

Jordan Gutterman, MD

Session 3: April 19, 2012

Chapter 00C **Interview Identifier**

Tacey Ann Rosolowski, PhD

0:00:00.7

This is Tacey Ann Rosolowski. I am, today, interviewing our third session with Dr. Jordan Gutterman. The date is April 19, and the time is approximately 3:15. So we're off pause. We're recording.

Jordan Gutterman, MD

0:00:24.0

Okay.

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Chapter 11

B: Giving to/Fundraising at MD Anderson
Funding Innovative Clinical Research: Some Institutional Obstacles

Story Codes

A: The Researcher
B: MD Anderson History
C: Discovery and Success
B: Critical Perspectives on MD Anderson
A: Critical Perspectives
B: Obstacles, Challenges
B: Institutional Politics
B: Controversy
B: MD Anderson Culture
A: The Administrator
C: Leadership
A: Personal Background
A: Character, Values, Beliefs, Talents
D: On Research and Researchers
C: Understanding the Institution
D: On Pharmaceutical Companies and Industry
C: Ethics

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Tacey Ann Rosolowski, PhD

0:00:24.7

So I just wanted to kind of put a little framework. We were talking before the official start of the interview that you wanted to reflect a bit on some of the administrative, departmental, institutional issues in which you were working over the—basically under four presidents now. So I just wanted to give a frame for that conversation.

Jordan Gutterman, MD

0:00:48.5

Yeah. Well, when I came here it was 1971, and I think I discussed kind of what attracted me here being [Emil] Freireich and a couple of other people from MD Anderson. [R. Lee] Clark had been here for many years. As I said, he was extremely supportive. He selected me, along with Dr. Freireich, to meet with Mary Lasker when she came in 1974, which was a key event medically and scientifically in my life. You know, it's just amazing the world that she opened up. And I'm not so sure we've talked in much detail about the world she opened up outside of MD Anderson, but at some point we might fill in the blanks on that. Not only in science and medicine, but kind of watching how she operated both within the government and the private sector and so forth, how she brought people together. As I said the other day, she had the greatest gift you can give a person as another person, and she was just a master at that. And so she came down here, and I discussed that.

Then I've also discussed previously, I think, also with Lesley as well as probably some with yourself, that—I'm not—I haven't done this with you, but I remember I went to this interferon meeting in 1975 where everybody thought that cloning genes and making recombinant molecules, biologics—many people said would never happen in our lifetime. I don't think Mary Lasker believed that. And I think I've discussed it previously, so I'm not going to go into it. I'll just mention it. In August of 1977—I always like to leave Houston in August. It's so intensely hot. I remember that summer saying, "How can anybody tolerate it?" I didn't think I would stay here that long, but—I mean, the first year I was here, way back in '71, '72. But in '77 we had a newborn—a young boy—a little boy that wasn't even one yet, so we couldn't travel. Mary Lasker called me, and her secretary—it would have been Albert Lasker's secretary—Jane had developed recurrent breast cancer. She said, "Jordan,"—and she sometimes swore—"God dammit, we've got to do something about this disease. Will you go to Sweden if I get you—and Finland—if I give you a million dollars?" But I think I've told that story, so I'm not going to repeat it.

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I think we've talked about all the preparations and the excitement about getting the interferon. It was called leukocyte interferon at the time. Finally it arrived, and we got FDA—Food and Drug Administration—approval to start the clinical studies in February 13, I think it was, 1978, with the schoolteacher. I won't repeat that either. Around that time, Dr. Clark had decided to retire, and his replacement, Dr. Charles—known as Mickey—LeMaistre came in as the new president. It's interesting; the inflection point is when we started those first patients. I think Clark was still in charge, but around that time—we could check the dates—LeMaistre came in as the first president. And I remember Mary Lasker returning here with Ann Landers, or Eppie Lederer—her real name—to Houston to visit [Michael] DeBakey. She came over, and I gave a short summary of where we were. We had already started the clinical studies. Mary and I had done a lot of stuff already. We had gone to drug companies, and I won't repeat all that because I think that has been discussed. So it's interesting that the year of LeMaistre's arrival was the year of all this intense activity and excitement and publicity. And not all of it was well received. Mary said she wasn't going to give a penny to an institute. Nothing about MD Anderson, it's just that she didn't want overhead. She wanted every penny to go to making the drug. And she's not the only one in my life that has had that—it was said to me many times. So she sent the money directly to the Finnish Red Cross to make the interferon, which I think has been documented. But it's interesting—this did not help me very much, which I agree with her. And I'm a bit of a rebel because I don't—you know—we were bringing—once the publicity started, patients were coming here, and the institute was generating income from a lot of the patients, I think. All of the publicity—I mean—this was many, many years ago now. But there was not complete support for this, as I said, in various areas of the institute.

Tacey Ann Rosolowski, PhD

0:05:39.3

Why?

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Jordan Gutterman, MD

0:05:41.4

Good question. It's probably multi-factorial. I think, first of all, people in general don't like other people to get credit or publicity perhaps. There may have been some concern about the credibility of all this. This was pretty bold. I think that's one of the lessons for students and others—there are different types of people. I want to do really, really bold and important things in life. For me, to do incremental things or do whatever everybody else does, to me, would be very boring. That's not what makes me—that's not who Jordan Gutterman is. And we can discuss that in terms of my own self-awareness and image of what I want to do. So you are going to rub—I mean—anybody who has done—I'm not saying I've done great things, but I'm just saying anybody who changes the paradigm, opens up new areas, gets people to think, perhaps, differently is going to rub people the wrong way sometimes. You can't avoid it. You can't be popular. And you have to develop, and I did. I mean, I came from a small, little town, and I still am a very shy person in many ways, but I can open up. I must have developed a very hardcore shell about this, and not a shell that it didn't affect me. It affected me deeply, but there were a lot of barbs and criticisms and pressures, including at the very highest level of the institute. I think I discussed in '84 when we made the big break—announced the big break in hairy cell leukemia publicly with The New England Journal paper. One of my colleagues accused me of making up the data with my other—one of my other colleagues—the person that worked with me, Dr. [Jorge] Quesada, who was very, very brave and courageous and honorable. And—you know—I think people believed it at the very top. I was asked to not go on McNeil/Lehrer. They had to clarify everything. So that was tough. I told you; we talked about “victory gin” and all that stuff back in 1984. The fifth of January, 1984—now, that is still a really interesting time. I always look at events. But I think for students and people, one day when they read this or hear this, I think that if your nature is to do major things, you are going to have to struggle. Nothing is easy.

Once I heard a little parable—that you don't climb a mountain on the smooth side. You have to climb it on the rough side. And so those steps are—it's a struggle. I could understand, perhaps, in retrospect, as I'm a little older, why the higher levels might be nervous about all this PR and all this type of stuff. So, I think it's multi-factorial. I'm not saying it's all jealousy. I'm just saying that, in general, the establishments like to maintain order and control, and bureaucracies do that certainly. And this place has gotten bigger and bigger and bigger, and it gets more ingrained. I still maintain—and we'll talk about this in a minute—that this institute is still a place, for various reasons including resources, if you are creative, you can still do things here in medicine and cancer research, for sure, that you almost can never do any place else. You probably could, but this is a place—the environment here—the place is very, very important. That's where I choose to do the work. I've grown to love what you can do in Houston and Texas even more when I tell you the next story in just a second.

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So after the approval of interferon, I mentioned I started a department, and we did a lot—we published a lot of papers. We ran a lot of trials. But they weren't that satisfying and fulfilling. They weren't really getting at the deeper roots. Now a lot of big breaks and understanding are beginning to take hold in terms of our understanding of cancer. In the early eighties—the discovery was made in the late seventies. The concept of the oncogene was finally recognized by a Lasker award for Mike Bishop and Harold Varmas, both of whom I got to know very well now on the Lasker jury. They eventually won a Nobel Prize, I think in '89. And I mentioned we weren't doing much work on those things, but it wasn't just oncogenes or a bit later suppressor genes. It was the whole result of understanding many of the complexities of cancer which are still not completely understood by any stretch of the imagination. I mentioned in the early nineties I learned a lot about the business end of drug development, and that was very educational. I think, as I said earlier—before in the tapes—I brought a lot of that knowledge, began to work with the pharmacists and reimbursements, and so there are many aspects of making new drugs in terms of an institute, of the economy of the institute, with the progress of the institute, and so forth.

Tacey Ann Rosolowski, PhD

0:10:51.3

Was there a similar discomfort at the administrative level for the negotiations that you were undertaking with drug companies?

Jordan Gutterman, MD

0:10:59.2

Oh yeah. Well, you have very—you know—very strict conflict. You've got to be very careful. In the end, you have to police it. I think that there was initially—when I first started working with Roche and Schering, not with Dr. Clark, but just in general. I think looking—scientists working with—collaborating—in fact, I wrote a piece in the nineties, as I began to wind down this department, about the war of the parts against the whole, how private sector—like in this case the pharmaceutical industry, the emerging biotech industry, the third sector that is the philanthropy and the foundations, and the government all seem to be at war with each other. And I just never see it. I mean, I never published that article. I still have it. It was about drug discovery—that you have to have all elements because there's part—we should not be dealing with pharma. We can't do really what pharmaceutical companies can do or even biotech companies. There is a thrust now in the government to make new translational research and drug discovery. There is a thrust here now at MD Anderson. I think you can do elements of it. I'm doing it, but I always reach out to these other elements. I mean, the Lasker Foundation, and I haven't talked much yet about the Clayton Foundation. I will. Without their support, much of this could never—or maybe none of it could ever have been done. I'll come back to a very key decision they made.

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That's the third sector they call the philanthropy—the foundations. That's one of the great attractions of Houston are these medical research foundations that are amazing. Big resources, very philanthropic, very few cities—I don't think any other city could equal that. So that makes MD Anderson a unique, special place to be in this wonderful medical center.

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Chapter 12

A: The Administrator

Department Chair and Section Chief: Leadership Issues

Story Codes

A: The Administrator

C: Leadership

B: MD Anderson History

C: Leadership

A: Character, Values, Beliefs, Talents

D: On Leadership

C: Evolution of Career

A: Professional Values, Ethics, Purpose

A: Critical Perspectives

B: Growth and/or Change

B: Institutional Politics

Tacey Ann Rosolowski, PhD

0:12:59.4

You mentioned last time—you told the story about that meeting when some of the oilmen who had been responsible for setting up the Interferon Foundation came to see Charles LeMaistre and kind of drew the line in the sand about interfering with your work. I'm wondering if you could reflect a little bit, when you were chair of the department, on the places in which the department functioned very well because of the way the institution is set up. And then conversely, some places where the department couldn't function because of some institutional roadblocks.

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Jordan Gutterman, MD

0:13:36.6

Well, we worked with a lot of compounds from companies. We got them—you know—we didn't start anything, but people knew me. And so they all wanted to work here; there were many people who wanted to work here because we have patients. We have a large department of very capable—many of these people have gone on to have leadership positions. For example, Dr. [Moshe] Talpaz worked on the CML—chronic myeloid leukemia—and I can't remember if we talked about that, but that was so exciting. Dr. Razelle Kurzrock worked with many of the growth factors. She's now head of the Phase 1 program here at MD Anderson and is the department chairman, doing extremely well and others—many others, actually, as well. And so—and a lot of them were—that was a wild group to manage because they were very, very strong-willed and very capable. I think we all did very well. I mean, actually, I don't recall today, right this minute, too many roadblocks other than the fact that slowly there were more and more control of drug trials, but we just kind of blended with the times. And I think—I don't recall that there was anything we wanted to do that was prevented.

I think the problem was internal in terms of the fact that I was spending a lot of my time going to committee meetings. I was known as someone who was always late, always brought articles with him, would not really listen to all the boring stuff going on, and would be reading constantly. That's just me. I just read. I had very little interest in the administrative aspects of it. I was thinking of new ideas and stuff, and that doesn't go well, and it should go well. You shouldn't be running a department if that's what you really prefer doing, and that's the other—another lesson. My heart was not in it. At first it was pretty exciting, of course. You are a department chairman. This was the end of '85, '86, when I took over.

Tacey Ann Rosolowski, PhD

0:15:40.1

How did that happen?

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Jordan Gutterman, MD

0:15:41.2

Well, the chairman—first of all, when I came here we were a section. It was called the section of immunology. Finally, after years and years of being labeled an immunologist—I think the label is dropping and will drop for sure with the new stuff that’s coming out. And I can see we are only going to get part way through that story today. That’s okay. And—you know—I’m itching to talk about it because it’s so fresh, you know? I get bored quickly. I remember reading—and I’ll answer your question. I think I forgot the question. Sydney Brenner, who won the Nobel Prize a few years ago for his work on the worm—but he really should have won a Nobel Prize well before then—he worked with [Francis] Crick. He discovered messenger RNA. And he won a Lasker—he won two Lasker awards. I know him pretty well. He’s quite a character—extremely humorous, brilliant, genius. I read once, in his autobiography, that—and he has told me this too—that once he has accomplished something, he wants to move on. He just doesn’t like all the details. It is like shooting that golf ball 350 yards, putting the little details on it—he wants to open up new ideas. I have the same personality. I don’t know if it’s a Jewish personality, but it’s certainly a personality, because he’s from South Africa. But—now, you asked the question—?

Tacey Ann Rosolowski, PhD

0:17:04.4

How did you become—?

Jordan Gutterman, MD

0:17:05.5

Oh, the chairman, yeah. So, the—we were a tiny section of three faculty members in DT—Developmental Therapeutics. Then as the interferon became well known—and people labeled it, I think, inappropriately as cancer immunotherapy. It was not immunotherapy, but it stimulated—all that work stimulated the National Cancer Institute to start a biological therapy program which is my preferable term. It is a biologic. It’s a natural substance. Yes, interferon does do some fascinating things to the immune system, and I think only in the last three, four, or five years as that work really matured into something pretty profound, but I don’t think the anti-cancer activity is primarily immunological. I think it plays a role. I don’t think we know that for sure, but that worked. And my chairman at the time, Dr. Evan Hersch, who I had met in San Antonio, was head of the section. I wanted a separate department, which was appropriate. And Freireich being Freireich said, “Of course, I think it’s time for—” It was called cancer, immunology, and—I’m sorry—it was called CIBT.

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Tacey Ann Rosolowski, PhD
0:18:29.0
Cancer, biology—

Jordan Gutterman, MD
0:18:29.8

Cancer, immunotherapy, and biological therapy.—CIBT. I just thought of something really, really interesting in terms of letters. I'll come back to that. This is amazing, actually, about CIBT. I'll come back to how the name has been truncated and now will be truncated for the last time into something with just a T. I'll tell you all about that—how it went from CIBT. In terms of my career, how something called IBT was the critical thing in my new work, and then that got morphed into BT, and then, as of the next day or two, it's going to be T. But I'll tell you about that. That has nothing to do with anything; it just is. Maybe there's a force there that controls that, but let's get back to the issue.

So I don't think, as a department, we were hindered too much. But I was really—I was getting bored with managing people, writing reports, evaluating people, a lot of infighting all the time, and a lot of these other people were feeling the ropes. They wanted their own things, and that's not easy. You know, Dr. Talpaz was very capable, and Dr. Kurzrock, but they are all strong-willed. Dr. Lopez, who I didn't work too closely with but is very talented, is still here. He's a great entrepreneur. And many others wanted their own programs. So I think that gradually the head of medicine, Dr. Irwin Krakoff—who Freireich had big problems with—I think he could see—at first I was kind of the golden boy, the new department head with all this—we had just gotten interferon approved and all this stuff. And for the first four years or so, things went very well. Then there was a lot of grumbling, and I think it's because I didn't pay attention to being an administrator. I wasn't a real good nurturer of this kind of chaos. Freireich does it in a genius way. I just don't know how to do it.

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Chapter 13

A: The Researcher

Going on Record with New Research: Avicins and Nutrition

Story Codes

A: The Researcher

A: Personal Background

A: Influences from People and Life Experiences

C: Discovery, Creativity and Innovation

C: Faith, Values, Beliefs

C: Professional Practice

C: The Professional at Work

A: Overview

A: Definitions, Explanations, Translations

C: Patients

C: Cancer and Disease

B: MD Anderson History

B: Growth and/or Change

B: Obstacles, Challenges

B: Institutional Politics

B: The Business of MD Anderson

B: Controversy

C: Portraits

D: On Texas and Texans

D: On Philanthropy and Volunteerism

Jordan Gutterman, MD

0:18:29.8+

So in the mid-nineties—and by the way, LeMaistre was still the president until ‘96—’92, ‘93—somebody who worked for me who played a key role in the new thing initially, and she was trained as a botanist. Her name is Mary Blake. She came to me with a manuscript of a paper, which I can still find, on genistein, which comes from soy and other plant products, about inhibiting a process that is involved with cancer. She’s a botanist, and she said, “Why don’t you work on plants?” She knew I was pretty much a vegetarian, and I had major passion about nutrition. My interest in nutrition really comes from my mother. Growing up in a tiny town where we had a big garden—and I think I told you the story when she died—maybe I didn’t—in 2004 about the carrots and all?

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Tacey Ann Rosolowski, PhD
0:21:46.2
No. Uh-hunh (negative).

Jordan Gutterman, MD
0:21:48.8

I guess I didn't even tell you about her death, which I will come back to. I'm jumping a little bit around. Mary came to me and said, "Why don't you work on plants?" And it just was the perfect time. I can still remember exactly where I was in my office when she walked in with this article. I'm going to put that aside for just a minute. Why don't you work on plants? That started the whole thing in terms of my head and gradually what happened.

I'm backing up now. I've told the story in some detail, but my father died in '74 and how I happened to be in Norfolk, Virginia. So in 1984, in January, she was here visiting in Houston. She was here for that McNeil/Lehrer show—it was now Lehrer—where I was—you know—under such stress because I was told not to go on, and I drank the gin and so forth. My mother was always concerned about distress—always concerned. She said, "Jordan, why do you do this?" And she was very proud and all this stuff. On May 15, 1984, I was in my office. It was in the morning—about 10:00 in the morning—and my brother called me. It shows you that lives go on with all this work that goes on. He was my brother Lawrence—my fraternal twin. He's a physician and was, at the time, in private practice in Columbus, Ohio. He had gotten a call from a neighbor who said my mother was too tired to get out of bed and that he was going to travel there, but he couldn't get there, I think, until the next day. I'm trying to remember, again. So I made arrangements to go. We both made arrangements to go. And we got there, and she was—my oldest brother lived in Norfolk, in Virginia Beach. They put her in the hospital. She was jaundiced, and I knew she had cancer. It was obvious—just—and so we walked in the room, and she was yellow—completely jaundiced. She had a massive liver. And she had this beautiful smile. She was just—I—recently we were in Virginia visiting my older brother. I remember on her eightieth birthday there was this picture of her in the Norfolk newspaper because she always came to visit me on my birthday and then would travel at the end of the day—she would come two or three—a week ahead of time, and then—I'm sorry—the next day because my brother was born the day after I was, right after midnight. So she could visit both sons on their birthdays, and then she would travel, even at the age of eighty, by herself. She was healthy, but she was getting older.

Tacey Ann Rosolowski, PhD
0:24:54.6
What's your mother's name?

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Jordan Gutterman, MD

0:24:55.6

My mother's name was **Satoris**—very unusual name, probably—and I want to tell you a story about that name in a minute. It's a little diverse. We're going to have to do four sessions, I can see that, because the Avicin story is quite a story. It makes the interferon sort of like, excuse the term, foreplay for the—and maybe it is. Pretty heavy foreplay, maybe, but—but I'll tell you about **Satoris**.

So we went there, and we knew it was liver metastases of something. We got an oncologist, and they did a biopsy. We determined it was pancreatic cancer, which, ironically, is a death sentence today, still. And even though we know a lot more about it, there is so much to be done there because it is diagnosed so late. It's ironic; As a sidetrack, there are people, including here, who I would have to say almost boast about the advances we're making in the treatment of lung cancer.

[redacted]

So there's so—and this is what angers me. This is what drives me, because there are so many people today, tomorrow, and the next day that are going to die of these diseases. I have a lot of ideas scientifically and medically. I'm not the only one, of course—how we can get this—I mean—we're treating way too late. And we need drugs that work on some other cells. We can get into the science, and this was why I changed fields.

But anyway, my mother—we determined there would be—I consulted with a friend of mine who I knew from—in fact, I roomed with him for a few weeks when I first came, before my family moved in 1971. So I knew, very well, an Australian guy. I called him. I said, “I don't want to make the decision by myself, or my brother, let him make the decision. She's eighty years old.” And, of course, he concurred—no chemo, just supportive care. Now, my mother never talked about this, and this was typical of her. She was sort of a denier. She knew what she had. There was no doubt. But it was never spoken, and she didn't want to talk about it. I honored that.

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My mother would often call me in college, even medical school, and so forth and so on. A friend of hers—she had a lot of friends with ovarian cancer. “Ruth, they opened her up, and it’s all over,” or, “Molly, they opened her up. It’s all over.” This was a constant theme with my mother of—so she was quite aware of disease. As I said, rounds with mom, but cancer in particular. She knew what she had. She probably knew what she had for three months prior to just succumbing to it. She didn’t want—just her dignity. She would never take chemo. My mother was a beautiful lady, beautiful until she died, very meticulous about her dress, her hair, but not in a vain way necessarily, not in a bad way. She never made anybody feel—I mean—she wasn’t a movie star. I’m just saying she just was real proper. She was the old-fashioned proper lady. And there was no way she was going to tolerate chemo.

This is not easy to talk about because the time is coming up. I mean, certain dates mean a lot. April, when my dad died, means a lot. We’re still in April—May. And so we got her home, and we got private nurses for her. My brother and I—my two brothers and I—we all decided we would—there were some family resources from some property and that we would pool those. That’s what my dad would want—would have wanted, of course. I mean, he was so devoted to my mother. He had been dead for ten years.

We brought her home. That’s what she wanted. We never even asked her. We knew what she wanted. We knew my mother. She wanted to be in her home, in her bed. We brought nurses in around the clock. I came back almost every weekend to see her—not quite. She lasted until—she died the fifth of July and was diagnosed—you know—clinically on the fifteenth, sixteenth of May, so about—what?—six or seven weeks? The last time she ever sat up was on Father’s Day, which was actually the twelfth birthday of my third child and daughter on June seventeenth, which was actually the—my daughter was born, in retrospect, on Watergate. I would—with me, with my life and dates, I always have—it’s how I remember things and make sense out of stuff. So my daughter was born on the seventeenth of June.

Both my parents were here in Houston. It was the last trip my dad took because he was in early heart failure on that trip. And the last meal she sat up—but she could barely sit up—and then she went to bed and could never get up again. She was on morphine. I mentioned nutrition because it was my mother, when I was a little boy, always, always, always was emphasizing eating modestly—excuse me—and fruits and vegetables, especially vegetables. And it wasn’t easy, in retrospect, compared to today where shipping was so easy. In the Midwest today, with the Whole Foods and all that type of thing, you can get so much healthier foods. But she was big on frozen stuff during the wintertime, which in retrospect is pretty smart because you retain a lot of the nutrition approach—you know—stuff that is shipped.

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I remember being in Milwaukee once. I just remembered this. My daughter was living there back in the nineties, going into a supermarket in the wintertime for some vegetables, and they were horrible. I mean, because they had been shipped and sitting around. Who knows what I was eating other than some fiber? You know, it could have been cellulose. But my mother always had—she always said, “Get the frozen stuff.” You know—the snap frozen—so that was a pretty good invention, if you think about it. But she always had fresh vegetables when they were available.

This is going to be difficult. I’ll tell you the story, but then I’ll make it the link to the comment, “You should work on plants.” So on the fourth of July, I decided I was—I had to get back to work. My mother was kind of in and out, and this—we didn’t know if this would go on for a day or two, a week, or even a month. And she would want me to go back to work. So I went in to see her for the last time, for the very last time, and sat next to her bed. She was sort of in and out, but she was somewhat lucid—no pain, a lot of morphine—and she smiled. I held her hand. And then she said, “So-and-so,” I guess one of the nurses, “went out and got fresh carrots for you. They are in the bottom bin.” So her last days she wanted me to have carrots. So I went—and I loved it, you know? And that was it. I never saw her again when I left. Why don’t we stop it just a minute.

Tacey Ann Rosolowski, PhD

0:32:57.6

Sure. Of course. Okay.

Jordan Gutterman, MD

0:33:01.0

I don’t know, maybe—it seems like yesterday—maybe it was four years ago, I get an email, and I see the byline of it. The name of the woman was **Satoris Culbertson**, and I said, “Oh my God, what is this?” An email appeared from a woman who actually, as it turns out, was a PhD psychologist at Kansas State University in Manhattan, Kansas. Her grandmother, whose name is Mary Bruno, who is still alive, who lives in an old town in Missouri, lived above my parents store in Flandreau in the 1950’s—1951—and she was a new mother. She had a little boy. And when she had her first granddaughter—this girl, who was the daughter of her—her daughter’s daughter—she told her daughter, this woman, **Satoris’s** mother, “I want to name a woman, a girl, after the most beautiful person. I’m sorry.

[The recorder is paused.]

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Tacey Ann Rosolowski, PhD
0:34:18.4

That's all right. We're back after a brief break.

Jordan Gutterman, MD
0:34:20.7

And this little—I'm sorry—and this little girl is born with dark, brunette hair, just like my mother had in those days. This woman, Mary Bruno's daughter, named her little girl Satoris after—in memory to honor my mother. She called me and wanted to know everything about my mother because she had just had the little boy and now had two little boys, and she had just recently been married. I looked her up. I've never met her. She's a beautiful young woman—PhD at Kansas State. I need to maybe get back in touch with her. I had been in touch. There's no sense on spending too much time on this. I would love to talk about it, but I'm in touch with the grandmother who told me stories about my mother and my father and how my mother tended to all these young women with babies. The reason why—I met someone in Norfolk when we went back—another person just like this who just, when she saw me again, talked about my parents. They were always just taking care of people. So the tribute to my mother is just wonderful there. And so when this woman says, “Work on plants,” this passion I had—because I felt that the epidemiology of cancer was telling us—I'm not the only one who knows this, you know. The Japanese would come over here and begin to get the same cancers we do in one generation. So, it's an environmental thing.

I think what has happened—one of the many breakthroughs in cancer in the last 20 years has been the increasing appreciation of environment with genes. And we know this from smoking, and now with obesity. I mean, this happened before the big obesity thing happened. So I said I want—I just think there is going to be stuff in plants that I ate as a kid, that I ate the day before my mother died, that have never been discovered. And that was the impetus for starting this journey which will probably never end. But it keeps me young.

Now, I'm going to digress a minute because—to give my father equal time—because he had an equal impact on me. So the day before he died, I also was at his bedside. It was April sixth, a Saturday. That night was going to be the first night of Passover. He died the next day, April seventh, which was the first day, which this year was exactly the same. He was so short of breath he could barely talk, but he asked me about my work. He was the more intellectual of my parents, very emotional. My mother had the more tender side. My father was an immigrant and tougher. He was not—I mean—he was a strict man, but he just wanted to hear about the work.

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I was working at the time on melanoma. I had just come and was working—this was pre-interferon and pre-Mary Lasker, but just by a few months. I met Mary Lasker right after that. It's amazing. I could barely hear him because he was just gurgling; he had so much fluid in his lungs. And there was a baseball game on. In those days they had the Saturday afternoon baseball games. And Henry Aaron had just hit his—what—now I'm just trying to remember. Had he tied Ruth? I guess he tied Ruth, and the next homerun he was going to break the 714 homeruns of Babe Ruth. He was playing with Atlanta. I think they were playing the Cincinnati Reds, and they kept him out. They kept him out because they wanted him to break the record at home. And my father commented about the plight and progress of African Americans—blacks. That was one of his major themes is the underdog. You know, being an immigrant, he had this soft spot. I had such a hard time—and I don't want to get too much into it because it's probably not relevant for the work. Well, it is relevant for the work. This is the underdog. I think cancer patients are like this.

You know, this is why I have such a hard time with bureaucracies and decisions. We'll talk more about them with the next things, because I've had more roadblocks with the new work than I had with the interferon because things are more complicated. I think that's part of my personality too, not trusting authority figures, because my father came out of that. I mean, he never saw his parents. He never saw his sisters again because of authoritative rule, you know? Once the Iron Curtain came down, forget about it, and the Nazis and so forth. These all came from authoritarian—so it's not that I don't respect authority; I do. But when those authority figures overstep their bounds, I have to stand up. That was my father standing up for the injustice.

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And he just was—he said, “I can’t wait until the game Monday night to see him break that record. I know he’s going to break it at home. We’ll watch it together. It’ll be after the Seder, after the second night.” I remember him—no, no—he was—no, the Seder was Saturday night and Sunday night, and the game was going to be Monday night. He said, “We’ll watch that game together.” Well, we never watched it because the next day he died. And it was that passion for correcting wrongs and—you know—I think so many of these people come here—here and every place else—you can’t let the system destroy it. You have to break through these barriers. People are more comfortable, in my opinion, in maintaining the status quo for lots of different reasons. I’m not saying I’m better than anybody else; I am not saying that at all. It’s just my personality is different. I just won’t—I mean—I have been here forty years, so obviously I’ve done the right things. I haven’t broken any rules or stuff, but I’ll stand up—and I’m not as outspoken as someone like Freireich. That’s why I respect him so much. He makes me like a mute. I mean, he’s gotten himself—he’s got more courage than I do. But a lot of that came—my own stuff—has come from my father. And just looking at this, you can just see the compassion that he had for this black man who was going to beat the great Babe Ruth’s record. And he wanted to watch it with me and his other sons, I’m sure. And I thought we would. I mean, I knew he was dying as well. My mother was more predictable. So there’s this blend of mother, father, nutrition, passion, and all sorts of stuff. My mother came—was American-born. She came from very modest means, but American born. My father—you know the history.

So now I wanted a new idea because I hadn’t seen a whole lot of progress. The interferon was very gratifying, but I was over it already. Everybody was doing it. I was excited about the hairy cell leukemia, the CML. In other diseases like biloma and lymphoma and kidney cancer, we made a modest improvement of things. But I felt I had more in me, and I didn’t see the innovation going on anymore. Plus I didn’t want to probably run the department, and people didn’t want me to run the department.

So the final decision, actually, was made about 1994. I walked in for my annual—the annual review of the department and to Dr. Krakoff, the head of the division. And for the first time, I was shocked. The administrative executive—

[redacted]

She had a spreadsheet, and she said, “Your department only generated X amount of dollars.” We were a clinical department, but mostly research. I said, “What are you talking about? What do you mean generate an income?” I had never thought—that was not something we ever dealt with. How many papers did you have? What progress have you made and so forth? Not how much money that you make. Then Dr. Krakoff comes in, and he said, “This is paltry. You guys have got to see more patients.” I said, “Why? We’re doing research.” “No, not anymore you’re not. You’re going to have to generate income.”

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This was a terrible time for the institute—'94—terrible time. I think it was through some downsizing going on. LeMaistre was a master at keeping this place going, but we lost some employees. He, himself, retired in '96. It was not easy times. But I had already begun to think about plants. So this was the nail in the coffin. I said—you know—I don't want to do this anymore. I could see that the clinical departments, even though we still do fabulous clinical research here, there was going to be this increasing pressure, certainly on the chairman, to generate money and so forth and so forth. And I was getting increasingly excited about the idea of plants. But I had no idea what to do. So around this time, I went over to a lecture to an institute called the Institute of Biosciences and Technology, I think—IBT. That's the IBT of the CIBT. It's in the old Shamrock Hilton location.

What happened was Texas A&M had put up an institute here in the medical center, a small one, a division, in part at least, of a friend of mine now—a scientist I didn't know—Charles Arntzen—A-R-N-T-Z-E-N—National Academy of Scientists. He was the dean of Agriculture, I think, at Texas A&M. I didn't know any of this. I just knew about this institute. And one day I went over to see—hear a lecture by a guy named Erkki Ruoslahti from The Burnham Institute in San Diego on the integrins. On the way out—I had never been in the building; it had a nice auditorium that came up—and on the way out I said, "You know, this is—I heard a little bit about the institute."

Tacey Ann Rosolowski, PhD

0:45:26.7

Could you repeat the name? I'm sorry. I missed it.

Jordan Gutterman, MD

0:45:28.4

Arntzen—A-R-N-T-Z-E-N.

Tacey Ann Rosolowski, PhD

0:45:32.7

It is the Arntzen Institute?

Jordan Gutterman, MD

0:45:34.5

No, no, no, no. He was the—

Tacey Ann Rosolowski, PhD

0:45:36.1

That's what I meant, the name of the institute.

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Jordan Gutterman, MD
0:45:38.0

Oh, I'm sorry. It's called IBT—Institute of Biosciences and Technology, I think.

Tacey Ann Rosolowski, PhD
0:45:43.0

Okay. There you go.

Jordan Gutterman, MD
0:45:43.1

I think that's what it is. It was built by Texas A&M. And the whole vision, as I learned, was to bring some of the technology that A&M had had—particularly plants and to some extent agriculture and maybe—I don't know about engineering—and to see if they could create something. And this is the best kept secret in the medical center, because I can't imagine anything more exciting. I'm going to tell you, sometime, what came out of this thing. So on the way out, they had a guard. And I said, "Do you have any plant guys here?" Something like that. It was a bit—you know. He said, "Yeah, there's a real dynamic guy upstairs there, Charlie Arntzen." I said, "How do you spell that?" "Arntzen—blah, blah, blah." I went back. This was—now, I had a computer on my desk, but they were these big, huge things, and I didn't even know how to use it. This was in the nineties. It's amazing how fast we came. I'm sure I didn't look him up on the—well, there was no Google. I got his phone number. I used the thing called the phone that people used to use—you know—on my desk.

Tacey Ann Rosolowski, PhD
0:46:52.6

And probably a phone book too.

Jordan Gutterman, MD
0:46:54.2

And a phone book. I think we didn't have a rotary anymore. I still love the phone, by the way, because I love voices, and I think I can at least hear. The guy takes the call, and he's so dynamic. I learned very quickly he's in the National Academy, and his major interest in life, he said, was plants and human health—a marriage made in heaven. So in the next day or two I went over to meet him. He's as dynamic—ironically, he came from western Minnesota—Grandview, I think it is, Minnesota. It would probably be about sixty miles northeast of Flandreau where I grew up—a little town in Minnesota. His father was, I think, a farmer. And he had been at the University of Illinois, and—well, he was very famous. He made his work on photosynthesis.

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So we decided we'd try to work together. And what I decided to do is this woman named Mary Blake, I would put her over there. I would go to the Clayton Foundation, try to get some money for him, and start thinking of how we could work together. I got introduced to all these plant people, and I was in seventh heaven. This is always the case with me. Brand new—I didn't know anything except that plants look green, but that's about it. I knew nothing, and I love to learn a new field, because I could see studying something like that maybe you could find these things, and you could help people one day and all the challenge of it, the science of it—it was just so exciting. I love to go over there, you know? It was so different from here. So I went over to the Clayton Foundation, who had given me money, and I was introduced by Leon Davis.

How things happen—Mary Lasker—the best gift you can give is another person. So by now I had been working the Clayton Foundation for fourteen years. They trusted me. They knew the whole interferon story, and they had become entrepreneurial now. Now they were thinking about patents. They didn't make anything, nor did I, on the interferon story, and that's going to come back to be positive twenty, thirty years later. But I went over there with the idea that I was going to change fields, and I didn't know how they were going to react.

The chairman at the time, who is still a trustee, was C.W. Wellen, who was the personal attorney for Ben Clayton. We haven't talked about the founding of this foundation. It turns out the foundation, which has been the key to this whole new story, was founded by a man named Ben Clayton, based on one interest in life in terms of science. It is called nutrition. He lived to his nineties. He was cotton dealer. Anderson Clayton was a big company here. That's the MD Anderson family and the Claytons. The original \$500,000 came from the MD Anderson foundation namesake, and it was matched by the state. But Anderson had been in business with Clayton in cotton and, I suspect, oil. Who knows? They made tons of money. Ben was one of two sons—I mean—one of two brothers, and he started a medical research foundation called the Clayton Foundation. His attorney was this man C.W. Wellen, who was the chairman. He died, I think, in the late seventies, early eighties. I forget. I could look this up. It was, at the time, I think, around a \$400 million foundation—medical research foundation. I remember going over there and saying that I wanted to change fields. I had an abstract idea. And I remember Bill Wellen looked at me—they had three trustees, at the time in the room with some other people—and said, "You know, you've done it once. Why not? Let's go for it."

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Now, where in the world would you get someone to do that but Texas—but Houston? I mean, where could you do that? Where would someone give me a blank check and say, “I like what you said”? Ben Clayton would be proud—looking at plants. The connection with my mother and probably her mother eating carrots before she died—as a kid, eating parsley—going there, and Wellen is the lawyer of this man who made all this money but wanted to put money back for the good of humanity. And I go there and say, because I’m interested in nutrition—and I don’t think I knew it at the time because—you know—we didn’t have the Internet. And I didn’t probably know all that history about nutrition and Ben Clayton. He loved it. He said, “This time you’ll do it.” And actually, we have done it, but we’ll talk about it because he’s still there. I just saw him the other day. He’s getting some memory lapse and stuff, but he gets enough of it. And I—he is in his late eighties. No one gives him credit for anything. And I said, “Mr. Wellen, it was your vision. You did this, you know.” You’ll hear the story, but I said, “You did this.” We haven’t done everything yet, but we’re getting there. And he remembered. He said he remembered. One way or the other, he remembered. And he’s not that demented at all. I mean, he’s losing some stuff.

So we moved Mary over to that institute, and then she organized speakers on various plant topics. So I could—you know—learn the difference between a leaf and a root and bark, stuff like that. And ironically, by the way, Taxol had become sort of a big name around this time. So natural products and plants were kind of reemerging, because even today, 60% of all drugs are derived directly, still, from the plant, or our analogs are—you know—synthetic derivatives of plant products—60% of drugs. Around this time, however, the big pharmaceutical companies had decided to deemphasize natural products. They are very complex. They thought all this new stuff of 0:53:19.7 (???) (inaudible) synthesis would work. We’ll come back to that. But I was kind of swimming upstream in terms of the way the industry was going. I didn’t know that exactly at the time. I didn’t know anything about drug development other than the clinical stuff. I sure have learned it now.

So one of the lessons you and anybody listening to this or reading this voluminous number of words will learn is if you are energetic and motivated and have passion and this, that, and the other, you can learn all this. It’s the most fun of all if self-taught, then reaching out to other people that are smarter than you. I think I told you Mary Lasker—well, she always said, “Have someone who is older than you.” My thing is always be around people who are smarter than you. And that’s not too difficult for me because it’s easy to find people smarter than me. They may be in one area, but that’s okay. It doesn’t make any difference. So you just get rid of the ego.

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So we start bringing all these people in and nothing happens. I mean, we couldn't figure out exactly an organizing principle of what we wanted to do. And then—this was 1995—and then in the fall of—I would have to check the facts. Around this time in '95, Arntzen announces he's going to move to Ithaca, New York, to be president of the Boyce Thompson Plant Institute on the Cornell campus. I was devastated. What are we going to do? He's moving his whole team. The plant guys are gone; that's it.

So around this time, just as a slight diversion, I was asked by a couple people right before Mendelsohn got here, since I was no longer department chairman and I was writing a big review on interferon and I was doing a lot of writing—I actually took some courses in creative writing because I was trying to figure out what to do next, because I was thinking about plants, but we weren't doing anything—I was asked if I could bring in big pharmaceutical monies. So I did this for a while. That wasn't all I did, but I brought in a big grant from Monsanto. I mean, monies went to various—it was a very interesting program with very basic researchers. And I ran that program.

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Chapter 14

A: The Researcher

Establishing a New Research Focus: Experiments, Money, Organization

Story Codes

A: The Researcher

A: Personal Background

C: Professional Practice

C: The Professional at Work

A: Overview

A: Definitions, Explanations, Translations

C: Patients

C: Discovery and Success

B: MD Anderson History

D: Business of Research

D: On Philanthropy and Volunteerism

Jordan Gutterman, MD

0:53:19.7 +

We also got a big grant from one of the real success stories in biotech, from Boston Millennium, another grant working on diagnostic stuff, so I was staying very busy when he announced all this. Then one day Charlie called me up on the phone. This is a free-standing research institute on the Cornell campus, which is quite a stunning campus. And he said, “The institute owns an arboretum in the middle of the Arizona desert between Phoenix and Tuscan, closer to Phoenix.” And I remember his words. He said, “Some crazy botanist had collected seeds from desert plants from throughout the world, and most of these trees and plants and so forth were growing in the arboretum, and then he was also growing down at the University of Arizona in Tuscan because they had kind of a center there to grow these things.” He said, “Would you be interested in studying the body parts of these plants?” And I said, “Let me think about it.” It sounded pretty interesting, but I didn’t know anything. I mean, I—you know—I’m a hematologist, and I had a lab. I knew how to do self-culture work and stuff, but working on plants and chemistry and isolation—I mean, that’s—so I thought about it and did some reading. I realized that desert plants were initially looked at in the birth control days. I think the Mexican yam is in the desert. That was the basis of the birth control pills by [Dr. Gregory] Pincus and the company called Syntex. But in general, desert plants have been sort of ignored for rain forest plants, so this sounded interesting. Then I thought about this. What are the stresses that desert plants have to deal with? They have to deal with ultraviolet stress—I mean—huge out there in the desert. So they must have interesting chemicals that deal—you know—we have skin cancer and aging overnight, also dehydration. So I called him up, and I said, “Yeah.” He said, “You know, there’s a natural product chemist named Joseph—” sorry.

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Tacey Ann Rosolowski, PhD

0:58:19.5

Sure. Okay, we're good. Joseph Hoffmann.

Jordan Gutterman, MD

0:58:25.0

So he and I met in Tuscan, and we went over to see Joe, who unfortunately passed away a few years later. He was a marvelously mild man. But he had a lot of problems. He was severely allergic. I can appreciate this. He had asthma and all sorts of allergies. He also had just undergone a divorce. His first wife—I think he remarried—they had a daughter. His first wife is a very well-known writer, and I'm forgetting her name right now. She has written a book on nutrition with her daughter Camilla. I can't remember her name right this second. It's not someone I've read. I see her books all over the place. So he was having severe—you know—he was just going through a lot of personal stuff—a wonderful guy.

He agreed to make extracts from all these different plants and trees and stuff—from the leaves, from the bark, from the roots, from the pods, from this, that, and the other. And I hired a PhD who was actually doing some work for me, who was very good with her hands, very skilled. Her name was Kalpana. She was from India. Kalpana—K-A-L-P-A-N-A—Kalpana Mujoo—M-u-j-o-o. Her husband is a scientist here. They are both still here in the medical center. She was working for a colleague that collaborated with who was in my department—a pharmacologist—and I kind of took her over. She was working on some suppressor genes. I knew she was very skilled with her hands. She couldn't write very well, unfortunately. You know, she has two languages—Hindi and English—but this is not uncommon. I mean, let's go over there and try to write in Hindi or Chinese, you know? That's not an uncommon problem around here. I feel like Joe Hoffmann—you know—every time I go there, he was like this coughing and sneezing and blah, blah, blah.

Tacey Ann Rosolowski, PhD

1:00:29.6

Spring in Houston.

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Jordan Gutterman, MD

1:00:30.7

Yeah. So, we set up a little screen with an ovarian cancer align, and a few weeks later we began to get extracts. I didn't know what they were. And we began to screen. Before killing—so it's called—in retrospect—it's called a phenotypic screen. Most drugs are not discovered this way anymore. Most drugs you find a target of interest, and then you screen millions of little compounds until you hit one. That is traditional. But the old way of doing it, what I call phenotypic screens—functional screens—you set up an assay. You want to see that it either blocks or enhances, that it would translate from the test tube situation, in vitro, to the in vivo. This is kind of the old-fashioned way of doing things. And this was definitely going out of favor. I didn't know any—you know—this is a good example of not knowing a whole lot, and that's good. Because I think if I had read too much or talked too much, people would have given me thousands of reasons never to do this. But I was going by gut and intuition and some of this other stuff.

We went through many, many extracts. I thought we were just going to kill everything because of all these toxins. As it turned out—a little bit like the interferon story, where the impure stuff was just exactly like the pure stuff—these extracts from all these things didn't do anything. And then one day, Kalpana comes into my office—same office where Mary had come to see me—and said, “Dr. Gutterman, it looks like we got a hit. There is this extract of this plant that killed some ovarian cancer cells.” I was only modestly excited. It was nothing like seeing a platelet count going up in hairy cell leukemia or a Philadelphia chromosome disappearing in a CML patient, but that's because I'm a clinician, and I knew what that meant. I had no idea—and in fact, even if you knew what I was doing, I wouldn't have been very excited. It didn't mean much. But I called Joe up, and he said, “Well, let me try to purify that a little bit more.” I thought he would purify it a little bit more, and that would be it. And to our surprise, the killing was actually somewhat improved. It was still there. We took some normal cells, and it didn't kill them. Now it began to get interesting.

This was—and I remember flying out to Tuscan, by the way. As an aside, around this time, I decided to join the department that I'm still in, in 1996. It has gone through several iterations of names and so forth and grown from the department of a new guy who had just come from Canada around the time Mendelsohn came—unrelated—'96, '97. It was called, I think, originally Molecular Therapeutics. Today it's called the Department of Systems Biology. [Dr. Gordon] Mills is an MD/PhD, and he kind of left me alone. I mean, I'm a full professor, and I had Clayton funding to do this. And they gave me money for Dr. Mujoo and a couple of other—a tech and so forth. Not a lot of money, but they just said, “Do it.” As I said earlier, where else would you get this green—you know—blank check?

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Now, I wasn't seeing patients. As a department chairman, I had kind of gradually stopped seeing—I would go down on rounds and hear about patients. We ran—during the really exciting days in the eighties and early-nineties at that department, we had conferences every day, where we went over patients, and it was very—it was actually quite exciting because we—well, obviously we had made the big breakthrough already in hairy cell leukemia and CML, but we were doing other things. And we also continued that work. But I, personally, had gradually stopped seeing patients. That was a choice. The choice wasn't made overnight, but as I got more and more into the science, as I will tell the story, it became obvious to me that I—this was a conscious decision, that seeing patients—I couldn't handle both. I wanted to read and read and learn and learn and learn. I said, "I think I'm going to be able to do more good for more people one day if I can really understand what I'm doing rather than seeing individual patients." Other people make different choices.

Do I miss it? Yes, I miss the human side. I still get calls on people, and I'm still involved. I still go to conferences. And I haven't lost too much. You lose a little bit. I can't remember the names of the new antibiotics, but the principles are the same. But that was a conscious decision. For someone listening or reading and so forth—you know—as a physician, it doesn't mean that you absolutely—particularly now—physicians and many professions you get trained as whatever it is. Whether it's a lawyer, an architect, a physicist, physician—you can do a lot of stuff. That's the beauty of the world today. There's so much information you can teach a lot, and you can go to people.

So meanwhile, we got two or three or four other hits, but—you know—I could see that Hoffmann could only really concentrate on one or two things. So he began to concentrate on this particular one. I have no idea what the other ones are to this day. Then I went out there in the fall, I remember—October 1996—meeting with Arntzen and Mary. Now meanwhile, Mary relocated with a single child—she was a single mother—to set up this program in Arizona to collect all these tree and plant parts and coordinate—make sure Hoffmann was staying on track. He was a bit, to say the least, disorganized.

Tacey Ann Rosolowski, PhD

1:06:26.3

What was the name of the program? Did it have a name?

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Jordan Gutterman, MD

1:06:31.3

Yeah. It's called the Legume Project. I think these were mainly legumes—bean plants. I think that's the name of it. That's what Clayton called my program. Oh, by the way, I had to go back to Clayton and get money for him. They had to do an agreement with the University of Arizona. Meanwhile, Arntzen was up at Boyce Thompson—part of Cornell—again, and I got Clayton to put money into his lab. So now it was starting to expand. I forgot all this. Well, it was only after we got the hit. No, no, that's not true. In '96, I had to go back to them. In '95, they were supporting Mary and had a little money in Arntzen's Houston lab and my lab. When Arntzen moved, they transferred that money up there. Mary stayed—came back physically over here. And he coordinated with Arntzen. And then in '96, when we finally made that agreement with the University of Arizona and Hoffmann, she relocated to Tuscan because—

Tacey Ann Rosolowski, PhD

1:07:33.8

What was the agreement you made with the University of Arizona?

Jordan Gutterman, MD

1:07:37.6

Well—excuse me—the agreement was that they would only—that the Clayton Foundation would own all the intellectual property and they would give them money. I forget what the grant was to Hoffmann, but they gave him—I mean—they supported his whole program out there in an agreement, in exchange for the patent rights and so forth. And they still have some part of it, actually, today. Even eighteen years later they still have a potential role here. And so money was also being transferred—instead of A&M now, it went to—the agreement went to Boyce Thompson. And then we just continued this. I remember, by the time—by the way, around this time, '96—during that year is when Mendelsohn came in. For the first year, he kept everything pretty much and then gradually made changes, and more and more specializations were going on. It was more economy. And he does a magnificent job in terms of growth. I mean, he was a magnificent fundraiser. He himself had some interesting issues with a drug, Erbitux—conflict of interest potentials. He made a lot of money, but he was one of the early ones in targeted therapy. He went through a difficult period because he was on the Enron board and then on the ImClone board. Enron, we know the story, and also because he was head of MD Anderson. By the way, LeMaistre was also on the Enron board. So those guys were in the—

[The recorder is paused.]

Tacey Ann Rosolowski

1:09:17.3

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Okay, we're recording again.

Jordan Gutterman, MD

1:09:18.7

But—you know—I was kind of doing my own thing. I mean, I was in Mills's department. We were protected. We were considered to be a research department but had clinical privileges, and I was protected since I had my own money. I got more and more into the science, as I will talk about. The chemistry, the biology—I had to learn all this stuff. I mean, I had to learn about everything—plants. It was—it's stated that it takes a minimum of ten years to master a topic. There's probably more than one—there are many topics here. But it took me probably up until about 2006 that I felt even comfortable, and I still don't feel that comfortable with most of it. But I know enough now to have directed this program. And then I reach out to the best.

But back in '96, '97, '98, Hoffmann ran into a roadblock. He was getting sicker and sicker. He eventually passed away. He could not get pure compound. I had learned enough chemistry that we needed to get the structure of this stuff. So I was talking to a friend of mine that used to be at MD Anderson at Science Park, Tom Slaga, a PhD guy who is now in Denver. He said, "Why don't you go to Hauser Chemical there in Boulder?" I don't know anything about Hauser. It's a natural product company, and they had made all the Taxol for the initial clinical trials, which eventually Bristol took over, but in the eighties and early nineties—and they were in Boulder. They were looking for business because natural products were kind of fading. And Slaga was interested in plants and nutrition. He was head of Science Park research. That's out near Austin, in Bastrop, but now he lives in Denver.

So I flew to Denver and drove with him up to Hauser, met two natural product chemists—a guy named Bailey and a guy named Sherlock and a guy named Jayatilake. I think it's J-A-Y-A-T-I-L-A-K-E—Gamini—G-A-M-I-N-I. He and I began to work together a lot for several years. I still remember on September 1, 1998, the Clayton Foundation formed an agreement with Hauser to do this contract work to try to purify and get the contract. I had no idea. I thought it would take them—maybe because interferon took forever to clone and all that stuff. Now this is, again, the same excitement, because I had to learn about how you take crude stuff out of a plant. This was, by the way, coming from the seed pods, which is a renewable source. I obviously came to learn with the Taxol story that you can't—don't have to chop down trees. You get these pods every year when you renew—very exciting—lucky.

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October 15, 1998, my sixtieth birthday, I got a call from Gamini. We got pure stuff, and we got the structure, just like the interferon. We got the pure interferon, we got the structure, and we cloned it. I mean, this is really exciting stuff. So now I had to learn chemistry. I flew up eventually so see Arntzen, and he's not a chemist, but he had a guy named Meinhart—German guy from Munich—Meinhart Zenk—Z-E-N-K—visiting. Zenk is a terpene chemist, and this was a terpene—a terpenoid. It had five rings and stuff. I didn't know squat about what this was. I mean, I just knew that it was—a little bit about it. He looked at the structure now, and I see why he did it. There are three parts to the molecule—four parts, really. He pointed to three of the parts. He said that's a delivery system, and the warhead—the business end is on the side chain over here. Well, he was right on. He got it. He had it exactly right on. But now I see, in retrospect, how he did it, because he's an organic chemist. But still, it was very insightful. I didn't know what he was talking about, but I said I'll learn. And I've learned.

So now we have to figure out what to do, and we didn't have a lot of the stuff. We had to figure out what the mechanism of action—that's the next—there are two things you want to do. You want to find out how it works and if possible find out what the so-called target is—what the molecular target is. Generally, a protein—it could be a nucleotide like RNA or maybe—or DNA for cancer. We were starting with a black box. We had no idea. We just knew it blocked the growth of cancer cells; it killed them. We didn't even know how they killed. So that was my next phase now is to come back here and begin to figure out how this stuff works.

Around this time I was very lucky. Another scientist, a young woman, who was working for another Indian scientist who I hired—she was working for him in a PhD—her name is Valsala Haridas. She still works with me. She's my right hand and left hand and everything else—you know—scientifically, a marvelous human being. V—V as in Victor—A-L-S-A-L-A—Valsala Haridas—H-A-R-I-D-A-S. She was working for a guy named Aggarwal—Bharat Aggarwal—A-G-G-A-R-W-A-L. I first met him in Genentech, where he had purified something called TNF. And Dr. Aggarwal I hired her to work on cytokines, back when I become a department chairman. Only recently, like in January, he was accused of dressing up something like eighty manuscripts of reproducing the same data in different formats, and he's in big trouble, I think, unfortunately. I like him. He ran a very strict lab. Dr. Haridas wanted to have a child with her husband who is a scientist and didn't like the strictness of it. She asked for a job, and I liked her. That was one of the smartest things I've ever done—hiring her.

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So I sent her and Dr. Mujoo on the task of working on the mechanism of action. Dr. Mujoo, I might add, around 1980, moved on to another position because there were just reasons. It was just—she was very good at finding the original, and she made the original observation and discovery, and she was on the original patent. She'll benefit if there is any financial reward and credit. She is a co-discoverer; there is no doubt about it. But she—I don't know—rightfully or wrongfully, there were things happening in this department that just weren't going to work out for her to stay.

I'm not a control freak, but I had to have control of this program because it was so bizarre. In fact, the funny thing is today, finding drugs and working on drugs and academic centers now is becoming slightly fashionable. I was way out of place. And I can tell you, no one understood what we were doing or cared what we were doing or appreciated what we were doing. Again, a little bit like the interferon stuff, but I didn't care I just—and I—

Tacey Ann Rosolowski, PhD

1:17:24.9

Can I interrupt you just for a second?

Jordan Gutterman, MD

1:17:26.0

Yeah, of course.

Tacey Ann Rosolowski, PhD

1:17:26.3

I just wanted to ask, just for the record—

Jordan Gutterman, MD

1:17:29.0

No, you know what? I don't even give you a chance to even ask questions.

Tacey Ann Rosolowski, PhD

1:17:31.6

No, no, no. You're—because I don't need to. You're just covering all the bases. But this is just one little detail.

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Jordan Gutterman, MD

1:17:36.9

Yeah, of course.

Tacey Ann Rosolowski, PhD

1:17:38.3

Out in Tucson, the program was called the Legume Project—Program.

Jordan Gutterman, MD

1:17:42.5

I think so. I don't know. We could check.

Tacey Ann Rosolowski, PhD

1:17:43.4

Now, did you have a name for the chemical studies that were being done here to determine the mechanism of action? What was that called?

Jordan Gutterman, MD

1:17:50.4

Well, okay. So I knew once we got the structure, I was now familiar enough—in fact, just today I was looking for the book that has a set of—I have everything in my books in storage, and I can't find the book. There are a couple really wonderful books about the history of drugs. They're just so exciting. Don't forget, it was my father who said become a pharmacist. He lived next to that pharmacy. So mother and father are intertwined constantly. I'm not going to go back any more generations because I don't know enough. But they're always there—always, always, there.

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I looked up the history of how aspirin was named, and it was named after the plant—I forget exactly right now. I’m not—I’m starting to feel not very good here. I’m really winding down. But the name of the—they named it after the plant, and then it just—the structure of it ended in an I-N, so they came up with aspirin. I think the—it’s not aspergillus. That’s a fungus. But we can look up the name. So they named it after the plant and put an I-N at the end. So this comes from an Acacia victoria. I’m kind of an optimist, okay? And I’m really focused and determined. So I said, “Valsala, one day this is going to be important, so we got to get the name. It’s got to flow right.” And we were lucky. It comes from an Acacia—and I’m going to digress on that one in a minute and tell you kind of an extraordinary story about Acacias. But Acacia is A, and then comes—the victoria is the species. It was first discovered along the banks of the Victoria River, which is not, I think, in the state of Victoria, I’ve been told. I’m not sure where it is. It’s up near that area near Sydney, on the eastern—I guess that’s the eastern coast. So we named it A for Acacia and then V-I-C for Victoria. And the general structure of it—it’s got five rings and then two sugars in this side chain, which is really the action. But there is a generic name for these types of compounds that have rings—four rings or five rings—and sugars. They’re called saponins or saponins, which is a derivative of soap. Or soap is a derivative of saponin. If you shake them up they can form suds. And they don’t have a great track record. Digitalis is a saponin, by the way, so that was my great hope. The heart—the first heart drug from **Dropsy** back in ‘77—not ‘77—1777 or whatever it was. So that was a hope for me. But a lot of them are toxic.

So I had my concerns whether this was going to do anything. So that’s how we named it—A for Acacia, V-I-C for Victoria, and then I-N for the last part of the—the general structure of the saponin, which is not the greatest name in the world because people don’t like them. Fortunately, this has activities different from saponins, but that’s I-N—and I-N is good because a lot of antibiotics have I-N at the end. They look like drugs. So the name—it’s an easy name. It’s a pleasant name. V is a very strong letter. A is—starting with a vowel, it’s got a nice ring to it. You know, that’s the name. So we called it the Avicin Project or the Legume. I think Clayton probably, still on the books, calls it the Legume Project.

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Now, meanwhile, Clayton is getting more and more excited. I took him out to Tucson. They had these trees growing. And these Acacia's have thorns. That's how they deter animals from eating them. The trustees came out on a hot, fall day—probably October I think—but it's still 102 degrees out there. And we went out in the fields to see these. One of the trustees, Tom Brorby, who is now the chairman, was wearing—he told me just the other day. Just a week ago he told me this story that this was the first time he wore this suit—light wool Italian suit. He said the most money at the time that he had ever spent on a suit, tailor-made, blah, blah, blah, the whole nine yards. And he snagged it on a thorn out there. What in the hell is he doing with a suit? But he's Clayton Foundation, and they're very formal. I mean, I've never seen them without a necktie. So he snagged—he had to have to it. I've heard that story a thousand times. I still think he's—he's not mad at me, but he said, "Well, you better make some money out of this stuff for the foundation." He had to get that rewoven. I just heard about this a week ago for the umpteenth time—how I took him out and didn't warn him about the thorns in the field. It was hot. He was sweating in wool. It was just crazy. But they were excited—you know—and they were excited.

So we put a patent application in on what's called composition of matter. Again, I had to learn about patent law. Now, I had a great teacher. Charlie Arntzen probably could teach patent law. He just loves patents. And so Charlie was pretty involved in those early days. He didn't stay involved because—you know—he was—Charlie was working on edible vaccines. And just to show the interesting people you meet when you start doing these things—you never know. Charlie was in—he loves to travel. He was in either Indonesia or Malaysia, and he saw a mother holding a child who was crying. And the mother just took a ripe banana and took a little—opened it up, and took a small little piece and put it on her finger, and then put it on the baby's tongue, and the baby calmed down. And this—he got this idea. Why don't we make vaccines and engineer them in plants? It's cheaper, supposedly, than any other way of engineering vaccines. You put them in either potatoes or bananas. That's what he was working on. I'm not sure where that field is now, but that was—but it was—more for third world stuff. So he had a hard time getting funding from—you know—from places I would go to. He would go to the WHO and so forth. He's a very, very creative guy. I don't talk to him much anymore. I haven't really—he's not been involved in this work for about the last decade. But he was key—key to the instrumental. Who would have known? He goes up to Cornell, and all these things start and weave, and this thing happens.

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So let's see. This may be a good stopping point. I don't know. Let me think about this a second. So we're starting the work on mechanism—I'm starting to wind down, too, a little bit—we'll talk about that. I think probably we start publishing—well, first we had to get the papers, and then we start publishing work and the chemistry. We applied for a patent, which, by the way, was awarded. It's called composition of matter. That was, I think, awarded, I believe, in 2002. That's the most important patent because the structure—you know—you can get around it. You can modify it, perhaps, and stuff, but a composition of matter is considered to be the most important patent you can get.

Tacey Ann Rosolowski, PhD

1:25:29.5

Is that on here? Oh triterpene compositions?

Jordan Gutterman, MD

1:25:32.2

Yes.

Tacey Ann Rosolowski, PhD

1:25:33.0

Okay. It's pending here.

Jordan Gutterman, MD

1:25:35.4

Yeah, that's way—it must be way out of date.

Tacey Ann Rosolowski, PhD

1:25:36.5

It must be out of date. Okay. Oh, here's one. Yeah. Right, triterpene compositions and methods for use thereof 2002—

Jordan Gutterman, MD

1:25:46.3

Yeah. That's it.

Tacey Ann Rosolowski, PhD

1:25:47.2

Okay. Yeah.

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Jordan Gutterman, MD

1:25:50.0

Arntzen et al, because they go alphabetical.

Tacey Ann Rosolowski, PhD

1:25:53.4

Yeah, Charles Arntzen, Mary Blake, Jordan Gutterman, Joseph Hoffmann, Gamini—

Jordan Gutterman, MD

1:26:01.6

David Bailey.

Tacey Ann Rosolowski, PhD

1:26:02.4

Yeah, David Bailey. I couldn't—I'm stumbling over that woman's name. But okay, great.

Jordan Gutterman, MD

Kalpana Mujoo. The Hauser people waived—the contract was that they would waive their rights to the few patents. So they're on the patent, but the patent is turned back over to Clayton. I think it's a good stopping point.

Tacey Ann Rosolowski, PhD

1:26:22.4

Okay. Let's—why don't we—? We'll terminate for today.

Jordan Gutterman, MD

1:26:24.2

I think we made a lot of headway. This is a whole story. It's a whole new career. It's a whole other story. Like I said, it's Act Two.

Tacey Ann Rosolowski, PhD

1:26:33.8

Yeah. Well, we'll continue with Act Two next time.

Jordan Gutterman, MD

1:26:37.0

It's so exciting, though. You haven't even heard the exciting stuff yet.

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Tacey Ann Rosolowski, PhD

1:26:40.2

Well—you know—you've been dangling this in front of me all this time, and I'm like, yeah. No, I'm glad to be in the story now. It's really fabulous.

Jordan Gutterman, MD

1:26:47.8

Oh it's—yeah—you know—we started a company in Seattle, and we got to the point to the clinic, and then they gave the technology back. I'm starting a company with a brand new accelerator here with state money. We're probably going to raise \$16 million. We're ready to go to patients. I mean, we're ready.

Tacey Ann Rosolowski, PhD

1:27:04.3

This is great. So to be continued.

Jordan Gutterman, MD

1:27:07.2

Oh, for sure.

Tacey Ann Rosolowski, PhD

1:27:08.4

To be continued.

Jordan Gutterman, MD

1:27:08.5

Plus we have a whole decade now of stuff. I can condense that down, but how it affects metabolism, and—oh, it's just—it just fits right in with the new—all this new work coming out with obesity and metabolism. It's just—I mean—we're just starting.

Tacey Ann Rosolowski, PhD

1:27:28.3

Well, it's 4:45, and we're closing off the interview for today.

Jordan Gutterman, MD

1:27:33.2

Oh, okay. Sorry.

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Tacey Ann Rosolowski, PhD

1:27:34.0

That's all right.

1:27:35.6 (End of Audio Session 3)