

## **Emil Freireich, MD**

**Session 1—October 5, 2011**

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### **Chapter 00A** **Interview Identifier**

*Tacey Ann Rosolowski, PhD*

**0:00:10.6**

I am Tacey Ann Rosolowski, interviewing Dr. Emil J Freireich. It's Emil, correct?

*Emil J Freireich, MD*

**0:00:17.8**

Americans say "ee."

*Tacey Ann Rosolowski, PhD*

**0:00:21.7**

How would you like me to say it?

*Emil J Freireich, MD*

**0:00:23.1**

J.

*Tacey Ann Rosolowski, PhD*

**0:00:23.4**

J Freireich at the University of Texas MD Anderson Cancer Center in Houston, Texas. This interview is being conducted for the Making Cancer History Voices Oral History Project, run by the Historical Resources Center at MD Anderson. Dr. Freireich holds the Ruth Harriet Ainsworth Chair in Developmental Therapeutics. He is also a distinguished teaching professor and director of special medical education programs as well as the director of the Adult Leukemia Research Program at the University of Texas MD Anderson Cancer Center. This interview is taking place in Dr. Freireich's office in the main building on the MD Anderson campus. This is the first of two planned sessions. Today is October 5, 2011. The time is approximately 9:20. Thank you, Dr. Freireich, for devoting your time to this interview and to this project. I'm very much looking forward to talking to you. As I mentioned before, you were interviewed in 2001 by Leslie Brunet on a variety of subjects, so I wanted to not cover all the ground. I'll be asking you some questions in areas that I feel were not covered in depth. The first thing that wasn't covered was something you already brought up, which is that you're called J, and that J doesn't have a period after it even though it looks like your middle initial. I'm wondering if you could tell the story about this strange—or mysterious—middle initial.

## **Chapter 1**

### **A: The Researcher**

#### *A New Idea and A Controversy: Transfusing Platelets in Leukemia Patients*

### **Story Codes**

A: Personal Background

A: Overview

A: Definitions, Explanations, Translations

D: On Research and Researchers

D: Understanding Cancer, the History of Science, Cancer Research

D: The History of Health Care, Patient Care

C: Discovery, Creativity and Innovation

A: The Researcher

C: Professional Practice

C: The Professional at Work

C: Collaborations

B: Devices, Drugs, Procedures

C: Faith

C: Portraits

C: Patients

C: Discovery and Success

### *Emil J Freireich, MD*

**0:01:58.1**

Well, when I grew up I was addressed by my family as “brother” because I had a sister. So there was “brother” and “sister.” In school, my name was Emil, but when I received my induction notice at the age of seventeen to go into the military, they required a birth certificate. As you know, I grew up in a very modest part of town, and we finally discovered that the city of Chicago did have a birth certificate. Lo and behold, the birth certificate said Freireich, Emil J, so I consulted my mother, and she said that when I was born she’d only been in this country about five or six years. She was young and didn’t speak much English, and the nurse said, “What do you want to name him?” So she said, “I want to name him after his grandfather whose name was Emil.” They were Hungarian, but they spoke German. They were located in that slit that was between Austria, Hungary, and Germany. She named me Freireich, Emil J. It was supposed to be junior, but the birth certificate had no “R,” just “J.” So I became Emil J Freireich, because it didn’t stand for junior, it didn’t stand for anything. It was just J. That’s how it happened.

*Tacey Ann Rosolowski, PhD*

**0:03:47.5**

Does that have any significance for you?

*Emil J Freireich, MD*

**0:03:49.0**

Yes, because Americans don't like this name Emil. It's kind of European. As you pointed out, many people—Americans—call it "ee-mil." The French call it "a-mil." But it's very European. And when I married my wife—my ever-loving wife—she didn't like the name at all, so she began calling me J, so everybody calls me J. Some people call me J Emil Freireich.

*Tacey Ann Rosolowski, PhD*

**0:04:24.0**

It just shows the power of that initial with no period after it.

*Emil J Freireich, MD*

**0:04:26.9**

When I write papers, as you know, the period always appears. Typesetters can't avoid it.

*Tacey Ann Rosolowski, PhD*

**0:04:34.2**

I did notice that, yes. They add things. Well, if you don't mind, I'd like to talk about some of the areas in which you've made contributions, specifically starting with the work on the continuous-flow blood separator. I know that you developed that with George Judson when you were at NCI from 1955 to 1965, but the one topic that really wasn't covered in too much detail in the 2001 interviews was how the blood-flow separator was developed technically once you got to MD Anderson. I'm wondering if you could tell me that story, and then about the trials that you began to run.

*Emil J Freireich, MD*

**0:05:24.4**

Did she give you the reprints I gave her?

*Tacey Ann Rosolowski, PhD*

**0:05:26.6**

Yes.

*Emil J Freireich, MD*

**0:05:28.0**

That's a nice story.

***Tacey Ann Rosolowski, PhD***

**0:05:29.8**

Yes, I did read it.

***Emil J Freireich, MD***

**0:05:31.6**

But of course it's very published, so it's very slim. I can give you a little more color. When we started treating children with leukemia and patients of all kinds, we recognized that whatever you did to kill a tumor inhibited the normal bone marrow, which is a rapidly growing organ, and the gastrointestinal tract. The gastrointestinal tract you can handle by replacing fluid, but the blood was a problem. We went to work on the platelets because the leading cause of death in patients treated when they had leukemia or otherwise was hemorrhage. The hemorrhage story is also told. It's very colorful because it had already been proven unequivocally that thrombocytopenia was not responsible for the bleeding. The science of that was volumes deep.

But we decided to do a simple, clinical thing. See, I'm a great advocate of bedside to bench and back. People think that if you discover everything in the laboratory, it will immediately apply. You'll call up some doctor, and he'll do whatever—give him a drug or something. But in fact everything that advances our knowledge about humans and human disease begins with clinicians observing patients, and then you can go to the library, so we decided to do that. We noticed that thrombocytopenia was present whenever they were bleeding, low platelets, so we did a retrospective study where we just looked at the charts and wrote down how often the nurses and the doctors noticed that the patients were bleeding, and we wrote down the platelet counts on those days, which we did on a regular basis, and we wrote what's a citation classic. It's a paper that shows that there is a direct relationship between the degree of thrombocytopenia and the occurrence of hemorrhage.

So then, now it's time to go to the laboratory. I went to the lab and I said, "Well, it's obvious we have to replace the platelets." So I took platelets out of my blood, and I got blood out of all these children bleeding to death. I put my platelets in, and all the in vitro tests of coagulation were normalized. I said, obviously there's something missing here. We've got to do an in vivo experiment. We have to give them platelets. Now there's a challenge. This may be more detail than you care about.

***Tacey Ann Rosolowski, PhD***

**0:08:23.1**

No, detail is good.

***Emil J Freireich, MD***

**0:08:24.3**

It's all in the paper. The first thing we did was recognize that the way blood was collected in the blood bank, once it's stored three or four days, the platelets are mostly dead; they disintegrate because there's acid and citrate. It's refrigerated, and that lends to clumping of the platelets and

so on, so we realized we needed fresh blood. When I had done it, I had fresh blood, but fresh blood is not something blood banks do. Blood banks operate on the basis that the blood is stored until needed and use the oldest ones first. If you use the fresh blood, you'll never have any blood in the bank. So we said, how do we get fresh blood? That was a challenge. It so happened that there was another young doctor working in the blood bank. His name was Alan Kliman. He was like most of us. We were serving our military time in 1955. I said, "Kliman, I want to get some fresh blood." He said, "Oh, yeah, we'll do it." So we got some donors. He bled them in the blood bank and delivered the blood to me, and we treated these children—home run.

But it was already established that it does not work, so how can you say that it does work? No matter what I did, it was just me talking. There was only one way. My mentor was Dr. Gordon Zubrod, who came out of the malaria program. The malaria program learned one thing during the war. As you know, more soldiers died of malaria than of war injury.

*Tacey Ann Rosolowski, PhD*

**0:10:36.0**

I didn't know that.

*Emil J Freireich, MD*

**0:10:38.1**

That was true during the war in the Pacific with the Japanese. They mounted the atomic bomb project, and they got the best brains in the country into a room and said, "You've got to figure out what to do about malaria." Out of that project came all the anti-malarials we use today—chloroquine and so on. Dr. [Gordon] Zubrod was in that program, conscripted, of course, and what they learned is that in order to detect anything, you have to eliminate the most powerful force in the human mind, which is bias. People conclude what they know about the world from experience that they had. Once that's true, everything fits into that because we're innately biased. We learn on the basis of what we've known.

The experiments which showed that platelets don't do anything were all conducted in animals. They were experiments where you remove the platelets by centrifuging and putting in platelet-poor blood, and these animals never bled, so it was obvious platelets weren't it. Moreover, in the animals that were radiated who bled, they found that there was an anticoagulant in the blood. It turned out this anticoagulant is a fibrinolytic enzyme, but that will come later.

So anyway, we had to eliminate bias, so we did the first prospectively randomized trial and transfusion in the world's history. What we did is we had children who were bleeding, and the blood bank agreed to give us one unit of fresh blood or one unit of bank blood more than seven days old in a random fashion, double blind, and then it was my job to assess whether it had any effect on the hemorrhage. These were children who had one m<sup>2</sup> body surface, about fifty or sixty pounds. They were all under ten. The small size helps enormously, of course, because their blood volume is smaller, so we conducted this study in a setting where the opposition both had certain

data. We knew it would work, and they knew it would not work, so this was very tense. We had all the safeguards built in—you can't talk, we can't know, you can't do.

After we had done ten or twenty children, Dr. [Emil "Tom"] Frei, my colleague for life, decided let's break the code. So in a situation like this, we had a very tense meeting. We had gathered in a room with the statistician who was in charge of analyzing the data with the opposition—Dr. [George] Brecher who ran laboratory medicine—world famous hematologist who had done all this work on platelets during the war. He invented the platelet counting method. He was very famous, very accomplished, brilliant man, European—Dr. [Paul] Schmidt, who ran the blood bank, and myself and my fellows, Larry Gaydos and my boss, Dr. Frei, in the room, with the statistician. Patient one, bleeding or no bleeding? Stopped bleeding—fresh. We did it one at a time. By the time we got through, it was 100% successful. Every patient that got fresh blood improved, every patient who got bank blood did not, and the measurements we made were objective and quantitative. We measured hemoglobin in the urine. We measured hemoglobin in the bleeding nose. We measured hemoglobin in the stool. We did bleeding times on the patients by stabbing and seeing how long it took to stop bleeding, so the data was not only the platelet counts, but we had objective data. Problem solved.

Don't forget bias. After the glow wore off, I got a call from Dr. [G. Burroughs] Mider, who was our scientific director, a very rough guy—pathologist. "Freireich, Brecher, and Schmidt tell me you're causing trouble." "No, sir." "Well, what's all this about blood? You have to have fresh blood, and you did this phony study, and it all came out wrong. If you don't stop making trouble, you're fired."

Well, I was young and easily intimidated, so I talked to Dr. Zubrod and Dr. Frei. Dr. Zubrod said, "Let's have a grand rounds." On the top floor of the clinical center there was a very luxurious meeting room, like the Hickey Auditorium. We had an NIH grand rounds on the subject of bleeding and platelets. The forces of evil—Schmidt and Brecher—presented the data that proved that platelets had nothing to do with it, unequivocally, and it was the gestalt; that was what everybody believed, and then we presented our little ten patients thing. Brecher got up and said, "Conclusion, it's a bunch of foolishness."

I have to tell you one other part. With the conversation with Dr. Mider, the claim that was made was that when the children needed transfusion, their parents would go down and donate fresh blood. I would interview the parents so I knew which ones got fresh blood, because if it was bank blood, no one went down to donate, so I was not only intimidated by being a troublemaker, but I was dishonest. I was cheating.

***Tacey Ann Rosolowski, PhD***

**0:17:35.9**

It wasn't really blind, so they claimed.

***Emil J Freireich, MD***

**0:17:39.5**

Cheating. So we had this grand rounds, and they presented and we presented, and, to his credit, with all the prestigious people from the clinical center in the room, Dr. Zubrod stood up and said, “Dr. Schmidt, if the doctors in my department order fresh blood, it will be your obligation to provide it.” Amazing that it took the courage of this man to do that even though his boss, Dr. Mider, was on the side of the blood bank.

After that, it was a simple matter to confirm the—well, first of all, we had to publish it. It got accepted in the *New England Journal*. Dr. Brecher refused to put his name on the paper. He was sure we were cheating, but Dr. Schmidt did—the blood bank director. From that point on, what we did is we systematically transfused platelets when the platelets were low.

We developed a very simple procedure for using plastic bags. The way we collected blood in 1955 was with glass bottles, rubber tubing, and steel needles. All of those surfaces take the platelets out of the blood and destroy them. During the war they had discovered the plastic blood bags, and the reason it was discovered was not because of platelets. It was discovered because it was a way to transmit plasma for battle wounds. The bottles were always breaking, so the plastic bags were very useful for transporting, but we found that plastic is non-wettable and therefore platelets don’t stick to the plastic surfaces. We adopted a collection technique where the steel needles were coated with silicone, therefore not wettable, plastic tubing, and plastic bags, so the platelets were not stuck to the surfaces but in the blood, so we collected platelets much more efficiently.

We also devised a little thing which is in the first paper. I have a slide of it. It’s a beautiful thing. We just took two bags, connected them to each other so that you can, in a closed way, collect a unit of blood, take out the platelets or plasma, put the red cells back in, collect another unit and run it to the second bag, and it was all closed so it was sterile and safe.

***Tacey Ann Rosolowski, PhD***

**0:20:09.6**

I was looking at that, and I have to say, I kind of tried to map out the process for myself. Was the idea that you gave one unit of blood that was rich in platelets to the patient, and then you returned the other unit, which was rich in red blood cells, to the donor?

***Emil J Freireich, MD***

**0:20:28.8**

Correct.

***Tacey Ann Rosolowski, PhD***

**0:20:29.2**

Okay, so I understood it.

***Emil J Freireich, MD***

**0:20:31.3**

Actually, we took platelet-rich plasma, so we only separated supernate and precipitate. The platelets are centrifugally light so they stay in the liquid part. The red cells are heavy, and the white cells are heavy. So we collected supernate and precipitate. Precipitate went back to the patient; supernate went to the side bag. Second unit, same thing, side bag, so we had two units of platelet-rich plasma for transfusion.

Now, during the one unit of blood transfusion, we worked out the quantities. We knew that you needed one unit of blood which contained approximately  $10^{11}$ —if you're familiar with that kind of numerals—platelets per square meter of body surface area of the child. And that transfusion would result in the increment of 5000 per mL, so we had the quantities all worked out. We knew that two units would give you roughly ten or twelve, so we knew how to treat hemorrhage. We knew where the hemorrhage began because we had this relationship—so. So we systematically began to replace platelets.

We had no trouble getting volunteer donors because all these children had parents and friends. By the time we had done that for a year or two, one of our fellows, Dr. [Jules] Hirsch, eventually came here and did a retrospective study and showed that bleeding is the cause of complications and death. It was essentially ninety-five percent reduced. So the cycle was completed.

***Tacey Ann Rosolowski, PhD***

**0:22:12.7**

Can I ask you just a quick question. I wanted to go back just to that moment when Dr. Zubrod stood up. I think it's hard for people who aren't scientists to understand exactly how dramatic those moments are and how much rides on them.

***Emil J Freireich, MD***

**0:22:33.2**

Dramatic—everybody stopped breathing.

***Tacey Ann Rosolowski, PhD***

**0:22:36.4**

What could the consequences have been if he hadn't done that? What might the consequences have been for him if his boss had taken a different attitude?

***Emil J Freireich, MD***

**0:22:46.7**

Well, I don't think that was the problem. What's going on in the scientific community is credulity. Since the evidence was so conclusive, that to change the paradigm required people to overcome their internal bias, which is very difficult. It's like convincing Obama that his plan is no good. Once you've got it in your computer, it's very hard to change direction. It's kind of like a gyroscope. So it was the intellectual courage. People couldn't believe that in the face of the

existing paradigm anyone would be willing to question it based on a very small study, so that's what impressed people. It's kind of like the king has no clothes. I mean, if someone is willing to say, well, you all think he looks gorgeous, but he doesn't have any clothes on. It's part of the human nature.

So that was a very courageous thing for Dr. Zubrod, and he did it because he was—both he and Dr. Frei were men of enormous objectivity. They were both devout Catholics, so they had faith in the truth, as opposed to convention, as opposed to the fundamentalist-type convention, so they were people of that kind of character. For me, none of those were issues. For the people digging the ditches, you don't care about the anatomy and the physiology and the biochemistry, you've just got to get the job done. That was me in the trenches just doing the work. The kids were dying, and we had to do it. You heard the Scotty Dinsmore episode?

***Tacey Ann Rosolowski, PhD***

**0:25:18.8**

I did.

***Emil J Freireich, MD***

**0:25:19.1**

That was the one that impressed me the most because we not only stopped his bleeding, but we were able to count the platelets after we stopped the transfusion and watch when the bleeding recurred in relationship to the platelet count. We redid in a patient what we had done retrospectively from the chart review, so we knew what the truth was, but the truth—it's difficult to see the truth. That's why progress is made by people who have that ability to see through the existing paradigms. So that's the platelet story.

***Tacey Ann Rosolowski, PhD***

**0:26:00.2**

What do you think gave you the ability to see through existing paradigms?

***Emil J Freireich, MD***

**0:26:05.6**

Well, because I was the guy with the shovel. There's a difference when you're in the library. Brecher was working with animals in a laboratory. When I came to the cancer institute, Dr. Holland had just left. He left four or five bleeding kids on the ward, dying, and since I was a hematologist and Zubrod gave me the job of curing leukemia, all the other guys that were there said, Freireich, you take care of those people. So we didn't have staff, we didn't have trained nurses, we didn't have equipment, we didn't have help. This was digging ditches. The kids were dying. I was there all day long and all night with the parents, holding their hands and bleeding to death and the ward is full of blood—blood on the ceiling, blood on the curtains, blood all over your jacket. It was like at an abattoir. It was—it's the digging ditches thing. You had to do something.

*Tacey Ann Rosolowski, PhD*

**0:27:14.7**

I think it's really hard for people to imagine that, because now the image of a hospital is so staffed and clean.

*Emil J Freireich, MD*

**0:27:20.3**

Yeah, sure—sure. That's actually what happened. Zubrod came on rounds one day, and after we sat down and talked about it—how much methotrexate and we were doing chemotherapy studies—he said, “Freireich, this ward looks like an abattoir. It's full of blood everywhere. Why don't you do something about the bleeding?” I said, “Yes, sir.” So you can't have prejudice when you're dealing with—when you're drowning. You have to breathe.

## **Chapter 2**

### **A: The Researcher**

#### ***Building the Continuous-Flow Blood Separator***

### **Story Codes**

A: Overview

A: Definitions, Explanations, Translations

D: On Research and Researchers

D: Understanding Cancer, the History of Science, Cancer Research

D: The History of Health Care, Patient Care

A: The Researcher

C: Discovery, Creativity and Innovation

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C: The Professional at Work

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C: Portraits

C: Patients

C: Discovery and Success

### ***Emil J Freireich, MD***

**0:27:20.3+**

That success occurred. We said, well, now they're all dying of infection. So we did the same thing; we did a retrospective study—Dr. [Gerald] Bodey [Oral History Interview], who is now retired—still here—number of white cells compared to the occurrence of serious infection. He showed another citation classic that if you lower the white count, the longer it's low the more likely you have a major infection. Obviously, we've got to have white cells.

Well, the problem was that unlike the platelets, which have a half-life and a circulation of about five days, the volume of distribution of platelets—you understand, the circulating blood has red cells and all the other cells suspended in plasma, but the concentration is not uniform throughout the body. It's higher in the spleen and in peripheral, small capillaries, so what we have to measure is kind of an average, and on average the volume of distribution of the red cells defines the blood volume because the red cells don't go outside the blood vessels unless you're bleeding. I'll come back to that too.

So when you inject the platelet, the volume of distributions are about twice that of the red cells because the concentration of platelets in organs like the spleen is higher than that of the red cells. They get through, and the platelets, which are small, tend to peripherally circulate and they drag, so their volume of distribution is about twice, so when you inject X amount of red cells, you get Y amount of increase. When you inject X amount of platelets, you get Y/2—you get half the increment.

So we radio labeled granulocytes from the normal donors, and the first thing we learned was that the volume of distribution was twenty times normal, and the reason for that is that the granulocytes operate like the fire department. That is, the normal situation for the differentiated granulocytes is in the marrow granulocyte reservoir. They don't circulate unless they're called upon. There has to be a fire alarm. The red cells all circulate continuously—the platelets—but the white cells don't. So when you inject white cells, the more granulocytopenic the recipient, the larger the volume of distribution.

Problem number two is if you label the granulocytes, once you inject the granulocytes labeled into a recipient, the half life and the circulation is six hours, because once the call goes out for granulocytes from the fire house, once they get into circulation, it's because they're needed. The message came from either a site of inflammation—a break in the vessel—so they're consumed peripherally, very rapidly—half life six hours.

So if you do blood counts on a normal person—you probably know all this. If I'm getting repetitive, you can stop me. In a normal person, when you do a blood count, he has 5000 to 6000 per mL circulating granulocytes. Why is that? It's because you've got infection all over the place. In a germ-free animal, his white count is ten. They're all in the fire house. When you inject them, they immediately go along the gum margins, around the rectum, all the sites of infection—the nose, the lungs—so they exit immediately. It's not that their life span is short; it's that their physiology is short. They want to go where the problem is.

So we tried our bags, and we got as many as we could and you shoot them in and nothing happens. The problem was obvious. It was dose. So my friend Alan Kliman and I—we had a cookout in his backyard, and we started to talk about how we could get more granulocytes. We came up with the idea I take credit for and he takes credit for. We got the idea of turning to patients who have chronic granulocytic leukemia and have white counts 300 times normal. They're diseased, of course, but the in vitro studies of granulocytes from granulocytic leukemia patients indicate that they're damaged but they're only about half as good. So we said, let's get white cells from leukemia patients and give them to our dying leukemia children to control infection.

Great idea. Can you imagine doing that in 2011 in the United States? It's insane. You're giving leukemia cells to dying children with leukemia. They're going to die of leukemia. They're going to get—but only in the clinical center, only with Frei and Zubrod would that ever have occurred, and we did it. We got patients with CML-benign phase that can live with these high counts for

very long periods of time, and we asked them to volunteer as donors, and we bled them continuously as donors. Of course, they had so many that as soon as we took them out, they put more in there. We actually published a paper showing that doing leukapheresis on these CML patients for a period of a month did not affect their survival or didn't make them sick in any way, so it was safe.

We didn't do that in beginning. We had to prove that, and when we gave these to the children, we worked out the whole physiology of granulocyte transfusion. We found the volume and distribution twenty times normal. We found the half life in the circulation, which ended up being about twenty-four hours instead of six, because once you fill the marrow granulocyte reservoir, they don't immediately go back to the marrow, they stay in the blood and do what they're doing. We showed the relationship between the pre-count, and we had a dose response. The higher the level of granulocytes in the recipient, the more likely they were to get cured. When we gave  $10^{11}$  granulocytes to these children, ninety percent of them had their bloodstream cured of infection and they were cured.

***Tacey Ann Rosolowski, PhD***

**0:35:16.5**

They were cured?

***Emil J Freireich, MD***

**0:35:17.1**

Temporarily. So we had the solution. The problem is there are lots of people with no white cells and there are very few patients with CML and most of them aren't going to volunteer to do nothing for a year. So we had to figure out how to get  $10^{10}$ —ten billion granulocytes from a donor. Well, obviously it's impossible because the number—that's the number in your whole body. If we got every white cell out of your peripheral blood we'd have enough for one transfusion.

But being stupid and young, digging ditches, I tried. So I went to work, read all the literature and studied flow dynamics, rheology. We studied the physiology of blood in the small vessels. We found that like the platelets, the granulocytes tend to roll along the margins so that the axial flow is red cells. We tried pushing blood through capillaries where the ratio of axial flow to peripheral flow was maximum, which is a very small tube. Then we tried to make it long enough so we could get, at the end, a very high concentration of white cells. This Rube Goldberg thing that I was working on required enormous positive pressure to push it through these capillaries, and it required a very long path for the blood, so if you came in my lab you'd see this tubing.

***Tacey Ann Rosolowski, PhD***

**0:37:27.8**

How long was the tubing that was required?

*Emil J Freireich, MD*

**0:37:31.0**

Oh, in order to get a reasonable separation it was maybe fifty feet—fifty feet of tubing through my lab. You had to have a huge machine pushing it very, very slowly.

*Tacey Ann Rosolowski, PhD*

**0:37:47.6**

So this was really the next evolution of the blood separator?

*Emil J Freireich, MD*

**0:37:50.5**

Well, I'm trying to figure out a way to separate them continuously, but it was obvious that the only way it would work would be centrifusion, and the problem with centrifusion is that the specific gravity of the white cell is only slightly less than the red cell. The way you separate them is you have to get the red cells to rouleaux. The rouleaux in the presence of macromolecules. They stack up like coins. That way the particles are larger than the white cells, and when you put them in the centrifuge, the sedimenting particles push the plasma out with the granulocytes and they end up in the buffy coat.

So we did all these experiments in tubes. We got blood from the blood bank that was contaminated with syphilis and stuff and had to be discarded. We did all that. If you came into my lab, it was like the hospital ward—blood all over the place.

*Tacey Ann Rosolowski, PhD*

**0:38:58.9**

Why were you trying to work for the continuous flow as opposed to the centrifuge? What was the advantage?

*Emil J Freireich, MD*

**0:39:06.3**

Well, the idea was that if I'm going to get enough white cells for a transfusion, I have to get the blood cells from your entire blood volume. Now, the one thing we learned was that when we started leukapheresing with the bags, no matter how many white cells we removed, the white cells in the marrow granulocyte reservoir replaced them very quickly. We knew that there was a large reservoir of granulocytes, but not in the blood. So obviously we had to process the blood. The obvious image was an artificial kidney, which removes pollutants and leaves the good stuff. So we needed something that would process the blood, remove the white cells, leave all the other formed elements, and mobilize the cells from the bone marrow, so we knew what we had to do.

So I was up there doing this stuff in the lab, and everybody knew crazy Freireich and all his tubes. One day, Mr. Judson appeared in my office. Why did he appear? Well, his son had chronic monocytic leukemia. He worked for IBM; he was an engineer. His engineering experience was with jet engines. He was one of the project officers that made all the—how to get the air and the

fluid and the fire. His doctor happened to be Jerome Block, who I think is now dead. He ended up in California doing oncology. Jerry Block was one of our trainees. He said, “Is there anything an engineer can do?” Block said, “This crazy Freireich on the trial floor is trying to do blood things. Go talk to him.” He came to me.

In our first publication, I describe what we actually did. He came in, and this is what I said, “This is what I want to accomplish.” He said, “Okay, tell me what you need.” So I sat down with pencil and paper and wrote the ten things that I needed—continuous flow, closed system, no hemolysis, rapid flow—it’s in this paper. So Judson listened very carefully. He was a very straightforward guy. He took this piece of paper—

***Tacey Ann Rosolowski, PhD***

**0:41:46.5**

Yep. Here are the ten things. It’s a really great list. Do you want to read it?

***Emil J Freireich, MD***

**0:41:51.9**

No, you can read it.

***Tacey Ann Rosolowski, PhD***

**0:41:53.1**

The leukocytes could be separated—

***Emil J Freireich, MD***

**0:41:57.5**

So Judson wrote them all down. I said, “There’s the job.” So he said, “Okay.” So he went away and I forgot all about it. I mean, crazy, simple-minded guy who’s never done anything biological, only works on jet engines. So I continued with my things and the tubes and the work. In two or three months—I don’t remember the exact time—two or three months later, who appears in my lab? Mr. Judson, and he’s got a briefcase full of mechanical things—metal screws, plastic tubes. He said, “Here it is.” No one could have been more shocked than me. I don’t think I have pictures in that paper, but I have pictures of the original equipment. It’s amazing.

So we put this together with screws and screwdrivers and bolts and glue and O-rings. We built the thing. You see, the secret to a continuous-flow instrument is how you connect the rotating and the stationary parts. That was the biggest challenge we faced. So we put these things together, and we got heart pumps from the heart machines. We got tubing. It was all done with make-up things that he could salvage from IBM’s—when projects failed they threw them in the storehouse and he salvaged them.

***Tacey Ann Rosolowski, PhD***

**0:43:30.1**

Why were you surprised when he showed up?

***Emil J Freireich, MD***

**0:43:33.5**

Well, because he didn't know anything about it, and I had been working my head off, and I'm ten times smarter than he is. Why didn't I figure it out? But he went to work—you know—he was an engineer.

***Tacey Ann Rosolowski, PhD***

**0:43:52.5**

It sounds like he's a trenches guy too.

***Emil J Freireich, MD***

**0:43:53.6**

And he came with a machine. I thought, whoa! So we tested it, and although it didn't work, you could see immediately that the concepts were there. So we got the centrifuge, we learned how to put—we had the bolt. The original centrifuge was upside down, so the blood flowed from top to bottom and the centrifugal force was horizontal, so how to connect the rotating and stationary parts was a very difficult problem. How do you do that?

Well, Judson looked in the literature, and he discovered that during the war the atomic energy commission people were separating isotopes centrifugally in ultracentrifuge, and they had worked out what's called face seal. A face seal is a combination of stainless steel and very high-quality Teflon plastic which has been engineered to be less than one molecule of water thick, so they're absolutely flat. In that circumstance, the flat faces can rotate continuously if the mechanics are right so they don't jiggle and there will be no crossing between the channels, so the thing is a circle.

Well, he went to Oak Ridge and he saw the things, and he went back to IBM and they made face seals. We had a beginning on that problem, and then the problem was every instrument that was continuous flow could separate, precipitate, and supernate. That's not a problem. That's not a problem. The problem was how to connect from the center of the centrifuge—how to collect the buffy coat.

Well, that was a real challenge because we had to devise a collecting system that would allow you to view the separation—we've got some beautiful pictures of that—so that you could locate the collector over the buffy coat, because the plasma comes from the top, the precipitate from the bottom, but the buffy coat is in the middle, so if you don't get the right ratio between the flow of platelets and red cells, you have to locate the buffy coat over a fixed collecting point.

So he had a plastic bottom. We did it visually and manually, and, by golly, we invented the first continuous-flow machine that could collect supernate, precipitate, and buffy coat.

Now, the collection efficiency was still very, very poor because of this problem of red cells, but I had done a lot of work on centrifuge and white cells, and we had studied all the macromolecules—fibrinogen and so on—and I came across a paper by a guy who is still working, Craig Thompson, who had invented a drug called hydroxyethyl starch. It's a synthetic macromolecule that is susceptible to glycolysis by human enzymes. He developed this in order to use it as a plasma substitute, so that in battle, instead of having to have plasma, which deteriorates and gets infected, you can use a synthetic macromolecule to replace the blood volume temporarily until they get out of shock and you can get blood and so on. It was very important during the war and during major surgery—during cardiovascular surgery. They had to use plasma substitutes instead of blood.

So I wrote to him, and he sent me some hydroxyethyl starch. It comes in various size—variety. There's a lot of stuff that has to go through—you don't want to know all the details. It worked beautifully in the test tube. Then we tried it in vivo, and it worked beautifully in vivo. It was about ninety-eight percent degraded in the recipient so that, although you retained some of it in your organs, it was not carcinogenic, and it didn't stay there forever because eventually your hydrolytic enzymes would break it down. If you used the right size hydroxyethyl starch, most of it was degraded or excreted by the kidneys, so we had a relatively safe product. We had to go through all that. It worked beautifully.

### **Chapter 3**

#### **A: The Researcher**

#### **Perfecting the Blood Separator in the Department of Developmental Therapeutics; Shifting MD Anderson Culture to Innovative Research**

#### **Story Codes**

A: The Researcher

A: Joining MD Anderson

C: Portraits

B: MD Anderson History

B: Building/Transforming the Institution

C: Discovery, Creativity and Innovation

B: Multi-disciplinary Approaches

B: Growth and/or Change

B: Critical Perspectives on MD Anderson

B: MD Anderson Culture

#### ***Emil J Freireich, MD***

**0:43:53.6+**

Oh, I skipped a very important part of the story. Put hydroxyethyl starch aside. That comes later. What happened—I'm still at the Cancer Institute, and Judson is doing this work. We wrote a letter to IBM saying, "We'd like Judson to work on this project." You know, he had other duties. As a compassionate thing for their employees, IBM—when it was rich—they said, fine, he can have full-time, get his salary, and work on this project with the Cancer Institute. So he came and worked in my lab full time and he'd go back to—because his son was in the hospital.

So we got to the point where we thought we might have something, so we had a demonstration. We had a patient with CML. We put them on this device we had, and Dr. Zubrod and Dr. Frei came and we showed them what we had. The seals leaked and everything went wrong, but they could see that the idea was right. So Zubrod agreed to write a contract for IBM. They estimated that in a year they could make an instrument that was sophisticated that would do what we had done with this hand-constructed model.

#### ***Tacey Ann Rosolowski, PhD***

**0:50:42.2**

Now when you hooked this particular patient up to this prototype, did the patient improve at all?

***Emil J Freireich, MD***

**0:50:50.0**

No. These were CML patients who were volunteer donors for the children to get the CML cells. Of course, they have a high white count, so their buffy coat is—if the thing is this high, the buffy coats are huge, so the ability to collect is relatively easy. When you take a normal person who's only got 5,000 white cells per mL, his buffy coat is very, very thin, and it's very hard to arrange it. It was set up to be easy, and of course it showed the principle. So they issued the contract to IBM, and they went to work. I don't recall the exact time—perhaps six or eight months later they delivered a machine. Since I was the project officer, I hooked my CML patient up to the machine. It didn't work. Pumps didn't work, the seals were leaking. I wrote a report. It doesn't work. Well, IBM had a policy that any engineer who undertakes a job and doesn't deliver on time is removed from the project, so Judson had to be fired. Dr. Frei and Dr. Zubrod put their genius heads together, and they decided the solution was to fire Freireich, that way they could say the instrument was fine. They issued another year contract to IBM to improve on the instrument and Judson was saved. So I was fired and Judson was saved.

***Tacey Ann Rosolowski, PhD***

**0:52:45.9**

This is about the time that you were shifting to MD Anderson.

***Emil J Freireich, MD***

**0:52:49.4**

Very close. But as an aside, I have been fired from every position I've ever had, so you would think I'm a total scoundrel, but I've only been fired for being successful, not for being a failure. This firing hit me deeply, but even more serious was the fact that within months Dr. Frei accepted the job at MD Anderson. Now, I don't know that it's useful for me to tell you why he did that.

***Tacey Ann Rosolowski, PhD***

**0:53:32.4**

I think you talked about that in the previous interview.

***Emil J Freireich, MD***

**0:53:35.4**

It was social, not scientific.

***Tacey Ann Rosolowski, PhD***

**0:53:37.9**

So we're talking about 1964, and then he left in 1964. I'm just trying to get the time—the date.

***Emil J Freireich, MD***

**0:53:46.2**

In '64.

*Tacey Ann Rosolowski, PhD*

**0:53:47.1**

In '64, yeah.

*Emil J Freireich, MD*

**0:53:53.9**

When he left, the balance of power at our institution—

**54:10.8** (end of audio file one)

*Tacey Ann Rosolowski, PhD*

**0:00:03.0**

All right. We had the recorder off for just a few minutes while Dr. Emil dealt with a phone call.

*Emil J Freireich, MD*

**0:00:11.1**

So when Dr. Frei left, the balance of power was such that I had created all kinds of antibodies. We had occupied too many beds. We'd kept too much—so—so it turned out the responsibility for the project went to a guy named Seymour Perry, who is now dead. May he rest in peace. He was marginally competent. One of my students was made head of the leukemia program, so I obviously had to leave. Dr. Perry, the day he was appointed, came to my office and said he thought it would be better if I left, because I was a big power and he was supposed to be—you know—it didn't work.

So I looked around for a job, and Dr. Frei offered me this job. I resigned my commission, after ten years, and got ready to move. In the spring, in about March, I got a letter from Dr. Frei—no, I got a letter from Dr. [R. Lee] Clark. Dr. Clark ran this place—this is a history, mostly, of MD Anderson. So he got Dr. Frei on purely social grounds. He was able to pay him a salary which was five times what he was getting at the Public Health Service. That money allowed him to raise his family of two incompetent mothers and ten children, which he did brilliantly. When Dr. Clark wanted to recruit me, he came to my house in Bethesda, had dinner with my kids and my wife. He wanted to be sure everybody fit into his private hospital. Clark ran the institution like you run your office. He was in charge of everything. And that's the way things work. When you have a general, things work. When you have a committee, it's just discussion. That's why MD Anderson exists, because of Dr. Clark. He was a giant of a person.

I resigned my commission in March, and I accepted the job at Anderson. He sent me a letter, and I got an appointment. My salary went up. Frei's probably went up more than five-fold, because mine went up five-fold. I was making \$6,000, and he paid me \$25,000. This is in 1965, so we were going to be rich.

And in March that year I got a letter from Dr. Frei saying, guess what, he was fired. Dr. Frei was going to be the scientific director; I was going to found my own department called Developmental Therapeutics. We worked out the name, the mission. So he got fired, and I got fired. So I went to look for another job. To make a long story short, I decided to come either way. So I came in July, and the first years at MD Anderson were extremely big. I may have already gone through this.

***Tacey Ann Rosolowski, PhD***

**0:03:58.3**

Yeah, in the first interview you talked about the issues that were making it so difficult.

***Emil J Freireich, MD***

**0:04:03.4**

So I don't need to repeat that. Dr. Clark was very loyal to the people who took a chance with him. When we came in as outsiders and disrupted their whole modus vivendi, there was friction. Clark tried to keep us going without offending the people who are here, so we did that by creating a department outside of the institution. Dr. Clark rented a mobile home and put it in a parking lot. That's where we had our labs. We rented a floor in Hermann Hospital for our patients. We rented a floor in an apartment building which no longer exists, across the street. We rented a storefront for some of our other laboratories.

(phone ringing)

***Emil J Freireich, MD***

**0:05:30.1**

So we created this department outside of MD Anderson.

***Tacey Ann Rosolowski, PhD***

**0:05:34.2**

And this was the genesis of Developmental Therapeutics?

***Emil J Freireich, MD***

**0:05:47.4**

Yeah. The blood cell separator—when we came here, things were compared to the clinical center—very primitive—because this place was based on the Mayo Clinic model. So that was to provide high-quality care—conventional care. But there was no clinical research to speak of. There were a couple of people—Denny Bergental had been here. There was a little bit of research, but we came in bringing the NIH concept, which was full-time clinical research. It required that we create all of our own resources, which we did, with grant money. When I was fired as head of the department of DT, I stated that there was never a year when my budget did not exceed my state budget. In other words, I never took a dollar from MD Anderson. It was all federal money or Cancer Society or Leukemia Society.

We were struggling to get the level of care that we were used to at the clinical center. For one thing, they'd never done platelet transfusions here, so I had to do platelet transfusions in my little lab. We had a 600-square-foot lab on the fifth floor, and I had one technician and secretary. We started, bought the bags, the platelets. We provided our own platelet transfusions. We had to do it on bone marrows because the way they examined the bone marrow was not the way the great Dr. Brecher did it.

When we got rolling about a year later—and there were no fellows and no trainees—we started with exchange students from Japan. They came out in a Japanese-American agreement. But what I was emphasizing was that Clark was able to support us in the face of enormous enmity from the existing faculty without compromising his loyalty to the people who were here. This took a man of great skills and vision. He was a person who knew what this place was going to be.

***Tacey Ann Rosolowski, PhD***

**0:08:52.1**

What were the questions or issues that the faculty had in the face of the work that you were bringing in?

***Emil J Freireich, MD***

**0:09:02.5**

Well, it was all strange to them. They were the world's authorities in cancer, and we did everything different. In the ten years before we came, they had 100 patients with acute leukemia. Today we get 1,000 new patients a year. It was just they didn't treat acute leukemia because no one knew how to do it. We had just discovered that at the clinical center. The pediatricians here had never used vincristine, which was the essential drug for curing leukemia. They'd never done platelet transfusions. White cell transfusion was out of the question, so it meant that the whole practice in the institution was going to change. Of course the patients flocked to us, because what they got from the conventional people was convention, and we offered them promise, hope. I've written several editorials about that's the importance of research. Humans cannot live without hope. Hopelessness is the greatest trauma a person has to suffer. It's like when the machine is just—well, maybe it will go through. And patients were flocking to us.

***Tacey Ann Rosolowski, PhD***

**0:10:32.9**

Can I just clarify one thing? You said your lab was really small, and yet patients were flocking. I'm curious, were you able to set up the equipment that enabled you to do the platelet transfusion?

***Emil J Freireich, MD***

**0:10:47.3**

Absolutely. We rented facilities, we had a trailer, and we had a building across the street.

*Tacey Ann Rosolowski, PhD*

**0:10:54.2**

So you replicated what you were doing at NCI?

*Emil J Freireich, MD*

**0:10:56.8**

Absolutely. And we did it quickly. It only took two years—two or three years. And we started a fellowship program. We got a grant to support fellows. We recruited and trained fellows. We trained some of the leaders in the world today.

Well, the important thing is the blood cell separator. I was slaving away at doing all these routine things, nothing original, when we got a call from the guy who managed the project for IBM. He said Perry was a catastrophe. They made no progress in the second year.

*Tacey Ann Rosolowski, PhD*

**0:11:36.6**

And this was in 1966 that you got that call from them?

*Emil J Freireich, MD*

**0:11:10.2**

In '66. IBM decided that after two years of work and making a prototype instrument, that continuing with the NCI was not useful, so they were either going to drop the project or take a bold move. The bold move was they built three machines at the current state of knowledge, gave us one. One went to Seattle, and one went to Buffalo, to Roswell Park. So I had a machine. We were back to the glory days. It was slightly improved over the one that I had rejected. They'd improved the pumps so now they didn't leak.

*Tacey Ann Rosolowski, PhD*

**0:12:39.6**

This was the 2990 model?

*Emil J Freireich, MD*

**0:12:41.5**

Right. They had turned the machine over so that you could look at the thing without a mirror. So they had made some changes, but the machine didn't work. So we started to work on it. We had to build harnesses. Our biggest problem was the seal. See that little valve up there?

*Tacey Ann Rosolowski, PhD*

**0:13:10.5**

Uh-hunh (affirmative).

***Emil J Freireich, MD***

**0:13:11.7**

That was the triumph—that little, teeny valve. What we decided to do—see, the IBM engineers who—Judson himself, he stayed with the project, but he was a very pedestrian engineer. They assigned two really bright, young engineers to the project, and these guys were working with us. They got the idea of putting holes on the face seals and putting saline across the face seals under pressure, and that little pressure gauge told you how much pressure was on the face seals. By doing that, we eliminated the leakage that was occurring regularly, so that made the machine work.

***Tacey Ann Rosolowski, PhD***

**0:14:05.7**

Let me just say for the recorder that Dr. Freireich has this valve mounted in a Plexiglas case in his office. It's about two inches in diameter, a pretty modest little thing.

***Emil J Freireich, MD***

**0:14:20.6**

Yeah, and that's what made it possible. Now we had a way to stop the leakage. We began to work on the machine, and, to make a long story short, of the three machines, we were the one that moved it forward. We started working with CML patients. It was easy to capture the buffy coat. Then we progressively improved it. I was fortunate to have Ken McCredie and Jeane Hester, who were the two geniuses who worked with me. They were really the leaders. Jeane Hester, who is still alive, God bless her. She was tremendously creative. And the two engineers from IBM, very creative guys. And we solved all the problems. We had to get rid of the bolts and screws and we made a disposable path and we made the automated buffy coat finding, had the pumps working and such. So we made the machine, and it became the product that led to the 2997, which was the commercial instrument. And that's the end of the blood cell separator.

***Tacey Ann Rosolowski, PhD***

**0:15:28.5**

Let me ask you a question. I read in another—maybe it was in one of your interviews. I can't remember if it was in an interview or one of the articles that you wrote. You said that it really took use of the machine at MD Anderson to bring it to the attention of the entire medical community.

***Emil J Freireich, MD***

**0:15:46.9**

Oh, absolutely.

***Tacey Ann Rosolowski, PhD***

**0:15:47.8**

I'm wondering what was the difference between having it at NCI?

*Emil J Freireich, MD*

**0:15:53.4**

Well, NCI didn't do anything after they dropped the contract. That was the end of it.

*Tacey Ann Rosolowski, PhD*

**0:15:58.4**

So it wasn't an issue. But if they had, would it have made a difference, if NCI would have perfected it versus MD Anderson perfecting it?

*Emil J Freireich, MD*

**0:16:06.5**

Of course. As I say in the paper, I have a patent on this idea, but I've never made a nickel because it was funded by federal dollars. So the difference is that by being at MD Anderson, we had the freedom to engage plastic companies to make the thing. You don't have the problems when working with the government. We were free—free enterprise. That was an era when IBM was intending to take over the health industry. They had an automated EKG machine, they had the blood cell separator; they were really going to run the health industry in the United States. IBM was big and powerful and successful in computers, and they could do anything. But, as you know, what happened is they got hit by antitrust, and they had to leave the health field. That meant that the blood cell separator development had to go elsewhere. But during the days that we were here, we had the freedom of IBM and their resources. We had Dr. Clark, who was able to protect us so we could do things that most people wouldn't agree to—you know—hooking patients up to the machine, pheresing them, pheresing CML patients then getting normal donors on an instrument that could kill them, giving white cell transfusion that ran radiated. A lot of things had to be undertaken that you can only do in an environment where there is strong leadership, and that's what Clark provided.

*Tacey Ann Rosolowski, PhD*

**0:17:51.8**

You've mentioned some of the other developments that came from the blood separator. I was interested in—there were a few things that you didn't speak about at length in your other interview. There was the development of the peripheral blood stem cell transfusion.

*Emil J Freireich, MD*

**0:18:07.9**

That's very important. I wrote a paper on that, and I think I gave you a copy of it.

*Tacey Ann Rosolowski, PhD*

**0:18:11.8**

Yes, I do have a copy of that.

*Emil J Freireich, MD*

**0:18:13.4**

Ken McCredie is the senior author on a paper in science in which we demonstrated that. Bun McCulloch in Toronto had been a pioneer in growing what he called hematopoietic stem cells. He showed that in a mouse you could get cells which could recapitulate the entire bone marrow environment and make all the white cells and red cells and so on, and these cells could be grown in vitro—in agar—so you could assay for them. McCulloch's conclusion was that the normal stem cells were destroyed by the leukemia so that patients couldn't be cured. We had some debates about that.

But Ken McCredie used the blood cell separator and studied the number of colonies stimulating the number of stem cells in the buffy coats, and in that paper we published in science, he predicted that we could collect enough stem cells to do an allotransplant based on the marrow collections. That paper resulted in an avalanche of development because to collect stem cells from peripheral blood takes two hours on a table with a needle in your arm. To get bone marrow stem cells you have to be hospitalized, you have to get multiple punctures in your hip, so you can't walk for a week, you have to be hospitalized overnight and get blood transfusion to replace the amount of blood that you lost. So why would anyone—? So the fact is that ninety of stem cell transplants are now done with the blood cell separator. That's probably its most important use.

The granulocyte areas stuck in the area of the dose problem. Ken McCredie was the one who developed the hydroxyethyl starch to increase the rouleaux and get the separation up, and then we used etiocholanolone, which was used for treating malaria, to get the white count up in the donors. Then finally, when the growth factors were discovered by Metcalf and people, we were able to use growth colony stimulating factor to mobilize granulocytes and stem cells in the blood, and then it all became easy. So now we could, for the first time, collect enough granulocytes to do white cell transfusion. We published the results on the order of 1,000 transfusions. We showed that, in the right circumstances, about forty percent of people could have their infections controlled.

Then I got fired again. The major reason for this firing was that we had displaced all the normal people from the hospital. Our service was so large and so successful that we had all the trainees. Dr. [Robert C.] Hickey, who was our director—the auditorium—called me to his office and said, "Freireich, every time I want to admit a patient, the hospital is full of all these dying cancer patients." So we had gotten hypertrophied to the point that we were out of balance with the rest of the institution.

We did a lot of things that made us unbearable, all successful. For the surgeons, at the beginning, they were delighted to give us all their dying cancer patients to do chemotherapy, but eventually we began to do chemotherapy instead of surgery, and we filled the house with lymphoma and leukemia and all these diseases, and we didn't have enough beds and all that. So the surgeons hated us. The laboratory medicine people hated us because we did all our own blood counts and bone marrows. We did the blood transfusions. Boy, they hated us. The medical people hated us

because they were doing preoperative histories and routine medical care, taking care of diabetes and hypertension, and they didn't get any patients; they only got consults.

The radiotherapists hated us because we did the first adjuvant chemotherapy studies in breast cancer. The consequence was, instead of getting lumpectomy radiation therapy, we gave them chemotherapy. Dr. Fletcher, who was a very colorful guy—a Frenchman—he's the one who did the first cobalt radiation in the United States. Too bad you can't talk to him. He stood up and said—Dr. Clark met with the department chairman every Monday morning to be sure the ship was afloat—he stood up and said, “Freireich, you're a murderer. You're denying these women radiation.” So the radiation therapists hated us.

When Clark lost his power base and was fired— One of my good friends, Joe Simone, gives a talk, and he says, “Institutions have no memory. The alternative is institutions don't love you. They're just institutions.” So Dr. Clark, for all the vision and creativity and energy he put into it, was fired, as you know.

***Tacey Ann Rosolowski, PhD***

**0:24:20.3**

You actually tell a good deal about it in your other interview.

***Emil J Freireich, MD***

**0:24:25.5**

I think there are others who know more about it than I do, but most of them are no longer here. But he ended up being fired, again, because he was so successful. The other health science centers revolted against the fact that we always got the biggest budget in the health science centers. The other presidents took him on and the politicians, so he lost.

***Tacey Ann Rosolowski, PhD***

**0:24:48.7**

I wonder if I could just ask you a question. From the beginning of my readings about MD Anderson, it seemed that there was always, at least in philosophy, a stress on interdisciplinary care. But on the flip side, when it comes down to the brass tacks of departments interacting or different specialties interacting, it seems to have broken out into these territories. So I'm wondering how you balance that.

*Emil J Freireich, MD*

**0:25:15.3**

Oh, yeah. Well, interdisciplinary care is something new. You see, high-quality care requires practice. It's like playing tennis or golf; you have to learn how to do it the best way. You can have a little bit of innovation, but the important thing is to do it perfectly. Whereas when you're in a research environment, you have to reject the status quo and do things that could be harmful and take chances in order to move the ball forward, so it's an entirely different environment and a different perspective. So as far as multi-disciplinary, it's always been multi-disciplinary. But the one discipline that was not here was medical oncology, because that was a new science. That's what we brought was medical oncology. As a new science, it impinged on the commercial side.

At the first meeting—I may have told this before. It's my favorite story. At the first staff meeting that I attended as a department head, Dr. Clark said, "Surgery cures cancer." And Dr. [Gilbert H.] Fletcher stood up and said, "Dr. Clark, radiotherapy cures cancer." We had just made the claim that we cured Hodgkin's disease, and I said, "Dr. Clark, chemotherapy cures cancer." So that's when multidisciplinary was founded. And as I said, when we started treating adjuvant therapy chemotherapy, the radiotherapists were still giving radiation therapy adjuvant, so we were competing, not integrated. But eventually we became integrated, because studies were done that made it possible. Modern care is multidisciplinary from the beginning because chemotherapy is a discipline, radiation therapy is now a discipline. The machines are much better than any accelerators, the proton machines, and surgery is much better. You can survive much bigger operations, and they do them with laparoscopes now. So now the strategy of treatment must be multidisciplinary, but it didn't at the time.

## **Chapter 4**

### **B: Institutional Change**

#### ***MD Anderson Changes Under Charles LeMaistre: Expansions in Leukemia Research***

### **Story Codes**

C: Portraits

B: MD Anderson History

B: MD Anderson Culture

B: Critical Perspectives on MD Anderson

A: The Researcher

***Tacey Ann Rosolowski, PhD***

**0:27:55.1**

So I see the distinction that you're making. I wanted to ask you one other question about the blood separator and then maybe go on to talk about the breast cancer clinic, because that wasn't something that you spoke much about in your previous interview. But in the paper that you gave me a copy of, the one that's forthcoming in—

***Emil J Freireich, MD***

**0:28:15.6**

No, it's already published.

***Tacey Ann Rosolowski, PhD***

**0:28:16.6**

Oh, it is already published?

***Emil J Freireich, MD***

**0:28:17.4**

Yeah.

***Tacey Ann Rosolowski, PhD***

**0:28:17.7**

Okay. It says that you say that you think the most important use to come for the blood separator is immunotherapy.

***Emil J Freireich, MD***

**0:28:29.5**

You bet.

***Tacey Ann Rosolowski, PhD***

**0:28:30.6**

So could you talk more about that?

***Emil J Freireich, MD***

**0:28:34.4**

The study that I've just completed—well, I was at the point where DT was going to be eliminated. When Dr. Clark got fired, the regents made the—I'm going to be critical of Dr. [Charles "Mickey"] LeMaistre. Dr. LeMaistre and I are good friends. And you can strike all the pejorative stuff. But he was a person who was the inverse of Clark. It's always true that when you replace a despot with 2IC, he's always the inverse.

***Tacey Ann Rosolowski, PhD***

**0:29:19.6**

What's a 2IC?

***Emil J Freireich, MD***

**0:29:21.3**

Second in command. LeMaistre, instead of being decisive and forceful and running the institution, was a manager, i.e. everybody else made decisions; all he did was make sure there was no fire. So when he took over this job, he didn't have any choice. DT was it, and everything else was struggling with us. So on his first day here, he sent a message to the executive committee, the medical staff, all the department chairs, that he wanted them to pick the person that would run the institution, not him, them. And that was his pattern. He was a compromiser and a manger. He eliminated my department. The first move was he hired a guy named Charles Conrad, who was the one who got shot. You'll learn about him. He was a military guy. He ran everything like you run a battle. He was in charge of everything, which means that innovation doesn't exist. Then the second thing he did was he vulcanized our departments. What we had brought to MD Anderson was not only the blood transfusions—the bone marrow—so we had that blood bank, we had pathology, we created an immunology program which didn't exist, we created an infectious disease program, we created a chemotherapy program. They decided that these programs were all too big, so they made them three countries, like they did to Yugoslavia. And they gave me the Department of Hematology. That would have been fine, except I did what I do naturally. Within two years, Hematology was the biggest department in the institution. We occupied all the beds. We had all the grants. We had all the fellows. We had all the patients. We had all the publications. We had the golden age of hematology. We made progress in lymphoma and myeloma and Hodgkin's disease, leukemia, childhood leukemia. Did I tell you I got fired from Pediatrics? That occurred very early. You know that story.

***Tacey Ann Rosolowski, PhD***

**0:32:21.2**

You talk about that, yeah.

***Emil J Freireich, MD***

**0:32:24.6**

I was here a year and a half, and I got fired from Pediatrics.

***Tacey Ann Rosolowski, PhD***

**0:32:30.5**

Could you talk about some of those research areas that you just mentioned? Does that include some of the immunotherapy advances?

***Emil J Freireich, MD***

**0:32:35.9**

Absolutely.

***Tacey Ann Rosolowski, PhD***

**0:32:37.4**

If you could talk about some of that, that would be great.

***Emil J Freireich, MD***

**0:32:38.8**

We brought in the BCG business, which was discovered by Dr. [Charles] Mantoux in France. Dr. Hirsch had a whole immunology program in which he showed that the immune competence was affected by the therapy and the disease, and it was a prognostic factor that would help us decide who was going to respond and who wasn't going to respond. Our pharmacology program, we had drug development. Now we have three departments doing that. We had a Dr. Loo, Chair of Pharmacology. We did all the new drugs that we imported from industry or from our own research went through pharmacodynamic and pharmacological testing. It wasn't just empirical. So we brought all that science with us. LeMaistre vulcanized it, and we were head of Hematology, and Hematology boomed, which was a bad mistake. We had all the money. We got grants. We did the Protected Environment Program. We were booming.

***Tacey Ann Rosolowski, PhD***

**0:33:48.4**

What was the Protected Environment Program? I read about that in one of your other interviews. Could you describe that?

***Emil J Freireich, MD***

**0:33:55.7**

Well, when we were at the Cancer Institute, after the platelets and the white cell transfusion studies, we had realized that it might be possible to make a person germ-free. And in experimental animals, if you take an animal and sterilize them as best you can and put them in this sterile environment and breed them so that the babies are delivered in a sterile environment, then you have a germ-free animal, and germ-free animals can tolerate 100% more chemotherapy than a normal animal, and the reason for that is that they have no organisms to kill them from infection. So we had the idea that white cell transfusions are great, but that's palliative. If we could prevent infection by making a person germ-free, we should be able to eliminate infection complications, so we began to work on what we called life islands. We created bubbles where people lived in a bubble, and the air was filtered, so it was germ-free. Everything that went in was germ-free. We also tried to sterilize the patient by giving him oral, non-absorbable antibiotics, cleaning the skin.

We made considerable progress in that direction at the Cancer Institute. When we came here, we immediately applied for a grant. We were funded, and we bought two life islands. We started to do that research. Dr. Bodey was the leader. Dr. Howe, who was the chief of medicine, who was my main competitor, went to Dr. Clark one day and said, "Freireich is torturing patients." Clark said, "Howe says you're torturing people. You put them in this bubble, and they have to live there without any contact with human beings for two months? This is horrible." But Clark always went with the future.

***Tacey Ann Rosolowski, PhD***

**0:36:35.3**

What were the results of your trials?

***Emil J Freireich, MD***

**0:36:37.4**

Oh, they were very good. We showed that you could reduce infections, not eliminate them. Well, it's very complicated. That's a whole story. You should talk to Dr. Bodey [Oral History Interview]. He's still alive. He'll tell you the whole story. But the problem is that it's impossible to sterilize a person, because we have organisms in places that cannot be eradicated—sinuses, gums; the rectum is a terrible place. Your perianal skin has all these glands that are full of organisms.

So we worked very hard to produce germ-free people. What we could do is get close, but not accomplish the goal. No one has accomplished that goal, in an existing person, to make them germ free. It has not been accomplished, to my knowledge. But we did show that in this protected environment, where the number of organisms to which you are exposed is greatly reduced, we could double the duration of remission because the patient could tolerate a higher dose of chemotherapy and the rate of mortality and infectious complications was half. We have used the protected environment in our hospital continuously for bone marrow transplant, for intensive chemotherapy, ever since we started in 1965, and we have two old nursing units that are protected environments now that we use on a regular basis.

***Tacey Ann Rosolowski, PhD***

**0:38:07.8**

How long did it take before MD Anderson returned to the idea of life islands, after they had told you to desist from that?

***Emil J Freireich, MD***

**0:38:14.7**

Oh, they never told me to desist. Clark always supported us. Howe said we were torturing patients. I went to Clark and showed him the data, he said, fine, continue.

***Tacey Ann Rosolowski, PhD***

**0:38:23.5**

All right. I misunderstood.

***Emil J Freireich, MD***

**0:38:25.9**

In the presence of a strong leader, you can do anything. In the presence of a weak leader, they respond to majority view. They're Obama-like—whatever gets me elected. That's all they care about. Clark was—he decided what he thought was right, and he did what he thought was right.

So anyhow, LeMaistre eliminated DT, and I was in charge of Hematology and made the same mistake again. We got the most grants, we had the most trainees, we had the most papers, we got the most patients, we filled the hospital, and they had to eliminate me as head of Hematology. So they gave me this Mickey Mouse title, Director of Adult Leukemia. It means nothing. They recruited a guy named Al Deisseroth. Deisseroth was kind of like Perry. He's still around. He works for the FDA. He's a nice man, hard worker, but just no talent. So the major thing Deisseroth did was he hired a guy named Michael Andreeff, who is still here. You might want to talk to him. He's very colorful. But Michael Andreeff came from Memorial Sloan-Kettering. There was a patient at Memorial Sloan-Kettering who got some kind of a disease and they called it Transfusion-Associated Graft-versus-Host Disease. The idea is that when you give these white cell transfusions, the immune cells attack host cells, and that results in myelodysplasia and it kills the patient. That happens when you get a bone marrow transplant. When you get a bone marrow transplant, you eliminate your immune system and you put in the donor's immune system and you get Graft-versus-Host disease, and that destroys your liver, the skin, the bowel. You get sick, and it kills people.

So these patients with leukemia who got white cell transfusions got sick, and someone said they got Graft-versus-Host disease, so they made a rule that at MD Anderson—it was in our bylaws—you had to radiate all the white cells. So from that point forward, the white cell transfusion project was stalled because when you radiate these white cells, you kill the stem cells, you kill all the immune-competent cells, you kill all the monocytes and macrophages, so you're left with fifty percent functional polys—not very effective. So if you combine radiation with the dose problem, that is the most we could get was fifty billion cells—you needed 100 billion—white cells fell into disrepute, and they're still in disrepute, but they found these peripheral uses for stem cells, but not for granulocytes.

We just completed a study, which I reported in Dubrovnik at our annual meeting of the Leukemia & Lymphoma Society, where we're trying to reinstate granulocyte transfusions that have not been radiated. We want to have the donor immune system react against the tumor, just like it does in the transplant situation—the so-called Graft-versus-Leukemia effect without Graft-versus-Host effect. And that's my current love.

So we just finished this study, and we treated 100 people in a randomized study, comparing radiated and non-radiated white cells, and it was marginally successful. We showed that the increments were better, the survival time was better, but it did not improve the response rate, and it did not improve survival. But that's the direction we're moving in. We're trying to get back to unirradiated white cells.

***Tacey Ann Rosolowski, PhD***

**0:42:37.6**

So what are you going to do next with these to improve the response?

***Emil J Freireich, MD***

**0:42:45.2**

Very good question. We're going to do what we did with the platelets. We started a study where we give white cells when you have no white cells, not when you have infection. By the time you have infection, the doses we give are too small to overcome the infection, and, secondly, because there was no inflammatory response, the infection destroys the tissues so that when you initiate the inflammatory response, it's too violent and the patients actually do get sick. So we're going to try to move to what we call prophylactic transfusion, like we did with platelets, like you do with red cells. When your blood count is low you get red cells. When your platelets are low you get platelets. That way you eliminate anemia, eliminate thrombocytopenia. We're going to try to do the same thing with the white cells. We're going to try to transfuse white cells when the white count is low and the patients do not have infection and see if we can prevent infection and prolong survival and response rate.

And there actually was a group of physicians in Beijing, China, at the military hospital in China, who have actually done this. They've interspersed granulocyte transfusion with chemotherapy, and they've demonstrated—it hasn't been confirmed yet, but in their paper they've demonstrated that you can prolong survival and improve response rate, so we're heading back in the direction of immunotherapy.

Of course, you'd like to do it in a sophisticated way. We'd like to be able to separate the immune cells from the neutrophils from the lymphocytes from the T-cells. That's going to take a lot of work.

*Tacey Ann Rosolowski, PhD*

**0:44:36.3**

What's involved with that?

*Emil J Freireich, MD*

**0:44:37.6**

Well, we're going to have to learn to separate, identify, expand in vitro. That's the secret to granulocyte transfusion. We're going to have to learn to get the stem cells to expand in vitro and have effective effector cells to do the anti-leukemia work for us. So that's what I'm working on now full time.

*Tacey Ann Rosolowski, PhD*

**0:45:02.0**

How long have you been doing that work?

*Emil J Freireich, MD*

**0:45:03.8**

It's continuous, ever since I was born—ever since we started on the blood cell separator. The goal was to eliminate infection. That's why we did the whole thing. Infection is still the number-one cause of morbidity and mortality in all cancers, because once you try to treat the cancer with a drug, it automatically—it's the specificity that matters. So the side effect is to suppress the normal hematopoietic cells and the normal immune cells. That's what limits chemotherapy. So if you have glioblastoma and you're getting chemotherapy to stop the glioblastoma, you're also damaging the bone marrow. Then you get infection and that limits the amount of chemotherapy, and that lets the cancer get away from you. So if we can do what we did with platelets and control infection—prevent it—I think we'll cure a lot more cancers.

## **Chapter 5**

### **A: The Researcher**

#### ***New Chemotherapy Treatments for Breast Cancer and Cultural Challenges to Research Innovation***

### **Story Codes**

A: Character, Values, Beliefs, Talents

A: Professional Values, Ethics, Purpose

D: On Research and Researchers

D: On Leadership

C: Discovery, Creativity and Innovation

C: Patients

C: Cancer and Disease

C: Discovery and Success

B: Critical Perspectives on MD Anderson

***Tacey Ann Rosolowski, PhD***

**0:46:11.9**

We've been talking for about two hours now, would you like to stop for today?

***Emil J Freireich, MD***

**0:46:16.5**

I have a noon meeting, but other than that I have no problem except my voice giving out. But your patience is probably giving out.

***Tacey Ann Rosolowski, PhD***

**0:46:24.04**

No. I'm good, if you want.

***Emil J Freireich, MD***

**0:46:26.2**

And I may have to transfer more money in the bank, if my wife calls.

***Tacey Ann Rosolowski, PhD***

**0:46:32.3**

Well, if your voice is going to hold out, let me ask you one more question, and then we can stop for today, because I will be coming back tomorrow as well. I wanted to ask you about the breast cancer clinic. That was something that was started up here at MD Anderson. The last time you were interviewed, you didn't speak very much about that. So these were the chemotherapy trials that were being discussed. I wonder if you could talk more about that.

***Emil J Freireich, MD***

**0:47:05.7**

Do you read *National Review*?

***Tacey Ann Rosolowski, PhD***

**0:47:14.8**

No, I don't.

***Emil J Freireich, MD***

**0:47:16.3**

There's a good article in *National Review* this last week about innovation. Our country is going through a—you know—when people are well-off, they want to protect their wealth. America is well-off. We're going into a dark ages, as you know, not only our economy but our whole philosophy. All the innovation in the world is going on in the third world—the Japanese, the Chinese, the Indians. The Americans, we're sitting on our fortunes. We want to control what we've got, so we're getting hardening of the arteries. The ultimate expression of it is this president who is trying to make us like Europe, totally socialist. In a socialist state, you can't tolerate anything new because you have the perfect system. So if you have the perfect system—socialism, where everything is free and run by the government—you don't need innovation. Innovation is a threat to the status quo. So innovation occurs during periods of great stress, like after the war. That's when NIH was created. In the post-war area was when we expanded and got all the marvelous new things.

America is going through this awful phase of hardening of the arteries. We're totally obsessed with safety. We ruined our economy because we're worried about clean air, so we can't drill for oil. We have to import it from Saudi Arabia for billions of dollars. We can't manufacture anything because it contaminates the air. We can't develop drugs because they're potentially dangerous. We're totally in a regressive mode. We have to save what we've got. Hug the trees. Save the trees. Don't build new trees; save the trees. Clean the environment. Don't use energy. Don't waste it. What does Obama say? Get your engine tuned up. Put air in your tires.

Do you remember when—? The previous Obama was a guy name Carter. When the Arabs raised the price of oil, Jimmy Carter said, "We're going to run out of oil. There's only so much oil." He forgot that there was no oil before Spindletop was discovered one hundred years ago.

People who have hardened arteries have no—I have a little slide I show. When you ask people what's going to happen in the future, the liberal will say, "Everything is going to be just like it is now—perfect," but the science writer is going to say, "Wait a minute. We'll be going to the moon. We'll have planets. We're going to have people replacing themselves and living forever. We can do anything." There's a big conflict of cultures, and in medicine it is horrible.

The federal government, through the FDA, has become so oppressive that the possibility of Americans discovering anything new is becoming progressively unlikely. You read about it in the papers all the time. It doesn't take a genius to think that if you put 10,000 people in a five-billion dollar building in Rockville, Maryland, and you give them guaranteed wages and a retirement program that after twenty years you retire and a better salary than the average American citizen, for life, they're going to do their job. Their job is safety.

Last night I was watching the EPA lady testify before Congress. You can't have fat in the food. You can't have sugar. We're going to have a law against McDonald's and God knows what else. But the FDA guys, with all this money, their careers depend on nothing ever going wrong. So I've got a drug that can cure cancer, right. I give a talk on this. I'm sure it will cure cancer. I have to apply to the FDA. They say, "Wow, if this drug cures cancer, it won't do me a damn bit of good. But what if one person in a thousand dies of a stroke? I'll be fired." Forget it.

The government is in a position where any innovation is too dangerous to undertake. So the answer is do nothing—status quo—USA 2011. It's a sad thing, because we were the world leader in science and technology and innovation. Now, we're totally out of it. Americans buy BMWs, not General Motors. They went broke. Americans throw away their light bulbs and we have to use these little mercury things and kill ourselves with mercury. Everything is status quo.

***Tacey Ann Rosolowski, PhD***

**0:53:35.0**

But the context was different when you were working with the breast cancer issues and the chemotherapy for that?

***Emil J Freireich, MD***

**0:53:42.6**

Sure.

***Tacey Ann Rosolowski, PhD***

**0:53:43.3**

So how was that different? What were you doing?

***Emil J Freireich, MD***

**0:53:45.7**

Well, that occurred at a time— Do you know how the FDA got worked out today? It always occurs in crisis. I wrote a paper—I'll give you a reprint of it—it's called *Freireich's Laws*. One of Freireich's Laws is success breeds enormous problems. Failure is no problem. And that's the thing; we live in a world where everybody's happy, like Europe. If you only work four days a week and you get three months vacation and everybody's happy and the country is going to the dogs and nothing is happening, fine. Well, anyway, we'll get to innovation.

Breast Cancer patients are dying. Ruth Harriet Ainsworth was a breast cancer patient. In the post-war period, America was NIH, all of America was NIH. The auto industry was booming, atomic energy was booming, the petroleum industry, petrochemicals, plastics, everything was booming. The Japanese had the American culture, as you know. One of the geniuses in Japan was a guy named Hamao Umezawa. Umezawa worked for the pharmaceutical industry, and he discovered that organisms made compounds which could kill bacteria. He became the godfather of antibiotic therapy. The Japanese developed the antibiotic industry under Umezawa's leadership. He discovered several of the antibiotics we now use today, but he made another amazing discovery. He discovered a drug called bleomycin. Bleomycin is a natural product which consists of about nine amino acids. If you purify it down to eight or seven or two, it doesn't work, but if you put the nine, it works.

So I was in my famous NIH phase, and I got to go to Japan. I met Umezawa, and he told me about bleomycin. I said, wow, we have to have it in the US. You can't use it in the US because it might hurt somebody. So you have to spend two decades killing innocent horses, cows, pigs, mice, guinea pigs, rats, plants, anything. Just keep busy, but don't give it to people—FDA. Clark—wait a minute, the Japanese have treated a thousand Japanese. Oh, we do not accept foreign data. We have to kill Americans. Clark got FDA to relinquish the role that they would not accept foreign data and insisted that they accept the Japanese data, and we have bleomycin. Bleomycin was one of the drugs that cured testicular cancer, as you know. It was working, so we were on a roll. We had a new agent that worked, and we had Clark.

Along came Farmitalia in Italy. The Italians, in the post-war era, were like the Japanese. They acquired the American macho, and their drug industry discovered a drug called doxorubicin. It was simultaneously discovered by the French. These drugs are called anthracyclines, and they had extraordinary activity in a number of tumors, particularly leukemia and lymphoma. The guy sitting right behind you, see that picture? The one with the red tie is Gianni Bonadonna, and Gianni Bonadonna was working in Milan. He cooperated with Farmitalia, and he got this drug, Adriamycin, which was read. He studied patients with breast cancer. He thought it worked, so he called us and said we should study Adriamycin. You've got to kill monkeys, dogs, horses. Wait a minute. Bonadonna had treated 500 women—Italian women. We don't accept—wait a minute. Bleomycin—you accepted Japanese. Okay, you can use Adriamycin. We did the first Adriamycin clinical trials in America. Ruth Ainsworth was one of the first fifteen people to get Adriamycin. And it turned out that Adriamycin is still the most important single drug for treating breast cancer.

*Tacey Ann Rosolowski, PhD*

**1:00:03.3**

Could you describe the trials that you did with that?

*Emil J Freireich, MD*

**1:00:09.4**

Those were the days when we didn't have to worry. Dr. Clark was there. We just gave it to women with breast cancer, and we got sixty percent objective responses and that was it.

*Tacey Ann Rosolowski, PhD*

**1:00:20.8**

What stage of breast cancer?

*Emil J Freireich, MD*

**1:00:23.2**

All metastatic. They all had to have measurable disease. But then, as you already intuited, we got the same idea we got with infections. What if we gave Adriamycin to women who were poor prognosis that might get metastasis? That was the advent of Adriamycin, which is still practiced today. Adriamycin, as you know, has unpleasant side effects. They lose their hair. For women, that's a bad thing. It also has cardiotoxicity. We had to learn to limit the dose. We did all that. One of our fellows, Jeff Gottlieb, worked that out. Daniel Von Hoff published it. So that's a classic picture up there. That occurred at a meeting of the AACR. Paul Carbone died suddenly on a golf course. He's the one who worked with us at the Cancer Institute, and he developed the CMF. He's the big guy. Joe Burchenal is the guy who developed 6-MP with Hitchings and Elion and Gianni Bonadonna. He's the guy who did all the anthracycline work.

*Tacey Ann Rosolowski, PhD*

**1:01:28.2**

And who are the other two?

*Emil J Freireich, MD*

**1:01:28.8**

He's still alive. He had a stroke and was out of work for about five years. Now he's kind of coming back, but will never be the same. He's badly disabled.

*Tacey Ann Rosolowski, PhD*

**1:01:40.1**

Who is the other gentleman in the photo?

*Emil J Freireich, MD*

**1:01:41.9**

Me.

*Tacey Ann Rosolowski, PhD*

**1:01:42.7**

That's you?

*Emil J Freireich, MD*

**1:01:43.7**

Yeah.

*Tacey Ann Rosolowski, PhD*

**1:01:44.7**

I didn't recognize you.

*Emil J Freireich, MD*

**1:01:45.9**

Much younger. I'm the one with the dark tie and the glasses.

*Tacey Ann Rosolowski, PhD*

**1:01:50.1**

Wow! I recognize the grin now.

*Emil J Freireich, MD*

**1:02:01.0**

So that's how adjuvant therapy started. Ruth Ainsworth was a very modest lady, school teacher, widow. Her husband died about ten years before. She lived very modestly, dressed very modestly. She had a very good remission. It lasted about a year and a half. When she relapsed, we treated her again but failed and she died. Then about six months later I get a call from this lawyer. She had us in her will. What's in her will, \$100? It turned out her husband had bought some chip stocks. She didn't know anything about them, and her estate was millions. I've forgotten what the exact figure was, but we got a big pot of money—millions. For me, that was wonderful, because we could build our department. I could hire more faculty and staff. I could buy more platelets. But Mickey—if I sound disdainful—he and I were very good friends; it's just that we had totally different views of the world.

I went to LeMaistre and I said, "That's wonderful. I want to have this for DT." He wanted to make himself famous. The way to do that was create these endowed chairs. We have about 100 endowed chairs, so instead of having a hundred million dollars to make the department great so it can make another hundred million dollars, you put it in the bank and you get five percent and it's useless. So if you look at all those endowed chairs up there, it's a big waste of money. We've got billions of dollars in the bank earning five percent that who cares about it? We should use that money to build the institution.

*Tacey Ann Rosolowski, PhD*

**1:04:14.5**

Well, why don't we finish up for today, and we can resume tomorrow?

*Emil J Freireich, MD*

**1:04:22.3**

Absolutely. So we made an endowed chair. This was the second endowed chair at MD Anderson—Ruth Harriet Ainsworth. I get ten or twenty thousand dollars a year, something like that. It's a big waste of money.

*Tacey Ann Rosolowski, PhD*

**1:04:41.2**

A nice memory for her, though.

*Emil J Freireich, MD*

**1:04:43.9**

Well, we could put the plaque up there. I could wear the coat. I don't care, but spend the money. What the heck? When you put money in the bank, the only one that benefits is the bank, not the institution. We should use the money to build structure that creates money. We create wealth by doing a good job in medicine and attracting patients and attracting industry and attracting drugs, curing cancer. That's our job, not endowing the banks. That's their problem. They can get the money elsewhere.

*Tacey Ann Rosolowski, PhD*

**1:05:20.4**

Well, why don't we finish up for today, and we can resume tomorrow.

*Emil J Freireich, MD*

**1:05:22.5**

Gladly.

*Tacey Ann Rosolowski, PhD*

**1:05:23.4**

Okay. Thank you very much.

Interview Session: 01

Interview Date: October 5, 2011

*Emil J Freireich, MD*

**1:05:25.5**

So we may have worn you out forever.

*Tacey Ann Rosolowski, PhD*

**1:05:27.5**

No.

**1:05:28.6** (end of audio file two)

**1:05:28.6** (End of Audio Session One)

## **Emil Freireich, MD**

Interview Session 2 — October 6, 2011

### ***Chapter 00B*** **Interview Identifier**

*Tacey Ann Rosolowski, PhD*

**0:00:02.1**

This is Tacey A. Rosolowski, interviewing Emil J Freireich, MD. This is the second session on October 6, 2011. The time is about 9:10.

Interview Session: 02

Interview Date: - October 6, 2011

## **Chapter 6**

### **B: MD Anderson Past**

#### ***A Commitment to Training and Education: A Failed Battle to Bring a Medical School to MD Anderson***

### **Story Codes**

A: Personal Background

A: Professional Path

A: The Educator

B: Education

B: MD Anderson History

C: Understanding the Institution

B: Building/Transforming the Institution

D: Understanding Cancer, the History of Science, Cancer Research

D: The History of Health Care, Patient Care

C: Portraits

C: Leadership

C: Obstacles, Challenges

C: Controversies

### ***Tacey Ann Rosolowski, PhD***

**0:00:02.1+**

So I wanted to ask you just a couple of followup questions, after the conversation yesterday about your research. Part of it is just my own curiosity. You said in the interview that you did in 2001 that it was kind of unexpected that you ended up going into hematology. It was kind of really a circuitous path. I'm wondering if you felt that coming as you did—from the side, in an unusual path—helped you be innovative in that field.

### ***Emil J Freireich, MD***

**0:00:59.9**

Well, sure. As I've told you, you've read my background. Ever since I was a young man I always wanted to be a family doctor, like my idol, the family doctor. But as my training went along, I kept getting fired from every job for the same reason—I always did more than I was supposed to do. So I had an internship at Cook County Hospital. I got fired because I got into a controversy over patient care with a nurse. Then I went to internal medicine because I figured that I had learned all the surgical techniques and OB and all that, and I didn't know much about medicine. It was very complicated. So I took a year of medicine. My professor, who I adored, got fired and asked me what I didn't know a lot about, and I said hematology. We had a terrible hematology

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professor. So he said, “Go to Boston.” So that was the beginning of a transition from a practice-oriented career to a research-oriented career. The new academic research environment was created in Boston in the ‘60s and ‘50s.

So when I got there, I was offered jobs in hematology, but the one that I was forced to take was the only one that paid. In those days, trainees all came from well-to-do families and didn’t need money, so they worked for free. But Dr. [Merrick] Ross at Massachusetts Memorial had a grant to study iron deficiency, so instead of learning hematology as a general discipline, I was thrown into an academic situation where I had to do research, so that was the beginning of my research career. Then, as I’ve emphasized in previous interviews, just because the dean at Boston University was the first assistant secretary of health in the country, and just because the NIH opened in ‘64 and I got drafted in ‘64, Dr. [Chester Scott] Keefer recruited me to go to the NIH in ‘65. So there I was in a research job, taking care of children with leukemia. Remind me of the question again.

***Tacey Ann Rosolowski, PhD***

**0:03:50.4**

I was just curious about the way that—I mean—oftentimes when people are thinking about how an individual’s career has become very successful and why they’ve been so innovative, it turns out that very innovative people often come to a field from outside that field, so they bring a broader perspective or a different way of approaching problems. So I was just curious to what degree you found that the case in your own career.

***Emil J Freireich, MD***

**0:04:18.8**

Well, my career was a natural flow. I was never in a position to make any decisions; they were all made for me. When I found myself in the Clinical Center of the NIH, there we were with all these dying children. You had to do something about it. It’s important to recall that when I graduated from medical school in 1949, the undergraduate career in medicine included nothing about cancer. In our pathology, we learned a little bit about how the pathology of cancer looked, but there was no such thing as treatment. There was no such thing as natural history or diagnosis, so from a medical point of view, we knew nothing about cancer. We didn’t know it existed.

As you know, the first inkling of treatment for cancer came out of the Second World War with nitrogen mustard in ‘44—Dr. Farber—’48—6MP—’49. When I went to the Clinical Center, the concept of treating cancer was really a whole new thing. As I pointed out in previous conversations, since Dr. Zubrod inspired us to do formal clinical trials, we began to convert the knowledge about the natural history of leukemia into quantitative data so we knew how many children died and how often, what the complications were. We discovered meningeal leukemia and how to treat it, so we just had to learn quantitatively about the disease. Are we done with that? Because I want to get back to education.

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***Tacey Ann Rosolowski, PhD***

**0:06:13.0**

Yeah, let's go on to that.

***Emil J Freireich, MD***

**0:06:17.6**

Well, I think in my career the things I'm famous for are patient care and research, but the third leg of the academic stool is education. Education was always a part of my research career. When we went to the Clinical Center, under leadership of Dr. Frei and Dr. Zubrod, we had all these young physicians who had no talents in research who were recruited to the Clinical Center largely because of their military obligation. The Clinical Center was staffed with physicians who were drafted but weren't activated by the Navy, Air Force, and so on. The people who needed them were the Public Health Service, so they recruited all these young, bright physicians usually referred by the chairs of their department as promising, young, intelligent, potentially research oriented doctors.

In my lectures—you mentioned the things I do now—in the lectures I do now, I give a lecture on the origin of science in the United States. As you know, our medicine was based largely on European medicine. In the '40s and '50s, the physicians who were academic were all trained in Europe. The American science began, really, during my lifetime. It's a new thing for this country. Really, the turn of the century is when the Flexner Report and all that stuff—

When we were at the Clinical Center and we had all these young, intelligent physicians, Dr. Zubrod and Dr. Frei and I recognized that there needed to be a formal training program in oncology. There was no oncology discipline. We were just thrown into the Cancer Institute with all these cancer patients, so the young physician scientists who came to spend their two-year military service at the Clinical Center—ninety-plus percent of them ended up in academia because the environment was so academic. That is, the backbone of what we did was create a teaching program for these trainees so that after two years they were oncologists, although the word didn't exist at the time. So really the first formal training program in cancer began at the Clinical Center. The other academic institutions in the country all recognized the power of what had happened in Bethesda.

***Tacey Ann Rosolowski, PhD***

**0:09:33.1**

Can you tell me what was involved in that first program? What were the courses offered?

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***Emil J Freireich, MD***

**0:09:37.8**

Well, we didn't have courses, they learned by doing. They rotated through my service and learned about who came in and how to treat it and how to classify it and natural history and how to do randomized trials. They rotated through the solid tumor service. They learned how to take care of breast cancer, colon cancer. So we had a complete medical oncology program, and the fact that they rotated became a training program. They had a formal, systematic exposure to all the diseases in a setting where the physicians were scientists and not treating but observing and recording and studying the natural history of these diseases.

I'll come back to that—when I came to MD Anderson—because the environment we created was totally unique, and where it was going at the moment was the rest of the academic medical centers in the country were all created on the basis that academics had three legs of the stool—patient care, research, and education. When the Clinical Center opened, there were no students—there were no medical students—there were no interns, there were no residents. And I recall, in my first year there, my job was to recruit patients, so I traveled to the academic medical centers in the D.C. area. I went to Hopkins and G.W. and Georgetown and all those places to tell them that we were doing research. We were treating children with leukemia. We were trying to figure out how to cure them. The comments I got from the senior—in 1965, I was thirty-eight years old. The professors were sixty-five, and they all came from the old school.

I remember, particularly at Hopkins, Dr.—I forgot his name. He was a very famous physician, one of the founders of the Association of American Physicians. But he got up and he said, “It's ridiculous to have an institution where the physicians do patient care and research and no teaching.” The stool is broken. But having a full-time research career was so productive. Then in the period from '65 to '75, academic medicine in the United States was totally transformed. All the medical schools developed academic clinical research programs, and they realized we had something with this teaching. So by 1964, the universities created a board exam in medical oncology patterned after this program that began at the NCI. So the point I'm making is that although we didn't teach undergraduates, graduated medical education was a component of my career from day one.

***Tacey Ann Rosolowski, PhD***

**0:13:13.3**

I was curious about how long it took you to recruit a critical mass of students from these other institutions.

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***Emil J Freireich, MD***

**0:13:20.6**

Oh, they came automatically. They were all in the Army, Navy—they all had commissions in the military, and their professors, like my professor, were contacted by Zubrod, Frei, or me. We went around and we told them there was an opportunity for these people to serve their—we called them Green Berets, because they could serve their military time in a peaceful situation rather than go fight in Korea, so it attracted the best and the brightest. The clinical associates that came to our hospital were the backbone of our research program. These guys were—they all became giants—[Dr. Vincent] DeVita; [Dr. George] Canellos; David Nathan, who won a Nobel Prize for his work at Hopkins; the guy at Children’s Hospital who just got the AAP Kober Medal. All these people became the scientific leaders in the academic medical centers around the world. Two years the NCI converted them not only into oncologists but academic oncologists. So all the universities were populated with the graduates, and all the universities began to mimic that. They had their own training programs, and then finally they realized that, like gastroenterology and cardiology, oncology was a specialty, and the specialty exam was created in ’64.

***Tacey Ann Rosolowski, PhD***

**0:14:56.9**

I’m starting to see why you said that that period between 1955 and 1965 transformed—

***Emil J Freireich, MD***

**0:15:03.0**

It was the golden age of medicine. It transformed all the specialties. What happened in oncology happened in cardiology. All the open heart surgery began at the Cancer Institute. It happened in neurosciences. All the studies of senile dementia—these were all people working around me. They were all like me—forty-year-old guys, fresh out of school, eager beavers in a candy shop. They had everything. They had patients, they had time, they had no responsibility. They did the research. They controlled their practice. They didn’t have a service obligation, that’s the main thing. I didn’t have to see people dying with sickle cell anemia. I just saw leukemia patients. The guys who did neuroscience only saw multiple sclerosis patients.

The secret to clinical research is to be able to control your service work, to manage your research as part of your service. That’s what MD Anderson—you hear Dr. [John] Mendelsohn [Oral History Interview] say, “Our patient care is research driven.” That’s what was discovered in the Clinical Center of the NIH. They discovered that the best patient care is research. The patients in research had the best chance of getting the best care.

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Training was a part of my career from day one. One of the reasons I came to MD Anderson—when Dr. Clark tried to recruit me, I had a job offer to go to University of Toronto, I had a job offer to go to Children’s Hospital, Harvard, in Boston. I could have gone anywhere, but the thing that Clark said that impressed me—I loved Dr. Clark. I hated him because he tortured me and fired me, but I loved him because of his vision of the future. He was a person—you know—when he took the job as director of MD Anderson, Houston was a backwater. The population was 200,000. They still had malaria. It was a very primitive community. But he saw the potential. He saw the oil industry. He felt immediately that Houston was going to be the biggest city in Texas, and when he recruited people, that’s what he told you. He said, “Houston is nothing, but it’s going to be the best, because we have everything. We have money, we have industry, we have culture, we have the water, and we have the climate. Houston is going to be the town.”

When I was thinking about coming here, he met with me and he said—you know—he was very impressed, as was everybody in the world, in what was going on at the Clinical Center. He said, “You know, the one thing the Clinical Center lacked was undergraduate education.” We had graduate medical education, but no undergraduate education. Dr. Clark, when he got a cancer center, he didn’t want it to be a cancer hospital, like Mayo Clinic. The first thing he did was negotiate with the University of Texas. The university—this is an academic institution. It’s not going to be like a TB hospital where people come to die. That was what the legislators wanted. The legislators conceived this place as a place like a TB hospital where you send dying cancer patients, get them off the street, get them out of their homes, put them in this place where they die. Not Dr. Clark. He was a surgeon. “We’re going to treat them.” And to do that, the very first thing he did, when he recruited colleagues from the military—you know—Dr. White to do surgery, Dr. Howe to do medicine—he recruited the backbone. The very first thing he did was recruit a basic scientist. He wanted to have research.

MD Anderson started off as a place with practitioners, not academic. They were all just doing their job, but he recruited basic scientists. He recruited Felix Haas from Galveston. They had three or four PhDs who began the research backbone of the hospital. And he insisted throughout that we be an academic—not a patient care—but an academic institution.

The very first idea he had was the basic scientists had to have post docs and undergraduates, but there’s no university. So they recruited post docs from other graduate programs around the country who came here to learn with the PhD’s working in the cancer hospital. But the post docs didn’t have any undergraduates who wanted to come, so Dr. Clark went to the university and said, “We have to have a graduate school.” Our graduate students had to drive to Austin to take their orals and their final exams. He said, “No. We have to have graduate school.” So the very first thing he did—we’re going to come to that when we talk about the PSTP—is it wasn’t just MD Anderson; it was MD Anderson’s Graduate School of Biomedical Science. And, God bless them, Dr. Grant Taylor, the head of Pediatrics was the first dean of the graduate school.

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When I came here in 1965, they recruited Alfred Leon Knudson, who is an absolute genius. He's a Nobel Laureate class scientist—physician-scientist. He was the dean of the graduate school. I am the longest serving full member of the graduate school. I don't have a graduate degree, but Dr. Clark felt I was qualified, and Dr. Taylor, and I became—I am still the longest-serving member of our graduate school—full member—and I don't have a PhD. But I'm better than all the PhDs.

After he got the graduate school, he convinced the regents that we had to have a health science center like there was in Galveston, like there was in Dallas, because he knew Houston was going to be the biggest city in Texas, and they had to have a medical school. So he convinced them to have the public health school. It's still there.

So when he was recruiting us—Frei and Freireich—he was chair of a committee of deans. There was the dean of MD Anderson—that was him—the dean of the graduate school—one of his employees—the dean of the public health school that he had recruited. Oh, and he also created a School of Allied Health, which is Ahearn [Michael Ahearn, MD ophp]. What was lacking was a medical school. So when he recruited us, I remember him telling me, "Freireich, we need to have a medical school," and it still doesn't exist today. Now you're talking 1965, so that's forty-six years ago. We need to have a medical school where the faculty is physician-scientists, where the first-year students who learn anatomy, physiology, and biochemistry learn it from working physician-scientists, so that all their knowledge is scientific. And when they get to the clinic, they're not going to go to Kelsey-Seybold and follow a doctor around; they're going to learn from professors who really know what they're doing—Freireichs who teach leukemia and DeVitas who teach Hodgkin's.

His vision was never realized, and one of the greatest frustrations in Dr. Clark's life was that when it came to the medical school, when he recruited us, he had already convinced the governing board of the Texas university system—I don't know what it's called, the Texas governing council for the university—that a medical school had to be in Houston. That was already approved. The medical school was coming. It was going to be staffed with outstanding physicians, and it's going to have not only cancer institute and heart institute and blood, everything was going to be research oriented in our academic medical center. Great triumph. I signed on immediately. That appealed to me enormously.

What happened, between the time I resigned my commission and I came here, Dr. Frei was fired, my department was eliminated, and he lost the medical school. It's complicated how it happened, but part of it was the war—Vietnam. That froze all construction. So although he had the money to build the Lutheran Pavilion, he couldn't do it. So although we were promised a whole ward with protected environment and beds, we had nothing but this little teeny lab because we didn't have a hospital. The research institute wasn't finished. We had no lab space. A big part of it was, as I mentioned before, political. That is, once the ball stopped rolling, at the same time the Supreme Court passed the one-man-one-vote thing—because all of west Texas was all Hispanic

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people and they didn't vote—but when the Supreme Court judged, then they got the vote, and the regents overruled the governing board of the medical center and moved our medical school to San Antonio. San Antonio got our medical school.

So our first year was no labs, no building, no money, no medical school. And then as we came out of the war and we began to get more money and we built our program, it was time for the medical school. Clark put his career on the line for that. He wanted a health science center in Houston. But the presidents in Galveston, particularly— See, what was happening is Galveston was the flagship health science center because of the Sealy money. Even though it was totally destroyed in a hurricane, they were still rebuilding it. They can't give it up because the Sealy money is put there and it can't be used for anything else, so you have to have Galveston. But Galveston was the flagship, and when Southwestern became University of Texas and grew in academic stature, that was a threat to Galveston, but they're 300 miles away. But Houston, that's fifty miles upstream, and the flow of patients and academics and grants and everything was flowing into Houston. The major opponent we had was Truman Blocker, who was the president at Galveston. The presidents at Southwestern and in San Antonio—all the university presidents—feared a medical school in Houston. And under Clark—they knew a medical school was coming, but not under Clark, because it was Clark—this would have been the greatest medical center in the country in a decade.

Dr. Clark's right-hand man was named Dr. Morton. Do you know Dr. Morton—Robert Morton? He was a radiotherapist, and he was Dr. Clark's political arm. He dealt with the regents. He made sure that we got all the money. When the medical school was denied to Clark, they not only gave him the medical school, they took the graduate school, the public health school, and the school of nursing away from MD Anderson and made a health science center—which is what they wanted—but they wouldn't give it to Clark. So what they did, because of his seniority, is they carved MD Anderson out of the health science center, and it didn't take very long for them to fire Dr. Clark. He totally lost his political capital in that battle—the battle with the other regents. As Clark was fired, Truman Blocker had retired as chancellor of the Galveston Health Science Center. They appointed him acting head of our health science center in Houston until they recruited a real one. At the first speech he made where I was present in the room, Dr. [Truman] Blocker said, "We're going to incorporate MD Anderson into the health science center."

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You see, there are only two institutions that own their hospital—Galveston, which is hopeless and will never be a major center because of geography, and MD Anderson. The other health science centers all have to use community hospitals. San Antonio has a county hospital, and Dallas has a county hospital. Tragically, our medical school doesn't have a county hospital. It has Hermann Hospital, a private hospital. What's going to happen to our medical school is what happened to Baylor. They're never going to make that an academic medical center. If you don't control your hospital, the financial pressures make it impossible to run the medical school. Ninety percent of your income comes from patient care, so if Hermann Hospital controls ninety percent of the budget, what does the president of the medical school control? Nothing, a few grants. So what happened to Baylor will happen to our medical school. It's never going to succeed. Hermann Hospital's interests are totally contravening to the medical school's interest. So Clark lost the battle. It was within a year that he was fired and they brought in Mickey [Dr. Charles A. LeMaistre [Oral History Interview]] with a search committee and all that stuff.

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## **Chapter 7**

### **B: Building the Institution**

#### ***Building the “Best Graduate Medical Education Program in the Country***

### **Story Codes**

A: Personal Background

A: Professional Path

A: The Educator

B: Education

B: MD Anderson History

B: Building/Transforming the Institution

***Tacey Ann Rosolowski, PhD***

**0:30:53.9**

Would you tell me about what happened to—?

***Emil J Freireich, MD***

**0:30:55.1**

I'm getting to education now. Go ahead. I can get back to it.

***Tacey Ann Rosolowski, PhD***

**0:31:00.0**

I was interested in how that educational leg of the stool got put back.

***Emil J Freireich, MD***

**0:31:07.7**

Well, that's the thing. So the medical school started with this ad interim dean, and then they hired the guy from the space program. I can't remember his name. He was hopelessly incompetent, and he had to start a medical school. A private hospital, a couple of rooms, and the only faculty they had was MD Anderson, so all of us became professors at the medical school. I was head of my oncology. Joel Moake was head of hematology. They recruited him. We were very close friends. We worked together.

So the medical school began with MD Anderson faculty, but the money rears its ugly head. They fired Clark. Dr. LeMaistre—others may have told you this, and it's my—I want you to be careful how you quote all this because it's going to hurt me. Dr. LeMaistre—I already mentioned this, but he was a very good friend of mine.

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*Tacey Ann Rosolowski, PhD*

**0:32:29.8**

Could I interrupt you just a second? All of this is being recorded, so if you prefer it to be off the record, I can turn off the machine right now.

*Emil J Freireich, MD*

**0:32:36.3**

No, I just want you to treat it gracefully.

*Tacey Ann Rosolowski, PhD*

**0:32:38.6**

Okay.

*Emil J Freireich, MD*

**0:32:39.4**

Dr. LeMaistre was chancellor of the University of Texas. I know the story of how he got to that position. It was not because of achievement. He was not competent. He was not a competent chancellor. The reason he got the job is that the guy that was chairman of the board of regents, Frank Erwin, was using the university as his political base to become governor of the state of Texas, and he ran the university. Mickey was, and always has been, a front man. He's handsome, he's thin, he gets his hair coiffed every morning. He has a deep base voice and speaks very beautifully. He's God's send to mankind. He's Mr. Perfect, provided someone else runs the university, which was Frank Erwin. Frank Erwin, as you know, got arrested on a DWI and his political career disappeared, so he resigned as chairman of the regents. They appointed a regular guy. The regular guy didn't want to run the university, so they had Mickey run the university.

Mickey insisted you call him Mickey, by the way. It's demeaning to me, but that's the way he liked to be addressed. I used to call him Dr. LeMaistre. He said, "Call me Mickey." So Mickey couldn't run the university, and it didn't take the regents five minutes to figure that out. So they had to get him a job without scandal. They don't fire people. So they made him chair of the research committee to replace Dr. Clark. At the same time, the no-good president of the health science center resigned. They told him, look, you can have your choice of jobs. Well, if he had a choice of that struggling institution and this enormously successful powerhouse created by Dr. Clark, with a great retirement program and everything in place, he took MD Anderson.

I was a candidate for that job. It's a tragedy that at that point in history they replaced Clark with Dr. LeMaistre. And as I mentioned before, LeMaistre immediately turned all the responsibility over to everybody else, and he became an administrative, not a—he wasn't a general; he was a secretary of state.

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I was running the medical school and teaching at the medical school. The students rotated—the undergraduate students—rotated through our hospital, because we had much better teaching than Hermann Hospital, who had a non-academic faculty. There was no one there who—they were all practitioners. They recruited a few guys like Joel Moake and the guy who ended up running the heart institute, so they had a few academics, but, to a large extent, the students were learning the way they did before Flexner. They learned apprenticed medicine. You follow some doctor around and do what he does. When the guy has swelling, you give him mercury. Why do you give him mercury? Well, we always give him mercury. Okay. So that's how they learned. Then there were us guys who were all scientists. We said, wait a minute—leukemia, hematology, science, blood. Well, the students hated the rotation order, because the kind of students they attracted were not academic types, they were practicing types. The mandate was produce family doctors. Family doctors don't think about science. So when they went to their class and they say, "Why are you giving him mercury?" They say, "Well, that's just the way you do it. Shut up and pass the test and go practice in Wichita."

So that situation didn't work at all. The students hated it. They didn't come. Some of the house staff liked it. That is, the graduate medical education was reasonable. But again, the people who wanted to be internists didn't want to learn the science of oncology; they wanted to learn everything—cardiology, et cetera. So again, the graduate medical program didn't work very well. There was only one thing that worked—graduate medical education. We trained the oncology specialists of the future. If a guy was a surgeon and wanted to treat cancer, come to MD Anderson.

So my situation with the medical school revolved around money. I was head of oncology. Oncology was the biggest service at Hermann Hospital. We were making tons of money. But what about the professional fees? I'm a full-time employee under contract. All the professional fees came to MD Anderson. The medical school guys realized that, "Dr. LeMaistre, we need the professional fees." "Yeah, but they're my faculty." "Well, we'll get our own faculty." LeMaistre compromised so that they kept the fees and we did the work. I staffed oncology with my trainees here—good oncology guys. We didn't have any money, so we applied for a training grant from the federal government. We got a good training grant. We began to—well, I'll tell you how the training program began. But anyway, the long and the short of it is that Dr. LeMaistre, in his perfect style, negotiated a settlement where they kept the fees and they had their own head and that was over. The relationship to the medical school disappeared in one day, because no one can have administrative responsibility when all the money goes to Hermann Hospital.

So that was the end of our connection to the medical school. I still have a joint appointment, but I go over there and give a lecture every two years. It's trivial. But graduate medical education was what we did here. It was just like NIH. What we did was make oncologists—surgical oncologists, medical oncologists.

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My specialty was leukemia. As you know, I started the department of Developmental Therapeutics. Dr. Frei was the first head, but I was deputy head. Frei and Freireich were like two arms of a body. I mean, I loved the man. I respected him, and he respected me. We had totally different personalities, but we were completely complementary. So Frei and Freireich didn't equal two; we equaled four. We were really—our brains were intermingled. We started this fellowship program in developmental therapeutics. It started with—I think I mentioned the other day—with the Japanese exchange students. We had a very good friend in Dallas, Dr. Hill, who ran the blood bank. He tried to recruit me, initially, so we were good friends. He had a number of these Japanese fellows come over to learn blood banking. He would send them up to rotate, and they would stay.

My first fellow was a Mexican. His name was Adolfo Isassi. He ended up being dean of a medical school in Mexico. He is a very smart, academic guy. Then we started to get these Japanese fellows. The important point is that our training program, which began with these foreign nationals, has populated the world. The first fellow we had from Japan, Nazemi Hurano, became president of a new medical school in Nagoya. He's one of the most famous academics in Japan. The second one we had who got the award as a distinguished alumni, Dr. Ohno, became the chair of the first Japanese cooperative chemotherapy group and he became dean of a medical school. He's still working, very famous.

When I go to Japan, and I go often, the famous academics in Japan have a party for me—a geisha party—and we sit and they all talk about old times at MD Anderson. We developed—I don't want to say singlehandedly, but almost singlehandedly—created academic oncology in Japan. From Japan, we began—as I said, we had Mexico. We had a young physician, Carlos Vallejos, who from—not Chile, not Argentina—what's the other one on the west coast? Anyhow, he was director of the cancer center there and very famous. We populated academic oncology around the world with our training program. We attracted them.

Then we began to attract some Americans when Americans realized that oncology, in universities, was a discipline. We began to attract and we trained some of the most famous medical oncologists in the United States—Larry Einhorn, who won the Lasker Prize for his work on testicular cancer; Bob Livingston, who became head of oncology at Washington University. We trained all the giants here—Hagop Kantarjian, who is head of leukemia; Bob Benjamin, who is head of sarcoma; Gabe Hortobagyi [Gabriel Hortobagyi, MD [Oral History Interview]], who is head of the breast cancer service. We populated the institution with academically trained people who came to DT to learn oncology as a science—research-driven patient care. So we created that element at MD Anderson, and we were very successful, which leads to vulcanizing our department.

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When Dr. LeMaistre eliminated DT, the training responsibilities devolved to the various departments. Then, as I say, he gave me hematology, and hematology got too big. They hired this guy, [Al] Deisseroth. They vulcanized hematology. It was too big. So now we have leukemia transplant. See, we brought immunology, infectious disease, pharmacology, hematology, molecular biology—all the disciplines came through DT, so when they finally vulcanized leukemia, I was head of the leukemia service. Dr. LeMaistre realized that he had Conrad running the hospital. He had Fred Becker recruited to run the basic sciences in laboratory medicine. He needed someone to run the clinical science, so he invited me to be vice president for clinical research. There was nothing I would rather do than that. So we had a meeting, a typical LeMaistre meeting.

All the LeMaistre meetings were the same. You do the talking, he listens, and then he says, well, this and that. No decision is ever made. He had a sign on his desk, you never make a decision, because if you make a decision, it's going to come back and bite you. So he never made a decision. It was part of his public presence. So he said, okay, it's a great idea. It was Dr. Hickey's idea, actually. Dr. Hickey was an academic surgeon. He was the director. Dr. LeMaistre appointed him so he wouldn't have to worry about directing the hospital, and he had Conrad running the medical oncology. He said, "It's a great idea, but before we do it, we don't want to upset anybody, so you have to get approval from Dr. Becker, who is vice president of research, and Dr. Conrad, who is the vice president for patient care, and you'll be vice president for clinical research."

At the time we had a clinic center grant, which I was the PI on, and we had a whole ward on Three West, which was our clinical research center, so I was already running the clinical research program here. So I went to Fred Becker [Frederick Becker, MD [Oral History Interview]], and Becker said, "Wow." Do you know Fred Becker?

***Tacey Ann Rosolowski, PhD***

**0:47:07.3**

Uh-hunh (affirmative).

***Emil J Freireich, MD***

**0:47:07.7**

Is he on the thing?

***Tacey Ann Rosolowski, PhD***

**0:47:09.0**

No.

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***Emil J Freireich, MD***

**0:47:09.9**

Fred Becker is another giant. He said, "Great idea. Just what we need. Freireich, you and I, we can work together." Then I went to see Conrad. Conrad said, "Clinical research? If it's patient care, it's mine. There's no clinical research." So I went back to LeMaistre and I said, "Dr. Conrad—Becker is totally on, but Conrad"— He said, "Wait a minute, I have a note here from Fred Becker. Fred Becker says, 'There's no such thing as clinical research. If it's research, I'm in charge.'" Becker—swine. What he told me was the inverse of what he wrote. So LeMaistre said, "Okay, you can't get approval from two vice presidents. You're out." So I got fired again. I've been fired eight times by LeMaistre. He couldn't tolerate me. Well, we're actually good friends. He comes up and puts his arm around me. So I'm missing a big part of the story. Can I take notes?

***Tacey Ann Rosolowski, PhD***

**0:48:37.9**

Sure.

***Emil J Freireich, MD***

**0:48:45.1**

He realized that he had Conrad who did no research. He had Becker who did lab research. He needed this vice president for clinical research. He had a brilliant idea. He needed a chief academic officer, what DuBois is now. That was a brilliant idea. He looked around at who he could get, and he selected Andrew von Eschenbach. He's probably on your list to interview. I hope you interview him. He was the head of GU surgery. He's a surgeon, a very accomplished academic surgeon. He and I were very good friends. We worked together on many projects. He became chief academic officer. Wow.

He did many good things. He was chief academic officer for about a year. The first thing he did was they built this building for all the administrators. He said, no, let's put the faculty over there. We need more room over here. He was a very strong advocate in the faculty. It didn't take long for Dr. LeMaistre to realize he created a monster, because now he had someone who was actually doing something, which was bad for him because there was going to be conflict between him and Conrad and Becker, which was just what he can't stand because he'd have to make a decision. He never made a decision. So [Andrew] von Eschenbach was fired after a year, and he went to the FDA. But von Eschenbach, during his time, realized that although we were the most powerful graduate medical education organization in the country, we didn't have a graduate medical education program. So he called me to his office and said, "Freireich, you've done a lot. Why don't you take over education?" And it was actually his idea to create a core curriculum and have a place where the graduate medical trainees can go for guidance in their careers, other than their subspecialty.

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At the time, grand rounds were being run by Dr. [Aman U.] Buzdar, who is another one of my very good friends, a Neanderthal from India or somewhere. Dr. Buzdar was running grand rounds. I was interested in teaching, and I used to go. We had maybe ten to twenty people coming to the Hickey Auditorium every week. It was a dying enterprise. Von Eschenbach called me up and said, “Why don’t you take over grand rounds?” And I did. So of course I made grand rounds a major teaching thing because we focus on research. We don’t have a one-hour seminar; we have multi-disciplinary presentations. It’s now the number one teaching program in the institution.

*Tacey Ann Rosolowski, PhD*

**0:52:22.0**

So that was in 1997?

*Emil J Freireich, MD*

**0:52:24.3**

I think so.

*Tacey Ann Rosolowski, PhD*

**0:52:25.7**

Yeah, 1997, Institutional Grand Rounds is what the name of the program—

*Emil J Freireich, MD*

**0:52:29.4**

The core curriculum became part of the GME program, and then we got an organized GME program. We recruited people to be head of GME, and Dr. [Stephen P.] Tomasovic was made vice president for academic affairs. Then, when von Eschenbach was fired, they hired Margaret Kripke [Oral History Interview], and Kripke, first class lady, scientist, quality person. She looked at what we were doing, and she said, “Freireich, why don’t you take over graduate medical education?” Fine. So she told Tomasovic [Stephen Tomasovic, Ph.D. [Oral History Interview]] to take me.

Tomasovic controls all the education activities in the institution, but he hasn’t got a single doctor on his faculty. All the directors are librarians and stuff. So Tomasovic said, “Good idea.” So they made me director of medical education. But they didn’t want me to be director of anything because, be careful, first thing you know I’d take over the whole thing, so they called me Director of Special Medical Education, meaning that I only control things that Tomasovic lets me control. And that’s a position I still have, which I’m delighted to have. It is seventy percent of my activity that I spend on graduate medical education, and I love it, and the fellows love it. We have the best Graduate Medical Education Program in the country, believe me.

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## **Chapter 8**

### **B: Building the Institution**

#### ***A History of Institutional Grand Rounds, The Core Curriculum, and the Physician's Assistant Training Program***

### **Story Codes**

B: Building/Transforming the Institution

B: Multi-disciplinary Approaches

B: Research, Care, and Education in Transition

C: Understanding the Institution

B: Education

B: MD Anderson History

B: Institutional Processes

C: Education at MD Anderson

***Tacey Ann Rosolowski, PhD***

**0:54:04.0**

I wanted to ask you for a little bit more detail about each of these activities. Institutional grand rounds, what did you do to transform that?

***Emil J Freireich, MD***

**0:54:15.1**

What we did is instead of having a speaker talk for an hour about his research, we made it lively. We insisted on there being multiple speakers—three to four—because if you tell a guy, “I want you to tell me about your research. Take an hour,” he’s going to tell you everything. There’s going to be tables and the P values and such. And the only people who attend grand rounds in seminar are the people who are interested in that area—ten people. We’ve got 1,000 faculty. Ten people come. So in order to get people from all disciplines, it has to be multidisciplinary. So I managed grand rounds so that every session limits the speakers to fifteen or twenty minutes, so they have to present summaries. That means that anyone not working in the field will be informed about what he is doing. Secondly, we made the rounds multidisciplinary. So if we talk about laryngectomy, we have a surgeon or radiotherapist or medical oncologist. If we talk about apoptosis, we have a cell biologist, we have a clinician who is working on chemotherapy, and we have a guy working on DNA. So we make the rounds appeal to a broad audience; we make them lively and fast, so grand rounds is successful. We average about 150 people, not ten. It’s a fantastic academic institution. We record it. People who can’t come because of their clinic on Friday can watch it on their TV. I do it when I’m out of town. I watch it. It’s great education.

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The core curriculum is mandatory. The GME committee—I'm an ad hoc member of the GME committee which consists of all the GME program directors. They elect the chair. I'm kind of an ad hoc member. I chair the curriculum subcommittee, and the curriculum subcommittee has members from all different graduate medical education programs. We review our core curriculum on a regular basis, and we analyze—the students testify as to the outcome. We get quantitative measures of whether they're learning. They get a little exam with each thing. We have a report every quarter from Marilyn Greer's department in academic affairs. So our core curriculum is really academic.

*Tacey Ann Rosolowski, PhD*

**0:56:50.1**

How were the decisions made about what the core curriculum should include?

*Emil J Freireich, MD*

**0:56:55.1**

Well, it's me. I'm absolute dictator.

*Tacey Ann Rosolowski, PhD*

**0:57:00.8**

So tell me, Dictator, what does the core curriculum—what was the logic of it?

*Emil J Freireich, MD*

**0:57:03.7**

The logic of the core curriculum is if you come here to be a radiotherapist, the least you have to learn is the basics of oncology. You have to know biochemistry. You have to know pharmacology. You have to know medicine. You have to know cancer. You have to know lung, colon, breast, everything. So the core curriculum creates, for the first-year graduate medical trainee here, a core of oncology knowledge that you'll only get at MD Anderson.

So if you're going to be a surgeon, you're going to know everything. If you're going to be a gynecologist, you're going to know everything. If you're in medical oncology, if you're a radiotherapist— So the graduate education committee voted unanimously that all first-year graduate medical trainees here are required to take the core curriculum. They are required to attend eighty percent of the sessions. If they can't attend in person, they are allowed to do it online. We record them all, and they are on video. They are required to assess the course, whether it fulfills their needs or not, and I report regularly to the graduate education committee on how we're doing. As I say, we have a committee of people who are interested in graduate medical education—multidisciplinary. We have educators, physicians, scientists, so on. We meet regularly and supervise it, so it's really an academic exercise. It's institution-wide.

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***Tacey Ann Rosolowski, PhD***

**0:58:31.6**

So what are your findings in the performance of the students and how they go on?

***Emil J Freireich, MD***

**0:58:39.0**

It's the best training program in the country. It's highly effective. There are some subspecialties. Like people who come here to do radiology, they don't like the core curriculum. But I keep pressing on their program director and say, "Look, you're going to be a radiologist, go to Hermann Hospital, but if you come to MD Anderson, you're an oncologist." And oncologic radiology is going to be a specialty, so you better know about oncology. You've got to know about mitosis and metastasis and cell proliferation and chemotherapy and so on. So, at least for now, the training program directors all embrace it. As I say, the vote is unanimously in support of the program. It's assessed and we present the results of the student evaluations, the faculty evaluations, and the performance of the students regularly at the graduate medical education committee which meets quarterly. We give a report at that meeting on how they're doing.

***Tacey Ann Rosolowski, PhD***

**0:59:42.4**

Now, that program started in 2000. How many students did you start with? How many students do you handle now?

***Emil J Freireich, MD***

**0:59:48.5**

Well, we currently have—I'd have to look for those statistics, but all of the first-year graduate medical trainees are required to take it, so it's 140 or 150, something of that order.

***Tacey Ann Rosolowski, PhD***

**1:00:03.7**

Wow. We haven't talked about the physician-assisted continuing education. That came in the same year.

***Emil J Freireich, MD***

**1:00:11.9**

Well, we'll deal with that briefly. I can't recall the year, but it was while I was here that a famous chairman of medicine at Duke University—I'm blocking out his name right now, but it will come to me in a moment. He decided that there should be a career called a physician's assistant. He invented the idea. The idea being that physicians are poor at some aspects of patient care. What they're good at is their brains. He was very academic. His name was Don Seldin. No, that's one of his students in Dallas at Southwestern. His name will come to me in a moment. But anyway, he created the idea of having a medically trained person who is not an MD but can do anything an MD can do physically but not make the decisions. That's the doctor's responsibility.

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He called them physician assistants. It was kind of slow to catch on. A number of academic centers began to do it, but being a great innovator that I am, I sensed immediately that something was important here. I was head of DT—

*Tacey Ann Rosolowski, PhD*

**1:01:49.5**

What was it about the idea that you thought was so important?

*Emil J Freireich, MD*

**1:01:53.1**

Well, I'm coming to that. I was head of DT, but I never separated myself from patient care. I insisted that if I was going to have a faculty, I would be at least as good, if not better, than everyone on my faculty. So I was the best doctor. If you had to consult somebody on leukemia, you'd come to me. And to maintain your competence, you have to practice. Not in the usual sense of tennis, you have to do patient care.

But as I got more and more administration, the department grew. We ended up with 250 employees and thirty faculty. It began to impinge on my patient care time. When I heard about this idea of a physician assistant, I was the first physician at MD Anderson to recruit a physician assistant. The first problem was how to pay them. So I went to the PRS and I convinced them that my income—that they could pay them the amount of income that my practice accelerated as a result of this PA. And within a year it was proven that the amount of income I generated with a PA was more than the PA's salary, so the PRS has taken over the PA funding. So they're funded just like the doctors, out of fees for service. The consequence is that the way it works is when I get a new patient referral from a doctor, he calls me. "Dr. Freireich, this is the chairman of the board of General Motors. He needs the best doctor in the world." "Yes, sir. I'll take him immediately." He comes in and the first person he sees is my PA. The PA takes a detailed history, a physical. She spends an hour with the patient, and she can afford to because she's not being billed at the rates I'm billing. When she gets done with all that, she orders all the laboratory stuff, and when everything is ready, she presents the case to me and I make the decisions. The consequence of that is the number of patients I can see has expanded by tenfold.

Well, the PA idea—my first PA—I can't remember her name. The PA that really mattered has recently retired. She's an absolute genius. I forget her name. Anyway, so the idea of the PA thing—it didn't take a year for every doctor in the hospital to realize what had happened, particularly the surgeons and the medical people. They realized that if I'm in the OR four hours a day, three days a week, and patients are coming to the clinic every day, if my PA can do the histories and physicals, get all the lab stuff, I can come in and decide what kind of operation is needed and go to the OR. So it caught on immediately, and the number of PAs grew.

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Kathryn Boyer—she's retired. She married one of our faculty and had a baby. I still deal with her every day, but she was just fantastic. It takes a personality of a person who is excellent as a doctor but just goes so far. They don't want the responsibility. So you can find people who love doing— It's like nurses. They love doing the care, but they don't want to make the decision as to whether you get your lung taken out or your brain fixed.

So anyhow, the PA program became very successful, and Kathryn Boyer formed an association—the PA Association. They had seminars, and they worked like the Graduate Medical Education Program. Although she founded it, I was the principal faculty member. Eventually we recruited a gal who was even better, the one who runs it now. I'm blacking out her name. It runs itself, and I just help them. I'm not administratively responsible for it. It's a terrific program.

***Tacey Ann Rosolowski, PhD***

**1:06:17.2**

So does MD Anderson train physician assistants?

***Emil J Freireich, MD***

**1:06:22.5**

Yes.

***Tacey Ann Rosolowski, PhD***

**1:06:23.1**

Okay, and then there's also the Physician Assistant Continuing Education Program?

***Emil J Freireich, MD***

**1:06:26.4**

Yes.

***Tacey Ann Rosolowski, PhD***

**1:06:27.5**

So tell me about the differences between the two.

***Emil J Freireich, MD***

**1:06:30.4**

Well, when the PAs are here, it's like the core curriculum. If they work for a thoracic surgeon, they only do lung cancer, but they have to be competent in cancer. So they have a CME curriculum where they have to be competent in the new developments in leukemia and everything else. And that curriculum is run by the PA people themselves. Then the other question was—?

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***Tacey Ann Rosolowski, PhD***

**1:06:53.2**

Oh, I was interested in the actual training program for the physician assistants themselves.

***Emil J Freireich, MD***

**1:06:59.4**

Well, there are formal training programs at the academic medical centers all around the country. We don't have one. But the PAs who want to do—we have a graduate medical program for PAs. So the ones who get PA degrees from Baylor—most of them come from Baylor, some from the Health Science Center—they come here to do a clerkship. If they like oncology, they do graduate medical training here, and they become faculty.

***Tacey Ann Rosolowski, PhD***

**1:07:25.6**

And then there's the continuing education?

***Emil J Freireich, MD***

**1:07:27.5**

Yeah, that's the existing—to stay broadly based, like our core curriculum. They can't just worry about themselves. They have to be competent in chemotherapy, what's going on, what they're patients might be eligible for.

***Tacey Ann Rosolowski, PhD***

**1:07:41.0**

So the continuing education came in 2000, and I'm just interested in the way that's the same year as the Core Curriculum. So there was this sense that, wow, there's a lot going on. There's a lot everybody has to keep up with. So that was the rationale. Interesting.

***Emil J Freireich, MD***

**1:07:57.1**

Yeah. I give more credit for the PA program to the PAs than to me. I was just psychological support. But the Core Curriculum was my baby. Now, the Physician-Scientist Program—okay. So, when Tomasovic appointed me to this position as Director of Special Medical Education, it reduced my clinical time to thirty percent, and I had seventy percent of my time now for education. Prior to that, the educational activities were always grafted on my clinical administrators. Now I had a position, thanks to Dr. [Margaret] Kripke, where I could focus on education, which I love. And why did I tell you that?

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## ***Chapter 9***

### **B: Building the Institution**

#### ***Creating Patient-Oriented Research in a Complex Scientific and Institutional Context***

### **Story Codes**

B: MD Anderson History

B: MD Anderson Snapshot

B: Institutional Processes

D: On Research and Researchers

D: Understanding Cancer, the History of Science, Cancer Research

D: The History of Health Care, Patient Care

C: Portraits

C: Understanding the Institution

B: Education

D: Cultural/Social Influences

A: Critical Perspectives

***Tacey Ann Rosolowski, PhD***

**1:08:53.0**

You were setting up the context for the physician-scientist.

***Emil J Freireich, MD***

**1:08:57.3**

The first thing I decided to do is— I learned, when I came to MD Anderson, that the secret to success in anything you undertake is money. The reason I succeeded in DT [the Department of Developmental Therapeutics] is we went and got grants. The reason we had a training program is we got a federal grant for a training program. We paid our students. We didn't have to welch off of the institution. We didn't have to beg for money. We got grants from the Cancer Society and the Leukemia Society. We were active in fundraising. We got endowments from our patients. So when I got this job as Director of Special Medical Education, the first thing I had to do is raise money, so I went to the granting agencies, and I discovered a thing that had just been created either the year of or the year before I applied, which was called the K-30. One of the things I'm most proud of is the Association for Patient-Oriented Research. It's 10:30. How much time do we have left?

***Tacey Ann Rosolowski, PhD***

**1:10:16.5**

Another hour.

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***Emil J Freireich, MD***

**1:10:20.9**

Okay. The NIH has a—research in general has a structural problem. The structural problem is that the ethos in the country is that if you want to cure a disease, if you want to improve health, you have to hire a bunch of basic scientists, put them in a laboratory, and have them discover everything about everything. If you clone the human genome and you get all the cells and culture and you do tissue culture and biochemistry and you do all the basic science, then these geniuses who get the Nobel prizes—there's never been a Nobel Prize for a doctor. They're all geniuses. When the geniuses work out all the basic knowledge, then they call some stupid doctor who just dispenses pills and he cures cancer. And that's an ethos that exists in the United States and in the world. Everybody believes that the way you solve problems is to do basic research. That's why the director of the NIH is a basic scientist. That's why the director of the National Cancer Institute is a basic scientist. They've never seen a sick person, and they don't know what cancer is all about, but they do know how to clone genes and grow bacteria and culture and lab and get grants, so the entire federal grant money flow goes to laboratory science.

Now there's a minority of us who realize that in fact not ninety-eight percent but 100% of advances in our ability to manage disease in man began at the bedside, with a doctor. The flow of knowledge about disease is not from the lab to the clinic; it's from the clinic to the lab, like we did platelets. I had to have a bleeding patient to go to the lab and figure out that it worked then go back to the patient.

In the United States of America and in the world, this ethos that clinicians are dumb, idiot, stupid guys who just apply basic science is universal. So the flow of funding to this day is to support laboratory science. If you're doing regular research—you're growing leukemia cells in culture, you're throwing a chemical on them—it's called regular science. The philosophers of science call this regular science. Regular science says you just do what comes next. If you know how bacteria grow and you throw it in and they don't grow, well, you want to find out why they don't grow. So you put more in and find out if they grow faster. It's nothing to do with humans. It has nothing to do with disease. It just— Do you mind obscenities? It's just friggin' around. That's what you get from Josh Fidler [Isaiah Joshua Fidler, DVM, PhD [Oral History Interview]]—basic science. He understands metastasis. His understanding of metastasis has nothing to do with metastasis in the clinic. It's all fairytale. Fidler's work will never contribute to the health of anybody. He gets cancer cells out of a mouse. He grows them in culture until they're automatically growing, which never happens with human cells, then he shoots them into the vein of a mouse and he gets spots on the lung—metastasis.

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I've written an editorial on this, and it's been published. Fidler's metastasis models are all laboratory stuff. He's famous because that's what people think is important. They don't care about curing metastatic cancer. They don't want to understand how cancer metastases occur in the clinic. They want to get grants and work out this—and they have this ideology. It's like church—basic science.

So there's a handful of people who do clinical research who recognize that basic science is useful in their thinking, but the important part of advancing and understanding disease is to study disease. Leukemia in a mouse has no relationship to leukemia in man—none. The things learned in a laboratory can be applied by clinicians if the information is relevant, but the observations begin at the bedside. And there are no exceptions to that. If you look at how did chemotherapy begin? Did some genius, like Dr. [Sidney] Farber, go to the patient-scientist lab and put methotrexate—and then it worked in children? Hell no. He had an idea that it would grow and he gave it to children. Everything that's occurred that's advanced the health of man has occurred because someone made an observation in a sick person and then tried to understand it. AIDS was done by doctors in practice.

When I went to medical school, the dean of our medical school was a guy named Andrew C. Ivy. He won the Nobel Prize. He was the most famous physiologist in the United States. He became dean of the school of medicine. The medical schools loved to do this. The dean—to teach people how to be a doctor—is a basic scientist. He doesn't know anything about medicine. His specialty was peptic ulcers. He had worked on animals, and he developed the acid theory of peptic ulcers. When we were medical students, we had more lectures on peptic ulcers than any other disease. We understood it totally, because in dogs, when you do this and you cut the nerves and you put acid—you had ulcers. If you do this and that, it goes away. We understand peptic ulcers, and some dumb doctor in Australia made cultures of the blood and found that there was a bacteria that causes ulcers. The acid has nothing to do with it. If you want to cure peptic ulcers, which is now a historically over disease, you give antibiotics.

And that's the story of medicine in the United States. We have this illusion, and certainly all the managers do, all the directors, all the head of NCI, NIH, all the senators. Everybody believes that we need more basic science. We need Fidler. Do metastasis research. Get a prize—a Nobel Prize. It doesn't do anything for metastasis. Nothing Fidler has done applies to man at all. It's all silly. We have patients—well, he does this in his lectures. We have patients with ovarian cancer, if you take their blood, they've got cancer cells running around 200,000—they don't have metastasis. It just stays in the belly. It's got to do with the biology of the disease that we understand—the doctors.

Anyhow, there are a handful of doctors working at the NIH, working on disease, and they said, look, maybe if ninety-nine percent of the budget goes to laboratory guys—to Fidler—maybe we could put two percent—maybe we could make it three percent—for clinical research. Oh, well, that's—more basic science.

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There were some people who convinced the NIH that maybe there was something to this clinical research thing. They refused to admit that 100%—not ninety-nine—of advances in care of patients occur by physicians taking care of patients who then work it out in the laboratory. But they were willing to say, maybe a couple of them, so they created a program called the K-30.

The K-series of grants were awards for training. They trained, essentially, basic scientists. But some guy made a mistake. It slipped through. So the big basic scientists who ran the cancer—the NIH, all these—you know—what’s the name of the guy who runs the NIH? He’s world famous. He cloned the human genome, never helped anybody. The guy who runs the Cancer Institute got a Nobel Prize for discovering an enzyme. He’s director of the Cancer Institute. But somehow they said, well, we’ve got all these training grants. Maybe we ought to have one for doctors. The number thirty—K-30—the other twenty-nine is— So they made this program, K-30, and they put some money there. I looked through things and said, “Aha. That’s for us.” So I applied for a K-30 grant. I figured the way to succeed in my business is make money.

Well, my friend and mentor, Dr. LeMaistre, discovered that a man named Jon Tyson, who is a pediatrician over at the medical school, had also prepared a training grant for a K-30. So the dean of the medical school, in consort with our leader, decided that the likelihood—since there were a very small number of these grants—that two of them would come to the Health Science Center was very unlikely. So we opt to combine them. So we had a meeting, and I presented my grant, Dr. Tyson presented his—which was totally stupid—and the decision had to be made by people who knew nothing. So the decision was obvious. Mickey said, “Tyson will be the PI and Freireich can be the co-PI.” So we had a joint program.

The title of the K-30 grant was Physician-Scientist Training Program. So we send in the joint award, and we got it. It was an award for five years. Within the first week it was obvious that we were mixing apples and oranges. We planned the curriculum, and Tyson called me into his office. This is an arrogant, young, unaccomplished, stupid guy. He said, “Freireich, let me tell you how we’re going to run this course.” What? He said, “The first thing you have to understand is how to do a randomized clinical trial.” I said, “Gee, you’re the one who can teach me.” You know who did the first published randomized trial in the world? And this young shit—excuse me—this young twerp is going to lecture me in his office. So that meeting was very short. I left.

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To give you an example, in his first lecture he told people how accomplished he was. He chaired a multi-institution cooperative group involving several hundred women who delivered babies. The scientific question being investigated was, when the baby is delivered, do you cut the cord at one inch or two inches? And after two years and millions of dollars, they discovered that one inch was better than two inches. Now that's research from which no one had ever benefitted because we were immediately saying cord-blood stem cells, you have to cut it as short as you can and squeeze out— He was an absolute goon, but he's one of these goons—you know—there are people who are stupid but are humble, but when people who are stupid are arrogant—you know—it's like Adolph Hitler. He thought he knew more than I did. He'd never done anything. I'm the one who cured childhood leukemia, and he's lecturing to me.

So within a week, the courses were— Our students came to our courses, their students went to their courses. A couple of their students listened to our courses. We had it broadcast over there. At first he dominated all of it, and then I insisted that we do some. The first one I gave he sent me an email and said, "I enjoyed your lecture." But the two came totally apart. By the third year, then we had to fight over the money because he needed this for students and I needed this for that.

***Tacey Ann Rosolowski, PhD***

**1:25:07.2**

What did you focus on in the portion that you administered?

***Emil J Freireich, MD***

**1:25:11.1**

Physician-Scientist Training Program.

***Tacey Ann Rosolowski, PhD***

**1:25:13.4**

What were the components of it?

***Emil J Freireich, MD***

**1:25:15.9**

Well, the curriculum was how to do clinical research, what the principles are, a little bit of statistics, randomization, clinical trials, observation, and experiences. I give a lecture now to the students still on the essence of clinical research—objectivity, quantization, objective measurements, lack of bias. So our course was terrific. We attracted good students.

As we were going along, I got the idea that our students were learning a subspecialty, but they're not certified. It seemed to me that we ought to separate the academic physician scientist whose profession is research from the physician scientist who is practicing scientific medicine. They needed a credential. So I decided the credential they needed was a graduate degree—a master of science or a PhD So I went to the graduate school and I said, "I want to have a graduate degree in

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patient-oriented research.” Whoa! There’s no such thing as patient—patient care—there’s no research. Inject leukemia cells in the tail of a mouse; that’s research.

If you can get a PhD working on mice, why can’t you get a PhD working on people? It’s a little more complicated. People are a little more difficult to control. They’re not pure, inbred species with the same sets of genes—identical twins. With one kind of leukemia cell—Dr. Fidler is still working with L1210 that was isolated in 1953. There’s 10,000 different mouse leukemias. They all have different patterns of spread. You have to understand what makes them do that. So we went to the graduate school, and we met with what you might call skepticism.

***Tacey Ann Rosolowski, PhD***

**1:28:07.1**

I can imagine.

***Emil J Freireich, MD***

**1:28:08.6**

It’s difficult for a basic scientist to understand clinical research because the system is inverted. You see, a basic scientist wakes up in the morning and says, “Gee, wouldn’t it be nice to know how—? Let’s work on that.” A physician-scientist comes to work in the morning, and you’re bleeding. Dr. Freireich, what are you going to do? The physician-scientist is presented with his problem. The laboratory scientist can work on anything he wants. [Dr. Joshua] Fidler, take some mice, shoot in cells, Nobel Prize. The guys who got the Nobel Prize this time—immunologists. They put T-cells in mice—Nobel Prize. Sick patients? Some dumb doctor will figure out how to use this basic knowledge to cure humans. That’s the ethos.

So we met some resistance, but I’m not modest, so I was persistent. I convinced people slowly, one at a time, and eventually we got through to the curriculum committee, we got through the academic standards committee, we got through the executive committee.

Dean [George] Stancel [Oral History Interview] —the dean said it would degrade the graduate school if they had a program in patient-oriented research and awarded these inferior degrees to these stupid doctors who are not Fidler—basic scientists. As I say, I’m not modest, and I worked with Dean Stancel. We were good friends. After about a year of pressure, the dean agreed to have a program which he called Patient-Based Research. See, it’s not patient-oriented, it’s not that you’re working on disease, it is that you’re working on basic problems and it’s based in patients—patient-based research. Okay.

So we started that, and the students that we had enough money for, we enrolled them in the graduate school. We created courses that were minimum requirements. We had a curriculum. We started graduating students with masters. And actually, I’ve taken three students in my lab that are PhDs. Okay, the grant runs out in five years. I can’t recall the year. You probably have it.

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***Tacey Ann Rosolowski, PhD***

**1:31:18.7**

Yeah, it started in 1999, so I guess it ran out in 2004.

***Emil J Freireich, MD***

**1:31:23.4**

Yeah, '04. Okay, in '04, Dr. Freireich is seventy-seven years old. I'm now eight-four. Old age. The second culture, in addition to bias in favor of basic science, is we're very age biased. We have to give young people an opportunity. So the whole granting program is biased against elderly people. One of my students, DeVita, when he was director of the cancer institute, created a program called Outstanding Investigator Awards. The idea being instead of a basic scientist saying—you know—we did this and this, and that's brilliant; it's basic science—maybe we could look at their productivity. Instead of these fairytales that we're writing grants. When you want a grant, you write a fairytale. We know this and we do this and we did these experiments. If the fairytale appeals to other fairytale writers, then you get a grant. But if it's going to be useful, it's supplied by private practice.

So I had two big PO1s, millions of dollars. I had the Clinical Center grant. Over the years, particularly the last decade, all those grants I lost competitively. In about a half of them, I actually got the word—I still keep the reviews. You get anonymous reviews. "Dr. Freireich is very accomplished and very famous. He's had a great career. But maybe it's time for young people." So when I began to see age bias appear in my grant reviews—oh, the time came for the renewal. The arrogant SOB at the medical school, Jon Tyson, wrote a memo to Dr. Tomasovic saying, "I don't think we should go together because they are so different." He felt that our program was a drag on his program, so if he could write his own he would get renewed. So he withdrew, and we were to write our own. So I said, well, if we're going to write our own, it's not going to be Freireich as the PI. I had to recruit someone really smart. So I found one of my ex students who is really a genius, Dr. [Razelle] Kurzrock.

***Tacey Ann Rosolowski, PhD***

**1:34:27.9**

I'm sorry, I missed her name.

***Emil J Freireich, MD***

**1:34:35.0**

K-U-R-Z-R-O-C-K. First name is Razelle. She's from Canada. She came here after she'd worked with Carlo Croce in Philadelphia, so she had a laboratory basis, but she was a clinician. When she came to DT she became a physician scientist—outstanding. She was teaching in the course, and she and I had regular interactions. I came to trust her as my 2IC. So I asked her to do the grant, and she did. And the outcome was that we got funded and he didn't. And Kurzrock became head of the K-30 program.

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She is totally outstanding—totally outstanding in every way. She’s become head of her own department. She runs the Investigational Therapeutics. She runs this program—the Physician-Scientist Program—and had done an outstanding job.

The problem is that we still have Dean Stancel. So we push the dean every academic year. See, the difficulty is that this program is what’s called a ‘small p’ program. So when you look in the catalog, it’s not listed as a program and it doesn’t have a faculty. It’s listed as miscellaneous. So if a student wants to do patient-oriented research, he has to know somebody who tells him how to get into it, because you can’t get into it through the graduate school. The catalog and all the administration, which are all PhDs, make every effort to divert graduate students from going into this program. But it’s very popular with the PhDs. They love it. In our program, two-thirds of the students are PhD students because they want to do patient-based research. They want to have their research applied to the clinical problem. They’re motivated by cancer.

So we face this tremendous impediment, and every year we go to Dr. Mendelsohn and we go to Dr. Kripke and we go to the dean and we go to the executive committee and we went to the graduate education committee. They all say, yeah, it’s very good. No one can budge the dean. So when Dr. DuBois became director, we went to DuBois. He said, “I got a good idea; let’s get a consultant.” So we invited Gordon Williams, who was the head of the K-30 program at Harvard, who has one of the best programs in the country. He’s a founder of the Clinical Research Association. He’s a very eminent guy, endocrinologist. He’s a friend of DuBois. Then we had him down to look at our program.

At Harvard, his program is a program, and ours is just as good as his and it should be a program. He met with Dean Stancel for an hour, and when he came out, I said, “How’d you do?” He said, “No progress. He won’t budge.” He met with Dr. DuBois, and Dr. DuBois knows all about that recommendation. We have it in writing that patient-oriented research is a legitimate graduate school program and should be a ‘large p’ program.

So the dean has just retired, but he’s still acting dean. We’re hopeful that once we get Stancel out of the way, it will be approved. It’s been approved by all the committees in the graduate school except the dean. And it’s really tragic that one person has that much power. It’s just not right, but I think the reason he has that much power is because the Graduate School [of Biomedical Sciences] was taken away from MD Anderson and put in the Health Science Center. Then Dr. Mendelsohn was able to negotiate us back into it. Sixty percent of the faculty and students are all from MD Anderson. The reason people come to our graduate school is not the Health Science Center. That’s a backward institution. They come to be at MD Anderson, the number one cancer center in the world.

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So finally, the dean agreed that we jointly issue the MD/PhD degree. The MD/PhD program is still totally based in the medical school. We pay for half the MD/PhD students. I served on the committee for five years, but they—Dr. What's-her-name that runs the program, she decides—it's totally based in the medical school.

So we have a problem with the graduate school establishing. I have advocated from day one that we get the graduate school back. We should have our own graduate school—MD Anderson's—just like Clark. Clark got the graduate school approved when we were just a dink institution. Now we're the number one cancer center in the world. We certainly should have our own graduate school. So we've got the tail wagging the dog. The Health Science Center runs the graduate school, and we're the faculty. It's really ridiculous. It depends on how the new dean goes. Dr. DuBois and Dr. Tomasovic have assured me that to form our own graduate school is just too expensive, so they don't want to do it. They want to stay with this joint arrangement, but we have to have more influence on the graduate school, so that's where it stands.

We have a committee that runs our graduate program. We have two or three PhD's on it who are very good. They are translational scientists. We have a couple of good MDs. We've graduated about fifteen or twenty masters, PhD programs in the decade, and Kurzrock runs it. We fight every year to get upgraded to a full 'p.' We've been to everybody. It will succeed. It's just a question of time. Whoever the new dean is, is going to—he won't have the power that Stancel has because he's based in the medical institute. The new dean is going to be jointly appointed, probably more importantly here, and it should go smoothly. So that's a very important part of our training.

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## **Chapter 10**

### **A: Professional Service beyond MD Anderson**

#### ***Advocating for Patient-Oriented Research and Patients***

#### **Story Codes**

D: Understanding Cancer, the History of Science, Cancer Research

D: The History of Health Care, Patient Care

D: Business of Research

A: Critical Perspectives

D: Cultural/Social Influences

A: Activities Outside Institution

#### ***Emil J Freireich, MD***

**1:34:35.0+**

I think that once you come to MD Anderson, you get the Core Curriculum. You're now an academic graduate medical education specialist. If you do research during your training, which you should do, and you get grants and you cure disease, you should have the tools of science that are not taught to physicians. Physicians learn medicine rote. It's not an academic exercise. When you get internal medicine, they tell you how to do things. They don't tell you why you're doing things. So physicians who want to be scientists have to get science training. They have to take our courses. We have courses in clinical research. We have a course in translational research. We have physician-scientists who teach the students and whose labs they work in. So that's going to happen, and then we'll have a complete graduate medical education program. We'll be able to train outstanding specialists or practitioners. We'll be able to train academic scientists who do their practice science-driven. We're going to train physician-scientists whose practice is controlled.

Every doctor on our faculty here practices like NIH. They have their own thing, and they know what to do. Dr. Wood does renal surgery. He's the best in the world, but that's all he does—renal surgery. He's a scientist. So the physician-scientists have to control their practice, they have to focus their research, they have to understand disease. So they have to have those tools, and they get that through the Physician-Scientist Training Program. So you get the core curriculum. Then you do your research. Then you get your PhD degree. Now you're on the faculty. Now you're a professor.

#### ***Tacey Ann Rosolowski, PhD***

**1:43:46.1**

The three legs—the three legs of the stool.

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***Emil J Freireich, MD***

**1:43:49.4**

And it's going to begin here at MD Anderson. That's what keeps me going. Every year, I get a note from the PRS Retirement Board, which says, "Freireich, you can retire at sixty percent of your salary at thirty years. And your salary goes up, because your optional retirement program kicks in. So if you retire, you're salary will go up." So I go home, and I tell my wife, "This is serious business. If I keep working, I'm losing money." She says, "You have to do what you want to do." So I'm now in my forty-sixth year.

Eventually they're going to fire me because I'm useless, but I really enjoy this phase of my career where my focus is on graduate medical education. I still fully participate in the leukemia research program. The Department of Leukemia is run by one of my students, Dr. [Hagop] Kantarjian, who is an absolute genius. He's like any great professor. You know, you train students who are better than you are. He's better than I ever was. He is really brilliant, competent, energetic, a wonderful person. The Leukemia Department is the best in the world, so I'm very proud to just hang in there. I do a little research on white cells and stuff, but I hang in there. I attend all the teaching sessions. I interact with all of our fellows, because the fellows who come here in medical oncology, they have to decide if they're going to be nephrologists or hematologists or leukemia. We have to attract the best and the brightest from the medical oncology program into the leukemia program. This year has been a very good year. We attracted two really super guys. I play a role in that because I participate in the teaching programs and I try to stimulate the research and I—so I participate in all the departmental activities.

So we have five hours of departmental activities a week. I participate fully in all that. Then I still have—I keep a few patients that—I don't take new patients. I don't attend on the hospital service, because I have a policy that if you're in the hospital, you have to see your doctor seven days a week. I don't work seven days a week.

I had a fatal heart attack in 1987. I was saved by being on the TIMI trial at Methodist, and then I had a bypass by a brilliant surgeon. I've just been very lucky. I'm way outside of the ninety-five percent confidence intervals for survival. But fortunately, my brain still works, so I keep working.

***Tacey Ann Rosolowski, PhD***

**1:46:53.1**

And you've been travelling too.

***Emil J Freireich, MD***

**1:46:55.8**

Well, I'm going to do less and less of that. Traveling is getting so painful. I went to Dubrovnik, my wife and I. It took us two days to recover. It's thirty hours on a plane. You can't sleep, eat. Who needs it? The days of face-to-face meeting are over. It's too easy to communicate

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electronically. I can talk to anyone in the world in ten nanoseconds. It's nice to have collegiality face-to-face, but the way the world is, in my new world, the work comes to MD Anderson. I don't have to go there. I don't go to Japan anymore. If they want it, they can come here. I decided after this trip to Dubrovnik that I'm not going anywhere. I can travel domestically. I go to Chicago, but I'm not going to go around the world. It's just—it's not worth the effort. It's not worth the time. I spent eight days going to a conference. I learned a little bit, but I could have read the abstracts in one night. And everybody knows me, and I know everybody, so I'm better off thinking.

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*Tacey Ann Rosolowski, PhD*

**1:48:17.2**

Can I ask you some questions about those—?

*Emil J Freireich, MD*

**1:48:19.6**

So I don't like traveling. Dr. [Michael] Keating [Oral History Interview] is the opposite. He likes to travel. He's gone all the time. Dr. Keating is a person who depends on human contact for him to think. I'm a person who thinks—pencil and paper and Internet. Go ahead, your questions.

*Tacey Ann Rosolowski, PhD*

**1:48:41.2**

I wanted to ask you about some of those national and global organizations.

*Emil J Freireich, MD*

**1:48:46.0**

Oh, I want to tell you about [Lawrence] Einhorn. So the way that happened is—

*Tacey Ann Rosolowski, PhD*

**1:48:48.4**

So this is the Association for Patient-Oriented Research?

*Emil J Freireich, MD*

**1:48:55.2**

Yes. More and more—I told you about all the geniuses at the NIH. I actually liked them. They're all nice guys, but they just don't know anything about research. They're lab guys. Fidler is a pet peeve of mine because he gets so much attention, and LeMaistre had a thing for him. They gave him a medal and now to win the Nobel Prize, the president of the AACR, and he's famous. It's all good research, but it's just lab research. It has nothing to do with cancer. That's what I call phenomenology. You want to study goldfish physiology? You get a Nobel Prize for studying immunity in goldfish. That's wonderful. As a society, we can afford that. But it hasn't got anything to do with leukemia.

So 600,000 Americans are going to die of cancer in the United States of America. Why is that? Because we're not working on cancer. We can cure cancer; we just have to do it, but Fidler is not going to do it; physician-scientists are going to do it.

So the geniuses—the money, which began—the grant program began as clinical research. Eventually, the basic scientists said, "Hey, there's money." The peer review committees that review grants are unanimously eighty to 100% laboratory scientists. There is not a single study section at the Cancer Institute where the majority are physician-scientists—not one. So all the money flows to Fidler, clinicians.

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Okay, so if you're working in a university and you want to be chairman of the department of medicine and you have to do research and you have to publish, it means you have to get money. The only way you can get a grant is do lab research. So the smart guys at the medical school say, "I'll do a post doc with Fidler, shoot stuff in mice, write a grant, and I'll get money. Then I can get some fellows, I can write papers, I can get elected to the National Academy of Sciences." See, I'm not in the National Academy of Sciences—Fidler is and Mendelsohn is. No doctor ever gets elected. Only Larry Einhorn—he's the only one. He nominated me for the National Academy of Sciences, and I was rejected, passed over by some guy working in a lab.

So the young academics realized that the only way they can get promoted to assistant professor and associate professor is do lab research, so they did lab research. You have to go where the money is. The reason there is a Cancer Institute is that Congress put money there. Otherwise, no one would work on cancer.

Well, I told you that science in the United States, in medicine, began with the Association of American Physicians. These were professors who trained in Europe and came back and they learned European science and they learned physiology and so on, so they formed a scientific organization. All the professors, they published all the papers. They trained all the doctors. But the medical schools had very little science and research. That was just done by the professors. So if you want to become a professor in the United States, you could either go to Europe or you could study with a professor, and if you studied with a professor, you learned to do what he does and you write papers and you do experiments with mice and test tubes. The first thing you know, you might or might not get a job. But you need a society where you can become presentable. So in 1914 or 1920—I don't remember the exact date—these young associate professors formed another society—The American Society for Clinical Investigation. To get into the Association of American Physicians, you had to be a proven leader/professor, so they were called the Old Turks. To get into the Society for Clinical Investigation, you had to be a Young Turk. You had to be an associate professor or wanted to be a professor who is doing lab research, publishing, and getting ahead in academia.

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When I was working at Boston University, I got elected as a Young Turk when I was—whatever year that was—'65. I was forty. You have to get to be a Young Turk before you're forty-five, because if you can't produce before forty-five, you're never going to be an Old Turk. So how do you get to be a Young Turk? Well, you have to do research, and if you're doing research and you have to have a place to present it and you'd like to go to the meeting—and the Young Turks and the Old Turks met together in Atlantic City. They formed a thing called the American Federation for Clinical Research, the Young Squirts. And the Squirts formed their society about 1930, and we went along happily that way until the late '50s, and the three societies met together back to back. So it started with the Squirts, and the assistant professors presented their papers. The Turks and the Old Turks could hear their papers and could tell if they were good, and they criticized them and helped them get ahead. Then the next day, we go to the Young Turks, and they presented their papers to the Old Turks to prove that they can get ahead. Then there's the AAP, where all the professors talk about how great they are, and they actually have an honorary luncheon and so on. And all of this is honorific.

Now, to get into the Squirts, you only need to write one paper, so there were lots of Squirts. To get into the Young Turks, you have to make it under forty, you have to—only ten a year or something get in, so it's an honor if you're a Turk. But to get into the Old Turks, that's really an honor. You have one out of forty get in, and that's a lifetime badge.

So I climbed the academic ladder the usual way. I was a Young Turk at Boston University. When I went to NIH and I wrote my papers up about white cells—good stuff about mechanism of anemia—laboratory stuff—nobody ever benefitted from it—I got to be a Young Turk. Then I started publishing on leukemia, and when I came here, Rulon Rawson, who was our dean, recommended me, and I got to be an Old Turk. So I have all these credentials.

So the Squirts realized that to be a Young Turk they had to publish. In order to publish, they had to get grants. In order to get grants, they had to do lab research. So the societies—the Squirts—were the first to become a basic science society. They talked about clinical things, but basically they did Fidler stuff—mice and test tubes and chemicals. Gradually, the Young Turks became a basic science group. Gradually, the Old Turks became a basic science group. I went to every Old Turk meeting from the time I got elected in '65, and every year the speaker became more and more lab oriented. The last one I went to, about five years ago, the guy who is now the NIH director, the famous—cloned all the genes—he was guest speaker at the Old Turks. He didn't even have an MD.

So these societies became basic science societies. Well, if you want to move up the academic ladder and become an assistant professor or associate professor, this is the route you have to go. Well, the Young Turks decided that the way to get grants was to work in with the federated societies. These are the basic science societies—the science for physiology, for biochemistry, for pharmacology—all the basic sciences together in what's called the federated societies. So the

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Squirts left the clinical meetings and moved to the federated societies because that's where they had to present their papers in order to get grants. They had to do lab work.

***Tacey Ann Rosolowski, PhD***

**1:58:59.0**

That whole clinical focus has just disappeared.

***Emil J Freireich, MD***

**1:59:05.9**

This is a catastrophe for the US. This is even worse than the FDA. It's the same problem. You see, things always occur when there are crises. If there's no crisis, the natural trend is to go back to stability, and stability is no innovation. The way you can be stable is everybody does laboratory research, no upset. The money is distributed. It's all peers. The patients die of cancer.

So the AFCR left. Now, there are a handful of Neanderthal physician-scientists who didn't like that, because they didn't want their Young Squirts training in their departments to go to the federated societies. So the guy I mentioned, Gordon Williams, was the one who wrote an editorial in the Young Squirts' newsletter, and he said, "If the Squirts have left clinical research, we need to form a society for the Young Squirts who do clinical research." I read that editorial, and I said, wow, here's my man. So I dashed off a letter to Gordon Williams, and I said, "I am totally in support of this. We ought to start it immediately." He said, "Wait a minute. I got this idea from a guy named Bud Robertson, who works at Vanderbilt."

So we were all Old Turks, and we said what we're going to do is we're going to meet at the next Old Turk meeting—[Dr. L.E. "Bud"] Robertson, Gordon Williams, and Freireich. We're going to invite people we know who are totally committed to this cause. So we invited—my recollection is—four other people, maybe five. One of them was Ed Ahrens, who had written the book—a very famous book on—I can't find it. He wrote a book which documented what I just said, but not just talk. He went to all the NIH review committees, laid out all the peer reviewers, laid out all the grants that were awarded, looked at all the subjects, and he wrote a book with all that data that demonstrated that the flow of money was progressively away from clinical research to basic research, and it was impacting health. We're not getting any clinical research.

So Ed Ahrens came and a guy named Jules Hirsch, who worked at Rockefeller University, a very famous guy in body composition. Then we had the lady who ran the grants program for the research centers, and so on. We had about seven people. We decided to form a society. We're the founding members of that society. We called it the Association for Patient-Oriented Research.

Now, we tried to get back with the Young Turks and Old Turks, but they didn't want us. They were already laboratory guys. So we have to start this whole progression over again. We have to get a clinical Young Squirt, a Young Turk, and an Old Turk Society of Patient-Oriented Research. So we started the society in what year?

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***Tacey Ann Rosolowski, PhD***

**2:03:11.4**

In 1998.

***Emil J Freireich, MD***

**2:03:13.4**

In 1998, and Bud Robertson was the first president, and I was the eighth president. It's struggling. It's not going to make it.

***Tacey Ann Rosolowski, PhD***

**2:03:26.1**

Oh, really? Why?

***Emil J Freireich, MD***

**2:03:28.4**

Why? Because they made the mistake of hiring a doctor to be the director of the cancer institution. It was a big mistake. You don't allow doctors—and that's when all this clinical stuff began. I'm blocking on his name right now. He was a radiologist from Hopkins. He became the director of the Cancer Institute. He made the diagnosis immediately that there was no funding for clinical research, so he created the Clinical Translational Grant Program. He got all the directors together. He embarrassed them into realizing that there was no patient-oriented research, there was no ongoing clinical research, and he convinced them all to set aside some money in a pot, under the director, to give grants to people who would do what they call translation research. You don't want to call it clinical research because they've got to do laboratory. But they are going to take all this Fidler stuff and apply it to patients. That's the paradigm. If we discover everything in a lab and we give it to some dumb doctor, he'll know how to cure cancer—translational research.

Unfortunately, he was a radiologist. He was not a doctor, but he was a radiologist, and he still believed in that paradigm. He didn't recognize the fact that the inverse is the case; the translation occurs from the patient to the laboratory because if you're not working on clinically relevant problems in the laboratory, you're working on goldfish. That's fine. You can cure goldfish. And we can have more healthier goldfish, but we're not going to have healthier people.

So the Translational Research Program was funded, and it was called Clinical Translational Science. All the academic institutions that were hurting because they couldn't get any money for clinical research became translational research centers, and all the people at APOR applied for grants, and they all got it. The guy who was the chair elect of APOR decided to form a society—the Clinical Translational Research Society. In the first round of the awards, the Health Science Center got—that shows you—you know—Tyson. Tyson became the thing. And Kurzrock's

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program, our K-30 program, got funded. Now Tyson is back in charge, so you know where that's going to go, straight down the pits. That was the end of funding for our clinical trial program.

***Tacey Ann Rosolowski, PhD***

**2:06:35.7**

The existing paradigm is really strong.

***Emil J Freireich, MD***

**2:06:37.4**

So the CTSA lasted one round, and then it went away. The guy who started all this, he's gone—I forgot where he went—and they got a basic scientist back in. We're back on track. The people who were in APOR have gone to this CTSA thing to get money. We met with the CTSA at our annual meeting to try—the main purpose is advocacy. We have to convince— We're never going to convince the National Institute of Health that clinical research is important. The only ones we can convince is Congress. Those are people who are sick, and their parents are dying of cancer, and they want progress. And when the Nobel Laureate goes to Congress, they say, "What progress have you made?" He says, "Oh, we've made great progress with translation." "How much money are you spending on clone research?" "Zero."

So eventually we have to—we have an advocacy organization, which includes these guys and APOR and the AFCC. They're coming back, the Young Squirrels. But there's not enough money. APOR has no money. We tried to make money from industry, but industry worries about conflict of interest. They can't mess around. So we have no money. CTSA program is fading down. The money has been reduced. The Young Turks are still getting money from the federated societies—the basic sciences. So we don't have the money. We have a lobbyist, but what could have worked did not, so we need another strategy. Leaders of academic medicine have to get to Congress, because it all starts with money. If Congress says—it's like MD Anderson. There would be no MD Anderson if the legislature didn't pass a bill to have a cancer hospital. Roswell Park is the same thing—the legislature—because the legislature represents the people. The NIH represents the scientists. As they used to say, you lick your own ass. You don't go outside your circle.

So APOR exists, but it's not functioning well. People aren't joining. We don't have any money. But the idea is right. So we're going to have to get to Congress some way. For right now, as we said in the first session, this country is—we're only worried about safety. We don't care if 600,000 Americans are going to die this year from cancer. They're just sick.

***Tacey Ann Rosolowski, PhD***

**2:10:06.1**

It sounds like you have to wait out—

***Emil J Freireich, MD***

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**2:10:07.6**

What we're worried about is the economy, Greece, the stock market, safety, no drilling, no energy, clean air, clean food, no drugs. So we can't make any progress with the legislature, because the legislature— We had a bill in the legislature four years ago to get around the FDA squelching new agent development. It was called the Patient Rights Bill or something, and I was an advocate. We went to court. We won in regional court a couple of times. The general idea was that if a patient and his doctor want to undertake a treatment, the FDA can't stop it. Why should they? But the bill failed, not for lack of support, but for lack of priority. There were just so many things pressing on these people. Now it's can we even run the government. The guys elected to Congress have got to cut the budget. You can't talk about money for clinical research. They're trying to fight for money for NIH even. Can you imagine? Can you imagine reducing the budget for basic research? Fidler? My God! The guy who is director of the NIH goes to Congress and says, "We'll become a backwards society if we don't shoot cells in the tails of mice. Just cure people? That's terrible."

*Tacey Ann Rosolowski, PhD*

**2:11:55.3**

Dr. Freireich, we're almost at 11:30, so shall we—?

*Emil J Freireich, MD*

**2:12:05.5**

I've worn you out. I've still got a few topics I want to cover, but you've done very well.

*Tacey Ann Rosolowski, PhD*

**2:12:11.1**

Absolutely. We've done very well. Why don't we stop for today, and we can make another appointment and continue. The time is 11:25.

**2:12:27.7** (End of Audio Session Two)

## **Emil Freireich, MD**

Interview Session 3 — October 11, 2011

### **Chapter 00C** **Interview Identifier**

*Tacey Ann Rosolowski, PhD*

**0:00:03.8**

This is Tacey Ann Rosolowski. I'm in the office of Emil J Freireich, MD. This is our third session together. The date is October 10, and it is about 10:15. I'm just recording the identifier. Dr. Freireich is finishing up an email, and he will be with us shortly. Here we go. Ten minutes early. Good morning.

*Emil J Freireich, MD*

**0:00:27.8**

Good morning. You look bright and awake this morning.

*Tacey Ann Rosolowski, PhD*

**0:00:32.3**

Well, I'm glad. It's 10:30. I've got to be, right?

*Emil J Freireich, MD*

**0:00:35.7**

Now come the hard questions.

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## **Chapter 11**

### **A: Overview**

#### ***A Critical Need to Fund Patient-Oriented Research***

### **Story Codes**

D: Understanding Cancer, the History of Science, Cancer Research

D: The History of Health Care, Patient Care

A: The Researcher

A: The Clinician

D: Business of Research

A: Activities Outside Institution

A: Professional Values, Ethics, Purpose

C: Patients

***Tacey Ann Rosolowski, PhD***

**0:00:38.3**

Now come the hard questions. There were a few more questions I wanted to ask you about the national organizations, and then I had some things I wanted to ask you about MD Anderson and some personal things. Then we'll be set, and if there's anything else you want to talk about—

***Emil J Freireich, MD***

**0:00:57.3**

Oh, good. So you want to stay until midnight?

***Tacey Ann Rosolowski, PhD***

**0:01:00.2**

Sure. Why not? Can we order out for food?

***Emil J Freireich, MD***

**0:01:03.1**

We can.

***Tacey Ann Rosolowski, PhD***

**0:01:06.5**

Well, last time we talked about the Association for Patient-Oriented Research, but we didn't get to the Global Organization Against Leukemia. I read that you were part of the organizing committee for that in 1998, and you served as its first president. I was wondering if you could tell me about that global initiative and what that meant and just how that institution was set up.

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*Emil J Freireich, MD*

**0:01:31.8**

Well, the real authority on that is Dr. Keating—Michael Keating. He trained when I was head of the department, so we've been colleagues for all the time. When he formed the Global Organization Against Leukemia, I was on the board, so I helped advise him, but I'm not the expert. The global business is, of course, my boss's business, Dr. [W. Ralph] Vogler. He just made a great video where he was in some—Mongolia, I believe it was, or something. But my orientation is more—I'd rather cure leukemia than spread the word. That's other people's problems. That's a public health issue. I'm a research guy.

*Tacey Ann Rosolowski, PhD*

**0:02:28.6**

So what is your involvement, and why did you decide to be involved with it if it's not what you—?

*Emil J Freireich, MD*

**0:02:34.9**

Well, I'm just a member of the board, and we review the budgets and the plans for expansion and it's a personal favor to Dr. Keating, but it's not a big deal for me.

*Tacey Ann Rosolowski, PhD*

**0:02:46.2**

Okay. Now, that organization was one of the cosponsors of the conference that you were recently attending in Croatia, in Dubrovnik?

*Emil J Freireich, MD*

**0:02:56.4**

Yes, it was.

*Tacey Ann Rosolowski, PhD*

**0:02:59.5**

I was curious about that whole phenomenon of these international collaborations and conferences and what you felt was coming out of that, how fruitful it's been?

*Emil J Freireich, MD*

**0:03:17.3**

Not a big deal for me. The international meetings are very important because it does allow for person-to-person interactions, and it does disseminate results of research. So the international meetings are quite important, and they do lead to collaborations. Some of the international collaborations are quite significant, but, as I say, not my cup of tea.

*Tacey Ann Rosolowski, PhD*

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**0:03:49.0**

What are some of the international collaborations that you feel—?

*Emil J Freireich, MD*

**0:03:52.3**

National?

*Tacey Ann Rosolowski, PhD*

**0:03:52.9**

National or international—that have been very influential in your area of research?

*Emil J Freireich, MD*

**0:03:58.9**

Well, Dr. Zubrod and Dr. Frei created the first cooperative chemotherapy research group in 1955, and that had a big influence on the way clinical research was done.

*Tacey Ann Rosolowski, PhD*

**0:04:21.2**

What was the name of that group?

*Emil J Freireich, MD*

**0:04:22.4**

That was called the Leukemia Cooperative Group, and it evolved into what is called Cancer and Leukemia Group B. It started out as a collaboration between Dr. [James] Holland's group at Roswell Park and our little group at the Cancer Institute. So there were only two institutions, but it immediately caught on, and a lot of people got interested. The focus was on childhood acute lymphoblastic leukemia, where we were making big progress. Then it expanded to all the cancers, so it became cancer and leukemia. It became Group B because the group at Memorial Sloan-Kettering formed a cooperative group. It was the second one, but in order to distinguish them, they called themselves 'A,' so the first one became 'B.' I was involved with them until 1962 or so, when we decided to concentrate on combination chemotherapy for children. I haven't had much to do with them since. When we first came here, I was active in the Southwest Oncology Group, and we did some studies with AraC, which were quite important. But then again, I preferred to work on innovative things. The groups tend to focus on applied things. If I claim that four drugs are better than three, they'll do a big study and spend a million dollars and get an answer that no one cares about. I'm on the innovative side.

*Tacey Ann Rosolowski, PhD*

**0:06:12.5**

Okay. I'm just trying to get a sense of how all those groups function and what their roles—

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***Emil J Freireich, MD***

**0:06:16.9**

Those groups are all—you know—they do applied things. APOR [Association of Patient-Oriented Research] was primarily a lobbying group. That is, we tried unsuccessfully to divert some of the money being spent on laboratory research to patient-oriented research, and we're still trying. And there may come a day when actually people will wake up and realize that all the advances in treatment begin with research on patients with disease and allocate at least some of the federal money to studying patients instead of laboratory stuff. So APOR was primarily a lobbying organization, not as much a scientific organization. We have plenty of scientific organizations. The International Society of Hematology, International Oncology, American Society of Hematology, which is international, ASCO, which is international. We have plenty of that.

***Tacey Ann Rosolowski, PhD***

**0:07:28.8**

I think maybe I—

***Emil J Freireich, MD***

**0:07:32.9**

I did spend time on ASCO.

***Tacey Ann Rosolowski, PhD***

**0:07:34.7**

What does that acronym stand for?

***Emil J Freireich, MD***

**0:07:36.8**

American Society for Clinical Oncology—it's the largest cancer clinical research organization. It was founded in '63, and I was one of the initial people to feel it was important. I've been a member ever since '64, and I attend annually. I was elected president in—I don't remember the exact date, maybe '72 or '73. When I was president, I started the *Journal of Clinical Oncology*, which is very important to the society, and I also started the commercial exhibits that generate a lot of income for the society.

***Tacey Ann Rosolowski, PhD***

**0:08:29.2**

What does that mean “generate the exhibits?”

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***Emil J Freireich, MD***

**0:08:32.0**

Well, when we have a commercial exhibit which is educational, but the pharmaceutical industry has exhibits, and they pay the society to use the space and have the exposure, so the society gains income. That income is used for awarding scholarships to young, promising scientists, supporting areas of research that are not being supported by NIH and so on. So ASCO is good thing. I like ASCO.

***Tacey Ann Rosolowski, PhD***

**0:09:00.7**

Now when you started, you said—what was it about that organization that you felt was really promising?

***Emil J Freireich, MD***

**0:09:07.1**

Well, when I graduated from medical school in 1949, we learned nothing about cancer treatment or patient care. It was like mental illness. You just put all those patients somewhere to die. During my graduate medical education, we didn't learn anything about cancer research or treatment. I trained in hematology. But in 1946, the Americans discovered nitrogen mustard and began to treat lymphatic malignancies. In 1948, Dr. Farber reported on methotrexate doing temporary remissions in children. So by the time I did my training in hematology, we started to treat leukemia, but the other cancers were largely ignored. When I went to the Cancer Institute, that's when the focus on cancer occurred, because people go where the money is. In the initial cancer effort, Congress realized that cancer was becoming a major healthcare problem, and they put money in place, and people—young physicians—began treating cancer. So that was important.

We were working on leukemia, and we needed a forum to present our information, so initially we presented our stuff to the American Association for Cancer Research, the AACR, but the AACR is an organization of laboratory-based scientists. Dr. Fidler [Isaiah Joshua Fidler, DVM, PhD [Oral History Interview]] and Dr. Kripke [Margaret Kripke, Ph.D. [Oral History Interview]] have both been president. The clinical papers were relegated to the last half day, so if they began on Wednesday, Thursday, and Friday, on Saturday morning we got to present our papers. None of the laboratory scientists attended. The first time I gave a paper at AACR, besides the chairman and my wife, there was only one other person in the room. There just was no interest in clinical research.

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A number of physician-scientists got together and decided that we ought to have a society for clinical oncology because we would have a forum. That society met the first time in, I think it was '64, and we met the day before AACR, because we were all cancer researchers, so we could go to the ASCO meeting the first day, and then continue in the AACR. Our papers weren't on Saturday morning. They were before the meeting, and we had an audience that was interested in that material. So ASCO boomed, and by the time I was president—whatever year that was—I should have something on the wall about that. I guess I don't.

***Tacey Ann Rosolowski, PhD***

**0:12:36.9**

I'll be able to find it in your CV.

***Emil J Freireich, MD***

**0:12:38.5**

It's in my CV. So the year I was president, we started the journal, we started exhibits, and the consequence was that ASCO boomed because we had money, and AACR had very little money. All they got money from were instrument manufacturers, so AACR decided to separate from ASCO because ASCO was too big and they were too small. AACR separated from ASCO, and that separation is maintained to this day.

Well, in the meantime, in 1955 or 1956, hematology was an important discipline. There wasn't an international society. Dr. [William] Dameshek, who founded the journal *Blood*—the most important public—like the *JCO*—an important publication for hematologists—also founded an American Society for Hematology. And again, I happened to go to the founding meeting, and I was a lifetime member of the American Society of Hematology.

But hematology was dominated by benign hematology. Hematologists did red cell, platelet, white cell stuff, but the malignant hematology was restricted to us weirdos mostly working at the Cancer Institute and Roswell Park and so on. So when we sent our chemotherapy papers to ASH, we got treated the same way we were by ASCO. Our papers were put on the last session on Saturday morning. By the time you gave your paper, there was only two other people in the room. It didn't work for ASH, so the malignant hematology moved from ASH to ASCO. But once we cured childhood leukemia and we had treatment for CML, malignant hematology became quite important.

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At the same time, benign hematology became trivial. There were fewer and fewer patients consulting benign hematologists. The American Society for Hematology tried to recover malignant hematology, and to a large extent, they have. Most of the cancer hematological malignancy papers go to ASH, which meets in December. Very little goes to ASCO, which meets in the spring—usually June or May. There's kind of a little collaboration between the two societies because most of the people who do malignant hematology also treat cancers, so there's collaboration. The hematologists had to treat leukemia to make a living, so the society recognized that.

Under the leadership of our chairman, Dr. [Hap] Katarjian, we're trying to form a new society called the Society of Hematologic Oncology. The reason that occurred is because we started these meetings at MD Anderson in the fall, before ASH meets in December. We had these meetings in September. We started in Houston, and we alternate elsewhere. The last one was in Dubrovnik. The next one will be in Houston in '12. But the problem is that it's gotten so big that it's time for us to have a big society. So Dr. Katarjian suggested to ASCO that they have a day for hematologic oncology, but ASCO doesn't want to fight with ASH, so we're going to form our own society. Things evolve quickly.

***Tacey Ann Rosolowski, PhD***

**0:16:58.2**

They do. Is there anything else that you wanted to comment on about organizations of that kind, or societies?

***Emil J Freireich, MD***

**0:17:07.5**

No, I think they're important for exchanging information, but in the modern age, face-to-face communication is trivial because everything is so electronic. I met with the head of our library the other day. She said, "What should the library be doing?" I said, "Just keep the electronics going." You can do everything from your iPad now. If you want to talk to someone about a paper— So the face-to-face meetings that were important in the early days for networking, for getting ahead so the young people could get promoted and get their work recognized, is less and less important, because now, when you publish a paper, everybody has access to it. The indexing and the electronics are so fantastically efficient that these big society things are less important for scientific communication. It's a good place for the young people to expose their research to their seniors and get ahead and so on and so forth, but that function is really not terribly important. What's important is communication. Now we have virtual meetings, everything is on TV, everything is on the Internet. The iPods are so fantastic. So all those old ideas are anachronisms. It's nice.

But APOR is important because we do have to lobby, because the direction of research is more in the control of the public. It's like the Tea Party people say, "We want to do what the people want," and the Democrats all go to Congress and say, "We serve the people," i.e. we know what

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they want. And we're in the same boat. The academic scientific community, they know what's important—clone the genes, treat the mice, metastasis, all that stuff. That's important. If you know everything about mice and tissue cultures and cells and culture, then leukemia will just go away. But the reality is realized by the people. If 600,000 Americans are going to die of cancer, well, we're working on metastasis research, shooting tissue culture cells in the tail veins of mice. When are we going to work on people? Well, let's do translational research. So now we have the Society for Translational Research. The idea was, okay, you've discovered all this basic science, now let's use it to treat people. That's a great idea. But again, translational science has degenerated into laboratory research.

If the public wants us to cure cancer, they're going to have to put their money where their mouths are. They're going to have to support clinical research. That's what APOR is all about. AACR will never advocate for clinical research. They are strictly laboratory research. And as I pointed out in our last interview, all the sections are manned by Nobel Laureates who won the Nobel Prize for discovering genes. No Nobel Prizes are given to people who cure leukemia. That's trivial.

***Tacey Ann Rosolowski, PhD***

**0:20:59.4**

It seems like it's a real basic cultural prejudice or bias.

***Emil J Freireich, MD***

**0:21:05.7**

It's one of the enormously attractive ideas that so appeals to your imagination that it's hard to face reality. People are born with a clean slate, and then they progressively accumulate biases, and those biases are difficult to break through. Of course, the bias that every teacher and every academic— If you go into the academic communities, they're all left-wing, bleeding heart liberals. They're all geniuses. They've all discovered Hippocrates or mice or Nobel Prizes and now they're authoritative and they know what we need—more of them. As far as cancer patients, they don't have to worry about that.

Like I said in the last interview, the difference between a scientist and a doctor is the doctor faces— This morning, for an hour at rounds, we saw three patients who were under thirty dying of leukemia. One was a guy in the military, a martial arts guy. He's got advanced leukemia, badly treated. One a twenty-six-year-old girl with horrible disease. I mean, come on. We have to get on with the problem, and only the public can make that known. Now, the problem is that there are only 600,000 Americans going to die this year, and that's a small number. The rest of them, they don't worry about cancer. They're going to prevent it. That's one of my pet peeves. If we're going to prevent cancer—you know—all the early detection models only increase the number of patients with cancer; it doesn't do anything to the mortality. The mortality stays the same.

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Prevention is not better than cure. Cure is always what works. All the progress made in medicine has depended on cure, with the possible exception of small pox vaccination, which quelled an epidemic, but in modern times more people die from disseminated small pox vaccine than die from small pox, as you know. Vaccination is useful to stem epidemics when you know exactly what the antibody and the viruses are. But as far as cancer prevention, outside of quitting smoking—which is self-evident. Treatment is the way to go. People are dying, they need treatment.

When the AIDS people needed treatment because they were dying—they were all twenty-year-old, healthy guys but a small minority of the population. By the way, AIDS was discovered by a doctor at the bedside, not a laboratory guy. They started to do culture viruses and treat it in vitro and do randomized tests. Well, the AIDS guys said, come on, let's start treating AIDS. They marched in the streets, because the AIDS guys were already activists. They're homosexuals. They were used to parading in the streets. When they got AIDS, they paraded in the streets and they got on treatment and now nobody dies of AIDS anymore, unless you can't afford it. You can go to Angola, and you don't have the drugs. But AIDS is essentially a chronic illness now.

But cancer patients are not activists. They're not politically active. They go along being normal, healthy people believing that if we do mammography and PSA we'll prevent cancer and it will go away. Just support laboratory research and discover all the genes, and we won't have any problem until the day comes when the doctor says, "Oh, my. You've got leukemia." I better go see a doctor, not the guy working in a lab. We've got to go see a doctor who is treating leukemia. And we now cure ninety percent of children. We cure twenty-five to thirty-percent of adults with leukemia. We cure converted chronic granulocytic leukemia to chronic disease, and none of this—

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## **Chapter 12**

### **A: Overview**

#### ***The FDA as a Barrier to Research Innovation***

### **Story Codes**

A: Critical Perspectives

A: The Researcher

A: The Clinician

D: Understanding Cancer, the History of Science, Cancer Research

D: The History of Health Care, Patient Care

D: Politics and Cancer/Science/Care

D: Ethics

A: Professional Values, Ethics, Purpose

C: Patients

***Tacey Ann Rosolowski, PhD***

**0:25:39.9**

What needs to be done to increase those numbers—the rates of success?

***Emil J Freireich, MD***

**0:25:44.5**

We have to get funding for clinical research. That's what APOR advocated. We said to the NIH, look, why don't you have—? They have eighty-five study sections—biochemistry, physiology, etc. Why don't you have one for clinical research that's staffed by physician-scientists? Let's fund the best clinical research. How about that? Forget it. They added two clinicians to one of their study sessions. They said, see? We got them there. They're a minority. They don't direct the flow of money. So it's going to take legislation.

I work with the Abigail Alliance. There's an outfit called the Abigail Alliance, which was founded by the father of a lady who was—I forgot how old Abigail was. She was very young—twenty-two or twenty-three. She got head and neck cancer. They treated her. Everything failed. She was ready to die. Dr. Mendelsohn had worked on the epithelial growth factor receptor antagonists. They were in clinical trial. She didn't qualify for the clinical trial because she'd had this and that, so she couldn't get the drug, so they appealed to the drug company to give her the drug, and the FDA said, no, you can't do that. You can't get the drug if you're not eligible for the clinical trial because it will detract from the clinical—you know—it's all this crazy reasoning. All of which is false. So she died. She never got the drug. Her father formed this organization called the Abigail Alliance. He recruited family members whose loved ones had died being denied treatments which would have saved their lives.

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When we first were working with Gleevec, the very first trial, the FDA required us to do a randomized trial—Gleevec versus conventional therapy. I had a patient with CML who was on the board of directors of Novartis—rich, powerful guy. I wrote to Novartis, to the president, and said, “This man is not eligible for the clinical trial. If you give us Gleevec, we can save his life.” They wouldn’t do it. The whole drug development process now is run by the FDA. The FDA is manned by failed physicians. The guy who runs—[Dr. Richard] Pazdur was on our faculty here. He was a so-so, average guy. He’s been in the FDA for ten years. He doesn’t know anything about anything, and he decides what needs to be done.

What does industry do? They say, well, we’ll never get a drug approved unless Pazdur approves it. So when they get a drug and want it developed, they go to Pazdur. So they now have an organization where the regulators in industry, the regulators in FDA—I’ve written an editorial about it—it’s right there—are the ones who direct research, not the geniuses who discovered drugs, who developed drugs, who treat patients. They’re out of it. It’s all done by guys with pencils who are desperate, protecting their careers. That’s what the word bureaucrat means. Bureaucrats protect their job. They don’t want to cure cancer. It’s a horrible thing.

So I worked for the Abigail Alliance. We got a judgment against the government. We had a bill introduced in the legislature, and we almost got it through. The idea was that if a patient and his doctor want access to an investigational drug, they should provide it at cost so that nobody is harmed, there’s no danger to anyone who didn’t volunteer, there’s no public foray, there’s no danger to the manufacturers, no danger to the government. It’s just insane that we don’t do that, but today it’s true. People are dying every day with drugs that could be—could be—curative and they can’t get them because of this stupid law. So we have to get our heads screwed on right. The public has to awaken to the fact that the government, which created the NIH, which created the Cancer Institute—there wouldn’t be any cancer research if it wasn’t for the government—the representatives of the people.

We need to have, as everybody has said, legislative relief. The FDA has to get out of the way of drug development. Drug development is between the scientific community and the afflicted patients. If you have cancer of the lung and you come to MD Anderson and the world’s greatest lung cancer doctor says, “Here’s the drug I think is good for you,” what’s the government got to do with that? It’s insane. It’s what happened in Russia when they had Lysenko-ism. You know, Lysenko was a scientist who declared that there was no heredity, because the Communist manifesto was everything is environmental. We’re living in a country where the government makes science. They tell you what you can and can’t do. It’s ridiculous. And we talk about freedom? When you get leukemia or are dying of leukemia and come see the world’s greatest leukemia doctor who has cured more patients of leukemia than any living person, before I can give you the drug that I think is good for you, I have to get approval from Ricky Pazdur who has never treated a leukemia patient in his life and never will—insane. Why are we doing it? You know the answer?

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These things always occur in times of panic. You see, the liberals believe that—all the intellectuals and professors believe that they know what's good for everybody. Those stupid people out there— So it's always a time of crisis. The FDA began when there was a manufacturer who sold sulfanilamide or something and fifty people died of toxicity, so the government said we have to have a law that says the products that are sold to the public have to be safe before you can market them. Great idea. So the FDA began on safety. Well, as usual, you get a government program and it escalates. Safety got worse and worse and worse.

Then there was the Thalidomide disaster. Here's a drug that was completely safe. You could have studied it in a laboratory for fifty years and never predict that it did what it did. When you gave it to pregnant women, their children came out without arms and legs. Ten years after we knew it happened in the clinic, scientists in laboratory finally figured out how to reproduce it in a mouse. There was no way this could have been prevented by anybody. There was no knowledge base. It's just one of the realities you have to face. But Congress had the solution. FDA now must approve any drug that is marketed to the public for safety. Okay. Well, I already explained to you how that works. If I'm in the FDA, and the manufacturer says here's the drug that cures cancer, they say, "Well, is it safe?" Well, if you give it to mice in a lethal dose it would kill them. Well, maybe you ought to give it to horses and cows and rhinoceroses in Africa—anything to delay it because if it kills anybody it's your ass in a sling.

The FDA has this award named for Frances Kelsey, who was the one who didn't approve Thalidomide in the United States. It was approved in Europe. In the United States, she didn't approve it, so no Americans had Thalidomide disease. So they made a medal for Frances Kelsey. Well, why didn't she approve it? Well, it was sitting on her desk while she was on vacation. So that's the best and FDA can do; you just don't do anything. If there is no drug, there is no danger and there's no progress.

So they were doing okay. We finally figured out how to kill enough mice and convince enough people that you could get some progress, and then another tragedy. What was the tragedy? I can't remember. Another tragedy occurred, and Congress passed a bill that the FDA has to decide not only on safety but efficacy. So now you can't market anything as effective until the government says it's effective. Well, anyway, the whole thing is insane.

The medicine has to go back to the academic medical community. There's no way the government can intrude on— There's no other area of research where the government decides what research can be done—none—maybe atomic energy. But in medicine, the government decides everything, and the government people are all bureaucrats. Some of them are scientists. The scientists who work for the government do research. They don't mess around with sitting around the desk, approving drugs. Well, anyway, how did we get onto that?

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***Tacey Ann Rosolowski, PhD***

**0:35:50.3**

I can't remember.

***Emil J Freireich, MD***

**0:35:52.1**

I can't either. APOR—so APOR is advocating for the public to recognize that cancer is a major healthcare problem. They have to put funding in the hand of physician scientists who are working on humans with cancer. We have this MD/PhD program that I told you we can't get by the dean. Dr. Kurzrock has this slogan. If you can get a PhD working on mice, why can't you get a PhD working on people? What's the answer? The answer is that if you're working on people, it belongs to the government—bad situation. We've got to rectify it, and it's got to be done like the AIDS people. We've got to get the cancer population marching in the streets and saying let's make progress and stop kidding ourselves that safety is—

Oh, the efficacy situation. What was the efficacy one? I forgot what the crisis was, but we have a number of examples where we have drugs that are very effective for five percent of people with a given disease—CLL. They go to the FDA and they say it's not effective enough. So the five percent can't get the drug because it doesn't work in more than five percent. That's legislation, and it's actually a guideline that the FDA adheres to. It's insane.

***Tacey Ann Rosolowski, PhD***

**0:37:34.7**

I think I've gotten a good picture.

***Emil J Freireich, MD***

**0:37:36.6**

That's why APOR is important. We have to lobby. The guy who sponsored the legislation for the Abigail Alliance—and I was one of the litigants—was the senator from Kansas. Do you remember his name? But he didn't run for re-election. He ran for the presidency, and he didn't win. So that legislation is floundering. It never got through the rules committee so it never got voted on, but it certainly would have passed. And the idea was that—well, investigational drugs should be made available to patients and academic physicians. I'll give you a reprint.

***Tacey Ann Rosolowski, PhD***

**0:38:25.8**

Yeah, I'd like to see it.

***Emil J Freireich, MD***

**0:38:27.9**

It's right here. I keep my latest diatribes on my table in case people will read them.

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*Tacey Ann Rosolowski, PhD*

**0:38:35.7**

I may even have read that when I went online. I think I saw something to that effect online.

*Emil J Freireich, MD*

**0:38:39.9**

It's an editorial. It's not citable.

*Tacey Ann Rosolowski, PhD*

**0:38:43.4**

Okay. So I think I've gotten a good picture of that whole cultural and political dilemma.

*Emil J Freireich, MD*

**0:38:52.0**

From my perspective.

*Tacey Ann Rosolowski, PhD*

**0:38:54.8**

Yeah. In terms of the areas of research—I mean—I know you feel that clinical research needs to be done—but in terms of the community of clinical researchers that you know, what are the most promising, exciting areas of research that can be undertaken or followed up on right now to help with the leukemia problem?

*Emil J Freireich, MD*

**0:39:18.1**

I'm not sure what you want me to say.

*Tacey Ann Rosolowski, PhD*

**0:39:21.6**

Well, I'm asking kind of a state-of-the-field.

*Emil J Freireich, MD*

**0:39:25.1**

Anyone who has—you know—one of the greatest experiences that a human being can have, after you satisfy all your physical needs—you know—sex, food, music, whatever—the greatest personal human satisfaction comes from discovery. If you work out something that no one ever has done before you, that is an exhilarating event, and once you've discovered something, you become a new person because you now believe that you can discover anything. If I discover a little, teeny thing, I'm willing to tackle something bigger and bigger and bigger, and first thing you know, you want to cure cancer. So it's been studied systematically, scientifically, that young people who make discoveries early in life are the ones who make discoveries later in life, because it builds confidence and a curiosity that allows you to discover things.

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So my personal view about transferring things from the academia to the public is a trivial problem. That occurs instantaneously. When the first clinical trial of Gleevec was done, Novartis couldn't make enough Gleevec. When the first polio vaccine was proven effective in a randomized trial, they couldn't make enough polio vaccines. So the transfer to the community is a trivial problem. That occurs immediately because the public and the caring physicians want the best for their patients. Regardless of what the skeptical community believes, when a patient comes to a doctor, he really wants to help you. With the exception of some rogues, that's an ethic. What we need is an environment where people can investigate. What makes humans human is freedom. If a person is free to investigate what he thinks needs to be investigated, things will happen. If people have to get federal approval before they can do research, they're dead in the water.

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## **Chapter 13**

### **A: Overview**

#### ***Leukemia as a Key to Understanding Cancer***

### **Story Codes**

A: Overview

A: Definitions, Explanations, Translations

A: The Researcher

A: The Clinician

D: Understanding Cancer, the History of Science, Cancer Research

D: The History of Health Care, Patient Care

D: Cultural/Social Influences

A: Professional Values, Ethics, Purpose

C: Patients

***Tacey Ann Rosolowski, PhD***

**0:42:15.2**

I guess I was thinking about some more specific examples too. I mean, in the area of what's going on with leukemia right now, what do you think are the most exciting, promising avenues that people are following?

***Emil J Freireich, MD***

**0:42:31.2**

Oh, well, I've written extensively on the subject. I'm going to give a talk to the History of Medicine Society next month, and the title of the talk is that the cure of cancer goes through leukemia research. If I were controlling the NIH budget, I would put the major part of the budget into clinical research and leukemia research. Why is that? With the other cancers, we have the problem of understanding what's wrong with them. You have a lump in the breast. You take it out, look in the microscope. It looks like the kind of things we've seen where women had cancer all over the place in the breast, so it looks like cancer. Take it off, radiate, operate, do everything. Unfortunately, it doesn't make any difference. The surgical approach to localize cancers—breast, pancreas, bowel, brain—made the observation that if you take the cancer out surgically—mechanically—the likelihood of it recurring locally is higher than likelihood of it occurring distally. So the obvious thing is to take out more. The surgical business got to the point—when I started cancer research—where the treatment for breast cancer was a hemibody. They took off the upper quarter of the body, and it didn't affect the mortality, until Dr. Fisher did this great experiment where he randomized women to getting just local treatment and radical treatment. It made no difference. So now we know that's not the answer. Okay. Well, the next step is local.

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Well, the important point is that, for all the solid cancers, we have no idea how to distinguish between things that look like cancer and things that are cancer, that are going to kill you. So the consequence is we do all these silly things—PSA testing for twenty years, killing men's prostates and torturing them until we finally, twenty years later, figure out it's no good, mammograms, X-rays—until we figured out the mammograms cause more cancer than they prevent. We don't have enough of an understanding of the biology of those cancers to know how to tell when a lump in the breast is going to end up in the brain. We talked about metastasis. The Fidler model of metastasis just doesn't fit with the clinical model, because we have patients with metastasis without a primary. So the occurrence of cancer is something we have to understand.

But the cancer problem resides with those cancers that metastasize. The ones that don't—when I was a young cancer doctor at NCI in 1955, we took care of a man who had a melanoma on his foot that was so large, it was larger than his head and it was bleeding and ulcerated. He came in, and we took off the melanoma, and he was cured. We have other patients who had melanoma this size and you take off their arm and they end up with brain metastasis. We don't understand the biology of the cancers in solid organs, but we do know that cancers that are metastatic are the ones that kill people.

I took care of women who had breasts that were the size of footballs, and we took it off and she was cured. It didn't go anywhere. But my sister had a three-centimeter lesion. She had a radical mastectomy. She had postoperative chemotherapy. She died in three years of metastatic disease. So we don't understand how to tell the ones that are going to kill from the ones that don't. Why is that? Part of it is the illusion that's created by the experimental models. We can reproduce metastatic cancer in animals—all species—and we think they understand it, but we can't reproduce it in man. And the experimental data doesn't fit with the clinical data. I've written an editorial on that. I'll give you a reprint if you want.

Leukemia is different. Leukemia doesn't have a local presentation. We don't look at the tumor and say, oh, this is going to kill you. Oh, this is not. Once we know you have leukemia, we know what its biology is. So there isn't any surgery or radiation therapy—all that garbage—prevention and so on—early detection. Leukemia is a systemic cancer from the start. And that's why all the systemic treatments for all the solid tumors were developed in leukemia, because we realize that, once you have the diagnosis, it's already systemic so we need systemic therapy. We don't need to radiate and surgery and all. We've got to get after it.

Well, the other advantage is we can examine the leukemia every ten minutes. If you have cancer of the colon, we get one crack at it. You might get two. We have this BATTLE study [(Biomarker Based Approaches of Targeted Therapy for Lung Cancer Elimination Project funded by Department of Defense] where they do biopsies every month, but for leukemia we can do it every day. Not only that, we can grow the leukemia cells in tissue culture. We can transplant them to immunodeficient animals so we can treat them in vivo and in vitro in the test tube, and all the techniques of understanding the biology of cancer come out of leukemia. We

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understand the chromosomal defect, the genetic defects, and what the genes are, how you control it, and how you regulate it. And that's the reason there is so much progress in the control of leukemia and lymphoma and the other systemic malignancies that don't respond to local therapy.

So I think if we propose that translation does not start with knowing all the things in a laboratory about a mouse and the cell culture, and we admit that studying people and the disease we want to conquer is the way to go, and if we admit that we can apply those resources to understanding the nature of leukemia, everything we've discovered in leukemia immediately transfers to the solid tumors—immediately.

The first adjuvant trial—I gave you one of my reprints. That's my discovery. It's now practiced universally. We now have neoadjuvant therapy, where when a cancer is staged to be potentially metastatic, they get treated with systemic treatment before they get local treatment.

We still have a lot of mysteries in leukemia, but starting with the fact— You see, if you want to understand anything—if you want to understand physics, chemistry, astronomy, anything—the way to do it is learn how to perturb the equilibrium. If you can shake it a little bit, you'll see what it does. And that's the beauty about leukemia. We can get the leukemia cells and we can do it. We can study leukemia in experimental animals. We can make leukemia in experimental animals. Starting from the disease, we can move backwards to the basic science. That's how everything works. That's how platelets work. That's how molecular genetics work.

I think I told you about the—it's part of my lecture I talk about—the discovery of BCR/ABL—the Philadelphia chromosome. That occurred because a pathologist was working with a laboratory guy to try to grow leukemia cells in the laboratory, and they were growing cells and discovered that if they put phytohemagglutinin in to get rid of the red cells, the cells would— And they started to look at the chromosomes. This was David Hungerford and Peter Nowell. They discovered that there was an abnormality in the chromosome—a little break on the chromosome. The first publication was an abstract—two paragraphs—and that discovery revolutionized the whole thing. It led to the realization that there was a neo gene. The neo gene, obviously we need something. It led to Gleevec, and first thing you know, CML, which used to have a median, average life span of three years—ninety percent mortality in five years—now, ninety-five percent of patients are alive in ten years, and all they do is take pills, like taking vitamins—amazing.

Now, we still don't know how it began—what caused the translocation—but the translation in the laboratory is occurring, and people are figuring out that when the chromosomes are in interface—when they're all scrambled up in the nucleus—that the BCR and the ABL genes are close to each other, so the possibility of a translocation exists. There's no virus. So by making progress in the clinic, we can understand the nature of the disease, and that's why I think when we cure leukemia, we'll cure all cancer, because everything we've learned in leukemia has worked in cancer. The idea of the small molecule started in CML, and now there are small

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molecules for every malignancy—epithelial growth factor for hormone receptors and so on and so forth.

***Tacey Ann Rosolowski, PhD***

**0:54:28.4**

I've never heard that term. What does that mean, a small molecule?

***Emil J Freireich, MD***

**0:54:31.8**

It's a— When I went to medical school in 1944, my advisor said, "If you're going to be a doctor, you have to read the Zeitschrift." The Germans developed organic chemistry, and they realized that you can make all kinds of things organic which had nitrogen and carbon. So they went to work systematically making every organic molecule you could, and they published 85 volumes called the Zeitschrift—the work—the writing work of organic chemistry. So if you wanted to get an organic chemical, you just have to look in a book, and it tells you how to make it. The Germans did that between the wars. So I learned German to learn the Zeitschrift. Well, our chromosomes are very complex organic molecules, but some of their functions have been worked out. Gleevec was discovered because it was recognized that the Abelson gene was responsible for phosphorylating other proteins which then became active genes. In order to phosphorylate a protein, this complex molecule had to have a place where it could attract ATP—that's the phosphorus. So they said, wow—the Nobel Prize has been given for this—if we make something that fits in the ATP binding pocket, they can't get ATP, maybe the whole thing will be disrupted. That's how Gleevec works.

So then the idea was if we can identify the essential operating part of any molecule, then we can make something that electrostatically fits in that site and will prevent it from doing that. Well, we have this gang in Harvard, where Dr. Mendelsohn is, called the Broad Institute. They decided to do what the Germans did for organic chemistry. They sat down and, with pencil and paper, generated every conceivable small molecule. Those are molecules that are less than 100 molecular weight or whatever—organic molecules—therefore biologically, potentially active. So today, if you have a target—you've heard of targeted therapy. It all started with Gleevec. You just go to the encyclopedia and look for something that might fit, and then you do high-throughput screening, which is you have robots that create—can test 1,000 pounds in an hour against a given target. You find the one that fits best, then you do the stoichiometry, and if it didn't fit perfectly, you look for something that is a little better. And that's the way it's going. So we have small molecules now that can tag every target, and that's a big discipline. That all started with leukemia, and now it's spread to lung cancer, to the EGFRs and everything.

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When you talk to lay people, they say, “We’ll never cure cancer until we find the cause.” That’s another myth. It’s like we’ll never make advances without basic science. It’s a myth. They are myths that are so attractive to the imagination that people believe them. And the myth starts with things like infections. If you know the bacteria and you can kill it, then you don’t get the infection. If you know the cause, you can develop treatment—if the cause is susceptible to treatment.

We know that the carcinogen in tobacco is responsible for ninety percent of the lung cancers that kill people, but we can’t get rid of that. So it’s one thing to know the cause, it is another thing to be able to do something about it. To our society’s credit, the government is helping reduce the burden of tobacco, but they prevent me from giving patients—dying cancer patients—treatment. They refuse to pass a law banning cigarettes. They refuse to pass a law banning alcohol. Alcohol is the second leading cause of cancer. It’s the leading cause of economic distress in our country, the leading cause of hospitalization, the leading cause of fire, the leading cause of death in automobile accidents. I mean, alcohol is the worst drug in our community. We ban marijuana, but we serve alcohol.

We have a faculty honors convocation where we honor people for research, and when you get done honoring people for their cancer research, you walk out in the corridor, and in the greatest cancer center interviewer the world, there are guys in white coats handing you glasses of carcinogen—alcohol. Drink, get drunk, jump in your car and kill somebody. What the hell. We’re so stupid. We’re regulating the wrong things. People worry about prohibition as a failed experiment, but it isn’t necessary to have prohibition. That was the wrong approach. If you pass a law outlawing alcohol, people can make alcohol in their bedroom. It’s easy. What has to be done is a social contract. We have to stop pretending that alcohol is good for you. Cardiologists tell everybody moderate drinking is good for your heart. Moderate drinking is bad for your heart and bad for your brain. It’s bad for everything. We have to have an ethos where we look at alcohol for what it is. But alcohol is a fine art. I might pay \$1,000 for a bottle of vintage, French red wine. Well, take that \$1,000 vintage red wine and hand it to someone who’s never had any alcohol, and he’ll go, “It’s horrible!” That’s learned. It’s learned behavior. We learn from our parents. They tell us wine relaxes you.

We ought to have a social contract that smoking is obnoxious. It offends people. Alcohol is dangerous. It kills people. It puts people in the hospital. If that’s the case, then when you come to my house, I don’t offer you alcohol. Fruit juice is okay. Water is even better. So we can’t ban tobacco. We have to have an ethos where it’s not—and we do that pretty well. When I go to the football game, you have to go out on the balcony to smoke. That’s okay.

*Tacey Ann Rosolowski, PhD*

**1:02:24.0**

Yeah, the regulations about smoking have really made a change.

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***Emil J Freireich, MD***

**1:02:28.1**

Oh, yeah. The airports—go in that room with all the other smokers. When I came here, the heads of the department smoked in our department head meetings—in the meetings. I was the one who said, “Dr. Clark, we ought to remove the cigarette machines from the cafeteria.” And Joe Boyd, our business manager, said, “Oh, no, Dr. Freireich. We can’t do that. We need the income from the cigarette machines.” I said, “What’s more important, the income from the cigarette machines or people dying of lung cancer? Let’s get rid of them.” So, to his credit, Dr. Clark did get rid of them. That’s what we have to do to alcohol.

We don’t need to understand the cause of disease to eliminate it or to control it. We need to understand how disease operates. How does it make you sick? Once we know how it makes you sick, then we can control it.

Diabetics—when I was in intern, my attending was a guy who discovered that restricting sugar in the diet of diabetics would prevent diabetic coma. His name was—he was a great man. But diabetes used to be 100% fatal. Juvenile diabetes, you never reached teenagers. We still don’t know the cause of diabetes, but diabetics have almost a normal life—not quite. But if they’re well-managed, they can live normally. We still don’t know what causes it. It may be genetic. It may be a contrast—that’s all good stuff. In the meantime, millions and billions of people are alive with diabetes, including my wife and my youngest son who take metformin and they’re alive. We don’t know what caused it. We have to turn the control of disease over to physicians who are scientists who work on the problem, not pretend you’re working on the problem by killing boll weevils.

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## **Chapter 14**

### **A: Overview**

#### ***The Partnership Between Basic Science and Clinical Research***

#### Story Codes

A: Character, Values, Beliefs, Talents

A: Personal Background

A: Professional Path

A: Overview

A: Definitions, Explanations, Translations

A: Professional Values, Ethics, Purpose

B: Multi-disciplinary Approaches

D: Understanding Cancer, the History of Science, Cancer Research

D: The History of Health Care, Patient Care

C: Patients

***Tacey Ann Rosolowski, PhD***

**1:04:57.1**

Can I ask you some questions about MD Anderson?

***Emil J Freireich, MD***

**1:05:01.3**

All you have to do is ask me a question, and I'll tell you some lies. And I don't have a noon meeting, I don't believe, so if you're not exhausted, we can do as much as you'd like.

***Tacey Ann Rosolowski, PhD***

**1:05:14.4**

Well, it'd be good to finish up today, if that would work for you.

***Emil J Freireich, MD***

**1:05:21.7**

I just have to take a peek at my schedule and make sure I'm right.

***Tacey Ann Rosolowski, PhD***

**1:05:25.9**

I think Joanne said you had a 12:30 meeting, or something around 12:30.

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*Emil J Freireich, MD*

**1:05:30.5**

I'm in good shape.

*Tacey Ann Rosolowski, PhD*

**1:05:33.9**

I want to—

*Emil J Freireich, MD*

**1:05:34.5**

But you're not in good shape. Do you need some water or some food? You're such a skinny little thing. You have to eat more.

*Tacey Ann Rosolowski, PhD*

**1:05:40.8**

I'm good. I'm good, really. I had a big breakfast.

*Emil J Freireich, MD*

**1:05:44.9**

Did you? Do you want a jellybean?

*Tacey Ann Rosolowski, PhD*

**1:05:49.4**

Oh, I saw your jellybeans out there.

*Emil J Freireich, MD*

**1:05:49.4**

I'm big on jellybeans. They curb your appetite.

*Tacey Ann Rosolowski, PhD*

**1:05:55.4**

No, I'm good. Thank you.

*Emil J Freireich, MD*

**1:05:56.8**

I'm a fat guy. You're a skinny guy.

*Tacey Ann Rosolowski, PhD*

**1:06:00.5**

I wanted to get your impressions about some institutional issues that are going on at MD Anderson right now, specifically the idea about global oncology.

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*Emil J Freireich, MD*

**1:06:17.0**

I'm neutral.

*Tacey Ann Rosolowski, PhD*

**1:06:17.7**

You're neutral?

*Emil J Freireich, MD*

**1:06:17.8**

Yeah, they can do what they want.

*Tacey Ann Rosolowski, PhD*

**1:06:21.8**

Do you think that the institution can be—?

*Emil J Freireich, MD*

**1:06:24.5**

All those things are important, but it's only important to people who think they're important. Global oncology, to me, is very derivative. If we cure leukemia, as I said—the people in the Congo are not treating leukemia as well as we do, but they will.

*Tacey Ann Rosolowski, PhD*

**1:06:44.4**

But what about the idea that—I mean—as I understand it, the mission of global oncology means basically to disseminate the same kind of healthcare under the MD Anderson name.

*Emil J Freireich, MD*

**1:06:56.2**

Marvelous. No one can be against that.

*Tacey Ann Rosolowski, PhD*

**1:06:59.0**

Do you think it's doable, though?

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***Emil J Freireich, MD***

**1:07:00.8**

Oh, sure. Sure. All it takes is money. As I said, I'm a great believer in freedom. If we have a treatment which costs ten percent of the gross domestic product, and we can only treat ten people out of the first million who have it, I'm in favor of it. Give it to the ones with the most money. They're the most successful. I believe in free enterprise. I believe in competition. Saving lives in Africa is an activity that people should engage in, and I'm in favor of it, but not me. I'd rather discover things that the people who are saving lives in Africa can use, because there were people saving lives in Africa when they were doing nothing. They were all dying.

***Tacey Ann Rosolowski, PhD***

**1:08:04.1**

What do you think is the most pressing institutional issue here at MD Anderson, aside from the tension between basic and clinical research?

***Emil J Freireich, MD***

**1:08:15.6**

There's no tension. There is total collaboration. The tension exists in the policy makers. We adore our basic scientists. I think I already told you, our course in patient-oriented research—we have more PhDs than MDs in that course. Our basic scientists want to cure cancer. That's why they came here. They're not working the medical school. They're working at MD Anderson. Not all basic scientists are doing "basic research" unrelated to the applied problems. Many basic scientists want to make progress. And when we make a clinical observation and we have to get support from our laboratory colleagues, they're right there, shoulder to shoulder. Our basic science people are with us all the way. They are very important. You can't experiment on people.

***Tacey Ann Rosolowski, PhD***

**1:09:11.4**

Who are some of the people you've worked with in that kind of collaborative relationship?

***Emil J Freireich, MD***

**1:09:18.6**

Thousands and thousands. The first thing you do when you discover something in the clinic is go to the fundamental knowledge that basic scientists apply and see if you can apply it. When I was a young physician and we were facing—we had children who were in complete remission who were in a coma. I called our neurosurgeon and said, "Let's do lumbar punctures." He said, "You can't do it. It's too dangerous. They're going to be herniated." So I talked to my colleague in pathology who is a basic scientist, and I said, "Let's figure out what's wrong with these kids." So he got all the autopsies for all the children who died in remission, and we put them on the table and looked at their brains and their spinal cord, and we realized they had meningeal leukemia. Then we talked to our basic scientists about how the spinal fluid works. We had David Hong working on spinal fluid physiology. We figured out that if we put it in here and shook it up, we'd

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get it up in the brain and could kill leukemia cells. It's a standard part of the treatment of curing leukemia. It all came out of a collaboration.

Many physician scientists have laboratories. The first step in understanding what you've observed clinically is to go to your own laboratory, but you are very limited in time and ability, so you need to find out who is doing that kind of thing. If you're looking for a virus, you need a virologist. If you're looking for a cell proliferation thing, you need a cell biologist. One of my closest collaborators was Bun McCulloch, who was the first one to discover stem cells in the hematopoietic system. He received the Lasker Prize. It's Nobel Prize stuff. He was the one that was responsible for motivating us to do the colony-forming thing and discover the things in the blood and allotransplant. So, yeah, basic science is—I have never said that we should not spend—I want to spend double the amount of money we're spending on basic science, but the problem is the translation. If you don't have the clinical arm, it's like trying to play the piano with one hand. If you want to make progress in controlling disease, we need the basic scientists to do the rhythm and the clinical scientists to do the melody, and then we get music.

*Tacey Ann Rosolowski, PhD*

**1:11:52.2**

That's a great metaphor.

*Emil J Freireich, MD*

**1:11:55.1**

Yeah. There's no either/or. No one has ever opposed basic science research. That's very important. But we can't ask the basic scientists to decide what should be done to patients. That's a patient-oriented decision, and the basic scientists and the patient-oriented doctors have to work together. It's like—I'm a big football fan and the game last Sunday—are you a football fan?

*Tacey Ann Rosolowski, PhD*

**1:12:28.6**

Not really.

*Emil J Freireich, MD*

**1:12:29.6**

The game was lost in the last six seconds of the game. When our quarterback had the ball on the three yard line and had the choice of trying to pass it—I mean—there were all these defenders—or trying to sneak in by running, he decided to pass it and it was intercepted. So the whole game turned on that nanosecond decision. Why did I make that analogy? I have no idea. Well, it makes the point that a football team—we couldn't have been on the three yard line if you don't have an offensive line, a quarterback, a running back. It's a team activity. All human activity is team activities. There's some moments when lightning strikes and you discover something great, but even the Nobel committee realizes that it's very rare that people discover things in a vacuum. They build on the knowledge base that we have, and all progress is collaborative.

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When I went to the Cancer Institute [NCI], the first clinical study we did was based on Lloyd Law's mouse model system. Dr. Fidler couldn't do any experiments without Lloyd Law's major discovery. What Lloyd Law did was he was a geneticist, and he learned how to make identical twins as a species of mouse. So today, all the mice that you buy from Jackson Laboratories are identical twins. So you can make a thousand identical mice of A, B, C, D. The one that became most famous was called L1210, which was named after Lloyd Law. His #1210 mouse model was perfect because this arose by taking one of those identical twin mice and painting coal tar on the hairs, and they got leukemia. That leukemia was so malignant that you could take it out and put one leukemic cell inside a mouse and he would die of leukemia in thirty days—one cell. How did he do one cell? It's brilliant how they did these experiments. Lloyd Law was my next-door neighbor. We couldn't have done anything without the basic scientists.

They run a culture of these cells through capillaries that are one cell thick, so they're in a line. They get the microscope and they cut the capillaries so there's only one cell. They put that capillary under the skin of a mouse and thirty days later he dies of leukemia. So Lloyd Law, when he retired we had a symposium, and Dr. Frei and I and Dr. Zubrod were invited to speak, because he was the inspiration behind all the early studies that we did in childhood leukemia. One of Lloyd Law's next-door neighbors was a guy named Abe Goldin, also a basic scientist. He wasn't interested in the biology of it; he was interested in the treatment, so he began to give drugs to the mice that had L1210 leukemia. Then we had a contract with Skipper and Schabel at Southern Research, and whenever we had a clinical question, they would set up a mouse model of the clinical situation and do the experiments in mice so we could do them in vivo. They did all the combination studies in the mice. So don't let me say anything negative about basic science. That's terribly fundamental. Everything comes from our understanding of the biology of things.

But, see, Fidler's stuff is different. That's not basic; that's applied. He studies epiphenomenon. The basic science is understanding how these tumors arise, discovering viruses and chemicals. Another next-door neighbor I had when I was at the Cancer Institute was—her name was Stewart. I've forgotten her first name. She was a lovely lady. She was in her mid-fifties. She spent her entire life trying to find out if cancers could be transmitted with submicroscopic particles. She discovered the first virus-induced mouse leukemia. Sarah was her name—Sarah Stewart. She was my next-door neighbor. We got very excited about that. We tried to do experiments that treat the virus leukemia, and, as you know, that research eventually led to the understanding of AIDS and the virus that causes T-cell leukemia in Japan. So every physician-scientist's career depends on collaboration with laboratory scientists because that's where the concepts come from.

So our first clinical studies were based on Law and Ed Goldman and Schabel and Skipper. They get all the credit. They're co-authors on all our papers. What is true is the illusion that patient-oriented research is not basic research. That's the trouble. Because there is basic—I mean—if you want to find out how leukemia is spread to the brain and kills children, you have to observe

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children. There was no model of meningeal leukemia. We had to discover it ourselves. When we did the pathology and found that the brains were involved, we then discovered that they had freely communicating internal hydrocephalus, which meant that we could certainly do LPs because there was no mass that would displace the brain, so we began doing lumbar punctures. We worked out the whole physiology of meningeal leukemia. We gave intrathecal stuff. We did X-rays to see what happened to the drug when we injected it. Everything depended on basic understanding of what you're doing. Since we can't experiment in people, we must experiment in a laboratory, and laboratory experimentation is the doyen of the basic scientist, but the basic scientist has to be susceptible to collaboration. He has to have an interest in the problem.

***Tacey Ann Rosolowski, PhD***

**1:19:15.2**

It sounds like a real feedback mechanism.

***Emil J Freireich, MD***

**1:19:17.0**

It's a real feedback mechanism. When we founded APOR, the first annual meeting we had we wanted someone who had a Nobel Prize for clinical research. We invited Dr. Brown of Brown and Goldstein. He's the paradigm of physician scientists. I love Dr. Brown. He's still alive—Southwestern University. He gave a lecture, and the title of the lecture was Bedside to Bench and Back, and the substance of the lecture—Goldstein and Brown won the Nobel Prize for discovering the things that make cholesterol and cured heart disease. As you know, heart disease is almost gone. I wish we could do that to cancer. And Brown said, the discovery of the anticholesterol agents began with the study of a single patient, and he put her picture up. It was an eight-year-old girl who was born with congenital hypercholesterolemia, and he was a young physician training for internal medicine. He had to take care of this little girl. If you have hypercholesterolemia, you die at the age of ten or eleven of atherosclerotic disease all over—brain, heart—all the organs are dead. So he said, I have to understand why this patient has hypercholesterolemia, so he took her and began to study it in the laboratory, and they drew on the basic scientist. Where does cholesterol get transported? How does it get transported? And they discovered that there was a defect in a specific enzyme which transports cholesterol from the liquid into the intracellular matrix, and when that enzyme was gone, it all accumulated in the blood and then all the cells that don't need it get it and the whole thing is there. There's the whole disease.

Now, he's a clinician, not a basic scientist, so he doesn't think about how it occurs. He wants to know how to interrupt it. So he went through the world literature, and he looked for compounds, like Zeitschrift and the Broad Institute. He looked for compounds that could affect the transport of cholesterol across the cell. He just searched the literature, and he found some Japanese guy who had worked ten years before and had discovered a molecule that could accelerate cholesterol transport into a cell. So they took that, and they went to the laboratory. They had the cells from

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this patient and put the—and they discovered the anticholesterol drugs and cured heart disease and won a Nobel Prize and created more human life than anybody currently alive.

You've seen the statistics. Less people die of heart disease than cancer now. So that's the paradigm—bedside to bench and back. So translation—I give a lecture on this to our students. The understanding of any problem requires that you start with the problem and then try to figure out how it got to be a problem. That's why basic scientists cannot do it. If you're working on mice, you cannot understand human melanoma. They don't have it. You can't work on elephants and giraffes. You can't work on bacteria. You can't work on test tubes. If you're going to understand the phenomena, you have to work on the phenomena. If you want to understand the stars, you have to work on the stars. You can't sit in the laboratory and make models of the stars. You've got to get a telescope and figure out what's going on. That's how Galileo got killed, because he insisted that the earth goes around the sun. They didn't want to believe that.

Basic science is terribly important, but it has to be done in a problem-oriented way. When we wanted to build an atomic bomb, there weren't any bomb manufacturers who could do that. They needed the guys who understood—they needed Einstein—to understand the laws of physics, but they had to have a problem. They had a direction. They wanted to create a bomb. If you put the geniuses together with the applied people, we had a bomb in no time at all. They did the same thing during the war. That's where Dr. Zubrod made us physician-scientists, because during the war—I think I told you this analogy already—more people died of malaria, so they created a malaria project. They got all the geniuses—the basic scientists, the laboratory scientists, and the doctors—and said get rid of malaria. That's what we need to do about cancer. That's what the Cancer Act was all about. Put the money out there so we can get all the basic science brains, all the translational brains, all the clinical brains in the same room and cure cancer. Let's do it. There's no reason not to do it. While people are worrying about global oncology, I want to cure cancer, because until we cure cancer there's nothing for global oncologists to sell.

***Tacey Ann Rosolowski, PhD***

**1:25:10.3**

What are the areas of—?

***Emil J Freireich, MD***

**1:25:13.4**

And don't write this, but we shouldn't be wasting our resources on global oncology, because we're where we should discover the cure for cancer. If we don't do it here, they're not going to do it in Africa.

***Tacey Ann Rosolowski, PhD***

**1:25:25.9**

What are the areas that you think MD Anderson is best placed to make advances in curing cancer?

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***Emil J Freireich, MD***

**1:25:32.5**

Clinical research.

***Tacey Ann Rosolowski, PhD***

**1:25:33.4**

In clinical research, but are there specific projects you think certain people are working on that are really promising—or certain areas of research?

***Emil J Freireich, MD***

**1:25:43.7**

A hundred percent of the projects people are working on are very promising. That's why they're working on it. People have to follow their nose. This business about targeted therapy, personalized therapy, it's a very—it's almost as appealing as prevention is better than cure. It's a nice idea. But that's an important area of research. That is, if you can find a reason that the cell is misbehaving, you can find something that will affect it. That's what we've got to do.

When we can cure ninety-five percent of patients with cancer, then we should spend our resources on global oncology. It's like polio. Until we proved the vaccine could prevent polio, we didn't give it to everybody in the world. And as you know, there are consequences with polio vaccination. There are some mouse viruses that have been transmitted to people and so on and so forth. All prevention strategies have a cost. People think—you know—the mammography thing, it's wonderful to have a mammogram every year, but that increases the occurrence of cancer—no doubt about it. Stopping smoking—that has no consequence. That won't bother you at all. Staying out of the sun—that won't bother you at all. Not drinking alcohol—that won't bother you at all, no side effects. Your heart will do just as well without alcohol.

So I went to the faculty senate and said, "I would recommend that we not serve alcohol at MD Anderson at the faculty honor convocation, which the faculty supports." The executive committee said, Freireich should be fired from the executive committee because he's offending people. I said, "The only people who want wine after a session are alcoholics. We're addicted to wine." Why can't we get done with the thing and have a glass of juice or sparkling water or something—you know—a Coke. We have to have alcohol. So they rejected it. Then they voted to exclude me from the senate because I was radical. That failed. So then, one day, I introduced a motion on the floor, and it had to be voted on. I got something like six votes. So I'm not the only radical.

***Tacey Ann Rosolowski, PhD***

**1:28:46.8**

No, you're not the only radical.

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***Emil J Freireich, MD***

**1:28:49.5**

I think MD Anderson's mission is to cure cancer, and in order to cure cancer, we have to have the best cancer treatment in the world, because if people are going to expose themselves to risk, there has to be a potential benefit. So there's no point in offering people innovative treatments unless we're sure that the potential for benefit exists, because everything has a risk. As you know, when you go to your doctor and he says, "I'll give you a shot of penicillin," there are thousands of people in the United States who die of penicillin toxicity today. So it's not to be taken lightly. You have to be sure that what you're treating is more dangerous than the penicillin you're going to get. The same is true of morphine, which is addicting. The same is true of digitalis, which causes arrhythmias. There is no preventive strategy—N-O preventive strategy—that doesn't have danger to the people who are engaging in that behavior.

A PhD wrote a book that, if you're interested, I'll give to you to read. It's called *Is Prevention Better than Cure?* She did a financial analysis for her PhD of all the preventative strategies she could find to prevent disease and analyzed the cost/benefit ratios, or the dollars-per-life cost, and there were no preventative strategies that were better than curative strategies. I'll give you the book.

***Tacey Ann Rosolowski, PhD***

**1:30:29.6**

Yeah, I'd be interested to see that.

***Emil J Freireich, MD***

**1:30:31.7**

Here it is. Want to read it?

***Tacey Ann Rosolowski, PhD***

**1:30:33.6**

Sure.

***Emil J Freireich, MD***

**1:30:35.4**

Don't you dare lose it.

***Tacey Ann Rosolowski, PhD***

**1:30:36.6**

I won't lose it.

***Emil J Freireich, MD***

**1:30:39.0**

Louise Russell.

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***Tacey Ann Rosolowski, PhD***

**1:30:39.8**

Louise Russell. Interesting. Funded by the Brookings Institution.

***Emil J Freireich, MD***

**1:30:46.7**

I don't know if it's still in print, but if it is, it's a valuable book. Don't you dare lose it.

***Tacey Ann Rosolowski, PhD***

**1:30:49.4**

I won't lose it. I promise.

***Emil J Freireich, MD***

**1:30:51.8**

I treasure it. I couldn't find the book that was written by Ed Ahrens. That's another treasure. I hope no one stole it. I should have looked for it when you weren't here, because you should read that one too. He documents the flow of money away from patient-oriented research—lab research. Gordon Williams, who was one of the three people who started APOR, was commissioned by the Division of Research Grants of the NIH to look at whether a clinical project had the same chance of success as a laboratory one. They published a paper which proved unequivocally that it doesn't. The study sections are all loaded with laboratory scientists, and these are not the laboratory scientists who are working on potential cures. They're the laboratory scientists who are working on their metastasis. You can build a whole paradigm in the laboratory of things that have no relevance to the clinical. It might eventually. The stuff Fidler did might be useful some day. It has led to clinical studies. There are people who have given Heparin to people to prevent the metastasis, and of course those studies were all negative.

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## **Chapter 15**

### **A: View on Career and Accomplishments**

#### ***A Legacy of Strong Faculty and Advances in Blood Cancers; Awards; Cancer as a Disease and MD Anderson Presidents***

Story Codes

A: Contributions

A: Career and Accomplishments

B: MD Anderson History

B: Critical Perspectives on MD Anderson

C: Portraits

C: This is MD Anderson

D: Understanding Cancer, the History of Science, Cancer Research

A: Personal Background

A: Character, Values, Beliefs, Talents

***Tacey Ann Rosolowski, PhD***

**1:32:08.4**

Interesting. Can I ask you to reflect a little bit on your years here? I was wondering, of all the work that you've done here, what do you feel most proud of or what do you feel has been of the most significance?

***Emil J Freireich, MD***

**1:32:26.1**

Well, I've already told you some of it. The first thing I'm most proud of is the training programs and the students that we've generated who have made an enormous impact on cancer and its treatment. These are students who are not like you go to a classroom. These are people who are motivated. Ken McCredie came from Australia. He was already a professor, and he came here to do scut work because he wanted to cure leukemia. Michael Keating [Oral History Interview], who is still here, was the same. Ken McCredie came from New Zealand. Michael Keating came from Australia. Hagop Kantarjian came here as a medical student in an elective. He's now head of the leukemia department. He's the most brilliant leukemia researcher in the country, in my opinion. Bob Benjamin, who runs our sarcoma program, came from the Baltimore NIH and came to MD Anderson. He became a giant. Larry Einhorn, who cured testicular cancer in Indiana—well, I went through this before, when we talked about it. That's the thing I'm most proud about is MD Anderson created an environment where people who wanted to cure cancer could come and do it. They didn't learn from us geniuses who had cured cancer, but they were in an environment where they could do it. Many universities have training programs. The medical

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school has a training program. You go over there, you can't do it. There aren't enough patients, there aren't enough doctors, and there aren't enough resources.

When you get to a place like MD Anderson, there's a critical mass. And they realized that with the Atom Bomb Project, with the malaria, there's a critical mass. You've got to have enough people so that people can focus on their function. It's like your body—you've got to have liver and eyes and hair and hands and feet and muscles. In order to attack cancer, you've got to have a critical mass. You have to have enough patients so that the heterogeneity of the patients can be understood.

We used to think acute myeloid leukemia was one disease. We now have thirty different categories of AML that are clearly documentable by molecular studies, so we have to understand the complexity of the problem, and that means people have to specialize. A hematologist in practice taking care of ALL, AML, CML—I mean—he's lucky if he can just do the best thing. If you want to make progress—you know—a guy like Keating, he works on CLL. He knows more about CLL than anybody in the world. We have people like Merrick Ross who know more about melanoma than anybody in the world. We have people like Christopher Wood who knows more about renal cell cancer than anybody in the world. We have a sufficiently large faculty so that people can become the world's most informed person about the basic science and the clinical science in that illness, and we realize that cancer—the one thing we know is it's complicated, baby. It's not like curing polio. It's not a germ and a disease. This is really complicated. It gets down to the basic genome—to the 25,000 genes and to the epigenes that change the genes to the protein-altering—there's probably a million different proteins that make us function.

So we need the critical mass. You've got to be big. You've got to have enough patients. You've got to have time to focus on one illness. When our fellows come here to train, they don't learn all of oncology. We have leukemia fellows who work on one kind of leukemia, and by the time they're here a year, they're the world's authority on that kind of leukemia.

So what's important about MD Anderson—and you already know that I'm very biased, and I believe that we all benefitted from the vision—you know—it's like Brown and Goldstein. Dr. Clark realized that if we're going to cure cancer, which is very complicated, we're going to need all the resources, all the specialties, all the patients, all the commitment to research, and he created a concept that—well, it was the bulb and the plant thing. You couldn't stop it. The idea was just fifty years ahead of its time. Those of us who came here were lucky to have an opportunity to work at it.

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MD Anderson is a truly unique place because of Dr. Clark. He set it up so that young people could work here without concern about their future. He had a retirement program. He set it up so that your salary depended not on how much money you brought in but on what your value to the team was, just like a football team. If you're the quarterback and you're the most important guy, you get the highest salary. So he set the salaries based on your contribution to the mission of the institution. And he was a Texan, and there's something about Texans. He believed that you could use any tools that you needed to get the job done, in this state and in this city. He had a vision of the economic success of the city, of the importance of the cancer problem, of the role of science and research, of the importance of outstanding physicians, in order to have the patients to study, outstanding laboratory—I told you already, the first guy he hired after he brought his friends in was a lab guy from Galveston. He realized that it will take science to conquer cancer, and he didn't want to just globalize what we know—you know—that was a Mendelsohn thing—he wanted to cure cancer. If we cured cancer in ten people in Texas, everybody in the world would have it in a year. Globalizing will take care of itself.

I think globalization is like food kitchens. It's good to help the poor and the starving, but it's more important to create an economy where everybody is working and pays for their own food. I don't like running food kitchens. I like working on agricultural science to make new kinds of corn. But it takes all kinds of people to run a machine.

MD Anderson is still a unique place. When Dr. Clark was fired and replaced by Dr. LeMaistre, the Clark direction was unimpeded. LeMaistre certainly didn't interfere with the development that Clark had started. In Mendelsohn's case, he already had experience at Memorial, running a division of medicine. He already had experience in doing translational science because he worked with scientists in California, and patients. So Mendelsohn actually enlarged the Clark concept to a very substantial degree. But, in order to do that, he—you know—global oncology, Fidler, and all that. He had to do all the things that were necessary to build buildings and get the money and make it possible. So, to a large extent, I believe Mendelsohn was a—I think all of our presidents were very successful, but they all benefitted from the Clark image—from the Clark concept—of what this place should be. I think Dr. DePinho has the same genes. We'll see.

*Tacey Ann Rosolowski, PhD*

**1:41:53.1**

As Dr. Clark?

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***Emil J Freireich, MD***

**1:41:54.3**

Yeah, and LeMaistre and Mendelsohn. I think he's of a breed that he doesn't—you know—if you want to destroy the Clark image, you have to do something destructive—you have to say, "Well, we're not going to accept patients from Florida," or, "We don't take melanoma." You make some silly rule that would interfere with its function. But in the absence of actively interfering, it's going to continue until the problem is gone. And I think I told you once, when I got the General Motors prize we had a press conference in New York. There were four of us—basic science, clinical, and translational. The first question the reporter said was, "When are we going to cure cancer?" And I gave, spontaneously, the best answer I've ever given, and it's the same one I would give today, and it is, "We're never going to cure cancer. Cancer is a part of the development of a very complex organism, like a human being. There's gonna be errors. There's always going to be cancer. What we're learning to do is control it." We can keep you from making it worse.

When people smoke, if you smoke twenty packs a day for twenty years, the incidence of lung cancer is only increased a hundredfold. The rest of the people don't get lung cancer. It's not that easy. Tobacco is only one part of the problem. There's something else going on that we don't understand yet—a genetic basis—something in the genes that makes the carcinogen make you get lung cancer. So if we eliminate tobacco, we'll control eighty percent of lung cancer. We're not going to eliminate it. There will still be lung cancer. We get lung cancer in nonsmokers—non-ever smokers. Cancer of the liver is caused by hepatitis virus. We can immunize everybody in the world so there's no hepatitis virus, but we'll still have liver cancer.

I say to students, when I give a lecture, cancer is the most important problem in biology. What is biology? Biology is the study of living things. What's a living thing? How do you define living? What is living and what is dead?

***Tacey Ann Rosolowski, PhD***

**1:45:03.1**

Oh, you're asking me?

***Emil J Freireich, MD***

**1:45:04.3**

Yeah.

***Tacey Ann Rosolowski, PhD***

**1:45:05.7**

Well, it eats, it grows, it replicates its cells.

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***Emil J Freireich, MD***

**1:45:10.7**

That's it. Life is defined as the ability to make a copy of yourself, so all living things have to make copies. Human beings begin as one cell, and by the time you stop growing, you have seventy trillion cells. Some of these cells have a lifetime of hours. We're constantly replacing all of our cells. Your hair is growing. Your cornea is growing. If you've got that much activity, there's going to be a mistake somewhere—cancer. So we'll always have cancer, but what we can understand is how to control it—a model of diabetes, of CML. Why should people suffer? We're always going to have cancer, but we're not going to suffer from it. That's the main thing. And probably we won't die from it, if we get really good.

I do another lecture—did you know Al Knudson? He was our first—no, the second dean of our graduate school. Dr. Clark created the graduate school. He hired Al Knudson. Al Knudson was a brilliant basic scientist. He worked out the molecular biology of retinoblastoma and showing that it was a genetic disease. He's the won all the prizes. I think he won a Nobel Prize. I don't know. But Al Knudson, when he was dean of the grad school, he knew I was a little funny, so we got involved in discussions, and we're good friends still. He gave a lecture to the students in which he said all species have a finite lifespan. Isn't that true? Elephants live and giraffes and bacteria and humans have a finite lifespan. Why is that? That's a basic biological question. Why do we stop living? So I said, all human beings, when created—fertilized—would live infinitely—infinitely—unless it's diseased or traumatized. So we used to debate that. Is the human lifespan infinite? His argument was based on running out of mitochondria and running out of that. My argument was that, as far as we can tell from the history of our species, the human lifespan has increased continuously and progressively.

Just about five years ago, in my talk that I give my students, there was a paper from Sweden. Sweden was the first totally socialized medical plan in the world, so they have vital statistics on every born person, and this guy showed that the maximum attainable lifespan has been increasing exponentially in the history of man. So the world's greatest philosopher, in my view, was Jesus Christ. And Christ said, intuitively, from his brain, that life is eternal. Once created, a fertilized ovum is going to live forever unless it's killed or gets sick. And I believe that's true. And everything we know indicates that true. As you know, the most rapidly growing segment of the American population is centenarians. The rate of increase in the proportion of the population that's over 100 is faster than the portion of the population that is under 10.

***Tacey Ann Rosolowski, PhD***

**1:49:51.8**

I didn't know that.

***Emil J Freireich, MD***

**1:49:53.7**

That is a fact—demographics. And as you know, most of the western countries are declining in

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population, and that's so that the bubble in age distribution is changing to this kind of a thing—a little point on the top. So, all the science indicates that we're going to live forever. Are we going to cure all disease? No, we'll always have disease, but we can control it. If you can have CML without any problem—one pill for ten years—if you can have diabetes and live for fifty years with a shot of insulin, we'll control all human disease. We're going to live forever. And I am confident that that is the case, not on the basis of any faith but on the basis of the science. The facts are that the lifespan of human beings has increased progressively over recorded time and will continue if someone doesn't stop it, like the FDA.

***Tacey Ann Rosolowski, PhD***

**1:51:11.0**

You mentioned earlier your award from General Motors. I was wondering if you would—because I've got—here is a portion of your CV here, and you have almost two pages of awards. I was wondering if you would comment on the ones that meant the most to you.

***Emil J Freireich, MD***

**1:51:29.3**

Well, the one that meant the most to me was the Lasker Award. The reason it did is because—and I just love this picture. Have you seen it?

***Tacey Ann Rosolowski, PhD***

**1:51:41.0**

Uh-hunh (negative).

***Emil J Freireich, MD***

**1:51:43.9**

I gave it to ASCO, and they have it in their archives. The reason this picture is adorable is this is Mary Lasker. Did you read the guy who wrote the Pulitzer Prize book, *The Emperor of all Maladies*?

***Tacey Ann Rosolowski, PhD***

**1:52:01.3**

No, I haven't read that yet.

***Emil J Freireich, MD***

**1:52:01.9**

Oh, good reading.

***Tacey Ann Rosolowski, PhD***

**1:52:02.9**

Yeah, I've heard it's good.

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***Emil J Freireich, MD***

**1:52:03.8**

Well, he explains how these people made cancer research—

***Tacey Ann Rosolowski, PhD***

**1:52:07.4**

And this photo was taken at the evening when your prize was awarded?

***Emil J Freireich, MD***

**1:52:09.9**

The awards ceremony. Here they are. Those are the awards. We each got a—what's her name?—the Angel of Samothrace, or whatever her name is.

***Tacey Ann Rosolowski, PhD***

**1:52:22.5**

Oh, the Victory of Samothrace.

***Emil J Freireich, MD***

**1:52:25.9**

Yes. She's on the bow of the ship that the Greeks used to go to battle with, and these are bronze statues with marble bases. I have mine at home. I'm thinking of giving it to MD Anderson, if they're nice to me, because my kids won't need it.

Well, this is Sidney Farber who described the first complete remissions in childhood leukemia. Dr. Farber is my idol. I have two idols—Dr. Farber and a gastroenterologist called Joseph Kirsner, and I'll tell you about him later. But Farber was a pathologist, so he cared about people. He looked at organs. But he was watching literature, and when the basic science discovery of folic acid was published, he realized it was a growth factor for hematopoietic cells, and he got the idea that— Another one of my good friends, John Laszlo's father, had shown that if you feed tumors to tumor-bearing animals, the tumors grow faster, so that the nutrients within a tumor are the essential nutrients for that cancer to grow. So Dr. Farber said, wow, if folic acid makes the blood grow, if I can get— Well, it turns out if you feed ground-up tumors to tumor-bearing animals, their tumors grow so fast that they necrose, outgrow their blood supply, and regress. So it's a form of treatment. Dr. Farber got the idea from Laszlo that if he gave folic acid to these children, their tumors would grow so fast that they'd lose their blood supply and they'd get better. So he gave them folic acid and they got worse. Now, that's never been replicated, and nobody knows if it really does make it worse, but he made that observation on a small number of children, and he called [Yellapragada] Subbarao, who owned folic acid and he said—by the way, what I'm telling you is a repeat of what he told me to my face, like we're talking. He went to the Eli Lilly guy who discovered the folic acid. His name was [Yellapragada] Subbarao, and he said, "I need a more potent folic acid, because this one is making it worse, but not worse enough. If it goes faster, it will get better." So Subbarao made analogs of folic acid, and it turned out to be an

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antimetabolite. That is, by putting a carbon ring on the central part of the folic acid, it would attach to the enzyme which activates it and wouldn't separate. So it became an anti-folic acid, and that was the first treatment of leukemia.

The concept of the antimetabolite that he discovered empirically as a pathologist is the basis for everything we know about the molecular biology of our DNA and all that, because it was the antimetabolites which allowed the chemists to do the basic science research to work out the building of the DNA and the RNA and all that stuff. That's from a pathologist looking at tissues from dying children with leukemia. It taught me something about science.

And this is Mary Lasker. Now, Mary Lasker was married to a guy who was a multimillionaire. He was a film man, and she collected art and did all the things multimillionaire wives do. She got interested in disease, and Dr. Farber discovered her and said, "Look, here's a project for you." And Mary Lasker became the people who created the National Cancer Institute. They're the ones who created the lobbying force that went to Congress that created the National Cancer Act, built the NIH in Bethesda.

***Tacey Ann Rosolowski, PhD***

**1:56:27.2**

Do you know what it was that got her interested in cancer, specifically, or in disease control? Was there a personal thing? I was just curious.

***Emil J Freireich, MD***

**1:56:37.6**

I don't know that. But she took it on as a cause. It's like global oncology. She decided it was something she wanted to do, and she had a lot of money. When we did the first interferon studies—when we discovered interferon for hairy cell leukemia, which was the greatest breakthrough in leukemia research ever, we couldn't get the interferon. It was too expensive. Mary Lasker sold paintings and bought interferon for us.

***Tacey Ann Rosolowski, PhD***

**1:57:06.3**

That's amazing.

***Emil J Freireich, MD***

**1:57:07.0**

And Dr. Clark is the one who talked her into it. When we had something that we needed to do, we went to Dr. Clark who said there are no obstacles. He had no obstacles on his horizon. If you wanted to fly a spaceship to Mars, he'd go at it—an amazing guy.

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So Mary Lasker and Farber created the Lasker Prizes, and they go for all basic scientists, just like the Nobel Prizes. Dr. Farber got the idea that maybe we should give a prize for clinicians who treat leukemia and cancer. So they had this event in—what year? I can't remember. But anyhow, they honored the people who made the strides that made cancer a treatable disease, and they're all in this picture. Here's one that I wrote an article about—M.C. Li. He was a Chinese escapee from the Communist Revolution. He was trained at Oxford, and his father was a Christian. He couldn't go back to China, so he stayed in this country, and he was a very imaginative guy. He's the guy who used methotrexate to cure choriocarcinoma. That started the whole thing—M.C. Li. He was a good friend of mine. He died of hypertension at a young age. He got fired at the Cancer Institute. He was a very good man.

This is Dr. Denis Burkitt who was an evangelist in Africa doing global oncology. He noticed that the African children were dying with this big lump on their jaw, and they died of a leukemic-like disease. He described a disease called Burkitt's lymphoma, which occurs not only in Africa but in the western world, and the reason it was important is it was the first disease that was clearly caused by a viral infection, and the Burkitt's Virus started that whole area of research. It got us to the DNA changing in mice—Denis Burkitt.

Here is my hero, Gordon Zubrod. He's the guy who came out of the malaria program, first director of the NCI, brought Frei and Freireich into the picture. He brought Emil Frei, my dearest, personal friend and buddy, dying of Parkinson's disease, tragically, and the young whippersnapper Freireich to NCI to start the thing.

***Tacey Ann Rosolowski, PhD***

**1:59:51.1**

That's great.

***Emil J Freireich, MD***

**1:59:52.1**

Wait a minute. Where's Jim Holland?

***Tacey Ann Rosolowski, PhD***

**1:59:54.8**

Here it is—1972.

***Emil J Freireich, MD***

**1:59:56.9**

Oh, no Jim Holland. Jim Holland is not there, but Don Pinkel is there. Don Pinkel worked with Holland on childhood leukemia. He got the credit, but Holland deserves it. Here's Joe Burchenal, who worked with Hitchings and Elion to get the first 6-MP—the first antipurine, which is, after we had antifolates, the antipurines worked out the whole molecular structure of DNA and RNA and all that and cured leukemia—very important.

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I don't want to get to the minor players. Here's a guy who doesn't belong here. This is Roy Hertz. He fired M.C. Li. He's a jerk, but he participated because he authored the first paper on choriocarcinoma. But he's worthless. That was Burkitt. That's Burchenal. This is Paul Carbone. You already saw him. Breast Cancer—very good stuff. Oh, and these are the two guys—Djerassi and Klein—who were both very low-class physician scientists—very unaccomplished, but they had the advantage that they worked for Sidney Farber, and Sidney Farber invented a thing called total care. In other words, he decided curing leukemia was one thing. Children were dying of hemorrhage. Djerassi started working on frozen platelets. I'm the one who solved it. Unfortunately, he got frustrated. Klein worked on infections and pain. So these two guys were Farber's boys, kind of like Frei and Freireich. And then here's Vince DeVita, who worked with Tom Frei to develop the MOPP, and this is Ngu, who worked on Burkitt's lymphoma in Africa.

So in this picture are the people who created the concept that cancer could be cured and treated as a systemic disease, and they're all here. They did it in one shot, and the year after that, the Lasker Prize went back to some biochemist for working on some enzyme or something. This is the only time that there was a clinical thing, and it's all due to Sidney Farber.

When I got fired from the Cancer Institute—you know—I've been fired from every job I've ever had. I'll be fired from this one too. Sidney Farber offered me a job. Did I tell you about my first paper? Sidney Farber—the first discovery I made at the Cancer Institute was the children with very high blast counts died of cerebral hemorrhage, and I made that in collaboration with a pathologist, Lewis Thomas, a dear, personal friend of mine. We wrote a paper, and Dr. Zubrod was afraid to publish it without some muckity-muck, so he invited Dr. Farber to come to NIH, and I got to present my paper. I was very nervous. It was 1956. I was, I don't know, thirty. There's the great Dr. Farber, and I present my paper, and when I sat down, there was Dr. Farber and Dr. Zubrod. I said, "Dr. Farber, do you have any comments?" He said, "It's such a wonderful thing to see all these young people trying so hard. It's wonderful. You have to keep it up. But as far as hemorrhage with the white count, that's all false. I already studied that problem, and I knew that the high white count had nothing to do with—"

*Tacey Ann Rosolowski, PhD*

**2:04:05.0**

Nothing like—you get an "A" for effort.

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***Emil J Freireich, MD***

**2:04:08.7**

End of my career. So the paper couldn't be published, and I went home and cried. My wife tried to encourage me, and I spoke to my friend Lew Thomas and he said, "Look, Freireich, this was research. We know it's true. I don't care what Farber said." So Dr. Thomas—who was in a different department—and I went to Dr. Zubrod, with Frei's approval. He didn't come with us. We said, "Here's the data. This is true. I don't care what Dr. Farber said." And the giant of the man that he was, he was willing to stake his whole career on research done by two Young Squirts. We were thirty years old, and he let us publish it, and of course it turned out to be true. Everybody in the world now recognizes that if you have high blast counts you've got to get rid of it, and we do pheresis. So that was the biggest moment of my career. What was good about it was the appreciation of what's important, getting on with it. Those are the pictures from NIH of the guys who did great things. That's the Distinguished Alumnus Award. I'm proud of that one, but the second most important one was the General Motors Prize.

***Tacey Ann Rosolowski, PhD***

**2:05:52.0**

And why is that?

***Emil J Freireich, MD***

**2:05:53.1**

I don't have a picture of the General Motors Prize. General Motors gave us a gold medal. Do I have a picture of it anywhere? This gold medal is 100% twenty-carat gold, and it's a casting of the three people for whom they gave the awards—Kettering, who was the clinical award; Sloan, who was the basic science award; and I forgot who the other one is. They gave three medals. Well, the winners of the Kettering award in that year were Frei and Freireich. We shared it, which I was proud to do. What year was it?

***Tacey Ann Rosolowski, PhD***

**2:06:45.1**

Yeah, I'm looking.

***Emil J Freireich, MD***

**2:06:49.8**

You've got a bad one. The one I have has an asterisk on the ones that are important.

***Tacey Ann Rosolowski, PhD***

**2:06:54.0**

Oh, here it is—1983.

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***Emil J Freireich, MD***

**2:06:56.2**

In '83, okay, so we'd been here—Frei was already at Harvard, and I was at—you know—it was a long time after we did all that stuff. That was all done in '64, so it's twenty years later. But the big thing was we got to meet—we got to go to the White House—to the Oval Office—and shake the hand of one of my idols—Ronald Reagan. And Ronald Reagan took a picture.

***Tacey Ann Rosolowski, PhD***

**2:07:26.4**

Wow, there it is.

***Emil J Freireich, MD***

**2:07:27.3**

Each one of us—our wives were in the background, but they were in the White House, and we each got to go up and shake his hand, one at a time. This is Smith—the chairman of the board of General Motors—that created the prize. So when I got home, I got a picture from the White House of me shaking the president's hand, and it's signed Ronald Reagan. I have it at my house. If MD Anderson treats me well, I'm going to give it to MD Anderson. The guy who did the video of this—you know—*People Make a Difference*. I don't know if you saw that video.

***Tacey Ann Rosolowski, PhD***

**2:08:07.6**

No.

***Emil J Freireich, MD***

**2:08:09.3**

It's available online. He came to our house, and he took pictures of all—well, he photographed all the things—the Lasker Prize, the General Motors Prize, the Outstanding Alumnus Award from NIH and so on. So they are recorded somewhere. So anyhow, that's the answer to that question. The reason the GM Prize was so important to me was that it was a cash prize, and I've forgotten how much it was. I think it was \$50,000. In 1983, I was still very poor, so when we got the General Motors Prize, it was the first moment in my entire life that we paid off our debts. We were out of debt. Up until that year, everything we did was on time—cars, house, health insurance—but when we got the GM Prize, we paid off all our debts, and ever since then we've been debt free. We don't pay mortgages on our house; we don't pay loans on our car. If we buy a car, we buy it. We manage like all people should, if they have a chance to do it. You've got to win the GM Prize to do it, though, because you never make enough money to fulfill your needs. You've got to get an infusion.

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For most of our young people today, the way they get it is from their parents. I mean, we have four children. One of them is totally dependent. She makes no money. She's a young thing. She's only fifty-three—no money. We have another dependent adult who earns maybe half of his cost of living. We have one angel son who makes a living, has no debts. And we have one daughter who is close. So that's how people get free of debt. What the GM prize is, is a parent. If the parents are smart and let their kids start off their careers debt free and live debt free, it frees them to do things. They can take chances. They can invest in the market. They can start a business. They can do all kinds of things. But if you start out in debt, you can't do anything. If you want to start a business, no one is going to give you any money if you already owe money.

*Tacey Ann Rosolowski, PhD*

**2:11:19.9**

It's a huge burden.

*Emil J Freireich, MD*

**2:11:21.4**

Yeah. So we need a system where everybody is debt free at some point in their life. That's what the government should do, and then leave people alone. You can tell I'm a right-wing conservative.

*Tacey Ann Rosolowski, PhD*

**2:11:34.7**

I can. Can I ask you a few more questions?

*Emil J Freireich, MD*

**2:11:38.7**

Anything. Yeah. I'm enjoying this. You want to buy me lunch?

*Tacey Ann Rosolowski, PhD*

**2:11:44.9**

Maybe.

*Emil J Freireich, MD*

**2:11:45.6**

I'm going to have lunch in about a half an hour.

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## **Chapter 16**

### **A: Personal Background**

#### *A Life of Work with the Support of a Strong Wife and Family*

### **Story Codes**

A: Personal Background

A: Character, Values, Beliefs, Talents

A: Professional Path

A: Inspirations to Practice Science/Medicine

A: Influences from People and Life Experiences

C: Portraits

*Tacey Ann Rosolowski, PhD*

**2:11:48.1**

All right. I have just a few more questions. I wanted to ask you some things about the private person behind MD Anderson.

*Emil J Freireich, MD*

**2:12:00.4**

Oh, my life?

*Tacey Ann Rosolowski, PhD*

**2:12:02.8**

Yeah, I know. Isn't that crazy? One of the things that struck me in one of your interviews is you said you had absolutely—in the interviews you did ten years ago—you said you had absolutely no hobbies, that you never did anything but work. I'm wondering if that really is true. What do you do when you want to relax?

*Emil J Freireich, MD*

**2:12:21.2**

Well, I'll go back a ways. I grew up in very modest circumstances, so just getting the essentials of life is what you did. You didn't have any time for fooling around. I did play basketball in high school, and I broke my leg. That turned out to be important in my life.

*Tacey Ann Rosolowski, PhD*

**2:12:43.1**

Why was that important to your life?

*Emil J Freireich, MD*

**2:12:45.0**

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Well, because it ended up keeping me out of the military, and that ended up with me going to medical school, and that ended up with me getting rehabilitation money from the state of Illinois, otherwise I never could have gone to medical school. I had no money. I had nowhere to get money. Scholarships weren't big enough to pay for everything. But when I got rehabilitation money, they paid for everything. They paid my books, my fees, my tuition. I lived at home. I rode the "L" to work, and I got my MD. What was the question again?

*Tacey Ann Rosolowski, PhD*

**2:13:20.6**

Things you do for relaxation.

*Emil J Freireich, MD*

**2:13:23.2**

Oh, relaxation. Well, when I was pubescent, the most important thing was sex. So when I was in medical school, I dated some high school girl, and we had reasonable sex, but when I got to be an intern, that's when I had sex. I interned at Cook County Hospital, and that was a community where everybody was under stress, because you had no money, you worked—we worked thirty-six hours on and twelve off, so you're always exhausted. You couldn't go anywhere outside the hospital. The nurses and doctors were—you know—if you had ten minutes, you went up to the OR and you had a little whoopee. But when I became a resident and we were paid fifty dollars a month and we had room and board, then I began to think. I actually developed a relationship with an intellectual—a left-wing, bleeding heart intellectual. Her name was Lenore Schwartz, and Lenore was an only child, raised by not rich but very well-to-do parents who lived in a very nice part of town that I had never been in before. Chicago was—well, all cities are like that. I lived in one mm above the ghetto. The ghetto was here, and then we were the next ghetto. They were up there in the high-rent district in Lake Forest. I met her through one of my friends who had money. He introduced me to Lenore. I don't know if I actually loved her as a person, but we were—I was twenty-two, and Lenore was rich and had a convertible. When we went out on a date, I drove the convertible. I was acting like a multimillionaire. She loved me, and I loved her, and we had wonderful times. She began to take me to all of the highbrow things. We went to the opera. I'd never heard an opera. We went to the symphony. I'd never heard a symphony. We went to an art gallery. She was a painter. We went to museums. We learned about anthropology. So Lenore Schwartz introduced me to a world that I hadn't even read about. I didn't even know they were out there, because when you come from the ghetto, everything is—just the next millimeter is as far as you're going to go.

So we decided to get married. She comes from a wealthy family, and I have zero. I didn't even have a car. So we went, like young people, to her parents, and we said, "We've decided to get married." Oh, wonderful. But to make a long story short, they said that was ridiculous. Lenore was working on her PhD, and she was an anthropologist and she was an artist, and dragging along some dying intern from Cook County Hospital was not for the family. They put up with me, but not very well. I didn't mix with their class very well.

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So as fate would have it, while I was an intern, fooling around with nurses at Cook County Hospital and dating Lenore, she developed acute leukemia. She was twenty-five or something, and at the time, the only treatment for leukemia was methotrexate and 6-MP. Prednisone had been discovered. She got all that treatment by the best doctor in Chicago, a guy I knew very well and admired. And during her illness, her family decided that I should stay out of it, because they felt that—they had guilt over the fact that we didn't get married and she was going to die without having something she wanted very badly. So they were full of guilt, and if I came back in the picture—we still loved each other, so they wouldn't allow me to see her. I didn't even see her until she died.

***Tacey Ann Rosolowski, PhD***

**2:18:46.7**

That's a very sad story.

***Emil J Freireich, MD***

**2:18:50.4**

And I wasn't invited to the funeral either. So after that trauma, my focus was on just succeeding, and social things became trivial. I just had sex. It was just—you know. But then I met my wife, and the way I met my wife was when I got fired from Cook County Hospital, I decided to take a residency at Presbyterian-St. Luke's, which is the inverse of county hospital. It's a private hospital. But we had a free clinic called Central Free Dispensary, and that was the teaching service which was run by the chief resident.

I was very good at what I did, obviously, and I was recognized by being made chief resident, and the chief resident did the teaching in Central Free Dispensary. So when I became chief resident—now you move from an adventurer—from just having experiences—for the first time in my life I had responsibility. I had to teach the other fellows. I had to run the clinic. I was in charge. The head nurse in the clinic was a short, petite, blonde lady named Haroldine Cunningham, and she diagnosed me immediately. Here's a guy just having fun, brilliant, and does whatever he wants. He's always going to be successful. And she took charge, from the day I arrived. "Freireich, there are four residents waiting in the clinic for you to sign the patients." If I was out all night, she'd really read me out. So that was the first time I had a relationship with a woman that was significant. There was no love and no sex, but it was a relationship. She was not just a nurse; she was a force in my life. Do you want to know a lot about my wife?

***Tacey Ann Rosolowski, PhD***

**2:21:33.4**

Tell me about your wife, yeah. She sounds like she's been important to your career and your life.

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***Emil J Freireich, MD***

**2:21:36.9**

She's very important. She's more important to me than Tom Frei. She's the most important person in my life. She was a person of enormous character honed by her early experiences. She was the product of a mother who was a very attractive young woman from a Germanic family dominated by a father. You know, in European culture, the mother was totally committed to her children. All the children were schooled. They lived in Lake Forest, a very fancy community. Her mother was number, I think, four—three out of five or four out of six—somewhere in the middle. She was a very feminine young thing, and she fell in love with an immigrant Scott, who was a golf pro. His name was William Cunningham. Their family was totally against this relationship, but she married William Cunningham, and she got pregnant very quickly, and Haroldine was the first born. There were two that followed her. She has two brothers. Because her husband was a ne'er-do-well—golf pros, they mingle with—they're like me and Lenore—they mingle with the rich and live like the rich, but they don't have any money. So they lived in very modest circumstances in Libertyville, Illinois, a little town. She had six children and slaved along with no help and no money, coming from a well-to-do family.

To make a very long and difficult story easy, when Haroldine was, oh, ten or something—ten or eleven—her mother committed suicide and she found her. She had slashed her wrists. So Haroldine had to walk into her house and find her mother on the floor, dead. That changes people.

***Tacey Ann Rosolowski, PhD***

**2:24:09.1**

That's severe trauma for a child.

***Emil J Freireich, MD***

**2:24:10.5**

So her mother's siblings, of course, came to the rescue. Her older sister, her Aunt Bee, was married to a physician and had one child. She offered to take in Haroldine, so she became Cinderella. She was taken in by her Aunt McGrew who had a daughter who was Cinderella, who was the queen, and she became the—she took care of everything. She had to do the laundry and clean the house and do all that stuff, because her niece was Miss America.

So her siblings—her two brothers—were farmed out. One went to one of the other siblings who had a farm in Illinois, and the other one—I forgot who he went to. But the three children were farmed out to siblings of the mother. The father was, of course, worthless. He continued playing golf, and he was an alcoholic and pretty much worthless. They all loved him. He was a nice man. He meant well, but as far as a father was concerned, he was zero.

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So Haroldine grew up in Lake Forest. She came from modest beginnings but was adopted by Aunt McGrew who lived in Lake Forest. She was now upper class. She went to Lake Forest High with all the rich kids, and when it came time to choose a career, all of her classmates went to college—fancy colleges—Harvard and Yale and all that. But she decided to be a nurse because her Uncle McGrew was a doctor. Auntie Bee wasn't into ten years of supporting poor Haroldine. She didn't have that much money. Don McGrew, the husband, died and left Auntie Bee with the money. So she had enough money, but she had to manage it, and she had to work to stay in the upper middle class section they were in. Auntie Bee really pushed her in the direction of nursing because you take three years and you're done. You make a living, and you're done. And 100% of nurses have jobs. So she went to nursing school, and she happened to be at Presbyterian. That's when I met her. She graduated and got a job in Central Free Dispensary. So that was Haroldine Freireich—Haroldine Cunningham.

***Tacey Ann Rosolowski, PhD***

**2:27:01.2**

When did you get married?

***Emil J Freireich, MD***

**2:27:03.4**

Well, when I was chief resident, during my year, the chief of medicine, who was a genius—Howard Armstrong—was fired. Again, because he was too successful. He built a program where all the house staffed work in the teaching service, and none of the residents and interns wanted to work in the private service with the rich doctors, so they organized and said, well, they had to get rid of the teaching service, so they fired Dr. Armstrong. When he got fired, he had no problem getting a good job at Cook County, but he was a physician scientist who worked in Boston during the war. He was very famous and very accomplished and rich.

So he called his residents in one by one and told them what to do. So when I got there he said, "Freireich, I understand from all the attendings that you're very good and you've learned a lot of medicine and what is it you need to accomplish your goals?" I wanted to be a general practitioner. I wanted to be a family doctor. And I said, "Dr. Armstrong,"—I may have told you this—"I don't want to offend you. You have a wonderful department, but the hematologist is a jerk, and we didn't learn any hematology." He said, "No problem. You have to go to Boston, and I'm going to get you a job with the best hematologist in the country." The three best hematologists in the United States were in Boston, and Howard Armstrong was important. He wrote me three letters of reference, and he said, "Take your 1946 Oldsmobile and go to Boston." So I took everything I owned, put it in the car, and I drove to Boston.

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I interviewed with the three greatest hematologists in the world, and they all offered me a job based on Howard Armstrong's letter of recommendation. I had to decide which one to take. Well, the most famous one was Dr. Dameshek, who founded *Blood*. He offered me a job. I wanted to go to Dameshek. The second most famous was Dr. Alexander. He was a coagulationist. I wanted to go with him. The least famous one was Joseph Ross, but Joseph Ross had gotten a grant from the NIH to study anemia, and he offered me \$3,000 a year salary. And since I had no source of income, no parents, I had to take Ross's job. So I went to work for Joe Ross. I was in Boston. I had \$3,000 a year income. I rented a room in a lady's house, so I couldn't have any women. There was no sex anymore. There was no drinking, no social life. I had to succeed at my job, and I was with some hard chargers, so I worked eighteen hours every day. I barely slept. Since I was the junior guy in the lab—we were the first to use radioisotopes off the pile. I used to spend sometimes three days in a row when I was just counting the samples. I had to do all the slave work. I set up the things for the experiments we did at Harvard, and I was working and no social life, but I'm very ambitious. I intended to succeed at this job. I met the giants of hematology—Bill Castle—so I was really doing great.

One day I get a call from Haroldine Cunningham. "I am coming to visit Boston, and I'd like to just have dinner with you." "No, problem. I'll pick you up at the airport." So I hadn't seen a woman now for months. I hadn't done anything. I was just working. So Haroldine arrived on the plane, and I drove my 1946 Pontiac to the airport—Oldsmobile—to the airport, picked her up, put her luggage in the car. I said, "What do you want to do?" Well, she didn't have a room or anything since she just arrived. I said, "Well, before we do anything, I want to show you my lab. I'm working my head off." So we drove to Mass Memorial Hospital. Do you know Boston?

***Tacey Ann Rosolowski, PhD***

**2:31:36.3**

A little bit.

***Emil J Freireich, MD***

**2:31:37.2**

Well, Mass Memorial is right next to City/County Hospital. It's in the ghetto of the city. So we drove down there with my 1946 Oldsmobile. No one would steal that car. This was in '53. I parked the car, and we went up to the lab, and I showed her—she was very impressed. So what do we do now? Well, we have to find a place for you to stay. So we went back to the car. Someone had broken into the car and stole her luggage. She had nothing.

So I went to the lady that I had my car said—you know, this poor nurse lost her luggage. So we went to the YWCA, and they took her in. We went to a store and bought some underclothes and a bra and some things, and she was at the YWCA, and I was working twenty hours a day. And Haroldine—our relationship had really become more than just—we never had sex, in the usual sense. We did necking and stuff, but we really developed a relationship. She ran the clinic, and we began dating. I saw her on weekends, and I really was very fond of her. When she came to

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town—you'll have to ask her—but she says she decided she was going to marry me when she came to Boston, and I believe that to be true. She didn't have a shotgun, but it was very close. She realized I was alone and lonely and working my head off and had no social contacts with anyone. I had no friends or colleagues or anything. So she really did intend to marry me. She came to town and lived at the Y, and I had a room. Then she got a job as a nurse at Mass General, so she was making \$3,000 and I was making \$3,000, so if we pooled our resources we could rent—we rented a room in a lady's house, which was an attic that had two rooms and an outside entrance. So we had a private entrance where the people who owned it couldn't tell us what to do, and we lived together, but we didn't—it wasn't a sex thing. It wasn't like modern people.

*Tacey Ann Rosolowski, PhD*

**2:34:26.1**

Oh, so you were sort of roommates for a while?

*Emil J Freireich, MD*

**2:34:28.7**

Yeah, we loved each other. We lived together. We spent all our time together. That was the only person I knew socially. So when I got eight hours off, I'd pick up Haroldine and we'd go out to dinner or go to a movie or go to our little apartment and talk about things or watch TV. So we became a couple, and after that went on for almost a year, she just said one day, "You either marry me or I'm going home."

I had three friends that I could trust. One was the chief fellow in our lab. His name was Stuart C. Finch. He's still alive, and he's still a very good friend of mine. He was married and had five children. He was a real family man. So I talked to Dr. Finch. I said, "Do you think this crazy nurse, should I marry her when I'm struggling so hard?" And then I had two other friends. These were two guys who were residents at Presbyterian-St. Luke's with me when I was a resident. One was a guy named Peter Bell Irving, and he was doing a fellowship in diabetes at Mass General. I consulted him. He was a bachelor and a swinger, and he got married much later in life. Then the third one was Oliver Wrong, who was another bachelor/swinger. And Oliver was a Brit who was training in metabolism or something like that with a very famous metabolic guy, and he ended up being chief of medicine at University College in London, a very famous guy. Peter Bell Irving ended up being very famous. So these were accomplished guys. I consulted my three friends, and they all said they thought it was probably a good idea. So I married her.

I had to work on a Friday. I had to count my samples and set up all the things and get done. We didn't have an experiment on Saturday morning. We normally did, but we didn't. So I got off Friday night at about 6:00, and Haroldine met me. We only had one car. We picked up my two friends, and we went to Beacon Street and found a JP, and we got married. Oliver Wrong was the best man, and Peter Bell Irving was the maid of honor, and Haroldine and I got married.

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Then we started being married and we had sex. First thing you know, fourteen months after we got married, we had a daughter—beautiful thing. Then fourteen months after that, we had a son. When she was pregnant with my son and the baby was a year and some old, that's when I got drafted in the military and went to NIH. And the rest is history. And ever since then, Haroldine Cunningham has been my one best friend, and we are really married. I mean, we are one. We got involved with our family. We had four beautiful children. We both adored large families, because her mother came from a large family, and we wanted to have twelve children. One of my best friends had four children. He was Roman Catholic. But by the time we got to number four—she had four children in six years—we were at NIH. We were making \$3,500 a year, which was less than what we made in Boston, because we only had one working; she was home. And in 1955, there were no disposable diapers. We lived in a house that we rented from an overseas State Department guy who rented it to us for a song, because he knew we were poor. And she had to maintain the house, wash the diapers, take care of our four babies, get them to school. We had one broken down car. So I tell ya, we worked hard. When I went to NIH—I think I already told you—I mean—we really worked hard. I walked in with nothing—no help, no nurses, no technicians. They gave me equipment and authority and do what you want. I had to recruit my own patients, take care of them, draw the blood. I had to do everything. And Haroldine—God bless her—supported me all the way, took care of our kids, took care of me, saw to it I had clothes and food and shelter and was interested in my work. She liked the kids. I told her what I was doing. When I got fired from NIH, she was the only one who stood behind me—Tom Frei, usually. So I love my wife. Did you see *Jerry Maguire*?

***Tacey Ann Rosolowski, PhD***

**2:40:17.2**

No.

***Emil J Freireich, MD***

**2:40:18.0**

I love my life. I love my wife. She was a part of everything I had done outside of my training, and we're very much one person.

***Tacey Ann Rosolowski, PhD***

**2:40:31.8**

You're very lucky.

***Emil J Freireich, MD***

**2:40:33.2**

Yeah.

***Tacey Ann Rosolowski, PhD***

**2:40:33.1**

That's wonderful.

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***Emil J Freireich, MD***

**2:40:33.8**

And she's a person of enormously high character because she came from a very fundamentalist background. She raised our kids. There's no fooling around with her. She's frugal, she's efficient, she's brilliant, she's clever, she's very resourceful, and she's responsible for everything I've done, because I couldn't have done it—even my fellowship. I couldn't have gotten through it without her. When we came to NIH—I'll tell you—she was pregnant with the second one, and she immediately got pregnant with the third one. We were living in a rented house. But she made it possible for me to work twenty hours a day and take care of the kids. We're a team. So she's the most important person in my life. More important than my mother, my father, my sister, my step-brother. She's really—she's what converted me from a child to an adult.

***Tacey Ann Rosolowski, PhD***

**2:41:45.8**

Is there anything that you'd like to add?

***Emil J Freireich, MD***

**2:41:47.4**

She had the advantage of being an adult, because she had a mother that she loved who died. She had five uncles and aunts who took care of her. She saw the virtue of the family structure. And she was very ambitious. She was a nurse, but she wasn't—she wasn't going to—you know—she worked all the time. When we were in Boston, she worked every day until we went to NIH. She was a nurse at Mass General, and she made a good salary. When she was pregnant, she had the baby and went back to work—tough lady. And she's still young and beautiful. Where is she in that picture? There she is, in the middle.

***Tacey Ann Rosolowski, PhD***

**2:42:35.9**

Oh, yes.

***Emil J Freireich, MD***

**2:42:37.3**

In the kind of—

***Tacey Ann Rosolowski, PhD***

**2:42:38.6**

A nice family picture.

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***Emil J Freireich, MD***

**2:42:40.3**

She's between my grandson and my granddaughter. And she loves our grandkids. She loves her kids. She's a wonderful mother, a wonderful grandmother, a great homemaker. She's a person of very high quality. I respect her.

So I'm sorry you got into that personal stuff. But as my hobby—my work has always been my hobby. I spend twenty hours a day—when I have a free day, I spend it with my family. I love my kids. For instance, I love football because my son has our four grandchildren—he lives in Austin, but he bought a license for the Texans, so eight times a year he comes to town with all our grandkids. They stay at our house. I love my grandkids. And the guy in the orange shirt is a senior in high school. He plays offensive guard on the high school football team. We think he's going to get a football scholarship. The skinny guy in the back, in the blue shirt, that's my oldest grandson. He's eighteen. He is a sophomore at UT San Antonio. We have to pay for his tuition and living, and we can't afford four. We can afford maybe six, but not four, so we've got to get some income for these kids to go to college.

Then my oldest son had a sterile marriage, and they tried. They got all the way to in vitro. The deal was for \$35,000 you get an eighty percent chance, so they went to China and adopted two little Chinese girls, and they're in the front there. We love them like they're our own. They're beautiful kids. And my oldest grandson, Chris, who is a step-grandson, is the one who fathered my great-grandson. So whenever I have hours, instead of playing golf—I tried golf. My sons play golf, because they have a lot of leisure time. Haroldine's father loved his grandkids. He was drunk, but when he came with us he would stay sober for a day or two. He'd drink in the evening. But he taught them all to play golf. Both my sons are golf players. My oldest son is serious. He plays in tournaments. The youngest son, he's just fair. So one day they said, "Dad, you ought to have a hobby. You should learn to play golf." So I had a family day, so they took me to play golf. Well, I played eight holes, and they said, "Dad, maybe you shouldn't play golf. This is not your thing." So my golf career was eight holes of golf.

And football I love because the kids come to town and we see our grandkids and I see my daughter. I love my youngest son. He's my favorite of all the kids. So, whenever I have a minute, I spend it with them, and I do what they do. So if they play football, I go to football games. My baby—Ellen is a soccer player. She's a goalie in soccer. I'm going to go on Saturday. We're going to see soccer. The football player—I have to go to a football game on Friday night in Austin. Emily is a dancer. I have to go to her dance things. Chris—they had a big birthday party for my great grandson. We had to go to that. He's two years old. He had a big party with all of his friends.

***Tacey Ann Rosolowski, PhD***

**2:46:18.4**

So it sounds like you're—

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***Emil J Freireich, MD***

**2:46:19.0**

So all my activities are what the family people want to do. My wife and I watch some TV in the evenings, and I like theater, so I go to the plays every once in a while. My oldest daughter was an actress. My oldest daughter was a hippie. She's the one in the blue. She's physically big. She's built like me. She's tall and wide, heavy. She was a Hair Generation baby. How old are you? Oh, you don't need to tell me.

***Tacey Ann Rosolowski, PhD***

**2:46:54.1**

Fifty-six.

***Emil J Freireich, MD***

**2:46:55.1**

She's fifty-seven.

***Tacey Ann Rosolowski, PhD***

**2:46:59.3**

She's a year older than me.

***Emil J Freireich, MD***

**2:47:01.6**

Yeah, so you're the Hair Generation too. She grew up smoking pot and hippie stuff with the boys and sleeping out and alcohol and all that stuff. We dragged her out of these commune-type things twenty times during her teens, when she was in high school in Houston. We had a rough time, but she finally got through high school. The way she did it was she got interested in drama. So she got into drama class. She practiced and finished high school. We got her into a drama program at North Texas State. Her academic things were so bad, she couldn't go anywhere but North Texas State. She got a baccalaureate degree, and she went to New York and acted and modeled. So she's done everything. She lived with all the gay guys, and all of her friends are dead now. She lived with them and sex and she did everything bad, and after a while, she got born again. She just got tired of all that. She came home, went to church, gave up all the bad things except alcohol. She couldn't shake alcohol, but she got a job as a teacher and worked with young people. She married a nice guy. But finally the alcohol got her, and we had to get her in rehab. She's now married to a straight guy. She's off the alcohol. She's off tobacco—fifty-seven. She had no children.

My other daughter had Crohn's disease when she was eighteen. She almost died. She had about ten years where it was touch and go. She got married to a wonderful guy, but they got divorced because of her career. She's a musician—plays the clarinet. So she's single and poor and we support her a hundred percent—Lindsey.

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And my oldest son is a great guy. He's the city engineer for the City of Round Rock. My younger son is a real estate guy. He works for Keller-Williams. So I have no hobbies except my family. So if they don't come to town—we're going through a phase now where my wife—we don't have help. She doesn't trust help. She's a compulsive obsessive. So if we hire someone, they never do it like she does. She has to do everything herself. So when they come to town, it's too much work for her. By the time the laundry—and we have a pool. They swim, and we go out and so on. She doesn't like them coming to the house, so we have to develop interests. So we're beginning to try to develop some things we like to do. I go to the theater with my daughter. She's an actress—Lindsey—and my wife is a realtor, so she loves homes. She looks at homes. She actually sold two houses in her career, but mostly she just likes real estate as a business. So we watch TV. I go to the football games.

One of my dear friends here, Bill Russell, was chairman of pathology. He's one of the people who recruited me here. He retired. He went to Florida, and he practiced for a long time and had a lot of money. When he died, his wife moved back to Houston because one of their daughters and their granddaughter lived in Houston. And she's a good friend, Marilyn Russell, and she loves baseball. So she takes Deeny and I to the baseball games. That's another hobby we have, but it's based on going with Dr. Russell. She's a lovely lady. She lives alone, but she had her daughter and her granddaughter in town. And professional friends—you know—the Freis, we do things with them. So everything I do has to do with work or family.

***Tacey Ann Rosolowski, PhD***

**2:51:08.5**

It sounds like it does. Well, I don't think I have any more questions for you right now.

***Emil J Freireich, MD***

**2:51:13.9**

Good. It's about time you got bored with all this boring stuff. As you know, I'm at the age where I enjoy reliving these experiences, but I shouldn't because I have to go forward or I'm going to get fired. So I still have a research project. I still contribute to leukemia. I'm still in charge of the training programs for graduate medical education. As long as I plan good things and we're doing well, I can still work as my main hobby.

***Tacey Ann Rosolowski, PhD***

**2:51:46.3**

Is there anything else you would like to add before we close off?

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***Emil J Freireich, MD***

**2:51:50.9**

No, but you should interview my wife. Now there's a great person. The guy who did the *People Make a Difference* series—I forgot his name now. He came to my house and interviewed my wife. She told him what my bad habits were.

***Tacey Ann Rosolowski, PhD***

**2:52:10.2**

Well, I want to thank you, Dr. Freireich.

***Emil J Freireich, MD***

**2:52:14.7**

Well, thank you. You are a trained listener. I should rent you by the hour. You're a psychotherapist.

***Tacey Ann Rosolowski, PhD***

**2:52:24.5**

Well, I hope I didn't do too much of that. But I want to thank you so much.

***Emil J Freireich, MD***

**2:52:31.9**

The best therapy people can have is to talk about their problems outside of their subconscious. It's to bring their problems to the surface. You have to know what bothers you in order to deal with it.

***Tacey Ann Rosolowski, PhD***

**2:52:45.5**

This is very true.

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***Emil J Freireich, MD***

**2:52:46.9**

When I was a senior in medical school, I met the founder of psychoanalysis. Franz Alexander was the chairman of our psychology department. In my graduating class from medical school, 180 graduates from University of Illinois College of Medicine—the largest single graduating class in the United States—fifty percent of the graduates wanted to go into psychiatry because Franz Alexander was so inspirational. He was the founder of psychosomatic medicine. He convinced everybody that all disease came from the brain, so you could treat diabetes by psychoanalysis. We used to go to the bedside and do what you did, talk to people with diabetes to get the out of a diabetic coma before we had to pull it. We did the same for hypertension. So psychosomatic medicine is a bunch of bullshit, but it was, at the time, a very attractive idea. And we thought, well, psychosomatic, if you're a psychiatrist, you can cure all disease, so we all wanted to be psychiatrists, but I signed up for psychiatry and I got fired. I was rejected, because in order to get into psychoanalysis, you had to be psychoanalyzed. So I applied for psychoanalysis to the best guys on our faculty, and they all said I was hopeless, so I couldn't go into psychiatry. I had to be a family doctor.

***Tacey Ann Rosolowski, PhD***

**2:54:18.9**

Well, maybe on that note we ought to close off the interview for today.

***Emil J Freireich, MD***

**2:54:24.1**

But that's true.

***Tacey Ann Rosolowski, PhD***

**2:54:24.8**

I believe you. I think that's a fabulous story.

***Emil J Freireich, MD***

**2:54:26.7**

Franz Alexander was my idol.

***Tacey Ann Rosolowski, PhD***

**2:54:28.2**

I think that's a fabulous story. Well, thank you very much, Dr. Freireich.

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***Emil J Freireich, MD***

**2:54:32.1**

But people say how did you get to where—? As you can see, everyone's life is a product of what happens to them. It's not what they decide to do. I became a doctor because I had tonsillitis in the ghetto, and I saw a guy wearing a shirt and tie, and I said, wow, I want to be like him. I got to be a hematologist because my boss got fired and said I had to go to Boston. I got married because my wife came and told me I had to do this family thing. People sit down with their kids and say, "What do you want to do?" That's not it. It's opportunity. You have to grasp what's in front of you and take your opportunity. The guys we've trained, the geniuses who are going to cure cancer, are all that kind of people. Michael Keating picked up his four kids and his wife, with no money, and came to train to work as a fellow at MD Anderson because he wanted to cure leukemia. He heard me give a seminar. I went to the international—that's one of the good things about the face-to-face thing is the young guys get to see some of the giants. At the time, I was the only one who was talking about curing leukemia, and when he heard about curing leukemia, he said, I want to do that. He took his wife and children, left his homeland, came to a foreign country with a visa, and for slave wages, and he's now number one in the world.

***Tacey Ann Rosolowski, PhD***

**2:56:09.4**

Looks like we're done.

***Emil J Freireich, MD***

**2:56:10.0**

Yeah, you going to get me soup?

***Female Voice***

**2:56:12.6**

I was coming to check on you.

***Emil J Freireich, MD***

**2:56:14.5**

She's such a great psychotherapist. I can't let her go. She's going to spend the rest of the day with me.

***Female Voice***

**2:56:20.5**

Okay, I'll get soup for both of you.

***Emil J Freireich, MD***

**2:56:23.2**

Were there any calls that I need to attend to?

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*Female Voice*

**2:56:29.6**

No, sir.

*Emil J Freireich, MD*

**2:56:30.3**

Okay, thank you for fending them off and giving me all that free time.

*Tacey Ann Rosolowski, PhD*

**2:56:34.9**

Well, it does sound like we can close off the interview at this point.

*Emil J Freireich, MD*

**2:56:39.3**

Sure.

*Tacey Ann Rosolowski, PhD*

**2:56:40.2**

Okay. The time is 1:15. I just wanted to say thank you again.

*Emil J Freireich, MD*

**2:56:45.7**

Have you eaten lunch?

**2:56:47.2** (End of Audio Session Three)