But still, that was only to create more awe and wonder and tremors. But I summoned up my courage, and I accosted him at a meeting in San Diego, and said, this is Cetus, and this is what we're all about. You can just imagine how we think of you, and we'd just like to talk to you about the possibility. He proved to be accessible and easy to talk to. He's probably the best example, but it happened with all the great people we brought together—once you broke through the accessibility barrier, you find that they're very pleasant people. And if you talk their language, and if you are interesting to them, or what you're proposing is interesting to them, they listen. And that happened every time.

Hughes: We're missing a few– we've got Glaser—

Cape: Glaser, Josh Lederberg, Francis Crick, Andrew Schally.

Hughes: Kary Mullis.

Cape: Kary Mullis and Hamilton Smith.

Hughes: Do you feel in retrospect that they did more than add substance through their names to the company?

Cape: Every one behaved in a different way. Oh, Hamilton Smith, who got the Nobel Prize for restriction enzymes.

Cape: The question was?

Hughes: How did they contribute?

Cape: As I told you, one of the things that I had to do was insist that they don't sit together at the retreats because that's counter-productive. We want to spread the joy around. They were pretty good about that. They were an inspiration more than anything else. Some of them would actually come in and spend hours and days at the bench as if they were supervising—supervising isn't the right word because they weren't—as if they were a member of the lab and trading ideas with the guys who were doing the experiments. And I think that was enjoyed enormously. Ham Smith was particularly good at that. They were very accessible, of course, at the retreats, but that was like two or three hundred scientists in one place, and it could be tiring.

One thing we never had them do, and I think this arose partly out of Don Glaser's experience at IBM where the board of scientific advisors acted like the

star chamber in King James the First's time: everybody had to present in front of this panel of austere judges, and somebody was for sure going to make a fool of you. We never did that. We never assembled them as a voting board. They were omnipresent, but as individuals.

Hughes: Was their main time at Cetus for these retreats?

Cape: Each of them individually would visit Cetus once or twice a year in addition to that.

Hughes: When they felt like coming?

Cape: Well, it required some negotiations—very busy people. It was just a question of setting it up and making it known that they would be around and telling the various people who would want to spend some time with them to make arrangements. Either they'd spend some time in an office with them, or, more typically, the consultant would come to their lab. And we had lots of other consultants, not just these six Nobel Prize winners.

Hughes:Francis Crick in the last thirty or so years of his life, although he's curtailed his travel very significantly recently, would move from place to place and sort of like an insect pollinating all around, he would basically be a good scout and a good carrier of who's doing what where and what's important in the world and where the next breakthroughs are going to be. Another person who was wonderful in this respect was an Australian, Sir Gus Nossal, who ran an institute in Melbourne at the time. He was a very good friend, and he has consulted with Chiron up until very recently. I don't know if he's still a consultant. He's been there for a long time.

He's an antibody person?

Cape: He's an immunologist, I think, but not particularly antibodies, not in the sense of monoclonals, not especially, but just cellular biology and immunology generally.

[End Tape 5, Side A] ##
[Begin Tape 5, Side B]

Hughes: I'm going back to the early days, and maybe I'm trying to make too much of how you were conceiving of this company as it was starting off. Was it in your mind that you did not want to model your company after the pharmaceutical industry, that you saw the science that you were trying to develop as needing to operate in a far more free-wheeling environment?

Cape: Well, we had that feeling, but I don't want to say we didn't want to grow up. It was, we didn't want to grown up and get sclerotic. We wanted to stay as creative

as we could possibly be because that was our strong suit. And you would have imagined that that presupposed a concept of a rational relationship between drug companies and the new companies. In fact we are more or less at that point now, but it took a long time in happening. One of the reasons it took a long time in happening—minor reason—a lot of the biotech companies, particularly after they started to hire some experts from big pharma companies thought that to grow up is to become a vertically-integrated drug company. The only company that has ever really accomplished that is Amgen. Even Genentech sold control of their company to Hoffmann-LaRoche before they reached that point. But it is interesting to observe that Genentech has contributed so much, has continued to be so productive, in the years since that Roche deal. It's largely because Roche and Genentech must have given a lot of thought to this pseudo-independence that Genentech has, which enables them to keep growing without getting sclerotic.

Hughes: In other words, are you saying that the relationship with Roche kept them from needing to become a pharmaceutical company?

Cape: Right.

Hughes: They could keep their biotech-ness.

Cape: Right. But I said that was a minor view. The major reason was the hostility of the drug companies to relationships with biotech companies. I think I gave you the ultimate example being Syntex which wouldn't even join our trade group because they considered us to be a bunch of promoters, and one big company executive more or less implied that we were a bunch of crooks. I think common sense ratchets into place. It doesn't just smoothly flow into place. Maybe the world "lurch" is the right word. But I think right now the consensus is that the drug companies already have in place the fixed costs to do regulatory clearance and marketing and production, and for a biotech company to try to spend money building that capability is a misapplication of funds. They should seek strategic alliances with drug companies where they do the discovery part, and the drug company picks it up at some point and carries it through to market, and that is the pattern that prevails today.

Hughes: But what were you thinking in that regard in those early days?

Cape: What we were thinking way back when, it occurs to me, was how can we keep our cash flow such that when the future becomes obvious—One of Gunther Stent's famous expressions was, "The future lies ahead," which says everything and it says nothing, right? As long as it isn't clear what it is, there's not much you can do except stay healthy and be there—Woody Allen, again. Showing up. You've got to be there. What we had to do and were very lucky in being able to do in the early years was to stay not only alive but also in a way never having to worry about cash flow, never having to worry about meeting payroll. For ten

years, we never had a crisis of that sort. And that was to find contract relationships with big companies that would basically pay all the costs, and then some, of any work we did. And between our work for Schering-Plough and for Bayer in Germany, and then shifting when Chevron and Amoco and National Distillers invested in us, again being paid for the work as we were doing it, just kept us solvent and growing all the time, to the point where at a max we had way over one thousand people. And subsidiaries in Palo Alto; Madison, Wisconsin; and in Amsterdam.

Hughes: Did you ever think ahead, that maybe ultimately your goal was to become a fully integrated company?

Cape: I think we labored under that illusion, yes.

Hughes: And you're saying now it's proved unrealistic.

Cape: We knew that the best deal would be with a drug company, but there were not drug companies particularly interested in such a deal. Genentech very wisely chose human insulin because the logical customer for that was Eli Lilly, and they could have a relationship with a drug company pretty fast.

Hughes: And so the products that you first began to develop didn't have as logical a pharmaceutical partner.

Cape: That's right.

Hughes: One could argue that Eli Lilly in a sense didn't have a choice.

Cape: They did what makes sense, but it's amazing how many people don't do what makes sense. Lilly could have taken the position that who needs human insulin? It's a minor product to the extent that there is a small market of people who react adversely to the insulin we make that is basically animal insulin. We can do without that. But they didn't. They did the smart thing.

Hughes: Did Cetus ever seriously consider developing human insulin?

Cape: We struck out on that. We tried to get relationships with various people to fund the work. I don't remember actually the moment where this was a very important thing to us but we weren't going to do it on our own. The number-one thing was to stay alive until some business model made itself clear to us that there might be a big market for a specific product. We couldn't really think in those terms until we had interleukin 2 and beta interferon, both of which we had intellectual property protection on, that might turn into blockbuster products. And I believe they're still Chiron's number one and number two therapeutic products twenty years later.

Hughes: I understand that in the ‘60s and ‘70s there was attention placed on the dichotomy between strategy and organization. You could say, we’ve got to get our business strategy going and then the organization will follow, or we’ve got to set up our organization and then we’ll figure out what our strategy is.

Cape: I don’t think we ever had in the ’70s discussions or thoughts on those grounds. Again and again I stress I *think*. Our primary consideration was staying alive, was staying solvent. Whenever we went for more money, we were relatively successful relatively easily, and those windows opened and closed and opened and closed, and we were very lucky. Genentech struck oil with somatostatin, but some of it must have brushed off on us because our public offering was so successful. We were looking for credibility, and we didn’t have a fixed business model. We shifted from Schering to Chevron and Amoco because that’s what showed up. It’s like the lawyer who says, in response to the question, what do you specialize in? And he says, I specialize in the problems of the people who come to through the door. There was a certain ad hoc aspect to what we did.

Hughes: But it sounds as though it was a science-based argument.

Cape: This is what we can do better than other people can do.

Hughes: You weren’t saying, we’ve got the prize business organization.

Cape: Definitely not.

Hughes: So the science was dominant.

Cape: Yes.

Hughes: Were the scientists dominant? Who was making the business decisions?

Cape: I would say mainly Pete and me. I think a typical successful business has a reasonably dominant CEO or CEO team. They have varying degrees of success in communicating with the board, and I think we were pretty good at communicating with our board. But no board likes to be in the position of running the company. They like to fine-tune it and stop this if they think it’s a disaster happening, and to change people if they think that’s necessary. And we communicated pretty well with our scientists. There was really not a wall between us. We didn’t operate on the basis of, “Shut up, this is none of your business.” I think we were pretty open in talking to people and we—I mean, there were periods of great frustration when things weren’t going right and things weren’t being cloned the way we wanted. We were frustrated by things beyond our control, such as, we were working for National Distillers in connection with the richest man in the world at that time, Donald Ludwig, in Brazil. We wanted to make alcohol out of manioc, and suddenly the entire manioc crop was destroyed by a virus, and all of a sudden the whole thing blows

up in your face. Or we had a biology-based process we were developing for Chevron, and one morning Chevron decided they weren't interested anymore. So what are you supposed to do? I cannot think of anything during that period of time where the scientists wanted to go this way and management wanted to go that way. I just don't think that ever happened.

Hughes: In a sense, you were a hybrid; you had the business and the science. George Rathmann was both, but most of the early people leading these companies were one or the other, right?

Cape: That's right.

Hughes: Where did that get you?

Cape: Well, as I told you, very briefly recapitulating, my family and people who knew me in the business world thought that I was wasting my time in academics, and the people who knew me in the academic world thought that I was wasting my time in business, and suddenly the venture capitalists informed me I'm a hybrid, and that's good.

Hughes: You were going into a hybrid industry.

Cape: It was not invented yet. That is one thing you will, I am sure, pick up from our business plan when we raised our first two million dollars. It was all promises and making no bones about the fact that they were all promises. It was all stuff in the future, and it was all based on there's got to be a pony in there someplace. I told you the Syntex story: we presented them with almost fifty things that we could do, and even we were surprised how quickly all of them were actually done by others. What we did was just clog our presentation to them with too much stuff.

Hughes: Do you think that there are substantial ways in which the early organization of Cetus differed from the other early biotech companies?

Cape: I don't know. There was nothing that they did that we weren't doing in terms of organization. For example, we had this process going to improve Schering's organisms that were making their antibiotic Gentamicin. And the system we had going required a team of a couple of dozen biotech guys, many with Ph.D.s, many not, to work around the clock such that there were cars in our parking lots at four o'clock in the morning. The biology sort of paced what they did. I mean, if they see it's in a certain stage, they've got to be there to do whatever they have to do. We never had punch clocks or anything like that. Everybody was just paid and they did what they did, and that sometimes required, as I say, weeks of unbelievable drudgery, but most particularly, time warp. By the same token, we hear stories—I wasn't there, I didn't see it, but I *sure* believe it—of David Goeddel moving a cot into his lab when he was cloning and expressing

somatostatin and working at it just like a computer nerd of ten years later—three days without sleep, and then whoa, he's out. And that's wonderful. But that's exactly the same way the company was run. He knows what he has to do. He doesn't need anybody to ride him. They knew what they had to do and they did it. And they were buying into the whole family effort.

Hughes: But why were they buying into it?

Cape: Because it was exciting. That's the way biology labs work now. It's exciting.

Hughes: And was it that same intensity and drive at Cetus, at least at times—I can't imagine how you could have sustained that.

Cape: Well, we sustained it for some years, I'll tell you that. I mean, different people might play the parts. How else do you think we could have encouraged Kary Mullis?

Hughes: But you saw that.

Cape: I saw that, yes. And you applaud it.

Hughes: What do you think it was? Was it the excitement of the science? Or was there also, okay, this company's got to succeed or I don't have a job? I also have now a financial investment….

Cape: Well, there's something of that, but remember, these were, just like now, terrible times. You may recall that the nation double-crossed the space engineers, and all of the guys at Lockheed were in Santa Claus suits, the equivalent in the 1970s of selling apples in the streets. Massive layoffs, ten, twenty thousand people. And here we hired as the head of our engineering, some guy from Lockheed who, thinking about whether or not he wanted to come to Cetus, was worried about the security thing. We were able to laugh with him six or twelve months later, saying, you were worried about security, and your wonderful Lockheed has laid off tens of thousands of people? When was the last person that we laid off? We didn't have too many problems. The only major layoff we ever had was when Chevron cancelled that project, and we had to lay off fifteen percent of our people. They were doing that job and there was nothing else for them to do. So, goodbye.

Hughes: It's three o'clock. You have to stop.

[End of interview.]

Interview 4, September 16, 2003

[Begin Tape 7, SideA]

Hughes: I was looking at the names on your CV of the earliest companies: Cetus Scientific Laboratories, 1971 to 1972. A research boutique?

Cape: No. We changed the name [to Cetus Corporation] simply because I thought it sounded better. I was always somewhat negative about generic-sounding names. We chose the name Cetus, and then we were stuck with that "Scientific Laboratories" for reasons that I don't remember. At some point we decided to become simply "Cetus," without changing the nature of the company at all. Depending on what you would call a research boutique, we were a research boutique briefly or for twenty years, I don't know. It serves a purpose sometimes to distinguish a company that basically is in research. If you think about it, where biotech has settled today, where the ideal relationship is with a drug company which does everything beyond maybe phase two clinical trials, you're still a research boutique. But when you're a thousand people—

Hughes: "Boutique" is stretching it a bit.

Cape: I find myself looking today at companies with six to ten people in them.

Hughes: That's a boutique, or a virtual company in today's parlance. Were you, in those very earliest days, aiming to exploit commercially, molecular biology, or was it biology in general?

Cape: Well, both. There are some insights that come from just genetic principles and could have been immediately applied to the challenges to antibiotic manufacturers, and we found that to a significant extent they were not applying them. I can't remember the specifics, but there were some reasons why, perhaps, it was a little bit dicey and chancy for them to apply certain genetic principles to the way they employed their organisms. But still, we pitched to them on the basis of inputs from our consultants, such as Arny Demain and David Hopwood, who was a specialist in streptomyces genetics—streptomyces (in the actinomyete group) are a brand of microorganism that are used to manufacture antibiotics—that we didn't think the drug companies were taking full advantage

of insights that have developed continually, even before molecular biology really took off. But needless to say, we thought that the real explosion in knowledge was going to be in molecular biology, and that, in fact, waited for recombinant DNA and monoclonal antibodies.

Hughes: I read something that made me wonder whether microbial screening—Glaser's apparatus and the things that developed from it—were regarded by you and others as kind of a bridge, a way to get to what you really wanted to do, which was exploiting molecular biology per se. Or was it not quite like that?

Cape: It was partly like that. If you examine, as you will, our business plan and the pitch we made in raising our first venture capital-type round of money, in other words, money other than that coming from the founders and their immediate friends, you'll find repeated reference to all the Nobel Prizes awarded since World War II. They were virtually all in molecular biology. Even Lederberg's work, which I believe was recognized in the middle '50s with a Nobel Prize, was work conducted in the '30s, '40s. But starting with the focus on DNA per se and subsequently, that was all molecular biology, and that was the unmined gold mine which we kept referring to. But in the meantime, since it wasn't at all clear; the crystal ball was still fuzzy as to which way this would go, we started off simply saying, that's not all: there's a whole bunch of other stuff, as exemplified in the know-how of some of our consultants, that really wasn't being properly applied and that we would start off applying that.

It served two needs. The most important need is survival. How do you keep money flowing in? And in successfully pitching to Schering-Plough that we could bring skills to bear on a problem of immediate importance to them, we were able to buy time. Even today, in financing challenges to small companies, bridge loans are very much in. If you can't get the venture capitalists interested now, but maybe in six months you'll be in a better position or the world situation will be more optimistic, bridge loans, use the word "bridge," are very much buying time. And that's what we were doing. So we were, I won't say treading water or just marching in place, but we were buying time.

Hughes: Whom did you approach in those very earliest days?

Cape: Mainly drug companies who were making antibiotics, because we knew that one way or another, the insights we had about how microorganisms grow and how microorganisms produce what are called secondary metabolites—In other words, antibiotics are secondary metabolites, whereas sugars and enzymes for digestion and stuff like that are primary; you can't make it through the day without those. But a bug may not make an antibiotic if it doesn't need to. It may be a waste of time and energy to make the antibiotic. So they're called secondary metabolites. But the point is that our know-how seemed to be appropriate, and a number of drug companies, most significantly Schering-Plough, took a chance on us. In fact, we did produce what we promised. We produced more highly

productive bugs for them to use in their production processes. It's not a world beater, but it kept us alive.

Hughes: I saw Upjohn mentioned.

Cape: We worked with Upjohn. We worked with Imperial Chemical Industries, which has evolved into AstroZeneca. We worked with Bayer, which is still around, which had an antibiotic very similar to gentamicin, which Schering-Plough had. And we kept alive. We also worked with a Dutch company called Gist Brocades, which made penicillin. But in terms of financial support, overwhelmingly important was Schering-Plough.

Hughes: In those very earliest days, was it you and Farley actually drawing up the contracts?

Cape: It's hard to distinguish. We've talked about the fact that there were five of us who were founders of the company. Don Glaser continued to be a professor at Berkeley, so we had access to conversations with him. But he was never working at the bench at Cetus. By way of contrast, Cal Ward, his brilliant postdoc, who I got to know also when I was in that same Stanley building [on the Berkeley campus] did come and work full time at Cetus on a number of things. Remember, we started off with his invention for imitating the sensitivity devices that make it possible for a doctor to choose which antibiotic to use for treating an infection. And by six months into our business plan, we decided, great idea, but you know what? If we can interest Schering-Plough in a totally different business model, we're going to go with that instead. But he remained in the company, and he remained very much involved in the scientific challenges that arose from that project.

Hughes: Did he leave academia at that point?

Cape: Yes.

Hughes: So he was full time at Cetus?

Cape: He was full time. Moshe Alafi was the chairman of the company, and he had experience in venture capital, had friends in the venture-capital industry, and he was very largely present. It's hard to say that he was operationally involved, but he was involved in much of the decision-making and we consulted him constantly. But you're right in saying that the guys who actually *did the stuff* in hiring new people, in contacting the drug companies for business development purposes, traveling to them, it was mainly Pete and me. Sometimes Moshe accompanied us on trips, and joined our negotiating meetings. To a lesser extent, so did Don Glaser and Cal Ward. On the other hand, it is true also that sometimes Cal, and sometimes Cal alone, and sometimes Pete or I alone, but frequently Pete and I together, would travel to Europe or to the East Coast,

where most of the drug companies were for operational reasons. On many of those trips, particularly in the negotiations with Schering-Plough, Moshe was with us, not only on the trip but in the negotiating room with the drug company. And on at least one occasion, and I think on more than one occasion, he came to Europe with us as well.

Hughes: It boggles my mind to think of all the matters that you had to handle in those early days. You described yourself as a hybrid, so that it wasn't impossible for you to understand both the business and the science. There still must have been an incredibly steep learning curve. Had you ever negotiated a contract, particularly with something as imposing as a huge, established pharmaceutical company?

Cape: No. That kind of thing was brought home to us when Standard Oil of Indiana, later known as Amoco, invested in us. One of the things they said to us in one of our meetings, was, "We have a culture gap between us. We don't say this to scare you, but all of us guys on our side of the table have lived in a world that is so far from the world you're living in now that we have a challenge in understanding you, and you have a challenge in understanding us. We're going to get through it, but we should recognize what it is. For example, we are bigger than Sweden."

Hughes: Did you ever feel intimidated?

Cape: They were human beings just like everybody else. And they were very decent to us. They didn't always understand our outlook, but they never actively opposed anything we wanted to do.

Hughes: I mean, by the whole endeavor. You not only had to put together a company, but a company that was breaking ground, that was doing something that hadn't been done before. But maybe you weren't even thinking in those terms.

Cape: We were and we weren't. There was an article in the *Chronicle* yesterday, or was it today, about how venture capitalists are looking for the CEOs of the companies that went bust in the dot-com boom. They still think those guys are great, and they're still putting money into them to try something else. When people talk about courage or fear or things like that, I think entrepreneurs have a genetic deletion for that sort of thing. We didn't go around scared all the time; we should have been perhaps.

Hughes: Or even just overwhelmed.

Cape: I really think I should have compared notes with my peers on this subject, the CEOs of other just emerging drug companies. Maybe we were all consumed by the need to put up a proper face of confidence and what-have-you, but it would have been a good idea to compare notes. But I do know, in comparison, family

that we left in the east who are terribly afraid of failure. And I remember at that time telling them, "Who cares? You start over again." You see many illustrations of that principle in the computer or the electronics field. You bounce back, that's all. We really never ran scared. (Donald Rumsfeld once expressed this same attitude to me at a Princeton cocktail party.)

Hughes: Was there a rough division of labor between you and Farley?

Cape: Hardly. There was an enormous overlap. I'd be inclined to say that in hand-holding in an external sense, shooting the breeze with our customers or our potential investors and what-have-you, that would be more Pete's job than mine. In terms of hiring and chatting with the scientists, that would tend to be more the kind of thing that I would naturally gravitate to. Obviously, the way that I've described it, Pete would do somewhat more traveling than I would. But in the summer of '76 there was a big international meeting in Berlin, and it was at this time that Pete and his wife were trying to have more babies, and that required him to be around more. The burden of the traveling and doing more of the externals, I just took it over, more than I had before, since he was staying home more than he had before. And in a way I never looked back. I had, for example, between '73 and '76 been learning to fly a little airplane, basically inspired by Calvin Ward who did it before me. Suddenly I was flying so much around the world in 747s that to spend time going around in circles at Oakland airport on Saturday mornings just to stay current didn't have any appeal, and I basically tailed off after that in flying a little airplane. And I think 1979 was the end of my career in that. But these are things I'm using as memory pegs for myself, so that starting in '76 I became myself more and more involved in the externals.

Hughes: As early as 1978, and it may have been even earlier than that, you were saying in print that Cetus should have a broad range of skills rather than a specific technology or a target. I got that from the oral history that you did for MIT in 1978. Let me quote: "…we will shortly select one or two target proteins. The important thing I want to stress is if they are the wrong selection, it doesn't really matter. They serve as a target for people that are trying to do things over the short run, and the important accomplishment is that you've got the skills finely honed at the end of the program."[5] What about that philosophy?

Cape: Well, that doesn't really develop the original point, which was, there are other things than recombinant DNA. Because we don't really know for sure which way the world is going to go, and we've got enough muscle, we think, to be competent on a number of fronts.

Well, a number of things happened in the ensuing years. First of all, we didn't understand the importance of explaining ourselves, particularly to the press.

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5. Interview with Ronald Cape:, April 19, 1978, Recombinant DNA Controversy Oral History Collection, Institute Archives & Special Collections, MIT Libraries, Cambridge, MA, p. 65.

Genentech not only performed very well, and that's the most important thing of all, but also demonstrated focus in that they were a recombinant DNA company—that's it. And I think to some extent, we were trying to differentiate ourselves from that. It also seemed like a good idea. But some of the things that we announced we were going to do in those early years, having to do with industrial projects and non-medical things and some engineering things that we were doing with our system, for example, struck some analysts as being fuzzy focus. "Why don't you decide what you are and do that?"

Well, just as a matter of timing and a matter of handling that aspect of it poorly, about five to ten years later, Genentech was doing just that, with founding Genencor and having certain other relationships, and was praised for having more than one iron in the fire. In retrospect, all of that controversy seems a little bit silly. The point is that in the early years, they beat us repeatedly in successfully cloning and industrially developing recombinant products like human insulin. We could say all we wanted about the fact that we were interested in more than that, but it also turned out that we were another year or two before we cloned important molecules. Now it all seems in retrospect not terribly important, but I do remember that it was important for me at that point to make the statement that we were more than just a recombinant DNA company.

Hughes: I know you were saying that recombinant DNA is not the only technology that Cetus is applying. But what I got out of that quote was the fact that you seemed to be honing your technology in a way that was not quite as product-driven as expected of a very young company.

Cape: Maybe, but… There's a number of things. First of all, Genentech's first product wasn't a product. Somatostatin never became an important product. But it was a blockbuster as a demonstration of capability.

Hughes: Right, and they didn't really expect it to be.

Cape: No, I'm sure they didn't. But the point is that they had demonstrated can-do, and we wanted to do can-do. I think I was saying there, it doesn't matter; if we could find a customer who would pay for us to do this or that, we'll do this or that – that's all that counts. Whether it's a big product or a small product is less important than that *we can do it*. And we will. And we did. But I don't think the important products for us, like for Genentech human insulin, which got clearance by the FDA relatively early in the game. That was great. It was another five or more years before we had interleukin-2 and beta interferon on the way.

Hughes: To belabor a point, perhaps: you don't remember having Cetus support projects that were largely to improve techniques, rather than aim for a specific product?

Cape: No, I don't remember that. Remember, we had three big industrial companies owning almost fifty per cent of our company—Chevron, Amoco, and National Distillers. We had a big project going with National Distillers to make alcohol from manioc in South America—continuous alcohol production. And we had it going on a small scale. That would have been fantastic and important. Maybe the markets wouldn't be what they are for a medicine, but they still talk about things like that with gasohol. And gasohol was used in Brazil, where the manioc was going to be grown, in cars. So it wasn't having to reinvent the society and how it would use the product. We were working with Chevron with another industrial project. Again, it wasn't recombinant DNA. But it was a project to make a couple of industrial projects in a coupled way, and possibly eat into existing markets for propylene oxide, that is an industrial chemical used in plastics. So we were actually actively involved in that. Remember, our number-one pharmaceutical project (beta interferon) was, of all things, financed by another oil company, Shell, and that did involve recombinant DNA.

Hughes: That was interferon?

Cape: That was beta interferon, which is still a major product of Chiron's.

Hughes: Why was Shell involved with that?

Cape: I remember Mary Lasker visiting us. She was from Texas, and she was very much into medical research.

Hughes: Particularly interferon.

Cape: That's right. She had with her top executives from Shell, which is located in Houston, and had until very recently been located in Emeryville – at least their research operation. It turned out to be our place, which is presently Chiron's place, in Emeryville. They just pulled out, hook, line, and sinker, just when we were looking for new expansion space. Sheer coincidence. And they built our pilot plant. They built the P3 facility.

Cape: So we were opportunistic. We found the money where we could find it. We found it with Chevron. We found it with Amoco. Amoco was funding different things with us, but always looking for something bigger, and it kept us alive. So we were under less pressure, if you like. Remember, in the middle of all that we went public and raised a whole pile of money when interest rates were twenty per cent. Our investment bankers pointed out that on the net hundred million or so that we raised, we could probably operate forever.

Hughes: When you approached these big companies, had you done enough homework to know where Cetus might fit into their agenda? Or did you present your technology, and then they said, oh, that would work very well with x..

Cape: Oh, it's a case of yes and no. You can always do more homework. Just like when we were formed and all the venture capitalists were saying what's the next big thing, and the next big thing was going to be—they used the word "medical" at that time. It turned out to be molecular biology and so forth.

After the Arab oil boycott in the early '70s, a change of thinking swept through the oil industry, where they all said, we are enormous. What else is potentially enormous that we could get into just in case things go from bad as they are today to much worse? And for many of them, it was biotechnology, which didn't even yet have a name. But medical applications with their enormous markups struck all of them as something they should at least find out about. And in point of fact, the three companies that invested in us did so in order to have a closer look over our shoulder to see which way we were going. So to present them with projects that allowed biology to solve problems that had previously been solved by chemistry, because all three of them had big chemistry divisions, not oil, but oil-derived chemicals. So they saw us as possibly able to develop new processes for them, and that's what we worked on for them. And that kept us alive when Schering closed out their financial support in the late '70s, when our contract ran out.

New processes for them without taking the risk and the expense of their having to develop in-house groups?Hughes:

Cape: Well, we did develop in-house groups, and we developed them on their buck, and when they decided to change their mind, we'd have to get rid of or lay off a number of people who were devoted to their in-house groups. For example, the propylene oxide project that I told you about, one day Chevron just announced that they had decided to terminate it. And we had to shrink our whole staff by 15 percent We had no choice. We didn't have too many bad experiences like that. But the point is that it was always the big company paying for the project.

Hughes: But Chevron and all the others could have said, okay, look at this new technology. Let's just hire some scientists and bring them in-house and start a recombinant DNA, or whatever, technology group. Why didn't they do that?

Cape: Well, to some extent they could and to some extent some of them did. But take a look at the way today a lot of big drug companies are stopping increasing the size and scope of their basic research people and using biotech relationships in order to accomplish the same purpose. It's much more efficient. And it's much easier—

Hughes: In the end?

Cape: Well, in the end, particularly if you decide to close down a project.

[End Tape 7, Side A] ##

Begin Tape 7, Side B]

Cape: Does the research staff have to be fired? That's somebody else's problem. And you buy yourself time by dealing with a small company that's already halfway there. Because the money is in finding a successful research result and building that into a market.

Hughes: And they could not have been sure that this was going to be the technology that got them where they wanted to get, could they?

Cape: No. Nobody told me this, but I think common sense tells me that if things had worked out, under certain circumstances, they might have said, okay, we've done this via this little company for a number of years. Now it's about time for us to start out on our own.

Hughes: Yes. And you see companies do that. You see Lilly do that, for example.

Cape: Or, like Lilly, you buy Hybritech. And a number of biotech companies have been bought that way.

Hughes: I read the introduction to the book you edited with –

Cape: Vivian Moses?

Hughes: Vivian Moses. *Biotechnology, the Science and the Business*. Did you know him because of his connection with [Melvin] Calvin's lab here?

Cape: Yes, well, we lived across the street from each other in Kensington. He's a very good friend. I'm going to see him in London.

Hughes: Well, give him my regards, because I helped in a very peripheral way to get the interviews out that he and Sheila had done with the Calvin Lab people. Anyway, you jointly make the point in the introduction to this book that biotech is a business that must make a profit. Yet, as is certainly implicit in what we said, this is an incredibly science-driven company. In these early days, what is the balance between the science and the business aspects?

Cape: Well, we were, if you like, searching for a business model that would give you very strange relationships between research and all other expenses. We were trying to generate a relationship with large companies where we would get a piece of the action from a product that, presumably, they would market and we would have handed over to them. Amgen is probably the only company that's really succeeded in doing this independently. And they are, compared to the size of a drug company, still rather small, although for biotech companies, well, they're number one in size. Genentech has got there, but they got there some years after Roche basically bought control of them.

Parenthetically, the two of them seemed to work out a brilliant strategy where Genentech seems to be an independent company, but it still is basically a Roche company. But it's not a good model. You can't really talk in terms of comparing two other companies, the percentage of research that Genentech spends compared to their total expenses, because the assumption is that you're going to turn over to somebody else or share the marketing with somebody else, and even Genentech is an aberration. The smaller biotech companies simply can't afford to do that, and I think that's one of the reasons that Cetus ended its life. It tried, on the basis of one product which tripped at the F.D.A., to build up the infrastructure that a drug company would have—the sales and all that. If you think about the articles in the paper today about Dell Computer and Hewlett Packard, they fire shots at each other about what percentage you have to spend on research. They're at least in the same ballpark, although one may be twice or three times the size of the other in terms of the percentage that they spend on research. If you tried to compare, let's say, Pfizer to, let's say, Amgen, Amgen probably spends more on research proportionately. I don't know if this is true or not, but Amgen's the only company that has followed the vertically integrated pharmaceutical company direction. Most other biotech companies don't follow through and bring a product to market all alone.

Hughes: Because they can't!

Cape: Because they can't. It's a stupid way to save money. They come to the point where they are recognized as being more productive in terms of new products – pipeline, in other words, and the drug companies have the fixed costs in place: the regulatory, the manufacturing, and the sales and the marketing, all that stuff. Why duplicate that? But the point is that it increases the denominator. Therefore, the percentage of research to your total expenses in a typical biotech company, then and now, is much higher than in a vertically integrated drug company.

Hughes: Are you saying that Cetus never had the ambition?

Cape: Oh, we did have the ambition. That's what killed us. We tried to become a drug company.

Hughes: But Genentech did too. Or at least Swanson says from the start that he had that ambition. He wanted Genentech to become a FIPCO, a fully integrated pharmaceutical company.

Cape: But the only one that did was Amgen. Now Genentech got sidetracked by this enormous investment by Roche. But they invented a new model, which worked beautifully for them. You could say they're a FIPCO, but they're a FIPCO owned by Roche.

Hughes: And you'd say the same for Chiron with Novartis?

Cape: Yes. Although that's a strange and different thing, and I don't know where that's going.

Hughes: Why is that?

Cape: You can check; this one is documented. The clear intent was someday, Roche would own all of Genentech. Someday. And I think that the specific language of the Novartis arrangement with Chiron is that that day may never come. [Note added in proof: it came in 2005/2006]

Hughes: So you have to think of the hybrid if you want to think in terms of full integration. And Amgen's the only one that's done it.

Cape: That's right. And nobody else is trying. Amgen had two blockbusters back to back. No one has ever had that before, and no one probably ever will again. With the Epo and the –

Hughes: Neupogen?

Cape: The growth factor, yes, Neupogen.

Hughes: When you and Farley and sometimes Ward were going around the countryside in those early days, did you promote New Biology as possibly able to become an engine of economic growth?

Cape: Yes. But I'd say, and we discussed this before, that we weren't terribly successful at that. A little bit of comparison I've made with people in other companies: they had the same problems, and if you think about it, it isn't hard to understand why. If making a gamble on a technology which cannot prove you right for ten years is what it's all about, it makes no sense for a fifty-six or fifty-seven year-old decision-maker at a big drug company to make that gamble. As I've said, it can't help his family; it can't help him. But if he *seems* to have made a mistake, it will kill his career. The big-company decision maker has everything to lose and nothing to gain. So you get a few really ballsy people, like the top management at Roche, who decide, well, nobody's going to knock us off; we're the bosses here, and we're not under threat, and we're going to gamble on this new technology. They bought PCR from us, and just a few months ago said they're going to be the leaders in the field of pharmacogenomics, individualized medicine, and PCR is a key to that. I'm sure they had it in mind that they didn't have to sell it to anybody.

Hughes: I don't think you give yourself enough credit, and everyone else that was around in those early days, because by the 1980s, any way you look at it, there's an industry.

Cape: Yes, but you don't have to be successful. Even Barry Bonds only hit .341; you only have to be successful about ten percent of the time and you're sailing. I'm just saying, we were thrown out of lots of places, maybe unceremoniously only once or twice, but essentially by many, many companies hearing the story and not buying it.

Hughes: Was it the recombinant DNA story or was it any of the stories that you might have told?

Cape: Any of the stories. Well, we used to have an easier time selling the old stories because they were more consistent with science that the executives had learned themselves at school.

Hughes: For example, laser screening, because that went back to the microbe-as-a-producer idea.

Cape: Exactly right.

Hughes: So recombinant DNA tended to throw them?

Cape: Except, it only takes a few successes before—You take a Genentech's tPA and human insulin and—

Hughes: Well, what about somatostatin? Was that not enough?

Cape: I don't think that there was a big enough market clinically for that kind of product, although it is a biological reactive compound.

Hughes: But I've heard that somatostatin was a proof-of-principle sort of project.

Cape: Oh, there's no question about it.

Hughes: Why wasn't the drug industry looking at that when Genentech was successful?

Cape: I don't know. The agricultural applications, bovine growth hormone, came directly from that.

Hughes: And how did that…?

Cape: That actually built on intellectual property of the University of California at San Francisco. I believe there's recently been hundreds of millions of dollars passed between Genentech and UCSF.

Hughes: I don't know about the bovine. I know about human growth hormone.

Cape: As a matter of fact, I believe that there were even lawsuits going on between Genentech and Roche, and those lawsuits continued after Roche made the investment in Genentech. "We're independent companies. You do your thing." I don't know the facts there at all.

Hughes: Was your job easier after somatostatin in selling this technology?

Cape: Yes, I'm sure it was.

Hughes: You would deliberately point to what Genentech had done with somatostatin?

Cape: I'm not so sure. I don't remember. But it had to be. I mean, people who are negotiating don't say everything they know or think to each other.

Hughes: But you could have used it just the way Genentech did, as, okay, we've done it: we've shown that foreign proteins can be produced in bacteria.

Cape: Oh, yes. Nobody doubted that.

Hughes: Oh, but they did in the beginning, didn't they?

Cape: Yes, except for the fact that the vast majority of the drug companies have a prejudice against proteins. Who wants proteins? They're lousy drugs! There are a few examples, like insulin. We want small molecules. You can take them in a pill.

Hughes: Well, was that what their hesitation was?

Cape: Partly.

Hughes: But surely they could have seen the benefits of having human hormone as opposed to animal hormones to give to human beings.

Cape: Let me ask you a question. The transistor, when it was invented, clearly was going to obsolete the vacuum tube as an electronic device. Therefore, you would think that the people who would be big in transistors and, ultimately, in chips would be RCA and General Electric, the people who made the tubes. So where did Intel and Advanced Micro Devices come from? The establishment gets pretty sclerotic after a while, and the people who are invested in existing technology amazingly don't see themselves becoming eclipsed. Although you do see examples. For example, take the replacement of glass by cardboard or by other packages. I remember when I was at Harvard Business School that one or another company who was big in bottles said, "We're not in the glass business; we're in the packaging business. We've got to be aware of all the changes taking place. We've got to be there." That's the way we would have expected the

pharmaceutical companies to be. But when you're selling, you don't walk in and tell the guy he's an idiot.

Hughes: Had you been using the term biotechnology?

Cape: I don't remember. We were using "bioindustry." At the Homestead Hotel, Bill Amon, who was one of Cetus's employees and had been in the chemical engineering industry for many years, organized the meeting of the American Chemical Engineering group, and it was called Bio something, Poised for Growth. In other words, he was very predictive of all the things we *could* do. I wonder what term we used then. I do know that when we formed the group that's now called BIO—and it was the major biotechnology companies, not including Genentech, who we got into it maybe five years later—we called it the Industrial Biotechnology Association, and so by the time it got started, we used that name.

Hughes: What year was that?

Cape: '81, '82 or '83. Les[lie] Glick was the guy who brought it together. Is he still alive? He was the head of Genex. In fact, IBA existed in his offices for a while. Harvey Price was the executive director of IBA until more or less the same time Genentech came in. And we got a new head and he lasted until the present guy, [Carl] Feldbaum, took over. (Carl retired last year.) There was a smaller group called ABC, the Association of Biotechnology Companies, and finally the two of them merged and formed BIO, the Bio Industry Organization. In fact there was a time, to be absolutely unambiguous about what we were talking about, we called it the New Biology. We were talking about stuff that didn't even exist in 1965.

Hughes: What did you mean by New Biology?

Cape: Well, everything from recombinant DNA to monoclonal antibodies to PCR to all those things that were invented from 1970 on.

Hughes: Was there a difference between the New Biology and biotechnology?

Cape: No. The term, "biotechnology" sort of took its place. So now questions are asked, what's a drug company and what's a biotechnology company? Can you do better than Supreme Court Justice Potter Stewart and pornography and say, "I know it when I see it"? Except for Amgen and possibly Genentech, a biotechnology company is discovery oriented and tries like crazy to make a deal with a FIPCO, somewhere along the line. Where along the line depends on how much money they've got, because everybody's got a picture of a curve that goes in terms of your value with time. As you get into Phase II it goes up, particularly if Phase III is successful, it goes way up. And at what point do you make a deal with the drug company? The drug company's taking a risk too. They usually

don't want to buy in early. Everybody's got good ideas, but unfortunately there's something called experiments, to see if it works, right? And the biotechnology companies are very big in here, and drug companies make their big deals in—Merck advertises, we do basic research for improving the human condition, all that kind of stuff. But when you analyze what makes them big, what makes them big is the deals they make with products. And a Pfizer will buy Lipitor from Warner-Lambert, and how do they do that? They acquire Warner-Lambert! That's how they become big, big, big, big. Although they were significant research establishments, nothing like before the biotechnology industry came along.

Hughes: Well, we've been skirting around it. Now let's leap into recombinant DNA at Cetus. The program, as I understand it, began in 1976. Could it have been begun before, considering that one, Stan Cohen was an advisor, and two, the papers on the technology were written in '73–'74?

Cape: I don't know how much sooner it could have begun. The world got wind of the potential of recombinant DNA, as well as its dangers, around the time of the Asilomar conference, which was 1975. There was in fact a moratorium so that you couldn't go forward very fast until the rules were promulgated.

Hughes: So that was a break in your thinking?

Cape: I'm making it up; I can't say all this for sure. But I'm sure it must have been the case. We determined that we had to get a real good person to head it up, and I think we hired David Gelfand in 1975. I'm not absolutely sure. It might have been 1976.[6] I know that Genentech was formed in 1976. I know that Tom Perkins and Gene Kleiner invited me to breakfast in the Intercontinental Mark Hopkins. They asked me did I really believe in recombinant DNA. They were minor investors at the time in Cetus, and I said, "Absolutely." And they had in their minds clearly at that time of financing Genentech.

Hughes: They were trying to get a second opinion before they actually went ahead?

Cape: You could say that. I mean, I might have been the third or fourth or fifth opinion, but since they had invested in my company, they thought I would be a good person to talk to as well.

Hughes: But it was not, and then we will also invest in your recombinant DNA program at Cetus?

Cape: Oh, well, nobody ever invested in a program. We decided what money to put up behind each program. Except to the extent that industrial investors like Amoco or Chevron would say, we bought some stock. Also, we want to negotiate a

6. According to his CV, Gelfand joined Cetus in December 1976.

contract to pay you some money and get some work done. So there weren't related, but we never had a financial institution telling us, we're investing in you and you will do this. Not that I remember.

Hughes: And that was 1975?

Cape: That was '76, I think.

Hughes: So Genentech maybe was off the ground.

Cape: Yes. I am always fuzzy to what extent they were off the ground at what point in time.

Hughes: They were incorporated in April of 1976.

Cape: That generally coincides with my memory. But I'm certainly not a prime source for that. I don't know. And, incidentally, Bob Swanson had been trying to get a job at Cetus for a period of months. Probably the best thing that ever happened to him is that, for various reasons, we didn't offer him a job. He was fabulously successful at Genentech.

Hughes: What were the reasons for not taking him on at Cetus?

Cape: I would be inclined to remember, and this is *really* reaching. I don't vividly remember. But I believe the reason is that we thought we'd be top-heavy in executives and that, number two, Kleiner Perkins had given us some indication, Tom Perkins in particular, that they didn't think we were running the company right. Under those circumstances it struck us as sort of weird that one of their employees was looking to us for a job. But I'd be inclined to stress, probably, the other. We were a little company; what do we need all of these people on top, we'd have more chiefs than Indians. But I don't really remember. But I do remember that it occurred to me repeatedly, oh boy, that was the best thing that ever happened to him. Because, boy, he became the star.

Hughes: Swanson came to you selling recombinant DNA specifically? I mean, that was the program he wanted to head?

Cape: I don't remember, but it makes sense. I did not remember that he was leaning on us to get up and running with recombinant DNA, but it makes perfect sense that he would have. Why would he not? And it makes perfect sense that he was entirely sincere in wanting a job. It would be consistent with what Kleiner and Perkins asked me at that breakfast, because they were focusing on recombinant DNA, and did I believe in it? I said, yes, I believed in it. That would be consistent with Swanson telling them the same thing, and he's going to leave [Kleiner-Perkins] and form a company and they should invest in it. All of that hangs together.

[End Tape 7, Side B] ##
[Begin Tape 8, Side A]

Hughes: Stan Cohen came on your board sometime in 1975. I haven't pinned the date down.

Cape: He was not on our board; he was one of our scientific advisors.

Hughes: I meant the scientific advisory board. I suppose he was talking to you about recombinant DNA.

Cape: Absolutely.

Hughes: You could say that inadvertently Stan Cohen had prepared the ground for Swanson's arrival.

Cape: Well, yes, but remember that the way we were proceeding was not the way that Genentech proceeded. Genentech, in retrospect, was smarter and got a faster jump on it, but they got a jump on it by not doing things inside. There was no inside. Genentech was, if you like, a virtual company.

Hughes: For two years.

Cape: For two years—The work was done by Herb Boyer basically spending most of his time hopping back and forth to the City of Hope Hospital, and I believe there's still lawsuits there, too.

Hughes: There are.

Cape: Right. I don't ever recall talking to Stan Cohen about the possibility of him doing that with us. At the time—and I discussed this a little bit with some of our major shareholders, like Chevron and Amoco—we thought the way to go was to build your own labs and do it yourself. Obviously that was at the cost of some time, and building our P3, and hiring David Gelfand, and all this kind of stuff. When did David Goeddel join Genentech?

Hughes: My guess is pretty early, like 1977-1978.

Cape: Ah, you see. The point is that Herb Boyer did all that work for Genentech!

Hughes: Well, Herb Boyer's post-docs did it.

Cape: Such is always the case.

Are you talking about [Axel] Ullrich and –

Hughes: No. Ullrich was doing the insulin.

Cape: In Howard Goodman's lab.

Hughes: Yes. It was essentially [Herbert] Heyneker, who was in Boyer's lab, and two scientists at City of Hope, Art Riggs and Keiichi Itakura.

Cape: Exactly right. Yes, I remember.

Hughes: It was a virtual company then. Genentech had contracts with City of Hope and UCSF. It also had a contract with Caltech, which didn't go very far. But getting back to Stan Cohen, because I'm interested in his early connections with Cetus. I wasn't thinking that you would contract with Stan Cohen. I imagine that he was saying to you and Farley that here is this technology he'd developed. But *he* didn't want to get into its commercialization.

Cape: [Interrupts.] You remember he told what's-his-name [Niels Reimers], that it wasn't worth patenting?

Hughes: He didn't say it wasn't worth patenting. He said that he didn't think he could patent it because some of the research money had come from NIH. He didn't think it was patentable

Cape: It was important enough to patent, but –

Hughes: Do you remember in those very early days when he first came on board that he was talking about the commercial potential of recombinant DNA?

Cape: Oh, *yes,* we talked about that a lot. But I can't remember the particulars of any single conversation. Why would we bother with it if it wasn't commercially important?

Hughes: Yes, and why would you have Stan Cohen on your scientific advisory board?

Cape: That's right.

Hughes: But do you see what I'm trying to get at? It wasn't as though Swanson appeared on your doorstep and out of the blue introduced a new technology. You *knew* about recombinant DNA.

Cape: Well, I was going to tell you a very short story about the fact that we had ongoing relations with, among other people, e.g. Ciba Geigy. The head microbiologist, Jacob Nuesch, at Ciba-Geigy came over, and we had a very friendly visit. I said, "Who do you want to talk to, Josh Lederberg? "No, no, no, I want speak to only two people in the Bay Area, Stan Cohen and Herb Boyer. That's who I want to speak to." And this was '74, I think.

Hughes: Really.

Cape: So I mean, they were aware, we were all aware that this [recombinant technology] was very exciting, super dramatically exciting. The question was, how to get started? Somatostatin as a demonstration project was extremely brilliant on Genentech's part. We spent a lot of time spinning our wheels trying to figure out what to work on. In the meantime, we didn't think it was any great rush. I don't mean we'd wait five years, but we could certainly wait a number of months, maybe a year or a year and a half, until Asilomar got behind us, the moratorium was over, we built our own labs, David Gelfand hired some people so we'd be able to do work inside, and we chose targets. And Shell's impending investment in an interferon project figured somewhere; they ultimately paid for building our facility.

Hughes: Do you remember what the considerations were early on as targets?

Cape: Mainly biologically active molecules. You'll see, when we look at that proposal made to Syntex. That was about the time we made the proposal to Syntex.

Hughes: I want to see that. You think that's in your trunk?

Cape: Oh, yeah. I'm pretty sure it is.

Hughes: People talk about the low-hanging fruit.

Cape: Human growth hormone and insulin.

Hughes: Yes. You look at what a lot of the companies are working on, Cetus perhaps being the exception, and they are pretty much the same things.

Cape: I haven't said, simply because it hasn't occurred to me to say, we were after human insulin too. We went out trying to sell it to this one and to that one, and we failed. Nobody would buy the project from us.

Hughes: Why was that?

Cape: We didn't have human insulin in hand. We were going to produce it. I don't know when Genentech got any money from Lilly. It may have been done on spec—I don't know.

Hughes: Well, the contract with Lilly was not signed until after Goeddel had cloned human insulin. In other words, Lilly wanted to see that it could be done, and then they were willing to sign a contract.

Cape: We were very interested in insulin. One of our consultants was Don Steiner at the University of Chicago, who should have gotten a Nobel Prize. He discovered

preproinsulin, in other words, the idea of a hormone existing in two prior states before it gets converted to the active state, and why, and how. We absolutely believed it. As a matter of fact, on one particular occasion, Don Glaser and I flew for one night to make a pitch in Europe. We slept overnight, I remember, in Brussels, we went to a meeting, and we flew home. That was it.

Hughes: To pitch human insulin?

Cape: To pitch human insulin, yes.

Hughes: To whom?

Cape: I believe it was a combination of two companies—Ciba-Geigy and Gruenenthal. And the meetings were held in Gruenenthal's offices, which were near Aachen in West Germany, which is right across the Belgian border, which is why we spent the night in Brussels.

Hughes: And what year might that have been?

Cape: I don't remember, but it was probably '76, '77, something like that.

Hughes: You didn't succeed?

Cape: Well, our business model was, we don't do it unless somebody pays for it. I'm suspecting Genentech spent their own money on it. Is there anybody around who remembers? Would Kiley remember?

Hughes: Oh, sure. And it's probably in the oral histories already. Interestingly enough, at the same time, Lilly had a contract with the UCSF group.

Cape: Really?

Hughes: Yes. The UCSF group now claims it did not know about the Genentech contract.

Cape: I'm not surprised. We had a few things like that. When we worked on a single-cell protein with Imperial Chemical Industries, they didn't tell us they had a parallel effort going. They were in a race with us to do it themselves, as opposed to letting us do it. They had the result of all our insights and all of their insight, and we had none of their insight and only our own, and we lost by a week, or something like that. And they told us, well, that's the American way.

Hughes: Were you a bit bitter?

Cape: Yes. But what can you do? I've come away from all of this with the feeling that big companies act like big companies, and they think they can push little companies around, and they do. No malice there. They do it because they can.

By the way, one of the funniest things that ever happened was when the ICI people came to Cetus with this project and asked David Gelfand, "What are the chances you can do it?" And he said, "Fifty-fifty." And they said, "That's good. How do you figure fifty-fifty?" He says, "Well, either it will work or it won't."

Hughes: That's great. Another possible impediment might have been the patent application by Stanford and UC on recombinant DNA technology. Did you pay attention to that?

Cape: I figured if it goes through, it goes through. Remember, patents in those days were sufficiently a point of argument, philosophic as well as otherwise. Could you patent life processes? There are many reasons to say yes, but a lot of people were saying no, and some people were saying it's not important, among them Wally Gilbert. In his business plans for Biogen and other things he was involved in, he would go around saying that patents aren't important, which of course is ridiculous.

Hughes: Why did he say that?

Cape: I have no idea. Never discussed it with him.

Hughes: You didn't think that, did you?

Cape: It never crossed our minds to slow us down. If it turned out that you had to pay a fee to Stanford and UC, you'd pay a fee to Stanford and UC. I believe that later on in our life, maybe in the middle of the '80s, we had made the posturing that we thought the patent was invalid or that we weren't going to pay it or something like that.

Hughes: Yes, Cetus stopped paying the license fee.

Cape: But that must have been under Bob Fildes's regime, and he was making all the decisions. But I do know that the fact that the universities had a patent on it had zero retardant effect on us going ahead.

Hughes: That's interesting and a differentiation from Genentech. Swanson, at the time that Genentech [was] being founded, hounded the Office of Technology Licensing at Stanford and, to a lesser extent, UC—because UC was not as active a partner—trying to get an exclusive license.

Cape: Well, Niels [Reimers] was handling the whole thing for both universities.

Hughes: Yes, he was. Niels refused to give an exclusive license. But that's what Swanson wanted.

Cape: But I didn't think that anyone ever assumed that Genentech would get an exclusive license, nor that it was necessary, but it would have been awfully neat for them to get it, from their point of view.

Hughes: It wasn't a slam-dunk decision on Reimers' part.

Cape: Really?

Hughes: I guess an exclusive license is one true way of getting a technology developed.

Cape: Do you realize that the total amount collected by UC-Stanford for recombinant DNA is less money than what we got from Roche for PCR when Roche already had an exclusive fifteen year license?

Hughes: No, I hadn't. [tape interruption]

Hughes: The recruitment of Gelfand: he was your top choice?

Cape: Yes.

Hughes: Why?

Cape: I liked him enormously, I thought he was brilliant, and he wanted to come. I'd totally forgotten it; hadn't thought about it for twenty years: there was a delay involved in his coming to Cetus. We negotiated the terms. There was a little bit of back and forth there that took a few weeks—his lawyer, our lawyers, all this kind of stuff, but that wasn't it. He was the top guy in the laboratory of Gordon Tomkins, who died of a brain tumor. Gelfand felt that he had to wind up, in a neat way, everything that was going on in that lab. That was going to take him some months, and he couldn't come to us until he was done with that. I don't remember at all how long that was. But that was something we were agreeable to.

Hughes: That's interesting because it shows intent on your part.

Cape: You know, time is more important than anything. On the other hand, it does show also how much, A, I was committed to recombinant DNA and, B, I was committed to getting the best guy I could find to head it up.

Hughes: Tell me a little bit about those negotiations, because the biochemistry department at UCSF was one of the centers of the firestorm in academia about commercialization of this technology. Obviously, Gelfand knew that this was going on.

Cape: I spent a lot of time with him at a meeting with him at MIT.

Hughes: Trying to recruit him?

Cape: It wasn't trying; I knew that it was going to be successful. We seemed, at the very outset, to like each other and agree, but we had to do it the right way. I subsequently met him and some other people in a meeting in Milan, and I wonder when those two meetings were. My guess is '75 and '76.

Hughes: Were you going to these meetings to keep up but also to meet people?

Cape: Both.

Hughes: Why did Gelfand come?

Cape: Oh, because it was then, and to some extent it still is, a lot easier to operate in a biotech company than in the university. In a university your typical good guy will be spending thirty percent, maybe forty percent, of his time writing grants. And it's a real pain in the neck; it's all bureaucracy, and it drives you nuts. You're dealing with the federal government, one way or another. It was our good luck—all of us, the scientists and the people who ran the biotech companies—to be on top of everything that was breaking scientifically in the world. There was very little distinction made between if a breakthrough came in a company or in a university lab, and Genentech is the most visible example of that. Another example of that is, unlike—in most fields, if a guy leaves the university and goes into industry, that's it; he's killed his academic career. There are many examples, and we had one, Norm Arnheim, who came out of a university lab to Cetus and went back as the chairman of a university lab at USC. It was happening all the time. So you could have your cake and eat it at the biotech company and, if you were lucky, get rich.

Hughes: So did stock options always play a role?

Cape: Always, always

Hughes: So it isn't just the promise of the science and its application. It's the fact that people have a chance of getting rich, which they know darn well they're not going to do if they stay in academia

Cape: Right.

Hughes: Do you think that's almost always a factor in recruiting people?

Cape: I can't say that I've studied it. My gut feeling would be sure, it had to have an effect.

Hughes: What did you and Gelfand discuss?

Cape: What the team was going to be like, what projects could be done.

Hughes: Do you remember talking to him about what commitments Cetus would make to recombinant DNA, in terms of money and program longevity?

Cape: Must have done, but I don't remember the specifics of it at all.

Hughes: Did you give him the responsibility to recruit his people?

Cape: Basically, yes.

Hughes: Do you remember where they came from? Were they from one institution more than another?

Cape: I don't really remember. Everybody in the world that was doing this kind of work was known to each other, and that was the pool you worked from.

Hughes: And a lot of them were right here in the Bay Area.

Cape: Like Kary Mullis. People like Art Riggs and Itakura had their own people, and sometimes we got one or two of them, or people that were one step removed from them. Everybody crossed everybody else's path. Ullrich and another guy came to see us too. And I talked to Howard Goodman at some length before he went to Harvard.

Hughes: Do you remember why all those people didn't come?

Cape: No. You are competing with some very attractive things, and to go to Harvard is certainly—

Hughes: Well, that's a hard one to beat. And, of course, the UCSF folk were doing their best to keep him at UCSF, which didn't work. In recruiting scientists, did you care at all whether or not they had any business sense?

Cape: No.

Hughes: You were going to handle that?

Cape: Yes, and we learned pretty soon that the red herring that you're going to have trouble with these academic prima donnas turned out to be a red herring. We really found the people extremely obsessed with success. The saying that went around was, if the experiments are working, everybody's gloomy, and they think you're not running it right or something. If the experiments turn out well, everybody's happy. If they don't turn out well, everybody's unhappy.

Hughes: Scientists obviously want scientific success. Well, scientific success in a company is obviously going to lead to corporate success, unless the business people are—

Cape: [Interrupts.] One of biggest problem that Genentech had was the fact that their scientists were giddy with their own success, and they would blurt out more stuff and show more data than was prudent. Certainly by drug company standards, it was appalling. There was a certain amount of mistrust of all of us [in biotech companies] as a result of the worry that these guys had no control over the scientists. I remember specifically becoming friendly with some of the people at Eli Lilly, and at a scientific meeting someplace in the South, the Lilly people were ordered not to talk to us, not to socialize with us, that we were spies and evil. It was really bizarre. Needless to say, we didn't pay too much attention to that.

Hughes: And you're saying that you at Cetus were tarred with the Genentech brush?

Cape: No, not necessarily. But it is true that they would show a sequence, and other people would go "click" and take a picture of it. This I have no proof of, but people told me they'd sometimes make a mistake or two in the sequence to deceive people who thought they were going to easily copycat them. They played that game with Amgen a few times back and forth. There was too much show and tell, a little bit too much show.

Hughes: What was Cetus policy in those early days about publications and presentation at scientific meetings?

Cape: It was very nonobsessive and very common sense: we count on you to use your own judgment. Remember, we're a team and we're in competition with other people. So for God's sake, keep that in mind, and your stock options are a way of having you keep this in mind. But it was never, ever a disciplinary problem. I can't remember a single episode *ever* of a person being called on the carpet for having blurted out too much confidential information.

Hughes: Were papers vetted before they were published?

Cape: Maybe by their scientific superiors.

Hughes: But not by the attorneys?

Cape: You know what? There must have been something. The value of our patent department was that they would go into scientists' labs and say, "You've got an invention here! Come on! Let's prepare you a patent application up here." And they'd facilitate the process. And then there was a lot of discipline applied by those guys on the keeping of notebooks properly, and stuff that might be more

sloppy in a university. But again, I don't recall anybody ever complaining about "There's too much control here, it's like a Gestapo"—never.

Hughes: Who were your early intellectual property people?

Cape: I don't remember having a law firm other than Heller Ehrman. Now that sounds to me a little bit narrow-minded.

Hughes: Meaning that you didn't have in-house counsel?

Cape: Oh, we had a lot of in-house. We had an in-house patent department of about a dozen people.

Hughes: Beginning when?

Cape: 1980, 1982.

Hughes: When you became public?

Cape: Yes, maybe a little bit before.

Hughes: But before that you were dealing with –

Cape: No, we had one or two people inside. Julius Tabin, who used to do patent work for the Salk Institute, was also one of our attorneys.

Hughes: Because he knew biological material?

Cape: Yes.

Hughes: I'm blanking on the name of the attorney who came sometime in the '80s.

Cape: Well, there was Al Halluin who headed our patent team, and later, Peter Staple. Michael Ostrach was head of our legal department.

Hughes: Do you remember when Al started and why?

Cape: Oh, we knew that we had to have the kind of almost camaraderie that would develop in an in-house person or persons, buddying it up with the scientists and going through the work and saying, you think you just spent a regular day, but you just invented something. So let's make a deal out of this.

From what I hear, scientists weren't used to thinking in terms of intellectual property.Hughes:

Cape: But I don't recall them getting their backs up about it.

Hughes: No, I'm not implying that. But it was a learning process.

Cape: We were very successful with PCR; we beat DuPont. They had a Nobel Prize winner testifying against us, and the jury ruled on about 250 counts, and we won on all counts.

Hughes: That Nobel Prize winner being Arthur Kornberg?

Cape: Yes. I thought his position that the technology, which has since proved to be perhaps more valuable than recombinant DNA, was obvious, well, why didn't anyone do it? Nobody was buying that argument. By the way, a friend of mine went to the hearing one day—it was the trail of the patent— and called me that night and said, "You're going to win." "How do you know," I said. He says, "Well, I listened to your guy [Kary Mullis]. He's nuts, just like an inventor. The jury's going to pick that up."

Hughes: Getting back to recombinant DNA at Cetus, please tell me about the P3 lab. This wasn't just taking on a minor technology. This meant building specific facilities.

Cape: Oh, yes, and we overdid it. David Gelfand had a lot of fun building that thing, I think. He with the architects that designed it. If you fired a bullet through the wall, the wall would reseal immediately—all kinds of things that I don't think the government had—maybe in their P4 establishment when they were handling Ebola and stuff like that. But as it turned out for recombinant DNA, although one should always expect the worst, no hazard has been revealed in all these years.

Hughes: But you didn't know that.

Cape: We didn't know that. So this was another illustration of the commitment to recombinant DNA.

[End Tape 8, Side A] ##
[Begin Tape 8, Side B]

Hughes: This is a quote from Farley in 1977 regarding recombinant DNA. "We made a decision to push genetic engineering aggressively, but we determined to keep it in perspective. It is a tool—a very useful tool at that—but is not an end in itself. If we are trying to solve… a problem and we can be very specific about what we need to do, then we can exploit the tool."[7]

Cape: Sounds very sober. If I were an investor, I'd much rather hear the Genentech thing: we are going to be the best in the world in this *incredible* new

7. Roger Lewin, "Modern Biology at the Industrial Threshold," *New Scientist*, October 5, 1978, 18-19, 19.

development. Everybody's going to be eating our dust. That's a lot more dramatic.

Hughes: I don't think Cetus had to worry about not showing up with glowing prose!

Cape: Pete Farley stated in 1980, "We are not going public!" That's like [California Lieutenant Governor Cruz] Bustamante saying, "I am not running in this election."

Hughes: I saw a reference to Cetus early work with *B. subtilis*.

Cape: Oh, yes, Shing Chang, who left us to go to Abbott, was a world expert in *B. subtilis*. The advantage of *B. subtilis* was that it's a gram-positive organism, whereas *E. coli* is a gram-negative organism, and that just creates a new class of bugs that you might use in production. We were banging that drum for a while. I don't think it ever went anywhere.

Hughes: I don't understand the significance of the gram positive and negative.

Cape: Oh, it's a totally arbitrary way of splitting all bacteria into two groups, one group that gets stained by the gram stain and one that doesn't.

Hughes: Yes, I know that. But in terms of production?

Cape: Well, I don't know of any *B. subtilis* systems that have ever been developed. I guess the answer was we don't need it.

Hughes: Why did you care?

Cape: Oh, it seemed to us to broaden the base of the capability; that's all. I'm making this up. For example, one of the things you have to do in harvesting the yield from a gram-negative organism is to bust up all the cells. And I think *B. subtilis* may secrete what it produces, and therefore you could almost make a continuous process—filter away the cells and just harvest the soup.

Hughes: That makes sense in what I've heard from some of the [inaudible] talk at Genentech, you know, the fact that you discovered that it could be excreted. I guess [inaudible]. But it went nowhere, as far as you remember.

Cape: As far as I remember. There was a cartoon in the *Chronicle* the other day that had this guy testifying: "To the best of my knowledge…", "As far as I can remember," blah, blah, blah. And it said at the bottom, "How you can tell you're dealing with a liar."

Hughes: When you brought in this technology, with a rather high-powered scientist at the head of it, and facilities being built, was there some jealousy at Cetus amongst the scientists who were *not* doing recombinant DNA? Was there some antagonism against the new guys?

Cape: Antagonism, I wouldn't say. But there was in the scientific community at large, between the biochemists or the "old-fashioned" microbiologists and the new guys, because in the academic world the new guys were getting all the headlines and sooner or later all the money. And that really hurt. And in the scientific community and to some extent inside of companies, I'm sure there must have been a certain element of, what are we, plow horses, and these guys are the racing thoroughbreds or something? I wouldn't say it ever became a major problem. I can't remember specific examples of it. But since it was all around me, in our dealings with academe and stuff, I'm sure it must have existed to some extent.

Hughes: One last question and we will end for today. In 1981, Tom White was named head of Recombinant Molecular Research at Cetus. What happened there?

Cape: Well, I think David, as I recall—On balance it's a question of how much you want to be an administrator and how much you want to do science. If there's somebody who's willing to do the administration and looks like he'll be good at it—By way of analogy, and I'm trying to reconstruct history which I don't remember too well: at Harvard, being the chair of the department is not considered an honor; it's considered a duty that somebody's got to do, and thank God it's only for two years or three years. Then you get back to doing what you love, which is the science, rather than spending your time in meetings and disciplining people and saying what can and cannot get funded. That's no fun.

In any event, I remember that the switch was made. I remember proposing it to Tom in my car returning from a meeting in Palo Alto. You're talking about the human factor that we were talking about at lunch. I remember driving back from a meeting with our people at Palo Alto, and the highway goes by the Coliseum when I started talking about this to him.

Hughes: Well, let's stop there.

[End of interview.]

Interview 5. October 28, 2003

[Begin Tape 9, Side A.] ##

Cape I heard the expression recombinant DNA through a very, very strange source, and that was I.F. Stone's son who was also a journalist. He came to me, and his notes would have to show that I didn't know what he was talking about at first when he talked about recombinant DNA. And that must have been in 1974 or so. I'm trying to think of my earliest memories on the subject. Another one is sort of funny. I think it was Michael Rogers, who is now the head of science at *Newsweek* and actually has a web page. He came to interview me about this whole subject around 1978 or 9, and I mentioned to him the fact that I had *not* been at the Asilomar meeting. A lot of people that I knew well were there, of course, like Josh Lederberg and Stan Cohen, to use examples. However, the funny thing to me was that in reading various reports about Asilomar, the best one was, in all places you would never imagine, but there it was, and I read it, and it was great. It was in *Rolling Stone.* He said to me, "Well, I'm glad to hear it. I wrote that."

Cape Have you interviewed Josh Lederberg?

Hughes No.

Cape He's a very good person to interview.

Hughes I know. He was an early, early early promoter of the commercialization of recombinant DNA.

Cape And also warning a lot of people who weren't listening, the drug industry that they shouldn't give up on anti-infectives. The war against infective organisms will never be won. It's a standoff, always a standoff, and equilibriums reestablish themselves over and over and over again. There's so much history that points this out, that how they can be so foolish to say that antibiotics have wiped it out? Besides which, antibiotics don't do anything about viruses, so how could you stop working on these?

Lederberg also predicted, if you like, these virulent strains of influenza, SARS, and AIDS. We just don't know the names of the epidemics that are coming along, as they always do, to a population that has never seen these organisms before. And the first confrontation is devastating. And he went on and on and on

in a much more sophisticated vein. This was in the sixties he was writing stuff like this. He continues to be a consultant for the government in one capacity or another for a lot of secret stuff.

Hughes Am I right in thinking that once Cetus's recombinant DNA effort got off the ground, that its initial aim was *not* human pharmaceuticals, rather it was products that were financed by Standard Oil and National Distillers.

Cape You probably read a remark by Jim McCamant. Recently I read some of the description of Cetus that sort of sounds like that and is completely wrong. In point of fact, it seemed, I think, to everybody at the time, including us, that the most likely big winners in recombinant DNA would be in the human medical field. However, yes, our principal investors were heavy chemical companies, and they were also interested in other stuff. And even people who weren't investors in us. The predecessor of AstroZeneca was called Imperial Chemical Industries, and they were an enormous company like Dupont. Part of their biological effort had to do with single-cell protein. We worked with them on recombinant DNA techniques to address the best possible single-cell organism with the highest protein levels or the most efficient way of producing them, stuff like that. We also worked with General Foods on converting used coffee grounds to edible (for pets anyway) single cell protein or SCP.

So yes, we broadened it beyond human medicine, but it would be absolutely wrong to say we were turning our backs on human medical applications and instead did that. It was in addition we did that, and a lot of the things that we were doing for Standard Oil of California, of Indiana, and for National Distillers, also an investor, were more in the field of what you would call industrial chemicals. But we were not principally using, as I can recall, recombinant DNA for those. The main heavy industrial application was that single-cell protein project for ICI. And just to stress the point, our final big investment by an oil company was not a stockholder. It was Shell Oil, and that was on interferon. So I rest my case. And they built our P3.

Hughes Shell did?

Cape Yes, it was their money that built the recombinant DNA lab.

Hughes Why would Shell support a project on interferon?

Cape I believe – this is sort of psychopop, or psychobabble maybe—that following the Yom Kippur War and the Arab oil boycott, many, if not all, of the major oil companies started to look around for other kinds of businesses with massive implications that they should be studying just in case it turned out that—as tobacco turned out for other people—long-term maybe [oil]'s not. A business without a lot of problems; it would be nice to have a backup. But it had to be a big backup. And different companies went into exploring biology in different

ways. In some cases, mainly investing in companies like Cetus and looking over our shoulders would give them some beginning familiarity with what was going on. In other cases, like Shell, they simply picked a medical application and were the chief financers of it. And, in fact, Shell did create a subsidiary called Triton, and that basically has evolved through various mergers and acquisitions and one thing and another to a non-Shell-related company, I believe, called Berlex, which is, in fact, Chiron's partner in—

Hughes Betaseron.

Cape You're right. Anyway, it was that rationale that was widely used. I never had reason to doubt the sincerity of that in dealing with Amoco, in dealing with Chevron, in dealing with National Distillers, and in dealing with Shell. That seemed to be where they were coming from.

Hughes Well, talk about the physical containment facility. Over lunch, you said something along the lines that it was overkill.

Cape In retrospect. It was being prudent in advance. Just like the Asilomar conference and the recombinant DNA guidelines that arose out of it would seem now, reflecting back, to have been overreaction. But prudent overreaction. How do you know that somebody's going to be safe? You can't just assert it, particularly since you're seen as self-serving by asserting it, and indeed you are being self-serving. When I think of the current controversies about so-called "Frankenfoods" and stuff like that, I definitely have the feeling that the lack of a demonstrated hazardous event is seen as proof of safety, which it isn't. Lack of evidence is not evidence of absence, right? And certainly some of the issues having to do with gene containment show that once the cat is out of the bag, it's very hard to get the cat back into the bag. Certain genetically engineered combinations and genes in corn seem to have found their way into corn where it wasn't intended to be. The famous monarch butterfly experiment turns out maybe not to have been as dramatic as it looked at the time. Nonetheless, the point is that these are new [genetic] combinations that evolution didn't come up with, and who knows what they may lead to, and what except the rush to profits would justify hurtling forward as fast as possible? The only thing I can see justifying it are the medical applications, and by and large, with some exceptions now, the medical applications have not met with that much opposition. People have sick kids and relatives, and they desperately want new approaches—cures for cancer and stuff.

Hughes Are you advocating a go-slow policy for the non-therapeutic areas?

Cape I'm not really advocating anything. I'm just saying that looking at it from the sidelines, I see people behaving predictably and in a self-serving manner and trying to pass off as proof of safety something that leaves me a little bit worried that that's not proof of safety at all. But the record is a good one. The record is

that there have been none of the catastrophes that were anticipated. But like we see with infectious disease, you sometimes find out something that you don't anticipate, and there seems to be some reason to go partly slowly. But as we see with the space shuttle, priorities start to get mixed up, and a person who is not involved in the thing might think that things should go more slowly, and there's a certain human tendency to push.

Hughes Let's now talk a little bit about the controversy in terms of the [NIH] guidelines that were formulated. And I believe that you were a part of that process on several different occasions. For example, in June of 1976, which is when the guidelines were first published, there was a group of industry representatives that met to discuss the NIH guidelines. Do you remember if you were involved that early on?

Cape Only indirectly. I do remember that I was involved, and my memory goes back to a confrontation with a Nobel Prize-winning scientist at Harvard. But it was a meeting I went to at MIT.

Hughes Oh, that famous meeting where there were signs with quotes from Hitler?

Cape No, that was at the National Academy of Sciences. I was there too. George Wald is the guy's name, and his wife Ruth was even more of an activist than he was, Ruth—

Hughes Hubbard.

Cape Yes. He got up, and with conspiratorial overtones, implied that all those evil men in industry have gotten together and said thus and such and done thus and such and plotted thus and such. I went up to him after the meeting, and I chatted with him a little bit and told him I found his remarks very interesting. Some of the points that he had made were on a piece of paper, and he handed it to me. This was a five-minute conversation after the main program, and I said, "You made reference to a meeting of industry, and I believe it's a meeting that I attended." I don't remember what the meeting was, but I sure remembered *then* what the meeting was. But as I say, this was back in 1975 or '76—you can look up when that meeting was at MIT. And I said, "I'm sure you would want to know from a person who was there that none of things that you mentioned happened. None of the plots or statements or actions that you were concerned about—I want to give you some comfort—they didn't happen." And he said, "You're a liar!" and he grabbed the sheet that he had given me out of my hands and stomped away.

That is all I remember about that meeting of industrial people. I don't remember where it was held or what was discussed, but I do remember how shocked I was that, in this case, as I saw it anyway, politics was running a person, a splendid scientist's brain, instead of wanting the facts or the truth. Coming right up to now, I have the feeling that one of the biggest mistakes that the proponents of

speed with the New Biology and all of the wonderful things that are going to come from it, if only the public understood, then we wouldn't have a problem, and that is absolutely untrue, as far as I'm concerned. They are oversimplifying, unbelievably so. There are many, many different kinds of truths, and people may have a series of priorities that have nothing to do with what a scientist's series of priorities are.

Not only that, but there's this whole subject that is sort of amusingly and entertainingly handled in Dan Brown's books, like *The Da Vinci Code*, that the religion versus science debate that's been going on for many, many years is easy to oversimplify. But the point is that if it's put in the proper hands, it can be described in a very fascinating manner, the bottom line of which is, some people can be very religious and very scientific at the same time. Go figure. And the conflicts that go on in their mind they seem to manage all right. Here is a case with George Wald where his politics and his science, or the matter of the facts that he was recording, might have gotten mixed up.

Hughes You testified at the Thornton hearing of the House Subcommittee on Science, Research and Technology in March 1977. Do you remember that?

Cape No. If I had a copy of it, I'd remember it. I remember, Oh, my God, I'm testifying in Congress.

Hughes That was the first time?

Cape Yes. It was really very fascinating.

Hughes Cohen testified in that same hearing, and I understand that your stances were not identical. He was from the very start saying that certainly federal legislation was not necessary. He did some experiments that showed that genetic transfer occurred under natural circumstances, which was supposed to obviate people's fears about genetic engineering.

Cape I don't remember enough about what I said or about what he said at the time to add anything to what you've told me.

Hughes I don't know if you said it at precisely this hearing, but you were saying generally that industry should be regulated.

Cape Well, as I said to you at lunch, I have the feeling that industry, without some regulation now, what specific regulation remains to be a very important detail—is like a football game without some referees or umpires. People kill each other. I mean it's pretty brutal. I early became suspicious of the Washington, inside-the-Beltway bureaucrats and staffers and what-have-you who think regulation is the answer to everything. They spend all their time in markup hearings for acts of Congress and in regulation creation, and they love it. As we find in security

regulations, smart people can get around them. What Stan Cohen may have been worried about, as well as scientific issues, is Gresham's law for currency that flows out to bad places. Scientists will simply move to places where there is no regulation. And, as a matter of fact, many of them did for a while. During the moratorium, particularly. Because time is everything. It's money, it's Nobel Prizes, it's everything. The first to get through the goal line is all that everybody remembers.

Hughes What did you think of the groups that did go abroad?

Cape I forget who they were.

Hughes Ullrich went to France to work on the human gene for the UCSF group.

Cape Well, are you talking about insulin or about human growth hormone?

Hughes I'm talking about insulin.

Cape I was hearing rumors at the time, and they still remain rumors to me; I have no first-hand knowledge. I do recall people saying that some people took things out of Howard Goodman's lab. I just don't know.

Hughes It was nothing that Cetus ever contemplated?

Cape I like to think that that's true. I don't remember anything that would contradict that.

Hughes You didn't have European operations at that point.

Cape Yes, but I imagine one could have found a university lab that would be available to you in any one of a number of countries. I just don't know. As far as I remember, we didn't contemplate it and we certainly didn't do it.

Hughes Here's a direct quote from a hearing of the NIH Directors' Advisory Committee.

Cape RAC.

Hughes RAC, in December of 1977. This, to remind you, is at the height of the push for legislation. There are a number of bills in both houses seeking to legislate control of genetic engineering.

Cape It is, by the way, a peculiar American habit of assuming that if something passes the United States, the whole world is going to follow suit. Considering the fact that that is manifestly absurd, you sort of wonder why these zealots get so worked up about trying to save humanity, which is what they're talking about. What are they going to do about India? What are they going to do about Japan?

What are they going to do about France? It's crazy. They never seem to think about that. They certainly don't talk much about it.

Hughes This is Ron Cape: "[The NIH provides] no review process regarding our plans, our protocols, our containment, and so forth….we can't…officially interact with or enlist the assistance of our government in adhering, as we are committed to do, to the NIH Guidelines. What we want is diplomatic recognition."[8]

Cape [You're talking only to?] Eli Lilly and Merck. We're the guys that are doing it, and you're not talking to us. It would be nice if you did.

Hughes "Us" being small biotech companies, which might not even have been called biotech companies at that point.

Cape They weren't.

Hughes In the same month, December 1977, you attended a meeting at the headquarters of the Pharmaceutical Manufacturers Association.

Cape Oh, yes?

Hughes Which was attended by representatives of Lilly, Upjohn, and Roche, John Adams of the PMA, and representatives of the Department of Commerce, the NIH, and the Office of Science and Technology Policy.[9] The topic was voluntary compliance with NIH guidelines by private firms. Do you remember, and can you remember any of the debate?

Cape No.

Hughes As you remember, the NIH guidelines did not cover industry.

Cape That's right; they never did. But they would review an industrial application if it was presented to them. So it would be pretty stupid to go ahead and draw the ire of people, justified or unjustified, and put yourself in that position, [by not presenting an application to them.].

Hughes I would suggest that review was preferable, not only by the so-called regulators, but for public approval. It was at a time when the public was getting all hot under the collar about the biohazard situation.

Cape That's a whole separate subject. I've got lots of opinions about that. You know who you should also speak to about the early days? David Padwa. He was the

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8. Susan Wright, *Molecular Politics: Developing American and British Regulatory Policy for Genetic Engineering, 1972-1982*, University of Chicago Press, 1994, p. 294.
9. Wright, p. 294.

head of a company called Agrigenetics. My memory tells me in 1983, they became an unfortunate victim of a down market, and he retired – brilliant guy—to Santa Fe, where I think he still lives. He must have some great memories of those days. He referred to some of these critics as Ayatollahs.

Hughes Was it in your mind as corporate executives to project a public image of concern about the potential biohazards?

Cape Yes. It seemed like the decent way to behave, and why not? You're not always in the spotlight; it's sort of good luck in a number of different ways. And how often do you have a visible chance in your life to take the high road on something? It's sort of self-serving to say that, but, yes, the answer is yes.

Hughes You also had Shell with deep pockets which was going to pay.

Cape I never consulted them on stuff like that.

Hughes I'm meaning, you had Shell which would come up with the money to build things like a physical containment facility.

Cape That's right.

Hughes Which maybe some companies couldn't have.

Cape Yes, but universities had them, I think. In any event, it was one way of looking as if we were going the extra step in compliance that we didn't even have to do, just in case. Not that we thought that there was any hazard, but why take the chance?

Hughes Do you remember hassle? I mean, there was quite a procedure, as you probably remember, where proposals had to be passed through RAC. I know some companies were concerned that in the course of that process, corporate secrets could be exposed.

Cape I don't remember ever discussing that. You should ask David Gelfand about more details. He was intimately involved in both the design and the construction of the P3 lab. He remembers stuff I don't remember or never knew.

Hughes Do you think he went to some of those RAC meetings?

Cape Yes, I do.

Hughes You didn't.

Cape Maybe I did; I don't remember.

Hughes Another thing that I know bothered Genentech, and I wonder if it bothered Cetus, too, was the fact that RAC had a 10-liter [production] limit.

Cape I remember that. Yes, it was a concern, I'm sure. If somebody had asked me at that time, I would have said it was a concern. I don't recall if anybody asked me, because sooner or later that won't do in production.

Hughes None of these things you considered to be severe roadblocks.

Cape Oh, they were going to slow things down, in a way that was okay.

Hughes None of this, obviously, was enough to deter Cetus from getting on the recombinant DNA bandwagon.

[End Tape 9, Side A ##
[Begin Tape 9, Side B]

Cape Companies with large investments, large sales, and a long tradition have a lot to lose and very little to gain by technology that might pay off ten years later. Little companies that are trying to prove themselves and have no investment in the way things are, but have a big investment in change, and are selling their ideas and their stock to people who would like to be part of change, have everything to gain and nothing to lose. That's built into the system. That's why the people who were selling vacuum tubes, who should have been the people who led in transistors and solid state stuff, didn't. They were aware of it, and they tried to keep up, but were not quite as dedicated to it. It didn't seem a matter of life and death to them. It does seem a matter of life and death to the innovator.

Were you involved in any way in establishing a biosafety committee at Cetus?Hughes

Cape Only indirectly. By that time Cetus was several hundred people, and I got reports about how things were going, but I didn't attend meetings or weigh in on much.

Hughes Would that have been Gelfand's primary concern?

Cape Yes. And ultimately, I imagine, facilities people.

Hughes Yeah.

Cape I was particularly struck by the inappropriateness—I'll just say inappropriateness; I don't want to ascribe motive at all—that the public should be comforted: there's nothing to worry about, all we're dealing with is proteins, proteins like egg white and stuff like that, innocuous stuff. Not mentioning that cobra venom is also a protein. I mean, it's a dumb argument to make. Or the paradox of when you're out selling stock you talk about the fact that you're

going to change the world, and what you're doing is the most important thing that ever came along. Then when people start raising safety fears, many of them sincere, you put them off and say, "It's nothing. Not to worry. It's just the same as everything else, you know. There's nothing new here. Why get so upset?" On the one hand you're trying to raise billions, and on the other hand you're trying to make nothing of it. You can't talk out of two sides of your mouth like that and be believed.

Hughes Ron, did you ever have doubts about the safety of this technology?

Cape No. Well, doubt is not the word I can address. I can say worries. But I was never really worried about it, no. That may be stupidity; I don't know. But I don't recall staying up nights worrying about it.

Hughes We mentioned in passing the *Chakrabarty* Supreme Court case, which brings up the issue of intellectual property in biotechnology, which has turned out to be a rather important aspect of the industry. What kind of attention did you and others at Cetus pay to that case.

Cape A fair amount. I knew [Ananda] Chakrabarty, by the way. I saw him at a lot of meetings. It was a General Electric patent. He was working at General Electric. It was the advance troops trying to see if living organisms could be patented. It was ultimately determined that, yes, they could be patented, which upset a lot of people. But I am told by investment bankers that it was very useful when companies like Genentech and us and others went public. [The patentability of living organisms] was such a questionable issue before it was decided that it was a big question mark which you didn't want present in the question, "Is this technology company ever going to make a lot of money?" The minute it became clear that you can patent things, suddenly you were in an area that people are comfortable with.

Another person you should probably speak to because he spoke at some length in those days about the fact that patents weren't important, and I'm sure he changed his mind subsequently. Being a Nobel Prize winner, maybe not then, but in retrospect, Wally Gilbert was repeatedly saying that he didn't think patents were very important.

Hughes On what grounds?

Cape I don't remember. Possibly that being first and running as fast as you can is what it's all about. If you can make it, and nobody else can, you'll be first to market.

Hughes In that regard, he proved to be wrong, wouldn't you agree?

Cape Yes. I'm making up what his argument might have been, his own company, Biogen, which was not first in the market in beta interferon, nonetheless caught up and surpassed Chiron.

Hughes So Cetus didn't take a public stance on *Chakrabarty*?

Cape I don't remember.

Hughes I looked at the *amicus curiae* briefs a long time ago, and there's something like a dozen of them, eleven of which are on the side of yes, one should patent living organisms. And one of those briefs is from Genentech.

Cape Now it's coming back to me. You're asking me, did I ever inveigh? I don't remember. I was very much interested and aware of the issues. One of them had to do with a non-recombinant DNA issue and, of course, Chakrabarty's was non-recombinant DNA also.

Hughes Right.

Cape And it had to do with antibiotics. "Well, they're found in nature. How could they be patented?" Well, yes, but it's more complicated than that. When they're found in nature, they're practically useless. There's a number of things that have to be done, not the least of which is find an organism that makes enough of them. You may remember that the original penicillin was made in a mold found in the lab, and it wasn't until, in a market in Peoria, I think, they found a melon that had a different kind of mold that made a thousand times as much penicillin as the one Alexander Fleming was working with. So you can patent and protect in different ways, not only the molecule itself, but [protect] ways of making it and stuff like that. The point is that there were a lot of precedents about patentable antibiotics. So if it's true for those which come from nature, why should it not be true for other things? Particularly when there's more input in manipulation of the genes. All the more reason to believe that human insulin, for example, doesn't exist as a commercial product at all. We don't kill people and extract the insulin; we kill pigs, okay? So it's a multi-faceted argument.

Hughes Yeah. Well, you said, and I paraphrase, that you were advised that the *Chakrabarty* case, when it came down in favor of the patentability of living organisms, help fundraising. But the *Chakrabarty* decision came down in June, 1980. You'd been fundraising since 1971.

Cape But not in the public.

Hughes Oh. That makes a difference.

Cape Genentech's IPO [initial public offering] was in the fall of 1980 and ours was in the late winter of 1981. And *Chakrabarty* was very fresh then. It was like, "See,

see, what did we tell ya?" And then everybody said yes, great. Patentability was no longer an issue. Remember, we raised our money, first of all, from a bunch of real crapshooters in the early '70s, and then from policy decision-making on the part of big companies who wanted to see what new technologies were available. They weren't getting bogged down in, are living organisms and products patentable? We'll get around to that. But at the present time we want to invest in some people who are doing it [biotechnology], was basically the decision. I don't think they were waiting on *Chakrabarty*.

Hughes Since we've segued into it, why don't you talk about the IPO? There's that oft-repeated statement of Pete Farley's that Cetus was not working up to a public offering. What changed?

Cape Well, we certainly weren't planning on it when he spoke, that's for sure. It was not our intention to do that, and it was sort of unimaginable that we could do it, particularly since we knew we were in a field that had no products in the near future. How can you go to the public without any products?

Hughes And how could you?

Cape Well, first of all, Genentech demonstrated the art of the possible, and then investment bankers started banging on our door. You know the old saying in the field of small-company fundraising: the time to take the hors d'oeuvres is when they're passing them around. That certainly had some applicability. But our planning in the '70s wasn't that we would never go public. We never sat around planning how we were going to go public. That's certainly true. We looked with the same amazement as everybody else when Genentech did. Genentech, remember, went public just about the same time as Apple. There was all of a sudden a bunch of new little upstart companies going public. And certainly they tested the appetite and found that it was very big.

Hughes And not satisfied by the Genentech offering.

Cape That's right.

Hughes So all these things were working to change your mind?

Cape Yes. Believe me, there were not enormously soul-searching doubts once it became demonstrated that it was possible to do it. And bankers were telling us that we could raise much more money than Genentech did at a higher value—And they were as good as their word; that's the way it worked out. We basically had to learn a new game and we did.

Hughes Cetus ended up having the biggest windfall.

Cape We were told that ours was the largest IPO of a truly private company to go public. The only exception that was mentioned was a government satellite business, which is called Comsat. But the point is, the government decided, let's put this into the private sector, raise money in the public market, and good luck. Whatever they do, we don't want to be in this business anymore. So that really wasn't the kind of thing we're talking about, which is small companies developed for a profit, being private for many years, then, like Intel in 1968, finding they've got products, they're leaders, they're good—go public. It seemed that in biology it was going to be a horse of another color; we were working to a large extent on industrial processes which would take a long time to be developed, so that somebody would really put them in practice, or products that had to go through the FDA, which was in itself a ten-year timetable to market. That seemed a little bit hard for us to grasp, because how can you sell this? Well, all you have to do is have one example of somebody doing it. We can do that! And we did.

Hughes Well, were you really convinced by that?

Cape Oh, yes! I mean, "Genentech Rocks Wall Street," that enormous headline in the *Chronicle* or the *Examiner* or wherever it was.

Hughes Well, you were convinced that you could do an IPO. That didn't really change your ideas about the long timeline that was needed to actually get a drug to market.

Cape That's right. We didn't think it would accelerate. But it enabled us to do a lot more different things. And remember, when Genentech raised money and we raised money was the height of that terrible economic circumstance where short-term money you had to pay twenty percent interest. Can you believe it? In other words, we could have lived forever on the money we raised, if that's the way we wanted to play it.

Hughes Amazing how times have changed.

Cape We're almost like the Japanese now, where interest rates are so low that it's hard to feel that the Fed can do anything by lowering them any further. I mean, you're close to zero.

Hughes That's right. Well, the outcome of the IPO was very successful. But there was something about having to jack up the stock?

Cape The bankers were concerned that the stock was not selling as well as they had hoped.

Hughes What was that about?

Cape Maybe it was misjudging the size that the market would gobble up and then be ready for a little bit more. So I believe that the so-called green shoe, which is a way in which bankers get a commitment from the company that even if they don't want to issue more stock, if the demand is so great the only way it can be addressed in an orderly manner is to have more stock available to sell, the company would sell more stock. Our green shoe never got implemented. I believe Genentech's did. So that was a sign that we were in trouble. And the bankers, I believe – my memory is very fuzzy on this – thought that what was needed is that some of our industrial investors, like Chevron, like Amoco, would buy a little bit of stock to sort of give the impression that there was demand. As I recall it – it's been twenty-five years – they didn't, so the stock stayed level for a long time.

The other thing that was astonishing about Genentech's IPO is that the shares went up from $35 to $87 in one afternoon. We never had that. We came in at $21 or $22 or whatever that was, and it stayed there.

Hughes Shortly after your IPO, Chiron had an IPO. By then the window had shut, so Cetus, were the last to really, for that time period anyway, were the last to rake in a lot of money with an initial public offering. Chiron did not do very well.

Cape I don't remember any of that.

Hughes What do you remember about being a public company and the difference presumably in management concerns or whatever?

Cape It had some of the predicted components, but nowhere near what they tell you about. I recently had a case with another company that went public, and they were going nuts with the significance of becoming a public company, like it was running their thinking, and it seemed to me to be an overreaction. We didn't change all that much. There were some obvious things. First of all, you've got to handle information differently, and second of all, you've got to be available to the public somewhat. A lot of companies have abused that in a manipulative way, as we know, and worse. From my point of view, some of that was a pain in the ass, because you'd like to just get about your business and not spend your time yakking on the phone to every Tom, Dick, or Harry that calls you wanting information. And yes, you have the public relations function as somewhat inside and somewhat outside. And also you're reporting responsibilities require more bureaucracy inside. Those are all addressable. You hire people to do them.

I'm not sure that my life changed all that much, except for one thing. I suddenly was sitting on top of a company worth half a billion dollars, which in those days was unbelievable, and aware of the fact that there was an enormous potential here. I'd never run a company with even as many people as Cetus had then, and we went up to 1200, 1300, 1400 eventually. I figured, yes, this is fun, but what

do I know about this? I'm a big investor and I want to protect the investment, and I think we should get in some professional management. We're highly visible now, and I think that's important. And we brought in a lot of people after that, which we wouldn't have done, probably, if we'd stayed private.

Hughes How about educating your employees about –

Cape Again, a necessary thing to do, having to do with secrets and trading and all that kind of stuff. But it wasn't that different from what you see today after the fiascos that have happened, where people are doing this ten times more obsessively, but nonetheless you have to do it. At Genentech they apparently posted the price of the stock every day. We never quite did that. But everybody knew. I can't remember in the whole history of Cetus there ever having been even an investigation of any of our employees or officers or directors or anybody's training practices.

Hughes How many shares one had must have been a subject of hallway conversation.

Cape Sure. But remember, that was eclipsed in advance by the stories of those Genentech summer students who are each millionaires for having come to work at Genentech. We couldn't match those kinds of stories. And it never got out of hand. I can't remember any unanticipated blowups on the subject of stock trading or the price of the stock.

Hughes I haven't come across any.

Cape I remember going to one of my Harvard Business School classmates, trying to sell him some stock in Cetus—sell him on the idea of calling his broker and buying some stock in Cetus. And he said something like, "Ron, I've analyzed the situation, and I'll be direct with you. You've got a great company. It's now selling at $22. I don't see anything significantly happening in the next five years to change it from $22. So it will still be $22. I'll take another look at it in five years, and then maybe I'll buy the $22. But not right now. There's no point. It's not going to run away from me." And he was probably sort of right. That was partly a function of overselling it. But remember, Genentech never saw $87 for quite a while, I think.

Hughes There was a dip.

Cape I think it maybe went down into the 50s and stayed in the 50s and the 60s. I didn't pay much attention to it. I should have bought stock. That's what I should have done.

Hughes What about the legal aspect of all of this? Who were you using?

Cape We used almost exclusively Heller Ehrmann. Julian Stern, who was the partner at Heller Ehrmann, was our secretary. So he wasn't on the board, but he was at all board meetings. We selected him in 1972. Never changed. He's still my lawyer.

Hughes He was an outside attorney? I mean, he was never an employee of Cetus?

Cape Right. We ended up having huge legal departments inside, patent attorney departments inside, travel departments inside. We had a dozen people or more in each of those departments. We had our own United Airlines computer.

Hughes Al Halluin came in 1983. He was an in-house patent attorney.

Cape Yes. It was his job to build up the in-house department. We had a centralized digital equipment system with a minicomputer somewhere, and everybody had a terminal. It was all hooked into the digital equipment minicomputer. Al said, "I want Apples for all my department." So that's what he did for about ten years. They all had Macs and everybody else had P.C.'s.

Hughes Isn't that funny? I got the impression that he was kind of a character.

Cape Not outlandishly so. It was a good environment to show personality and a little bit of attitude, but his was not outlandish.

Hughes What about publication policy?

Cape I can only say what I've said in speeches, because I don't remember anything else. It simply was never a problem. Somehow, by a combination of rules, procedures, having the attorneys viewed as helpers and enablers by the staff in a bunch of red tape that they didn't want to get involved in, helping them to write their papers, I can't remember a single problem.

Hughes Helping them to write a paper in a way that didn't jeopardize a patent?

Cape I'm not quire sure, to tell you the truth. I would expect that might be the foot in the door that would motivate the lawyer. On the other hand, it had to be seen as helpful by the scientists, because they don't suffer fools gladly. They will accept help but they won't accept intrusion. So somehow, through zillions of papers published and lots of patents applied for and issued, I don't remember having a management meeting saying, oh, we've got a problem. I don't remember it ever happening. There were a lot of things which we were supposed to have problems with. How do you organize all these prima donnas? How do you get jobs done? How do you this? How do you do that?

Hughes Do you think it helped in your case that you did come from a hybrid background? That you had spent a number of years in academia and also had the business education?

Cape I would like to think so, but I can't substantiate that. After all the dozens and dozens of pages [Paul] Rabinow publishes without comment about how terrible Cetus management was and how terrible this decision was and how terrible that decision was. He never analyzes the culture that permitted PCR to get invented and funded by a management that said, this is great for the culture but pretty crummy for money. It's never going to earn a penny. But what the hell? And this guy [Kary Mullis] is a kook. But what the hell? It's good because that's what's it all about. That's what these guys like to identify as their world: it allows eccentrics, and it encourages debate and derision and competition and all these kinds of things. Coming back to your question, does this [publication policy] end up with stalemates and knocking heads together and stopping creativity? It didn't seem to. I don't recall ever discussing it as a problem. Nor, at that time, did I ever hear of it being a problem at Genentech or Biogen or anyplace else.

Hughes Well, I heard that Swanson had to be persuaded. One of the arguments Boyer used was, okay, if you want to get top scientists, Bob, you've got to give them what they most want, namely publication rights and keeping up in their fields in the eyes of their peers.

Cape Well, we sort of took that for granted. We never had a fight about it. And yes, it's true that something must have filtered down from the top. I can't tell you what. I told you, I think, at one point, that I didn't really realize that after twenty years, until I saw all those women crying when Chiron was taking over and everybody was crying. So, I simply cannot remember fights [about publishing]. There were lots of fights among the scientists about protocols, about turf, about all kinds of stuff that scientists fight about. But policy on who's going to publish – none of that made it to top management.

Another good person you should speak to is Jeff Price, who, for many years, was our vice president of R&D. Another person you should speak to is Frank McCormick, who is now head of the UC Comprehensive Cancer Center, moving first to Divisadero, that new building, and now apparently moving to Mission Bay. He was our vice president of R&D, too, for a few years. See what they can remember.

[End Tape 9, Side B] ##

[Begin Tape 10, Side A.]

Hughes How would you describe the early culture of Cetus?

Cape Well, we wanted to be as much like a university setting and as little like business as possible. It seemed to us that Nobel Prize-winning accomplishments were engendered by whatever a university does and seemed to be hindered by whatever businesses do. It reminds me of what they say: you get children at five; they go to school; they're all ready to go and eager and really inquisitive, and the system knocks it out of them in three years. It doesn't take long to remove all that, right? Some magical formula that they apply in first and second grade, or something.

We were aware of that, but by a seat-of-the-pants kind of thing. And we always encouraged independence, even in our secretaries. I don't mean to demean them; I mean to say, there was no drawing lines as to whom you talked to or the laissez-faire component of trying to keep it informal and free. I resisted—I know this—an organization chart for a long time. People were *pleading* for it. We're an organization; let's have an organization chart. And I figured, oh God. I can see some things that might help, but I can see other things that might hinder, and I'd rather not have one. And eventually we had to have one like everybody else. I'm only mentioning that as an illustration of the point. I wish I could be more specific about what we did right, and what we tried to avoid doing wrong, but if I once knew, it ain't there anymore.

Hughes Things like the organization chart probably came in after the IPO?

Cape Probably, yes. I can't say that for sure because you might pull out an organization chart dated 1977. It's people like Jeff Price who would have them, if [inaudible] just as sick as me, kept it. You know, [inaudible] needs it at this point? A lot of people [inaudible.]

Hughes Getting back to culture [inaudible.] Were there activities? Genentech makes a big thing of its ho-ho's, for example.

Cape We didn't do anything like the ho-ho's. I personally would have regarded that as rigid and institutionalized fun-making. It was nonetheless a good idea. As a matter of fact, I was the first chairman of the Bay Area Bioscience Center, and they're having a celebration on their, I think, twentieth anniversary, and in memory of Genentech's ho-hos, they're having a brouhaha at PacBell Park. We had lots of parties. But they were more spontaneous.

Hughes On site?

Cape Yes.

Hughes Were you happy with Cetus culture?

Cape I liked it very much. I feel I was always accessible. A lot of people would come into my office and bitch about this, that, and the other thing. I'm not sure I responded with action in many of the cases, and occasionally I would. But I don't think I kept an apartness between myself and other people very much.

Hughes You had an open-door policy?

Cape I like to think that. It's so easy to say it from inside the open door, and for other people to feel differently. But a lot of people approached me a lot of times. It wasn't, "Fix this," but, "I want to tell you my aggravations and my frustrations." Kary Mullis to this day claims he still likes me, in contrast to everybody else at Cetus.

Hughes Why does he say he likes you?

Cape I told you, I thought it was possibly because I was in the room at the time. He was giving one of his usual speeches with pictures of his nude girlfriends and everything else. He was saying terribly nasty things about DuPont and pretty nasty things about everybody at Cetus. But he mentioned that I'm an exception to the rule.

As one example, I was selected as Scientist of the Year by some R&D magazine. And Scientist of the Year I'm not and wasn't. They gave me a prize of ten thousand bucks, and I invited all our scientists to Auberge du Soleil [restaurant]; i.e. I spent the money on *them*.

Hughes All right. The Pajaro Dunes conference.

Cape [Interrupts.] What year was that, '82?

Hughes Yes. Good for you. March of 1982. I want your perceptions of the meetings themselves, because there were certain people who criticized how it was handled. The theme was the commercialization of science, of course provoked by what was happening with the New Biology, and what should be the university's appropriate role.

Cape What were the reasons why it was criticized? Exclusionary?

Hughes Yes. The press was not there—

Cape All the universities that weren't there, like Princeton, like Yale, had their own meeting in Philadelphia a year later. I attended that one, too.

But yes, it was exclusionary. It was pretentious in the sense that those guys thought they ruled the world, and it was sanctimonious in the sense that it was hypocritical, also, that the various people were spending a lot of their time with pious platitudes, which many of them were breaking even as they spoke. Which was sort of dumb. I remember saying, "Just listen," most of the time. There's no point standing up and telling them all off; it was not going to accomplish much. I did whisper to one person, whose name I won't mention, that he was citing his university's purity, and he had in front of him an agreement that broke most of the rules he was annunciating. His answer was, "Well, I wasn't president when that was signed." Well, then at least bring up the subject and reveal it. He muttered it to me, but he didn't go any further with it.

Hughes The major criticism of the conference was that not much came from the conference, that there wasn't really any hard and fast policy.

Cape Well, why should Stanford and UC and Caltech preach to the world? There was some feeling of that.

Hughes And also it was a question of the fox guarding the hen house. These universities were at the forefront of this field and had a lot to gain by pursuing relations with companies and spiffing up their patenting activities.

Cape MIT did a really good job of that.

Hughes Who was there?

Cape Harvard, MIT, UC, Stanford, Caltech, and I think there was a sixth. But that's all I can remember.[10]

Hughes Do you remember who invited you?

Cape No. The two criticisms that you made are at cross purposes to each other. They didn't presume to preach. It was a workshop among people interested in working out how would universities and industry work together. And it wasn't intended to come to any definite conclusions; it was intended to explore possible problems and to find out if anything was working for anybody. If they had come out and pronounced something, then for *sure* the ones who were excluded would say, who the hell do you think you are? But since they didn't do that, what was wrong with getting together outside of the press and just letting your hair down and talking?

10.The five universities Cape mentions sent multiple representatives. In addition, there were invited guests, some from corporations, such as Cape and Donald Glaser. (Martin Kenney, *Biotechnology: The University-Industry Complex*, New Haven: Yale University Press, 1986, p. 86.)

Hughes There was an article in *Science* by Barbara Culliton.[11] My memory is that she made some of these criticisms herself. Does the name Albert Meyerhoff mean anything to you?

Cape No.

Hughes He was a lawyer for the Natural Resources Defense Council.

Cape That's an activist group representing "the people". I have nothing against them, but the only thing is, they appoint themselves.

Hughes We're getting the other side.

Cape I have no objections.

Hughes I'll quote what he said: "…Pajaro failed to address the vital issues surrounding conflicts of interest or the use of exclusive patents provided to business entities contributing to university research projects."[12]

Cape Well, first of all, I don't think it's true that it didn't address them. It didn't settle them. Secondly, the Act of Congress that followed by four years, I think, said something like, if you accept government funds, and particularly NIH funds, that's okay. You, the university, the recipient, are hereby delegated to do whatever you like with them—make commercial arrangements with them and so forth. The federal government is not going to come after you for its piece of the action.

Hughes Is that the Bayh-Dole Act that you are talking about?

Cape Whatever it is

Hughes That was actually passed earlier.

Cape Earlier than '82?

Hughes Yes, if we're both thinking of Bayh-Dole. Now, there was a fair amount of legislation in the early '80s designed to streamline the process for commercializing basic science.

Cape Right.

11.Barbara J. Culliton, "Pajaro Dunes: The Search for Consensus," *Science* 1982, 216:155-56 (April 9).
12.Albert H. Meyerhoff, quoted in Martin Kenney, *Biotechnology:The University-Industry Complex*, New Haven:Yale University Press, 1986, p. 84

Hughes It was getting away from the ivory tower idea of the ’50s and so on, in which the government was willing to fund basic science without any concrete end in mind in the near future. And that philosophy was shifting in the 1980s.

Cape The Reagan Administration had as a philosophy, which I somehow agreed with, that the way our country is organized, business is the vehicle in which commercialization takes place. The taxpayer isn’t a stockholder; the taxpayer primes the engine, and some kind of a deal has to be made by somebody on behalf of that series of inventions that takes place in the public sector. But the best thing to do is to leave it in the hands of the universities that got the grants. Whatever deals they make, good luck to everybody. The NRDC [National Resources Defense Council], for example, would say, that is not the United States that I believe in.

Hughes Well, the real critics were saying that these companies are taking the fruits of public support and making profits for their own benefit.

Cape Well, you’re saying exactly what I’m saying, but saying it in a pejorative way.

Hughes Yes, and it’s not me saying it; I’m summarizing.

Cape Profits is not a dirty word. That is the device by which these structures which were perfected in the United States—and we discovered recently that perfect isn’t the right word—but the point is that they were fine-tuned over many years to be the vehicles for making money out of inventions. Very rarely, like when you want to build an atomic bomb, the government will seize intellectual property. But generally, it wants to see it in a company whose people are obsessed with making money off of it. It makes money, it pays taxes, and that’s how the people get theirs. Or so the theory goes.

Hughes Would you not say that something on a smaller scale is also occurring to research universities? UC, for example, beginning sometime in the 1980s, begins to look at its patents. It’s been patenting all along, maybe not as ferociously as a Stanford or an MIT, but it has patents. But they’re not being licensed. They’re just sitting there.

Cape Well, UC Berkeley was famous for regarding patents as a pain in the ass and telling scientists to go away and stop bothering them.

Hughes You remember that from your days here at Berkeley?

Cape Yes. But again, hearsay. I didn’t ever go into the patent office with an idea.

Hughes Whereas Stanford, beginning in the late 1960s, has a very proactive patenting office.

Cape Nothing like MIT. I've seen MIT in action, and it's like ten times as powerful. It holds seminars and invites venture capitalists in, shows them everything that's going on, says, go to it guys.

Hughes When did that sort of thing begin at MIT?

Cape I don't know.

Hughes I would wager that it's been within the past twenty years or so.

Cape Yes, I'm sure.

Hughes It's a huge subject, the commercialization of science, and yet we're only skimming over it

Cape People have been discussing this just like discussing the health care system in the United States. You've got to go back to square one. Let's start from scratch, because if people take a look at what they see now and have certain venal opinions about various things, and I have my opinions about the hypocrisies of the universities—The best example I can think of was when I was negotiating with Tom Maniatis, who ended up founding the Genetics Institute, which did stay private longer than about anybody else as a matter of principle. But anyway, I wanted to make it a Cetus subsidiary, just like Cetus Palo Alto, Cetus Immune, and Cetus Madison. And the secretary of the Harvard Corporation said to me, in two adjoining sentences, "Our aims are loftier than yours. And we want a bigger slice of the company."

[End Tape 10, Side A]
[End of interview.]

Interview 6, December 18, 2003

[Begin Tape 11A.]

Hughes I thought we'd start out with a general discussion about management and strategy. And my first question is, how would you describe your managerial style?

Cape That's a difficult question, because I think it has to do with adaptation to a particular set of objectives. We weren't in a simple—I say simple just because I think it's easily definable—industry, like a Procter and Gamble would be or even a drug company would be in: a long-established company with many divisions, many people, and lots of bureaucracy-dictated things on the one hand, and lots of creative things on the other. But nonetheless all were within a format that you become accustomed to before you get anywhere near managing anything.

However, in biotech—First of all, let me dismiss the family business. I'm not so sure that any of the experiences, except perhaps attitudes and problem-solving, which are applicable to anything, or the skills that I had built up in my previous years in business in Montreal or at Harvard Business School were particularly useful in originating and running a new kind of company, a company in which you could run the fastest with the best people only if you were able to convincingly create a culture and an atmosphere for the people who would really do the productive work, in which they would flourish, in which they would be happy, in which they would work as long as necessary to do the job. I mean, in hours per day, days per week, and so on and so forth. And who were sufficiently good, intelligent, bright, smart, to be creative.

There's a lot been written about creativity, but I'd say our job was to select the people who had already demonstrated that they had what it took, whatever that was, and it didn't always have to be the same thing. And then, as I repeat myself, put them into a situation in which they would be familiar. It would be more like academia in culture than any industry had ever had before. But nevertheless it would have the imperatives that any industry must have: it must be focused; it must be directed ultimately to processes or products, and those goals and the harnessing of the energies and creativity had to be agreeable to the people who

were being harnessed. Which meant a totally new, and if I could put it this way, non-military, non-overly bureaucratic kind of organization.

Hughes Because the employees were coming from academia?

Cape Many of them were coming from academia, and those of them who came from industry had to have enough structure to keep them comfortable, but on the other hand had to relish the freedom that, if you like, they were escaping by coming to Cetus.

Hughes Because that was one of the reasons they came.

Cape Yes, that's right. To get to the point, for the first ten years, I don't think we, or for that matter, as far as I know, any biotech company had any trouble finding great people. Their record of accomplishment speaks for itself. It was important to motivate them, and I think most of us did a reasonably good job: the tools were there. There was enough to be able to pay them well, and to incent them, which most of them, some slower than others, and some with some reluctance, to regard stock options and the commercial way of rewarding as something that suited their life goals. However, I think Genentech probably hired the best examples of this, but we have our Nobel Prize to be proud of. Some biotech companies had a policy on secrecy that was good enough for the investors but loose enough for the scientists, who like bragging rights and who don't like to think of themselves as being mere cogs in a wheel. And I think I was adapted to that kind of management reasonably well.

Hughes Well, you'd been a scientist.

Cape Well, yes.

Hughes I mean in academia. You knew the culture.

Cape Well, I had in my head both the scientific feelings and the business feelings. To make a long story short, though, I think those questions are best asked of people who worked at Cetus.

Hughes The company, of course, was changing as time went on.

Cape All the time.

Hughes For those first ten years, would you call Cetus an entrepreneurial scientific research-based company?

Cape Well, I think we eventually evolved into a more focused company that had aspirations, as did many biotech companies, to someday grow up and become a new kind of pharmaceutical company, but nonetheless, a large pharmaceutical

company, vertically integrated. Of all the companies in the field who had that aspiration, I think the only one who really made it was Amgen. And even by today's standards, they're pretty small compared to the enormous results of the mergers.

Hughes When and why do you think Cetus developed that ambition?

Cape Oh, because we had specific products that we thought would be great news to people who were sick, and thereby cover ourselves with glory and reward our investors.

Hughes And Cetus would do the whole development, from lab bench to marketplace?

Cape Yes, but that was a conceit. In other words, it had to have enough capital invested in it to make it possible, an accumulation of capabilities that the drug companies had decades, possibly as much as a century, to accumulate. The presumption was that you could put all that together in a small company in a few years. I think that turned out to be asking too much and, also, getting illogical. The point was that biotechnology, the New Biology, the results of the Nobel Prizes from 1945 to 1975, were not embraced by the drug industry with any great, you know, shall we say, momentum.

Hughes But how much was there they could have embraced?

Cape Oh, they could have embraced all the kind of drugs that, for example, Amgen came up with, the kinds of drugs that Genentech came up with. I'll grant you, they were all proteins at first.

Hughes I was meaning more than recombinant DNA and the genetic technologies. When you're talking about the Nobel Prizes, are you thinking of the ones related to molecular biology and genetics?

Cape Yes. Virtually all related to molecular biology and genetics.

Hughes What else was there that could have been commercialized?

Cape As you know, we had certain instrument aspirations, but they were mainly always, because there weren't things you could buy that would do the job properly; we had to build them ourselves. It wasn't that we thought that there was big business in instruments. But anybody could have seen in 1980 that, hey, the drug industry already has marketing organizations, regulatory organizations, manufacturing plants and organizations. Well, what exactly do you know that makes you better than them? And the only answer that I could say would be that two things would cause you to try to make your own. Number one, that the drug companies didn't seem to be as eager to motivate, either by partnerships or by ultimately buying, at a great profit, biotech companies, to make that a viable way

to go. Although the Genentech-Hoffmann-La Roche deal showed amazingly what you could accomplish if you were good enough, and by good enough I'm talking about Genentech.

And the second reason was, the knowledge that—Take a simple commodity like a shirt. The person who makes the thread or weaves the fabric or, for that matter, puts together the shirt, makes less money on the shirt that Macy's does. So the further downstream you integrate and absorb, assuming that you can carry the costs of having those functions in your company, the more money you make. I'd say that was an illusion. The amount that you have to invest in that compared to the value of your creativity makes you an also-ran in vertically integrating and a leader in innovating. So now, at long last, there seems to be a rational relationship between the pharmaceutical industry, which is new-product short—they talk about what's in the pipeline, and they point to this or that large drug company and say there's a very meager pipeline—and the productivity of new products coming from the biotech industry. So that's one great advantage of a partnership.

Another great advantage of a partnership is it makes research a variable cost of the drug company, instead of having to sign up great scientists for a lifetime and reduce your work force in the creative area at your peril, to say nothing of the cost of the plans and the equipment and everything else that goes into research. You sign a contract with a biotech company, and if you like their production, you continue to contract, and if you don't like it, you terminate the contract. And if something new comes along, you can quickly help it and your company along in several ways.

Hughes Why would a Standard Oil sign up with Cetus?

Cape Mainly for the creativity. And the same thing with Schering.

Hughes I'm thinking of Triton, for example, with interferon. If I'm understanding right, the Triton part of the deal was development and production.

Cape Well, remember that came later, maybe reasonably soon later. The first deal was made with Shell, because Triton was formed by Shell. The point is that originally there were these oil companies that as an offshoot, if you like, of the oil prices of 1973, started to think, "How are we going to diversify?" The same as the tobacco companies, say. There are reasons to be concerned about the long-term future of selling tobacco. And they were similarly thinking of what are the next big things in the world that, with their enormous capital, they could possibly get into, and for some moment in time, many of them, focused on biotech.

Two or our largest shareholders, I've told you, were Amoco and Chevron. Our biggest customer was Shell. Another big customer and shareholder was National

Distillers, which had a gasohol program going with us. And those deals were not motivated by anything we had except creativity, the processes we could invent, not the implementation of them.

Hughes But you, Cetus, were in those deals maybe marginally because of the money, maybe 99.99% because of the money. But wasn't it also because they had a type of expertise that you didn't? You were on the creative end. You were doing what was closer to the basic research. Then these firms would either develop it themselves or give you the know-how to carry it to a marketable product. No?

Cape Partly yes. A project that we had with Imperial Chemical Industries— now it's morphed into AstraZeneca—was a large single-celled protein project. Or Chevron, with a coupled project having to do with fructose and a plastic precursor, and other such projects. Assuming we succeeded, it was never imagined that we would be the ones to put up the millions or billions of dollars that it cost to put up plants, nor did we have the know-how to do it.

We in those partnerships had sometimes weekly meetings or monthly meetings with them so that they were very aware of what was coming down the road and what challenges they might have to face down the road. In a couple of those cases, the economics changed as the Arab oil crisis drifted into the past and other winds of change came into the oil industry, such as, do what you know best and stay away from other things. But still, the actual dollars that would have to be spent upfront for capital structure of manufacturing were becoming important things to consider, notwithstanding how creative we might be.

With the drug companies, I would say the regulatory and marketing are more important than the manufacturing. After all, I believe Amgen as we speak is still making Epo[gen] in roller bottles, which is a not large-scale adaptive kind of way to grow things, but that's the best way they can make the recombinant product. What I'm saying there is that it isn't necessarily the case, although frequently it is, that the drug company has the technology to manufacture. They certainly have the capital to invest in it, which is perhaps equally important. So in theory what you say is right, but you have to deal with the specifics.

And one of the specifics that perhaps I haven't cynically just stated is, your job is to stay alive. Your choices each year are among the choices that you've got. And while you may map out a policy and a growth strategy that's very meticulously thought out over a fifteen- or twenty-year period, you may find yourself in a certain year where what you're selling, nobody's buying. You have to figure out how are you going to deal with that immediate thing so that you're alive next year in order to be able to continue. So you're dealing with a combination of philosophic, strategic, forest-rather-than-trees approach to where you're going, always conditioned by either the threat, as in 1974 where there were zero IPOs in New York in all fields, to when it became apparent through Genentech's experience in 1980, my god, Wall Street loves us. Suddenly, you've

got to say, well, there are a lot of things to do, but taking some of that money in is one of them, and right now. So present your best possible face, check it out with the lawyers, check it out with the bankers, but if you can do it, do it. And we're coming just about to the point where I somewhat backed away from hands-on decision-making. When we raised our hundred-plus million dollars, which was big stuff in those days, my feeling both as a shareholder and from a personality point of view was that we should get some experienced management in terms of what looked like our future, namely to sell drugs.

Hughes So that decision was made—

Cape 1980, about the time we went public.

Hughes Before Fildes came.

Cape Fildes was the result of it.

Hughes That's a big point because there's a tendency to say that things changed when Fildes came in. I think we should make it clear here that Fildes moved things along, but Cetus was already moving in the direction of a more focused pharmaceutical company, rather than activities in quite a wide range of fields.

Cape Well, there is a whole series of reasons. The main financers of our industrial projects basically lost interest in those industrial projects. At the same time, we were beginning to discover and produce interleukin 2 and beta interferon. It's easy to talk about things, but if you don't have a product to talk about; you're blowing smoke. But I do want to make it clear that I backed out of the CEO role because I thought somebody else could do it better. Okay?

Hughes And that person was Fildes?

Cape Eventually we hired Bob. It's interesting to reflect on the fact that pundits will write what pundits feel like writing. And sometimes the entertainment value or the stir-up-some-interesting-controversy value is more important than whether it's true or not. I know myself that we were really trying to find an experienced CEO. I do know that the scuttlebutt went around," Well, if they are, why are they taking so long about it? It's a phony search or a soft search. They don't really want to hire somebody, but their Wall Street people are telling them you'd better do this." That's just not so.

Hughes Why was it taking so long?

Cape Well, I guess we were hard to please. I don't know. I know we were doing a lot of interviewing. I remember one case where we were interviewing a guy who came out of Texas Instruments. I remember meeting him at O'Hare airport and

having a long interview with him. And he said, "How big is Cetus?" And it was several hundred at that point, and he said, "I think that is below the size I can easily deal with. I have a lot of experience in big companies, like Texas Instruments. I know when I have the proper infrastructure in place; that means secretaries, that means janitors, that means managers. I know how to run that. I'm not so sure I'd be good at building that from scratch. And I think you're still at scratch." That was one big shot—he ended up in the biotech industry. But my point is that I remember we were looking very hard, and we weren't finding anybody, and there wasn't an immediate problem that we were doing everything so terribly. It was just that it made sense if I was a large stockholder in this thing to have it run by somebody who knew how to turn it into a drug company.

Hughes I don't see what your being a large stockholder has to do with it.

Cape I thought it would be better for the company.

Hughes Because you were just too heavily invested?

Cape No. It was the fact that my future stake in the world depended on Cetus doing well. And I thought that was the best thing for the company.

Hughes So, you were trying now *not* to be a CEO. What did you see as your function at Cetus?

Cape Well, once we hired Bob—and there's a very strange thing. A classmate of mine at Harvard Business School wrote a book called *Passing the Baton.* That was in the early '80s. I was interviewed to be the subject of a chapter as to what this smooth transition was—smooth transitions being just right, nothing revolutionary. And as it turned out, things that looked very good in 1983 didn't look so good in 1991 or 1989. But it certainly looked at that time as if here was somebody [Fildes] who could do the job that was needed to be done and had done it elsewhere. I then went through a process which was basically cosmetic, although once [Bob] got in the saddle, his first title was COO [Chief Operating Officer], and he became CEO a year and a half later.

Hughes And you remained CEO for that period?

Cape Yes. But it was only nominal. As a matter of fact, when he was named CEO, one of the things that I was very happy about was the fact that the story in the papers was, it comes as no surprise to anybody. It's an evolutionary thing.

Hughes So what did you see yourself doing, then?

Cape Well, the thought I gave to it was the following. If I had not been a founder of the company, I should have just marched out the door and never come back. Being the founder, I represented to a lot of the creative people in particular some

philosophy or identification with how we started and what we meant, and that maybe my staying around in that capacity as chairman, but not CEO, might be worthwhile. I'm not saying it was the right decision, but that was the thinking at the time. I remember thinking at the time, that hey, every company does it differently, and two contrasting at that time were Chevron and IBM. At Chevron, when a CEO leaves, he leaves. He's out of there! He never even goes back in the boardroom. At IBM they've got three former presidents on the board, hanging around. History, like we were talking about at lunch. So, whatever works. And I thought that I could also bring some attention to the company by carving out a career in the non-governmental organization world, and possible the governmental organization world. I had a lot of friends in it.

Hughes You're thinking of BIO and organizations like it?

Cape Yes. And also that foundation to collaborate with Japan [the Harmony Foundation] and the fact that I found myself running into people that I'd met over the years, and on two particular occasions finding myself as member of a U.S. delegation. In one case, to the European Union, a meeting in Brussels. "Come on, Ron, join the delegation!" And another time, a little bit more formally, as part of a National Science Foundation delegation to a meeting in Tokyo. And that's what I did. I wanted it to be absolutely clear that I wasn't going to interfere with the way Bob ran the company. And that was basically the agreement between us. We would meet a lot, we would talk a lot, but we're not voting—*he made the decisions*. I made it clear that the underpinning of this was, if you succeed, you get all the glory, and if you fail, you get all the— It's like a baseball manager in a way. I know that sounds a little bit crude. To be around second-guessing, have people coming around him, and if they don't like what he's doing, bitch to me, didn't seem productive.

Hughes You did not allow that to happen?

Cape Well, if somebody I knew plunked himself down in my office I wasn't going to throw him out, but the attitude was such that that didn't happen very much. I can't remember any occasion where I went to Bob and said, "Hey, that's wrong. You've got to do this." Never happened.

Well, put Farley into this picture. We've barely talked about him. He, too, probably could have been absorbed in some way in Cetus.Hughes

Cape Let me give you just a simple recitation of the facts. When we started the company, he was basically, if you want to use the clothing business as an example, he was Mr. Outside and I was Mr. Inside. It was never, ever that vivid. I did a lot of the traveling and negotiating, and he did a lot of the scientific reviewing. It's like people who say, who wears the pants in that family? It's the wrong question. It's like, have you stopped beating your wife? It's assuming that there's some division of labor that's going to make you understand and make

you happy, and the important thing is for us and the people in the company to be happy. In any event, the emphasis was more external for Pete and more internal for me.

Hughes Did that mean he was largely the one that was out beating the bushes for funds?

Cape Yes. But more for contracts with the big drug companies.

Hughes Why he?

Cape He liked it. He was garrulous. He was an outgoing person. I don't much care for that. He liked to chat with strangers. I don't particularly care for it. That's what I told you when you first asked me to do this [oral history]. I don't much care for this kind of thing. Most of the people in the biotech business are more like Pete, I would imagine. The ideal example is a person who combines both, which is George [Rathmann]—[someone] who knows the science and can articulate it well, but also knows management and also has a way with people.

Hughes Farley is a physician. How adept was he at explaining the science?

[End Tape 11, Side A] ##
[Begin Tape 11, Side B]

Cape We're all adapting to changing circumstances, and Pete was very good at establishing personal relationships with people in other companies, like Schering, like Shell. That just worked well. And I was doing that too, but more involved with deciding among the scientific projects. I did most of the recruiting, if not all of the recruiting, to the extent that it wasn't done by other scientists of the scientific advisory board. I'd be inclined to say that Pete did very little of that.

But jumping way ahead, because I think it has a bearing on what you're saying, I think Pete became—and I'm guessing here because I never discussed it with him—increasingly constrained as we were getting larger. When Bob Fildes, who was a good friend of Pete's—Pete and I and Moshe Alafi spent a lot of time with Bob Fildes as we were visiting England and elsewhere. We hired our vice president of research, Steve Goulden, from Glaxo, which is the company that Bob was with [before Cetus, Brogen, and Bristol-Myers]. We socialized with him in England a lot. But I believe that it was Bob's coming in as the CEO designate that caused Pete to say, "This is not what I want to do." And very abruptly, without any discussion of it in advance, he called me up one day and said, "I am leaving the board; I am leaving the company. Good luck to you, good luck to me." It was almost devoid of any kind of hostility, but it was also devoid

of any kind of discussion. He had thought about this for a while, and he was out of there.

Hughes He didn't give you a reason?

Cape Well, there were other things he wanted to do.

Hughes He must have felt that he was being displaced, that his role in the company could not be as significant.

Cape That makes sense to me, but I do not recall ever discussing it with him. As I say, the one thing that struck me about the decision was it was presented as, "I have decided," not "I'm thinking about it. What do you think about this?" And there was not much to do except say, "Good luck." And he did get into other businesses. He got into two businesses that were not particularly related to what we were doing; more financially related, like leasing equipment and developing a new medical information system with an orthopedic surgeon, a friend of his in San Diego. He eventually got into such things as building million-dollar yachts on spec. So that's pretty far afield.

When I left hands-on involvement, I still was very much involved in board meetings and in policies and in budgets and in things like that. I used to be in Washington once a month for this or that reason. As you found, I testified before some committees at some point; that started in the '70s. I got to know a lot of people who were on the staffs of various congressmen. That led, as I mentioned in passing to you, when I was president of IBA [International Biotechnology Association], which is the predecessor of BIO, to a one-hour meeting with Al Gore because of one initiative that he had going. And I did all those things that were out of the building. I was away a lot.

Hughes Before Fildes came, who then was at Cetus on a regular basis?

Cape Well, when Bob showed up, we must have had 300 to 400 people. All the projects were being run, not from the top, but by one level below the top, by the head of research and the various project managers. The money raising was done basically by Pete and me together, dealing with our investment bankers. All of those functions went over to Bob when he took over. There was a lot of talk of the fact that we had industrial projects as well as medical projects, that we weren't focused. Strangely enough, when two or three or four years later Genentech did the same thing, I don't recall reading in any articles that they weren't focused. But what I'm saying is, I don't recall any articles anywhere saying, "Nobody was minding the store."

Hughes People were saying in the early '80s, at least according to Rabinow, that there needed to be more organization of the scientific enterprise; that there needed to be a vice president of research and development, and those things do happen..

Cape As I said, Rabinow repeated various people's assertions without verifying them. But since I refused to be interviewed, I feel I have no place criticizing. Steve Goulden was the VP of R&D from 1976 or 1977. And Jeff Price took over as vice president of R&D in the mid-eighties or early eighties, and at the end, Frank McCormick, who's now the head of the UCSF Cancer Center, was the vice president of research. There were people.

Hughes Well, maybe I read it wrong; I'll double-check it. There's a vice president of research and development, which is Jeff Price, right?

Cape And under him was Tom White.

Hughes And under him, as vice president of research, was Tom White.

Cape He was a much better molecular biologist.

Hughes Is that so?

Cape Jeff Price's background was not in molecular biology. There was a drive in which I offered that job to Tom. We were driving back from Palo Alto. We had a product meeting on IL-2 [interleukin 2] or something like that.

Hughes Was he the first?

Cape Maybe.

Hughes You're saying that Jeff Price's position had antecedents.

Cape Well, we had a vice president of R&D who I hired away from Glaxo in 1976.

Hughes Well, is there any credibility to the claim that there wasn't an organizational structure for scientific research?

Cape I do remember, and I think I talked about this once before, that there were a number of influences on the extent of bureaucratic structure. Remember what I said was my philosophy about how the thing should be run in the first place. There was also the awareness that—it's like the beginning of a love affair, where it's never going to be like this forever, so enjoy it while it's possible. You grow up, and things are changed. Partly as a function of size, you have to have some bureaucracy. But at some level, I always had the feeling—There's that story in the bible of the children of Israel didn't have a king, and they approached the prophet Samuel to pick a king, who ended up being King Saul. And he said, "Are you crazy? Why do you want a king? He's going to steal your women. He's going to make you fight wars. He's going to send your boys to die. Who needs this? A big ego on top running everything." And they said, "Doesn't matter. We want a king. Everybody else has a king. We don't feel equal to other people

because we don't have one." And so they got one. I always had that feeling, but was aware of the fact that reporting and writing reviews and knowing some feedback to the quality of the work requires a certain amount of organization.

Another limitation had to do with our size, as a result of which we developed a form which is known as matrix management. You have project leaders, but you also have departments. You have a department of molecular biology. You have a department of cellular biology. You have a department of biochemistry, and so on and so forth, because those are certain skills that you have to apply. And if each of those projects had to have their own people, you'd have three times the staff and be very inefficient. So there has to be, in some way, two bosses for a particular scientist, or his project or projects, if he does more than one, and his principle discipline. But again, in this burgeoning science, frequently the geneticists and the biochemists and the molecular biologists are the same guy. Nonetheless, there were things that made it a little more difficult to get organized than that glib statement implies. And we wrestled with how is the best way to do it. I know that.

Having said that, I told you once before that the guy who I liked very much, Jim McCamant, wrote a really glib thing: Genentech was this, and Cetus was into industrial projects. That's such an oversimplification that it doesn't tell you anything. The fact is that I don't think our industrial projects were ever the equal of our pharmaceutical products, once we got a few things cloned and saw some intellectual property that we'd come to medical product with. And that was always the prime intention of the company. But yes, we did succeed in striking contracts with, and getting investments from, heavy industry first, and that, if you like, rearranged our priorities for a while.

Hughes Are you saying that always in your thinking was movement towards becoming a pharmaceutical company?

Cape Focusing on the products of recombinant DNA, once it became obvious that that was a way to go. However, our first big recombinant DNA project was single-cell protein, which was a feed for animals. And we worked primarily on antibiotics for drug companies before the Amco, Chevron, and National Distillers investments (1975-1980).

Hughes But I also remember reading in the annual reports—probably in the early '80s, you say quite clearly that recombinant DNA was an important technology, but it was only one of the technologies that Cetus was using.

Cape It may have been an attempt to distinguish ourselves from Genentech, I don't know. One thing that has to be said about Genentech is the fact that of all the biotech companies, I think they would score highest on doing what they said they would do and sticking to doing what they said they would do. Having said

that, you'll notice two or three of their major products now are monoclonal antibodies.

I think when you look at annual reports, one of the biggest take-home lessons is reading the Amgen either '85 or '86 or '87 annual report. One year later, they were obviously going to be a billion-dollar company because they had two blockbusters. One year earlier, they weren't even mentioned in their annual report. That's how back-burner they were or how the results hadn't come out as to how terrific they were.

Hughes EPO hadn't been invented?

Cape EPO and GCSF, in other words, Epogen and Neupogen. They weren't even mentioned.

Hughes Well, I looked in your annual reports for PCR [polymerase chain reaction], and PCR doesn't appear until several years after Kary [Mullis] was talking about it at retreats, etc. I have it somewhere, exactly which year it does appear. Here we go. PCR is first mentioned in the 1986 annual report as "our powerful and unique DNA amplification technology." But it's not a featured product; it's just one of the things that Cetus is offering.

Cape When we decided to feature PCR, it was a challenge to graphically depict it in an entertaining and illustrative manner. I don't think we ever fully succeeded in that. I remember seeing the very first of the Jurassic Park movies and thinking, we should have gone to a Hollywood cartoonist. There is a DNA replication cartoon, video, that does it very nicely. With all our artists and all our advertising agencies and everything else, we couldn't come up—We tried to be too accurate in some ways.

There was a medical illustrator that *Fortune* magazine used in the '60s. His name was Francis Bello. Time-Life used him in their science resources, which is a series of hard-cover books that came out of the '60s. The accuracy is unbelievable. The little details that nobody would notice reflect what was known about the size and shape of those molecules at that time in each of his illustrations. But at some level, it's too much trees and not enough forest. The public can't appreciate that, and the aficionado thinks this kind of depiction is beneath him.

Hughes What I'm really trying to get at is, was Cetus slow in recognizing what a revolutionary technique it had under its roof?

Cape The answer is "Yes, but."

Hughes That seems to be a pattern.

Cape In retrospect, we had the tiger by the tail. To our credit, which I don't believe is mentioned in Paul's book, we had a culture in which nutsiness and craziness, to use Mel Brooks' expression, was not only okay, but a little bit of it was necessary. Cetus was unlike other companies like IBM in which some of the revolutionary stuff that went on there had to be done under the table because management had told them to stop it, and they just didn't stop it. In our case, yes, PCR was under-appreciated to say the least, but it was still fun. We knew it was going on. Kary got up at every scientific retreat and announced where he was. And sure, he took a lot of ridicule for it. But he was still funded. We felt it was necessary for our internal culture.

Hughes It must have been in the mid-1980s when people were resentful of Mullis for a variety of reasons. I mean, he was a difficult individual to deal with, and there were accusations that his probes were not accurate. He didn't want to have to sequence them, so he had a way of presumably telling how they were accurate. When people's experiments didn't quite work out, he was often accused of not producing the probe that was ordered, and a variety of other things—you know better than I.

Cape Let me tell you a story. At the time that DuPont was challenging our patent—this is now 1990—it was considered by many people high entertainment to go to the trial in San Francisco. And one of my friends called me after having spent two hours there as an entertainment. He said, "Ron, you're going to win this case." And I said, "I don't even understand how you can say that. You don't understand the first thing about the science." "Oh," he said, "But I know people. I saw your guy [Mullis]. He's crazy. That's an inventor. And the jury will recognize that."

Hughes There was a move within Cetus to get rid of him. They want him out. You meet, and I thought it was quite amazing, you gave Mullis a year. You demoted him from being head of the DNA synthesis group, but you gave him a year to show that PCR really works.

Cape Do we give him any help?

Hughes I presume you're paying him.

Cape Oh, we're paying him, sure; we're paying for the cycling machines and all this kind of stuff.

Hughes Fred Faloona was working with him in that period, and maybe there were others too. I don't remember. My point is that you'd given him a *year* to focus on getting this technology going.

Cape Some of us were more in love with this than others.

Hughes You don't remember that meeting?

Cape No, I don't. It's entirely plausible. I don't dis-remember it. There were a number of attempts to spin PCR out. Some of us lobbied very heavily and finally got a PCR division created separately to sort of insulate it from being competitive for budgets and things like that from the rest of the company. They even had their own t-shirt. Our emblem had always been a sperm whale, and their emblem was a killer whale.

Hughes And who was head of that?

Cape Hollings Renton. That was a way of making sure that it didn't get intruded upon too much. That's about the maximum interference I ever created. And if you'll look in Rabinow's book, you'll see that Bob Fildes always represents himself as a great fan of PCR. I say no more. However, the feedback from all quarters was, PCR doesn't amount to much. Wall Street didn't think it amounted to much. In other words, the feedback was, if you spin it out, where are you going to get money from? You're talking about a non-existent market. You're talking about a product that fills a need that nobody sees.

Hughes But there was a need. There was a need for a good way of—

Cape Finding needles in haystacks.

Hughes Yes.

Cape Like seeing if there's any DNA with a sequence of A's [adenines] in a blood sample.

Hughes But why isn't that a need?

Cape You're going to do this on everybody? It costs a fortune. Can't afford it. I've seen many examples of this in biotech. The very early prediction of pharmacogenomics was a little session I chaired, and the principal speakers were Eric Lander and Lee Hood in Davos at the World Economic Forum. The dream was that everyone would have a smart card, and that smart card would have not only their DNA sequence on it, but the changes in time of that DNA sequence on it. And that will make it very possible to customize both medicines regarding opportunity, regarding new drug applications, regarding who's going to benefit the most, and so on and so forth. And one of Hillary Clinton's staffers stood up and said, "We're not going to pay for that." The point is, these things in anticipation seem so expensive that you don't even want to think about them. It looks like overkill, when in fact it's the best idea in the world. And Roche just announced six months ago that that's where they're going, probably with help from PCR.

But to make a long story short, I also told you we got Roche to jack up the price dramatically in the closing months of Cetus. They saw so much value in it,

although they already had a fifteen-year exclusive license to use it. They still paid us $330 million for that.

Hughes And that wasn't enough to keep Cetus independent?

Cape No. We were going over the cliff with our expenditures from the clinical trials on interleukin-2. We were losing fifty million dollars a year. Go raise fifty million dollars today! We were losing that much per year.

Hughes Well, shall we go into the IL-2?

Cape If I can remember it.

Hughes I'm not expecting to discuss the science. The new immunoregulins—the cytokines and interleukins and all of those interrelated terms become the thing that biotech believes is the next horizon. Is that not true? Biotech first starts with trying to reproduce existing peptides.

Cape Commercially existing peptides, or polypeptides, or even proteins, like insulin.

Hughes But then everybody, not just Cetus, begins to get into this never-never land in which the commercial venture is based on science that is only just in embryonic stage.

Cape Yes, so much so that every time you have a meeting, someone puts up a new model of the immune system, and it's evolving all the time. Last week—that's no longer true. That class of compounds in the '80s was principally represented by the interferons and interleukin-2. And of course there's many, many more molecules. They are the ways in which cells send each other signals, and those signals are much, much more complicated than we ever imagined. It's one of those things where the more you know, the more you realize you don't know. A religious person would say, there's got to be design; this is too much.

Hughes Well, I know why companies were focusing on interferon, because there was that whole history of hype that they were the potential cure for cancer and infectious disease. People hoped for a revolution when recombinant DNA came along. As we know, it didn't pan out quite the way that people expected.

Cape Meanwhile, they're selling a full billion dollars worth of stuff.

Hughes Now.

Cape Yes.

Hughes But not then.

Cape Not then.

Hughes But not for the reasons that were hyped in the late ’70s and ’80s.

Cape Although it did cure sometime called hairy cell leukemia, didn’t it?

Hughes Yes. That was Genentech. I forget which of the interferons.

Cape Well, there was a time when there were ten different alpha-interferons. And the question was, do they merely represent an evolving towards something. We thought maybe that each of them would have some special role. And it turns out that what you were dealing with was the ’51 Chevy, the ’52 Chevy, the ’53 Chevy, all transportation.

[End Tape 11, Side B]
Begin Tape 12, Side A]

Hughes When people began the interferon program, they didn’t even know there were several types of interferon, right?

Cape That’s right, because they were getting it from foreskins, and other such sources, and as a result they were getting mixtures. And they had names that I have forgotten at this point.

Hughes They became alpha, beta and gamma interferon. Interferon seems to be a mysterious but an obvious thing to go for. Why interleukin?

Cape First of all, interleukin’s first name will give you a clue. Interleukin 2 was once called T-cell growth factor. So it was obviously a stimulant to the growth of T-cells. When we were kids, they talked about immunity being immune globulins—antibodies. That’s what they call humoral immunity, namely, it floats around in the blood. Those are mainly made in the lymphatic system, and so they’re called L molecules. Then there is what’s called cellular immunity, which means that lot of these other white cells, not lymphocyte necessarily, make a series of other molecules. It sort of reminds me of the way vitamins went, you know. At first there were one or two specific diseases, and then the nomenclature followed them. I mean, forget about all that. So, those were mainly made in the thymus gland, and they were called T-cells as opposed to L-cells. It turns out that the kind of immunity that comes from the cells that come from the thymus gland is called cellular immunity, and they’re called T-cells, and the antibodies come from the lymphatic system, so there’s sort of two groups.

It turns out that while the effect of interferon may be more generally understood—I don’t know what the specifics are—but the lymhokines and the cytokines were communications molecules— proteins sent out that turned on or

turned off, up-regulated and down-regulated, these various other cells. Those cells are very useful in ways that we were never told when we were taught about antibodies. For example, you know that killer T-cells have similar specificities to the antibodies, but they proliferate also selectively, and these various factors have to be made to give them a signal to do something. And that is, I think, still getting sorted out.

The first one that was clearly defined as a general T-cell growth factor was interleukin 2. So you couldn't go wrong if you wanted to multiply T-cells. If you were going after killer T-cells as a way to address a certain disease, it was a good idea to have some interleukin 2, if not in the patient, then in the broth where you're cooking them up. As a matter of fact, one of the reasons we went to interleukin 2 is we had a consultant, Steve Rosenberg, who was a big-shot doctor at the National Cancer Institute. He was on the cover of *Newsweek* because he told everybody that President Reagan had cancer. No one had ever heard of such a thing in those days, that you would come out and say things like that. So he was very famous, and he was working with interleukin 2. He wanted interleukin 2 to stimulate the growth of his T-cells that he was conditioning to attack people's cancers. And he was taking it out and multiplying it outside the body, and then goosing it back into the body. So he needed interleukin 2. I remember delivering to him at one of those retreats where Kary Mullis was possibly sounding out about PCR a vial of interleukin 2, and he said, "This is more interleukin 2 than exists [elsewhere] in the world at the moment." So we developed a relationship because we were able to supply him with it.

Hughes Well, he mentions that in his autobiography, *The Transformed Cell.* It was a tremendous boost, of course, to his research now to have plenty of IL-2 to work with. But as you know, the clinical results that you were getting were rather dicey.

Cape Well, there again, talking in terms of 2003, I'm appalled. If you take a look at the profile of side effects of interferons or interleukins, they're very bad. At the time they were described as not bad at all, because compared to chemotherapy they're not so bad. Compared to anything else, they're pretty gruesome. And some people are so upset by the flu-like symptoms, even if they know their cancer is responding, they won't continue. But the real numbers are that fifteen percent of the people react marvelously, and the others don't react at all. It's not a continuum. And the FDA said fifteen percent is statistically not distinguishable from zero. If they would use pharmacogenomics, as I was describing to you before, and find some gene sequence—you don't even have to know what it does—which occurs more frequently in that fifteen percent than in everybody else, you'd stop trying to sell everybody interleukin 2, and you'd concentrate on those people [in the 15 percent], and you'd be able to talk about a hundred percent response. But the drug industry doesn't think that way, generally speaking.

Hughes Well, explain why, and whose decision it was, to put so many eggs in the IL-2 basket. I read somewhere that Cetus put $150 million into IL-2.

Cape Today that wouldn't be very much. I've read that it now costs the drug industry $1.7 billion to bring out a new drug.

Hughes But then it was a lot.

Cape I'll say. Particularly in terms of how much money we had.

Hughes Well, recreate the thinking.

Cape We were determined to become a drug company, and we needed an approved drug to be a drug company. We even had a sales force selling generic anti-cancer drugs just so we had some people on the ground running to be ready when we got approval from the FDA.

Hughes Were you that confident?

Cape So it would seem.

Hughes Well, how much of this was Fildes' decision? The story is, he comes in, he's going to focus. What is he going to focus on? He's going to focus on cancer therapeutics. Is that actually the way it was?

Cape To the best of my memory, yes.

Hughes There are many kinds of cancer therapeutics. Was it just because—

Cape Because that's what we had.

Hughes That's what you had.

Cape I'm making that up, but it makes sense. And it makes sense, in retrospect, to say that the juggernaut got carried away with itself.

Hughes Is Fildes so all-powerful that he doesn't have to consult anyone? You've decided that you're going to step aside and let him make the decisions. You talk over things, but in the end he has to make the decision. That's what you told me today. Where is the executive board in all of this?

Cape Since when did boards mess around with specific operational decisions?

Hughes But this is a big one!

Cape Yes, you're right. In retrospect, what did the board do? In retrospect, the board decided that they had spent so much money that they couldn't afford to live as an independent company anymore. There was no way to turn this thing around. And the one thing they had to do was curtail the expenditure, right, and the second thing they had to do was find a safe harbor.

Hughes Meaning the merger.

Cape Yes.

Hughes But before that why don't they say, "I don't care what you say, Fildes. Yes, we need to focus, but it is too risky to focus on just this one product, or predominantly this one product." I don't know what else was being funded.

Cape Your question is, how could you be so stupid to put all your eggs in one basket. And you're absolutely right. It's one of the cardinal rules of business. You never want to have a situation where you're a one-trick pony—a lot of biotech companies are today.

Hughes But surely somebody was saying that. Weren't you saying that when you met with Fildes?

Cape Yes, but. I think we were all confident that we would get approval at that [FDA] hearing in the summer of '90. And we didn't. And that was basically a wake-up call that should have been responded to earlier. If I read that book [by Rabinow] properly, and you read it more carefully than I did, his statement is that the board, in saying stop this rate of spending, had lost its guts or lost its will. But I don't think there was enough money left to continue.

Hughes To do anything else.

Cape To do anything else. So it may have been very belated as a decision. But belated or not, it was the right decision to make. We're jumping off the cliff, folks. As a matter of fact, I think we did surprisingly well. I mean, our stock dropped after that FDA session from $21 to $5, which was below the cash we had in the bank. And when we merged with Chiron we got our $21 back. Did we have to lay off anybody? No. Did anybody lose any money? No. Did any projects have to get cancelled? No. So we escaped by the skin of our teeth, except we lost our company. And in that period, magnificently, due to the efforts mainly of David Gelfand and Henry Erlich and John Sninsky, we turned PCR from a Nobel Prize phenomenon into a commercially useful system.

Hughes I know there was dissention over the Nobel Prize being awarded only to Mullis.

Cape Well, it's one of those things. It could have gone both ways. You must have read some of the books and articles about the Nobel Prize. It's a crazy process. There

is reason to say that Kary uniquely invented it. There is reason to point to many other examples of somebody who didn't invent it, who had nothing to do with it, getting the Nobel Prize. There are other cases where somebody who invented it never gets the Nobel Prize. Einstein got the Nobel Prize for the wrong thing, for some trivial effect that he had invented, and not for relativity.

Hughes I was thinking of the current Nobel Prize in physiology and medicine for MRI.

Cape There's an example of a similar situation in the guy who invented the laser suing and winning part of the royalties. He didn't win the Nobel Prize, but he got part of the royalties.

Hughes Should the executive board have been more involved with the decision to put so much into the IL-2 basket?

Cape In retrospect, that is obviously true.

Hughes But at the time?

Cape I don't suppose at the time it was all that clear. I don't remember anybody standing up and saying, "I insisted that this was crazy." Nobody had a lot of people with experience there.

Hughes Fildes is, from what I gather, and I've never met the man, is a strong personality.

Cape: Yes.

Hughes: Do you think that he was controlling the show to a greater degree than other people might have? He came across as such a convincing and strong-minded individual that perhaps there wasn't as much due diligence or just plain attention paid to whether this investment in IL-2 was really a good thing to be doing.

Cape Because of all the crooks, who have in the last two or three years have been revealed as not only stealing from the investors, but also stealing from their employees, and building themselves big houses, and all this kind of stuff, the whole subject of what a board does has come under new scrutiny. In the case of most biotech companies, there may be appalling amounts of money spent, but they're spent on scientists and clinical trials, and a lot of that doesn't go the way you want it to. Every week you read about so-and-so announces they're stopping the clinical trials on this because they're not getting the results they had hoped for. We made that mistake in the case of something that was unfortunately too many eggs in one basket. And our whole future. That's called bet the company. And that's what we were doing.

Hughes Right. To put it in very bald terms, was the executive board to a large extent just a rubber stamp?

Cape It wasn't a rubber stamp as much as it was not as critical as it should have been. It's a very difficult thing to suddenly become too conservative and fear you'll never get there, because everything is a race. And there are many examples of races which have been won by a hair, and if it had gone the other way, the company would have folded but became one of the great success stories. I would imagine that with maybe ten different members of the Cetus board, each of them had a different daydream, and you do get carried away. In retrospect, it's very easy to say, it should have gone more slowly.

On the other hand, if the only penalty we paid was giving up the company's independence, and if we kept the value that had dissipated, maybe you might say, yes, you were awfully lucky to pull that one out. And maybe that's the truth. But we had to stop it then and look for merger partners. And that's what we did for the next year and a half. It was a happenstance meeting in the joint parking lot [of Cetus and Chiron] of Ed Penhoet and me, saying, hey, we're all in the same game, and we can pull your marbles out—that sort of thing.

Hughes You—and again I get this from Rabinow—had been to something like seventy-five different companies trying to find a strategic partner.

Cape I have no idea. I personally had been to maybe a dozen. All I remember vividly arepeopleinJapanweweretryingtotalktoaboutPCR,andalltheywanted to know is when are you going back to the FDA? That's all they wanted to know. I mean, can we talk about something else, please?

Hughes It's interesting to speculate what might have happened if IL-2 and PCR hadn't been on the burners at the same time. What would have happened to PCR if it was the only viable product, if there hadn't been anything else?

Cape It had its own problems. Not scientific problems, but strategic problems.

Hughes Meaning what?

Cape Meaning that it was so wonderful, and it was perceived as so wonderful by the scientific community that there was a lot of pressure on us to make it available without any commercial connection to anybody that wanted to use it. Driven to its logical extreme, you say, forget about the value and concentrate on the contribution to science. On the other hand, never having come to a satisfactory conclusion about that, we, and I think to some extent Roche, but I don't know, enabled it to get into the hand of tens of thousands, and maybe more, scientists, and the number of possible applications—well, they're countless now. PCR is so ubiquitous, it's in more situations than recombinant DNA. And a lot of those developments would have been impeded by too restrictive a policy. But we

never solved that dilemma, and that dilemma, perhaps, still remains to be solved. I think Roche may in fact incorporate it into an approach to pharmacogenomics. It might be very useful. Certainly it's been used repeatedly in courts. But there's not an enormous amount of money in that. In fact, we were still running the show when the first reversal of a conviction occurred and a guy was sprung out of jail. We worked with the FBI a lot at the time. In fact, I think Robert Muller, the current director of the FBI, came to visit me one time. But I'm not sure of that.

PCR didn't have a clear business model ahead of it. It was quite clear that in high-sensitivity diagnostics it had a future. Anybody could have figured that one out, and that's why Roche had this fifteen-year exclusive license to do just that. But there were bigger fish to fry, and I think there still probably are. There was some debate about how much money is in the instrument market, and how much money is in the selling of these enzymes, and, if I recall correctly, somebody has successfully challenged some of the patents on the enzymes and the kits.

I told you the funny story about the knockoffs, didn't I?

Hughes I don't remember.

Cape One of the key elements of PCR is the thermocycling. You have to heat it up, cool it down, heat it up over and over. (I gave one of the very first thermocyclers to a British science museum. It's sitting in London someplace.) It turns out that one of the debates we had with PerkinElmer that were making the instrument was, we wanted them to respond to the fact that there were really cheap knockoffs being made in Japan. And they had the feeling that they would build a Cadillac or nothing. And the point is that for one-third of the price, you could make something almost as good, and they were resistant to making anything less than a Cadillac, so we were sort of cut out of that market. So the knockoff market sort of developed. We got hold of one of those knockoffs. And what the PerkinElmer machine said—a little sticker—was something like "The purchase of this machine does not constitute a license for commercial applications of the outcomes of the experiments that it enables. We're happy, however, to discuss licensing terms with anybody who has such a commercial outcome. And here's an 800 number at Cetus to call." The Japanese put that identical sticker on their knockoff!

Hughes I want to hear about muteins. At one point, Cetus seems to have been making quite a thing about one amino acid change from the natural amino acid, and I wondered what that was about.

Cape The intention was to avoid forming inappropriate disulfide bonds. It turns out that there are three amino acids in the sequence of interleukin 2 that have SH groups on them. And an SH group can be reduced to an SS. [draws diagram] This is the molecule, and there's an SH here, which means it comes from a

certain amino acid, cysteine. You can remove these two hydrogens and form a bond between these two sulfurs. If you hydrolyze this, and certain breaking-ups of proteins end up in an amino acid, that's a diamino acid with a sulfide bond like this, and that amino acid is called cystine. At one point cysteine and cystine were listed as separate amino acids, and it's simply a result of degradation that produces cystine. It's a bonding between two cysteines.

Hughes But so what?

Cape I'm getting to that. That was an unnecessary digression. If this is the correct bonding, there's nothing to stop this one from bonding here, or this one from bonding [there.] There are two incorrect pairings that can take place. If you replace this with an OH, which changes cysteine to serine, I think, you can't get the inappropriate bonding. So this was a way of guaranteeing a much higher yield of the right shape.

Hughes Yes, because it becomes beta-serine.

Cape Right. That's why they got beta-serine. It also makes it a synthetic molecule that never existed before, and you can patent it. That's sort of nice. But you an also patent the "natural" mix, if made by rDNA [recombinant DNA]. And the "on" in betaseron is to get a suffix like interfer*on*. Gimmicky, but that's the way it is with trade names. It turns out that beta-interferon and IL-2 both have the same opportunity.

Hughes But the patent question was secondary?

Cape Yes.

Hughes Wasn't the mutein technology supposed to be generalizable?

Cape Maybe; I don't know. The same thing is possible in beta interferon as well. And it turns out we were very lucky. Both of those molecules are free of a real complication in protein pharmacology, namely, most proteins are coated with sugar; they are glycosylated. And these two molecules, interleukin 2 and beta interferon, do not have glycosylization. The proteins are naked. So we don't have to be worried about the immunology of it.

However, Biogen used a different approach altogether, beating us in the marketplace. And that had nothing to do with molecular thing, although they don't have this thing [knocking on diagram]; they have closer to the natural but made by recombinant DNA. They adopted a different labeling strategy in going to the FDA. In other words, they were claiming different things, claiming possibly one dose a week instead of two doses a week; whatever it was, I don't remember. But the point was, they took away half of the market in one year on

the basis of the fact that they were able to say to the doctor what the Berlex people or the Chiron people were not able to say.

And that was relatively recently, wasn't it?

Cape In 1993, this was the molecule of the year. No, beta interferon. Forget about interleukin 2. The same thing is true of beta interferon. Betaseron is beta interferon. But the same thing applies. It's a mutein. We had a hundred percent of the multiple sclerosis market in 1993; we had fifty percent of it in 1994, and [Biogen's] product just took over. It's like a horse race; you never look back.

Hughes The Cetus Health Care Limited partnership was created in 1983.

Cape Oh, there were a number of them.

Hughes Is that the first?

Cape I have no idea. There was a wonderful situation provided by the tax code, which was cancelled in 1986, that you could invest in a particular partnership that focused on a particular drug. Because of the high-risk nature of the partnership, you could take terrific tax losses on your investment; and if the drug should pay off and those royalty streams came in to you five, ten years later, you would do very well. These were very popular in the biotech industry up to 1986 when their tax advantages were destroyed. Though the idea of being able to invest somehow in one particular product is attractive, this [limited partnership] made it possible

[End Tape 12, Side A] ##
[Begin Tape 12, Side B]

Cape —to have the feeling of missed opportunities, everything from science to the last day we had a party to celebrate the amalgamation [with Chiron.] There were so many Cetus employees crying. I was very moved and touched and realized I didn't appreciate what we had.

I had this ankle problem where I had almost became unable to walk three years ago. And I went to a large number of sports medicine and orthopedic experts, including the head of the sports medicine department at Yale University. I got up on the table to have him examine my ankles, and he looked at my papers and somehow one of the doctors had made mention of Cetus. "Cetus!" he said. "I invested in Cetus." This reflects my sad feelings about the way the whole thing turned out. I got off the table and said, "Goodbye. I can see there's no point in continuing this conversation." And he said, "No. I made a lot of money. I invested in one of the limited partnerships."

Hughes The limited partnership wasn't invented by Cetus as a funding device.

Cape As far as I know, that's true. But we used it. There was a fair amount of opportunism in fundraising. I used the metaphor about the story in the bible of the warehouses in Joseph's dream. Perhaps more simple and to the point is the phraseology used in biotech regarding fundraising, which is, the time to take the hors d'oeuvres is when they're passing them around. Okay? So there were certain opportunities in various financial markets for various kinds of investments. And when I think of the agonizing time and detail that went into our initial public offering, which raised $100 million, and several years later, with all the people who had been our internal as well as our external professionals and investment bankers, were still in their same jobs. Suddenly the market heated up for selling some kind of security in Europe. We raised $100 million in three weeks—okay, let's go for it—and did all the paperwork and gave our investment bankers the green light, and they did it. It was practically like falling off a log. That's how different things were in those days.

Hughes Going back to the early days of Cetus. I've heard the name Saul Neidleman mentioned.

Cape First of all, he was and is, if he's still alive, a wonderful guy. Number two, he was the head of what you might call the Natural Products and Industrial Projects division or effort, going on at Cetus, the one that Jim McCamant thought was our major focus. One of the people who worked for him is a wonderful woman whom I was with on Monday of this week in Washington. She is now the president of the Maryland Biotechnology Institute. Her predecessor in that job is now the head of the National Science Foundation She is somebody you might also talk to about Cetus and Saul Neidleman, if you can't find him. And the last I heard he lived on the other side of the hill someplace, like Orinda or Lafayette or something. I have no idea where he is, and I spoke to Jenny about him recently. Her name is Jenny Hunter-Cevera, and she was in that group then. She's a good person.

Hughes By 1980 I have Neidleman as director of new ventures research.

Cape That was a euphemism. I mean, it doesn't tell you anything. It could be anything but it was industrial medicine—the ethanol project, propylene oxide project, that sort of thing.

Hughes So he was not a bench scientist?

Cape He was a projects scientist. He came to us from Squibb. But he was the principal guy in those.

Hughes We have only talked in passing about the subsidiaries of Cetus. Let's see how it goes in terms of formation. Cetus Palo Alto was formed in July 1980. And that's basically Stan Cohen?

Cape Yes. With a little bit of Stan Falkow.

Hughes It was formed to do what? Tell me as much as you can remember.

Cape To do whatever projects in recombinant DNA they could best do in a smaller organization in which the scientists would identify more closely and recapture, so-to-speak, the entrepreneurial spirit. It was the same idea as now you see what they call spinouts with an entrepreneurial sort of sense.

Hughes Incubators?

Cape No, it's called intrapreneurial. What it amounts to is a big company, like Pfizer, has a technology where the people who are doing it are very excited. Even Pfizer agrees—I'm making this up—that it's great, but it didn't make the cut for whatever reasons. Maybe it was too small, or maybe it was a market Pfizer just decided you can't do everything. So the guys say, let us form a new company. We're going to leave. We want to take the intellectual property with us. So, Pfizer, give us all the intellectual property, give us our freedom and what have you, and we'll give you twenty percent of the company, okay? And that has been done several times.

We were trying to recapture that kind of spirit in Cetus Palo Alto, in Cetus Immune, and in Madison, Wisconsin, in Cetus Madison, which changed its name, when W. R. Grace bought a fifty percent slice of it, to Agragenetics. And actually, that name still exists. Its original was W. R. Grace blending into Cetus, and the fact that it implies agricultural, which is perfect, is all forgotten. It was a division of Monsanto. Monsanto's gotten acquired. But I flew over it. The greenhouses are still there. It's still there! It was formed around Winston Brill, who was a brilliant geneticist at the University of Wisconsin.

Hughes Well, let's go back to Cetus Palo Alto. By 1980, you at Cetus Emeryville have a blooming recombinant DNA effort with Gelfand at the head. How are these two recombinant DNA units relating? Or are they?

Cape Well, I think the question at the time was how would they relate? Would they stimulate each other? Is this like Procter and Gamble, which has competing brands on the market and each has its own brand manager. You say, well, let's see how it works and see if it creates more competition.

Hughes Now, was that your idea?

Cape Yes. And I don't think any of them really worked. Cetus Immune was built around Hugh McDevitt. It had a great number of really terrific immunologists from Stanford on it.

Hughes Yes. Tom Merigan .

Cape Yes, Tom Merigan.

Hughes Gary Fathman.

Cape Gary Fathman, right. Ed Engleman, who was at the Stanford blood bank. And one or two others.

Hughes How much time were these people really there? These are all people with full faculty positions, and they have their own university research projects.

Cape Well, they're allowed twenty percent of their time [for consulting] by Stanford rules.

Hughes So they were serving as consultants?

Cape Yes. I do remember the physical facilities of each them, and there was action going on in them, and there were good scientists in them. Let's take just one person who was in Cetus Immune, Jim Larrick, a doctor, who is still forming companies, was a jack-of-all-trades. He was one of these renaissance men who one day would be doing ethnobiology with natives in the Peruvian mountains, teaching them certain elements of modern medicine, and they'd be teaching him about antivenoms and things like that. The next thing I see Jim doing is writing an article in, I think it was, *National History*, about the yak and how an entire culture in the Himalayas lives around the yak and all its various ramifications. And then most of his time he's spending at Cetus Immune, running some of our antibody projects. Jim Larrick now runs Panoramic, in Mountain View.

These were experiments in how can you organize and reorganize the way science is done with industrial targets. Cetus eventually became more than a thousand people, which by today's standards may not be much. In those days it was a lot. It's too big for that kind of excitement and everybody knowing everybody else's business and that sort of thing. And these subsidiaries were experiments in doing things differently. The question was, could they be done more successfully? I think the way they turned out, for whatever reason, and I can't really remember well what they were, Bob decided that they weren't sufficiently productive to continue. And the only one that he continued was the one in Wisconsin, which he continued by getting a big industrial partner.

Hughes Monsanto.

Cape No. He got in W. R. Grace. Ultimately, the solution to the cash drain of those efforts was that for every year we didn't put money in, after a certain amount of time, W. R. Grace would get a slightly bigger piece of it. Eventually, I think by the time we merged with Chiron, we didn't own any of it. But guess what? It's still there. And some of the agrafood or genetically modified food things that

you read about in the papers, both good and bad aspects of them, were actually accomplished in our Madison laboratories. They're still there.

Hughes Were these relatively independent groups?

Cape Yes, that's the right word, relatively independent. We wanted to know what was going on and if things were going fast enough to stick with our own fully own people. We'd try to say, what the hell? They were relatively independent.

Hughes Do you remember what, for example, Cetus Palo Alto was working on?

Cape No. My guess is growth hormone was one of them, but I just don't remember. Same thing with Cetus Immune.

Hughes Cetus Immune—there's Hugh McDevitt, an eminent immunologist. Did he have any relationship to the IL-2 project?

Cape Yes. As a matter of fact, I'd be inclined to say that of all the people who I remember was most instrumental in our deciding to give IL-2 the green light, probably a few years before Cetus Immune was formed, was Hugh.

Hughes Well, Cetus Immune formed just a few months after Cetus Palo Alto. It was formed in December 1980. That's before the IPO, too.

Cape We mentioned that in the IPO. We mentioned that in the prospectus. I believe [pause] that we made the decision on IL-2 before Cetus Immune was formed. It doesn't really matter, but I'm just trying to think of it. All the people we mentioned and a few more that were in Cetus Immune and Cetus Palo Alto were considered consultants to Cetus and were at those big retreats where Kary Mullis would carry on.

Hughes Couldn't one say, particularly pre-IPO—this is not even a public company yet—that this is pretty ambitious?

Cape Yes. But it was also very, very enjoyable. I mean, we were trying to figure out how people would work best in an industrial setting, and the central thought on all three of those subsidiaries is that maybe they'd do better in a smaller organization.

Hughes You were trying to accommodate the scientists?

Cape To motivate them, that's for sure.

Hughes With the idea, of course, that they'd be more productive, and that maybe you'd get products that were marketable. One of the things I'm interested in is the

balance between science and business interests in the early biotech companies. Do you have any comment to make?

Cape Well, I was aware of the fact that they might conflict, but I also considered it a red herring that they conflicted a lot. The only example I can think of, and it was almost a demonstration of a cultural principle, was PCR, where we were by no means convinced that there was any commercial future here, but it was wonderful to have that kind of nervous energy and creativity around. We wanted to preserve that even in the face of it might be possibly injurious to the body as a whole, basically the nutsiness and craziness. Universities have that problem too, don't they? They have some professors who are highly disruptive, and up to a point, university administrators tell themselves that they're doing everybody a favor by putting up with it.

Hughes We have ten minutes left. I think we can probably finish, unless you feel cut off.

Cape But you know where to get me.

Hughes I know where to get you—in various parts of the universe. Tell me how you first became involved with BIO [Biotechnology Industry Organization] and its predecessors.

Cape Well, Leslie Glick, who was at the time the founder and CEO of a company called Genex, which flamed out early—it was involved in making aspartame [a sugar substitute, trade name is Equal] from Monsanto, and that didn't work out somehow. So the company, I think, disappeared. But it was one of the major biotech companies in whatever year it was that we started it BIO, like 1981 or 1983 or whenever it was. A bunch of us, seven in particular, got together at the Philadelphia airport and decided that the industry needed some kind of an organization that could talk about mutual problems and challenges and initiatives, varying all the way from the scientific to the safety to the public relations to the congressional, and all those kinds of things.

Hughes Do you remember who the seven were?

Cape Well, I've been asked that question recently, and I can always come up with five or so. All the big ones that counted in 1981, except Genentech, which failed to join.

Hughes Why was that?

Cape "Who needs you guys? We're in a class by ourselves" kind of thing is the feeling I got about it. It was five years later, just towards the end of my tenure as president of IBA [International Biotechnology Association], that we finally coaxed Bob Swanson to change his mind.

So there was Bob Fildes from Biogen, there was me—this is pre-George Rathmann; Amgen was called American Molecular Genetics or something like that, Amgen—and Joe Rubinfeld, who eventually was an employee of Cetus. He was an old friend of Saul Neidleman's. Then there was a guy named Frank Pass, who was a dermatologist from Minnesota, I believe, who had a company I've forgotten the name of, and then there was David Padwa, Agragenetics. I'm getting up there.

Hughes George Rathmann does come in later, doesn't he?

Cape Not much later.

Hughes Were you head of the show?

Cape No. The first president was Lew Glick. Gabe Schmergel was there, too, the Genetics Institute. And that was the founding group.

Hughes What did you do?

Cape Well, we had meetings, we had speakers, we talked about issues, values, the role of science, the role of the public, Congress; we had politicians addressing us.

Hughes Did you have lobbyists?

Cape Not as many as BIO has turned out to have. There were several of us from IBA meeting with Al Gore right in the middle of my three-year stint—didn't do much lobbying per se, we were just trying to tell our story. We were deluded, as most scientists, I believe, are deluded, in thinking that the problems with the public would all be solved if the public knew and understood the facts. They were sort of obsessed with the fact that everything is science, not realizing that there are other issues involved, such as the freedom to choose, which is not a scientific thing. The United States, for example, supports its business by saying there's no scientific basis for labeling. If we're a consumer-driven society, we should understand that if consumers in Europe like to insist on knowing what genetically-modified foods there are in their stores, the FDA saying it doesn't make any difference is not an appropriate answer.

But we were at that time not lobbying too much, because we had the feeling that what we had to do was get the facts out and argue with Jeremy Rifkin whenever the opportunity came up. Those were the kinds of things we did. And, as you know, the meeting that BIO had in Washington last June, and which we are going to have in San Francisco this June, brings in 20,000 people.

Hughes Why was there the merger?

Cape With the smaller group?

Hughes Yes.

Cape Well, [inaudible] and if the right people were in the right place at the right time to meet to merge and be done with it all, I think it was the right decision. They're still fighting with issues such as, how are you going to arrange membership fees, and are you going to keep out the two hundred or three hundred companies that can't even afford a hundred bucks a year, where Genentech might be spending $25,000 or $50,000 a year?

A lot of the lobbying, since you bring it up, is done through BIO now, but so is a lot of it done through individual companies. Just as I believe it is true to say that the pharmaceutical industry does a lot of lobbying in Washington, and they've got the Pharmaceutical Manufacturer's Association with their lobbyists. But I'll bet Eli Lilly has their own lobbyists, and Merck has their own lobbyists.

Hughes I know Genentech does. Did Cetus have its own lobbyists?

Cape [Gestures "no."] Well, Bob pulled out of BIO for two or three years.

Hughes Okay. Final question. What do you consider to be your most significant contribution?

Cape Well, I think showing that it can be done. It's more luck; I mean, how could anybody pass up the opportunity, being at the right place at the right time and having the right background? I think that in heading one of the first biotech companies and seeing it mature to an appropriate value, which made a lot of people happy, in terms of working there and feeling fulfilled, bringing valuable products out, having a culture that nurtures still the only biotech Nobel Prize ever awarded. It's a bag of mixed things. I feel a very mixed feeling of missed opportunity and basically addressing opportunity. I feel very lucky to have been at the right place at the right time.

Hughes Well, thank you for all your time.

[End of interview.]

Curriculum Vitae—Ronald Elliot Cape, M.B.A, Ph. D.

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Career

1992—1997
Darwin Molecular Corporation, Bothell, Washington. Chairman.
Darwin is a company in the formative stages founded by world leaders in DNA sequencing and directed molecular evolution. These technologies will be combined to establish new paradigms of drug discovery, targeted therapy, and diagnosis.

1972—1991
Cetus Corporation, Emeryville, California. Co-founder in 1972. President, 1972- 1978; Chairman, 1978 to 1991; Chief Executive Officer, 1972-1985 and 1990 to 1991.

Cetus was a world leader in genetic engineering—the first company founded specifically to address the extensive business opportunities arising from significant post-World War II advances in the understanding of biologicid systems. The company was best known for its development of genetically engineered Proleukin® interleukin-2 (L-2), and Betaseron®beta interferon and the discovery and development of GeneAmp®PCR, the polymerase chain reaction process (recipient of the 1993 Nobel prize in Chemistry). Cetus conducted operations in Emeryville, California, and Amsterdam, The Netherlands. Cetus merged with Chiron Corporation in December 1991.

1971-1972
Cetus Scientific Laboratories (Cetus Corporation's predecessor partnership), Berkeley, California. Managing partner.

1971—1975
Cape. Farley Inc., Berkeley, California. President.

1956—1973
Professional Pharmaceutical Corporation, Montreal, Canada. President, 1960-1967; Chairman, 1967-1973.

1955—1956
Merck & Company, Ltd., Montreal, Canada. Purchasing and advertising departments.

Awards

1994 Multiple Sclerosis Silver Hope Award

1994 Fellow, American Academy of Microbiology

1993 Fellow, American Academy of Arts and Sciences

1993 Fellow, American Association for the Advancement of Science

1988 Communicator of the Year by the San Francisco Chapter of the International Association of Business Communicators

1987 Administrator of the Year by the Society of Research Administrators

1986 Achievement in Business by *Better Health & Living* magazine

1985 Scientist of the Year by *Research & Development* magazine

Professional Activities

Neutrogena Corporation, Board of Directors

Advanced Bioconcept Inc., Board of Directors

Cogito Learning Media, Inc., Board of Directors

GlycoDesign, Inc., Board of Directors

Neugenesis Corporation, Board of Directors

Sunol Molecular Corporation, Board of Directors

The Foundation for the National Medals of Science and Technology, Board of Directors

Neurobiological Technologies, Inc., Business Advisory Committee

Princeton University, Board of Trustees

The Rockefeller University, Board of Trustees

National Library of Medicine, Board of Regents

Committee on Biotechnology, Commission on Life Sciences, National Research Council

California Public Health Foundation, Board of Directors

Bay Area Bioscience Center, Founding Chairman

Canadian Medical Discoveries Fund Inc., Scientific Advisory Board

Medical Research Council (Canada), Standing Committee, Business Development

Scientific American, Board of Directors

Bio/Technology Magazine, Scientific Advisory Board

The Scientist, Editorial Advisory Board

Harmony Foundation, Founder and Director

Scientist-to-Scientist Colloquia at Keystone, Originator

The Keystone Center, Board of Trustees

The Keystone Center Foundation, Vice President and Director

Steering Committee Member, COBIOTECH, an international scientific committee for biotechnology of International Council of Scientific Unions (ICSU)

University of Pittsburgh, Adjunct Professor of Business Administration

University of Pittsburgh, Biotechnology Center Advisory Board

Princeton University, Advisory Council to the Department of Molecular Biology

Queen Mary College, University of London, Visiting Professor in the School of Biological Sciences

The Presidents' Circle of the National Academy of Sciences

The Delegation for Basic Biomedical Research

AAAS Committee on Scientific Freedom and Responsibility

The University of California Biotechnology Research and Education Program Advisory Committee

Berkeley Roundtable on International Economy (BRIE), California Business Advisory Committee, University of California, Berkeley

University of California, Davis, Board of Visitors, College of Engineering

Advisory Board for "A Study of Technology Transfer from Federal Laboratories to Industry"—University of California, Davis

Advisory Board to the Center for the History of Microbiology (American Society for Microbiology Archives and University of Maryland)

University of Waterloo (Canada), Institute for Biotechnology Research, Board of Directors

Advisory Trustee, Advanced Biomedical Science & Treatment Center, Oakland, California

Industrial Biotechnology Association—President, founding member, and member Board of Directors

Natural Sciences and Engineering Research Council of Canada, Advisory Committee on Life Sciences

Member of the Institute of Medicine's Committee for Promoting Research Collaboration

Delegation Leader, Citizen Ambassador Program of People to People International, for Biotechnology Management Delegation to Japan and the People's Republic of China

Member of Impacts of Applied Genetics Advisory Panel to the Office of Technology Assessment, which put together the report entitled "Impacts of Applied Genetics—Microorganisms, Plants and Animals"

Annual Reviews, Inc., Business Affairs Committee

Dynamic Fund of Canada, Ltd. (a mutual fund) Director and member, Investment Committee

Business Advisory Committee, Neurobiological Technologies Incorporated

Memberships (including civic and charitable organizations)

American Society for Microbiology, member and Foundation for Microbiology Lecturer

Society for Industrial Microbiology

Canadian Biochemical Society

Federation of American Scientists

The New York Academy of Sciences

Scientific Research Society of North America (Sigma Xi)

Royal Society of Health

San Francisco Opera Association, Board of Directors

San Francisco Conservatory of Music, Board of Trustees

Opera West Foundation, Board of Trustees

University of California Art Museum Council

Head-Royce School, Board of Trustees

Bay Area Council

Bay Area Economic Forum

San Francisco Exploratorium, Director's Council

San Francisco Performances, Business Advisory Council

Commonwealth Club of California

The Princeton Club of New York

Hobbies

Skiing, hiking, flying, music

Education

1967-1970
University of California, Berkeley. Molecular Biology and Virus Laboratory. Postdoctoral research in the laboratory of Dr. Gunther S. Stent, studying the relationship between metabolisln and genetics in infection of *E. coli* by bacteriophage T4. Holder of Centennial Fellowship of the Medical Research Council of Canada.

1963-1967
McGill University, Montreal, Canada. Ph.D. in biochemistry. McConnell Memorial Fellowship. University Graduate Fellowship. President, Montreal Biochemical Circle. Attended Third Advanced Study Institute of Molecular Biology, Spetsai, Greece. Research Director: Dr. John H. Spencer. Thesis: “Frequency and Distribution of Purine Nucleotide Clusters in DNA.”

1953-1955
Harvard University. Graduate School of Business Administration. M.B.A. degree with Distinction. George F. Baker Scholar (top 5 percent of class). President, WHBS radio station.

1949-1953
Princeton University. A.B. degree, *summa cum laude* in Chemistry. Ranked first in class

of 621 on graduation. Phi Beta Kappa in junior year. Albert G. Milbank Award (highest cumulative grades through junior year). George Wood Legacy Prize (highest grades in junior year). Student Medal of American Institute of Chemists. Sigma Xi. Research director: Dr. Gregg Dougherty. Thesis: “The Catalytic Alkylation of Sulfur.” President, Prospect Club. Extracurricular: crew, debating, club president.

Prior to 1949
Born in Montreal. Attended local schools. Ranked second in Province of Quebec matriculation examinations in 1949.

Publications

Co-editor of textbook *Biotechnology: The Science and the Business* in conjunction with Dr. Vivian Moses of Queen Mary College, Harwood Academic Publishers, London, 1991.

"What Is Biotechnology's Public Role After We Have Delivered What We Promised?" *Genetic Engineering News*, Vol. 10, No. 2, February 1990, page 4.

"Observations on the Future of Biotechnology." *SRA Journal of the Society of Research Administrators*, XIX, No. 4, 7-1 1, Spring, 1988.

Oral Testimony before the Senate Select Committee on the Pacific Rim, Hearing on "Economic Demands of the Pacific Rim on Educational and Social Institutions." San Diego, California, December 14, 1987.

"Harmony Fellowships: Fostering the International Growth of Biotechnology." *Biopharm Manufacturing* magazine, 1**,** No. 1, 14-1 5, November, 1987.

"Harmony Fellowships: A Proposal for a New Prestigious Program to Promote Reciprocal Biotechnology and Cultural Exchanges," presented to the Second International Exhibition of Biotechnology, Bio '87 Japan, Osaka, Japan, October, 1987.

"Biotechnology," presented to the Canadian Engineering Centennial, Montreal, Canada, May 20, 1987.

"Sharing the Biotechnology Leadership with Japan: A Proposal," presented to the "1ndustrial Biotechnology Associalion, Los Angeles, California, May, 1987.

"The Impact of Biotechnology by the Year 2000," presented to the World Business Council Conference, Palm Desert, California, February 15-19, 1987.

"The Success Story of Cetus: What Can Canada Learn?" presented to the Second National Research Council of Canada Industrial Biotechnology Conference, Montreal, Canada, December 4-5, 1986.

"The Future of Biotechnology." *Proceedings of the US-Japan Colloquium on Antibiotic Research and Biotechnology,* 75-76, organized by the People to People International Foundation and the Japan Antibiotics Research Association, Tokyo, Japan, November 5, 1986.

"Biotechnology - Who Are The Real Environmentalists?" *Cincinnati Environment, 3,* No. 1, 1, 3,6-7, July, 1986.

"Who Will You Blame When the Other Guy Wins?" (The Last Word) *Bio/Technology* Magazine, 4, No. 4,368, April, 1986.

"Future Prospects in Biotechnology: A Challenge to United States Leadership." *Biotechnology in Society,* 5-9, 1986. Pergamon Press Inc.

Testimony before the House Subcommittee on Investigations and Oversight of the Committee on Science and Technology on "Planned Releases of Genetically Altered Organisms: The Status of Government Research and Regulations." 21-35, December 4, 1985.

"Of Genesis, Genes, and Public Policy." *Research & Development* magazine, *27,* No. 11, 76-81, November, 1985.

"Commercialization of Biotechnology" Panel, *Proceeding of Biotechnologv Dav III; Biotechnology in Canada: What is Being Done and What Ought to be Done,* 119-121. University of Waterloo, October 28, 1985.

"Impact of Product Approval—Drugs." *Proceedings of The Toxicology Forum 1985 Annual Summer Meeting,* Given Institute of Pathobiology, Aspen, Colorado, 26-35, July 15, 1985.

"Conspiracy of Silence." (Editorial) *BioEssays, 1,* No. 6, 243, December, 1984.

"Brainstorming" Panel, *Proceedings of Biotechnologv Day II: University/Government/ Industry Interfaces in Biotechnology,* 78-80. University of Waterloo. November 6, 1984.

"On Deserving Awe and Envy." (The Last Word) *Bio/Technology* magazine, *2,* No. 10, 912, October, 1984.

"Biotechnology: Sayonara to the U.S. Edge." *The Commonwealth* (weekly newsletter of the Commonwealth Club of California), *LXXVIII,* No. 42, 347-349, October 15, 1984.

"The Biotechnology Industry: A Global Perspective." *The World Biotech Report 1984,1,* Europe, 1-14 (The Proceedings of Biotech '84 Europe, a conference held May, 1984, in London, England).

"Academic and Corporate Values and Goals: Are They Really in Conflict?" Presented to American Chemical Society, Kansas City, Missouri, September, 1982. *Industrial-Academic Interfacing* (ACS Symposium Series 244), edited by Dennis J. Runser, 41-49, 1984. Also, *Professional Relations Bulletin,* No. 30, 2-4, October, 1982.

"Challenges to Biotechnology Engineering in Industry and Universities." Presented at the North Carolina Biotechnology Center Workshop, Raleigh, North Carolina, April 14, 1983. *SIM News, 33,* No. 6, 29-34, November, 1983.

"An Industrial View of Biotechnology." *Proceedings of Biotechnology Day I: Identifying Opportunities in Biotechnology,* 5-15. University of Waterloo. October 6, 1983.

"The Corporate Mission in Research and Development—Reactor." *Partners in the Research Enterprise,* 117-118, 1983. University of Pennsylvania Press.

"What are the Lessons of the American Experience? Can Europe Stay in the Biotechnology Race?"—An International Conference held at the Amstel Hotel, Amsterdam, organized by *The Economist,* October 8, 1982.

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R. E. Cape, W. F. Amon, and S. L. Neidleman. "The Future of Biotechnology and the Role of Genetic Engineering." *Biotechnology Letters, 2***,** (5)*,*199-204, May 1980.

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"The Industrial Revolution in Microbiology." *Modern Medicine of Canada*, *34,* (12), 1619-1624 (1979).

"Microbial Genetics and the Pharmaceutical Industry." *Chemtech. 9* (l0), 638-44 (1979).

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Testimony before the House Subcommittee on Science, Research and Technology of the Committee on Science and Technology, "Science Policy Implications of DNA Recombinant Molecule Research." 89-106, March 30, 1977.

"Profit Opportunities—The Future." Paper presented at fall meeting of Commercial Development Association held at The Homestead, Hot Springs, Virginia, entitled "Biosystems Poised For Growth," 107-116, October, 1977.

Robert Bruner and Ronald E. Cape. "The Expression of Two Classes of Late Genes of Bacteriophage T4." *Journal of Molecular Biology*, *53,* 69 (1970).

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Ronald E. Cape and John H. Spencer. "Nucleotide Clusters in Deoxyribonucleic Acids. I. Isolation of Purine Oligonucleotides." *Canadian Journal of Biochemistry, 46,* 1063 (1968).

John H. Spencer, Ronald E. Cape, A. Marks, and W.E. Mushynski. "Quantitative Determination of Pyrimidine Nucleotide Clusters by a Single Spectrophotometric Measurement." *Canadian Journal of Biochemistry, 46*, 627 (1968).

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4/96

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Sally Smith Hughes is a historian of science at ROHO whose research focuses on the recent history of bioscience. She began work in oral history at the Bancroft Library in 1978 and joined ROHO in 1980. She has conducted interviews for over 200 oral histories, whose subjects range from the AIDS epidemic to medical physics. Her focus for the past decade has been on the biotechnology industry in northern California. She is the author of *The Virus: A History of the Concept* and an article in *Isis*, the journal of the History of Science Society, on the commercialization of molecular biology.