National Cancer Institute
Division of Cancer Epidemiology & Genetics
National Institutes of Health
Oral History Project
Interview with Dr. Stephen Chanock
Conducted on May 6, 2022, by Holly Werner-Thomas for
History Associates, Inc., Rockville, MD

HWT: So, diving in, my name is Holly Werner-Thomas, and I am an oral historian at History Associates Inc. in Rockville, Maryland. Today's date is Friday, May 6, 2022, and I am speaking with Dr. Stephen Chanock for the National Institute of Cancer (NCI), Division of Cancer, Epidemiology and Genetics, part of the National Institutes of Health or NIH. The NIH is undertaking this oral history project as part of an effort to gain an understanding of the National Cancer Institute's Division of Cancer Epidemiology and Genetics. This is one in a series of interviews that focus on the work of five individuals at the NCI-DCEG, including their careers before and during their time at the institute. This is a virtual interview over Zoom. I am at my home in Los Angeles while Dr. Chanock is in Shady Grove, Maryland. Before we get started, could you please state your full name and also spell it?

SC: Yes. My full name is Stephen Chanock. S-T-E-P-H-E-N, C-H-A-N-O-C-K.

HWT: Thank you. Dr. Stephen Chanock is a leading expert in the discovery and characterization of cancer susceptibility regions in the human genome. He received his MD from Harvard Medical School in 1983, and completed clinical training in pediatrics, pediatric infectious diseases and pediatric hematology, oncology, and research training in molecular genetics

at Boston Children's Hospital and the Dana-Farber Cancer Institute, Boston. Since 1995, Dr. Chanock has served as the medical director for Camp Fantastic, a week-long, recreational camp for pediatric cancer patients, which is a joint venture of the NCI and Special Love, Inc. From 2001 to 2007, Dr. Chanock was a tenured investigator in the Genomic Variations Section of the Pediatric Oncology Branch in the NCI Center for Cancer Research. He also served as co-chair of NCI's Genetics, Genomics and, you'll have to help me with this one—Proteomics?

SC: Proteomics, yes. you've got it.

HWT: Proteomics faculty for five years. In 2001, he was appointed as chief of the Cancer Genomics Research Laboratory, formerly Core Genotyping Facility. And in 2007, as chief of the Laboratory of Translational Genomics, both within DCEG. From 2012 to 2013, he served as acting co-director of the NCI Center for Cancer Genomics, and in 2013, Dr. Chanock was appointed director of DCEG, a position which he has held since. He has also received many awards for his work over many years, including director's awards at both the NIH and the NCI, and most recently, the AACR, American Cancer Society Award for Research Excellence in Cancer Epidemiology and Prevention. Does all of that sound about right?

SC: Yeah. That sounds good. Very good fiction. You were very good at making all that up.

HWT: (*laughs*) So I always like to ask people to describe their backgrounds in relation to their career paths. Of course, your father, Robert Chanock, was an NIH scientist himself and discovered RSV [respiratory syncytial virus] in 1957, I believe. We do not need to begin there, but I want to acknowledge that, that there's this connection with your father as a major NIH scientist. What was his influence, if any, on you? And would you consider him a mentor?

SC: Yes. He was my beloved father. A remarkable scientist and a wonderful father. He brought me to NIH in 1957. I grew up on this campus. I learned to ride a bicycle and used to play soccer on campus where Building 35 now stands. We used to go to the Cloisters on Sunday night and listen to the obligates sing the vesper service on the other side of the wall while enjoying a picnic dinner, often with other NIH families. I have all sorts of wonderful memories of NIH because it was literally my home. I grew up literally two miles away. As some have joked, it has been the family business. Although for me, when I was younger, I was a very serious competitive swimmer and very interested in music. And when I left to go to college, the last thing I wanted to do was to have anything to do with science or to go to medical school or do anything like that. I wanted to be a musician, a composer, and a conductor. So, I studied music. And went off to Europe to do that before deciding that, well, maybe medicine was the right calling.

HWT: I just want to spend a moment parsing some of those details.

SC: Sure.

HWT: Because I did read that you initially did plan not to study medicine but music. And then you graduated from Harvard Medical School in 1983, of course. So, what was the process there?

SC: Well, I mean, I grew up in a house where medicine was all around with my father and all of his visiting colleagues, some very distinguished Nobel laureates and giants in science and others who were great fun and enlivened the house. Albert Sabin was a mentor to my father, and we used to spend holidays with him. So, I had this exposure to these great scientists as people. And my mother was a very accomplished modern dancer and [she] went out and danced on tour when I was very young. And she loved the arts and music. And so that's where, you know, I tended to gravitate more towards that side of the equation. I was very good in math and quantitively was quite good, but I had aspirations to be a musician. So, when I went to Princeton University, I majored in music and during that time, between my junior and senior year I had a, I think it was, no, sophomore and junior year, I had a very remarkable experience. I lived for six weeks in Switzerland in the household of a man named Yehudi Menuhin, the great violinist. So I won't bore you with the details of how I came to that. But there were a group of young musicians who did everything from clean the house, cook. I was the tutor to the grandson so he could go to the Charterhouse School in UK. We all played music and we lived in the same house as Yehudi Menuhin, who provided comments and suggestions. And all these great musicians were coming every other day for his festival. And that was really very, very insightful. Because I had talent, but I didn't have enough talent. And I was in this very

intense, rarefied environment where I had the time of my life. I have friends who I've kept up with since then. But it was clear that I wasn't good enough to be at that level. I just didn't have that raw talent. And I thought to myself, what do I do?

And so it was very natural to think about what could I do that was socially very important. And medicine was that. So I'd grown up in a socially active family; my mother took me to multiple demonstrations in Washington and sent me to a Quaker School. My father believed in the public good. Virgil's famous saying, you know, "There is no greater good than the public good," which was a large poster that was on our kitchen wall from the time I can remember anything. And so, I decided to go to medical school, thinking that I was going to go into public health, Third World health, and make the world a better place. And so I went to Europe and studied music for a year after I graduated to finish some of the things that I'd started, and also because it would take a little bit of time to get through all the application and finish the courses in summers, etc., to do the premedical qualification. And I applied and luckily, you know, I very fortunately was accepted to Harvard Medical School. And so I kept up my music. To this day, every night I either play the piano or play the harpsichord for half an hour, 45 minutes. It's my release. My wife of 42 years, a wonderful person, can tell what kind of day I've had. Because whatever I go to play, she's not in science, and she'll just say, "Oh, it was one of those days." Or, "Oh, it sounds like you had a good day." (*laughs*)

HWT: I was going to ask you what instruments you play. I just have a couple of follow-up questions before we move on. One is, first of all, what is your mother's name?

SC: My mother's name is Beth Osgood Chanock, but she danced professionally as Beth Osgood. She actually danced with Martha Graham when I was very young. And she ran a studio here in Washington for years with a woman named Pola Nirenska, who was a very famous Polish dancer. And so she was engaged within the dance community. And her best friend ran the Alvin Ailey Dance Company. And so every year when they'd come dance at the Kennedy Center or Lisner Auditorium, they'd always have the cast party at our house. And Alvin would stay at our house sometimes. So I grew up heavily exposed to that modern dance and modern music scene.

HWT: What a remarkable childhood.

SC: Yes. I'm very fortunate. Yes.

HWT: Can you tell us a story, again, before we move on, again, you know, you said there were Nobel laureates and other scientists, very important people around. Can you remember a story to tell us that was influential?

SC: Oh, I can—I mean, there are lots. Just as an aside, I promised to finish writing this article about my experience with all these famous virologists who were all in our house. But I mean, that's a whole hour and a half interview telling you those stories. I think there were two people who really had a tremendous influence on me. One was a very controversial man who won the Nobel Prize who was my godfather, [Daniel] Carleton Gajdusek. He

was here at NIH in NIMH for years and he won the Nobel Prize for his work on the neurologic disorder, kuru.[1] Through my youth and early training, I used to spend a lot of time with him and his most unusual family, comprised of a remarkable cohort of young men brought over from the South Pacific for education. In truth, he was the most remarkable intellect I knew. He was always talking about the importance of medical research and medicine in society, he was an anthropologist as well as a physician-scientist, always observing humans and their context. Here was somebody who solved the horrific problem of kuru in New Guinea and learned something new in discovering what's called now called prions. And his motivation was this intense curiosity to solve a public health problem, as far away and as unusual as that world was from Bethesda, MD. And so, the importance of the context of science was impressed on me, subconsciously.

And the other person was really my father's mentor, whom my father worked with in two different go-rounds. I was born in Cincinnati while he worked with Albert Sabin, one of the developers of the live polio vaccine. And we kept a very close family relationship. Albert was a very challenging person on a personal level. But he was incredibly scrupulous, hardworking, and rigorous in his science. And so talking with him and being around him quite a bit, whether it was on vacations—his two daughters were a little bit older than my brother and I, but we would spend time with them. He was somebody who just thought in very structured ways. The decision of when to have dinner was a structured decision with him. He was a very rigorous person. But he always took interest

[1] Gajdusek was the co-recipient (with Baruch S. Blumberg) of the Nobel Prize in Physiology or Medicine in 1976 for work on an infectious agent which would later be identified as the cause of kuru, the first known human prion disease.

in what I was doing and always asked questions and would ask the tough questions. What are you going to do with this? Suppose you become a musician. Then what are you going to do? How are you going to pay the bills? What are you going to do next? Are you going to get bored with this? And in retrospect, that was really quite formative, having those—there's no other way to describe it—but volleys with him. When I was in medical school, he would come to Harvard, he and his wife would always take my wife and I out to dinner. And he always asked 101 questions. He was intensely interested. He called me his scientific grandson. So it was a very special relationship.

HWT: Wonderful. Well, I'm glad that I asked. Those are some of the stories that I'd love to hear more about if we had more time. And I'm sure you'll have some of these in your own article. What about at Harvard Medical School? Did you have mentors there?

SC: I did. I certainly did. I'll tell you the, what really shaped my career was two things. I'll go back to university, for all four years, my roommate and closest friend is a gentleman who's still alive, his name is Bob Massie. He's a hemophiliac and was infected with HIV very early on. And he's one of these long-term survivors [controlling who many, including] Tony Fauci and company have written papers about him. He's an Episcopal minister and taught at Harvard Business School in ethics. He is my closest friend and he's godfather to some of my kids. I was best man at his wedding. He was an usher at mine. And I lived with him for four years in a college dorm. And he was giving himself shots of Factor 8. And he had certain kinds of challenges with walking and terrible arthritic pain. And I learned to manage that as a friend. Not really thinking I was his doctor, but just

heavily exposed to that. Seeing just how debilitating a chronic disease can be. But also, just marveling at how well he overcame that and how his spirit and his desire to do things triumphed over just about all the physical disabilities and barriers that were thrown up in front of him. So that was a formative experience.

Then the other was with my late brother's fatal cancer diagnosis which occurred when my wife and I were living in France for a year where I was studying music. I had just gotten into Harvard Medical School. We were in this little town on the coast of Normandy where we were living for a year and naturally very excited. Unfortunately, a day or two later, my beloved brother was diagnosed with a pediatric cancer. He was a little bit older than I. So when we came back, my first year of medical school was really tinged by his illness. He was treated at the National Cancer Institute by a man named Phil Pizzo, who was head of the Pediatric Oncology Branch, who eventually recruited me. Phil was a marvelous mentor. But that was something, going through my first year of medical school, having my brother very sick, I traveled back and forth. And he passed away just at the end of my first year of medical school. I took my finals at the NLM with a proctor, who was a friend of one of the deans.

So those two things sort of set me on a course towards pediatric oncology, particularly towards catastrophic illness and remarkably how people face these very substantial challenges younger in life. So in that setting, some of the people that I then started to come in contact with, I was naturally drawn to when I was a medical student, were some of the pediatricians, especially the pediatricians at the Dana-Farber Cancer Institute, the

Jimmy Fund, where I eventually trained in pediatric oncology. And so there are people like Stephen Sallan, a marvelous person who was the head of the clinical service at that time and Sam Lux, who was head of hematology, who have been lifelong mentors. And they're each, you know, well up there. I'm sixty-six and they're a bit more, I'm not going to say exactly how much, because I know they may not like that. (*laughs*) But I started to talk with them. And so by the time I finished medical school, I knew I wanted to do pediatrics. And I knew I was headed towards some form of complicated serious illness, whether it was hematology, oncology, or infectious diseases.

That was the time when AIDS was just breaking. So I set up, as a resident, the very first AIDS clinic at Boston Children's, and saw the first kids Boston. I wrote papers on the first case reports under the mentorship of Ken McIntosh, Professor of Pediatric Infectious Diseases at Harvard. It was a funny coincidence that he had actually trained with my father 30 years before, or 20 years before. (*laughs*) So the personal connections and the personal experience clearly shaped how and what decisions I made—or perhaps were made for me. So for me, it was never a question. I don't think I ever once in my professional career wondered, well, what do I do next? Why am I doing this? It just, it seemed obvious, or it was very clear why the next step was very important and where the compelling questions were.

HWT: Incredibly rich stories. I have a follow-up question. I wanted to ask you more about your time at Children's Hospital anyway. So I'll tie that in, in terms of what you learned, what you're talking about and also what you contributed there. So yeah, let's start there.

SC: So, I mean, I was affiliated with Boston Children's for, I don't know, I guess eight or nine years. I went to medical school and then I was an intern and a resident, and then I did two fellowships back-to-back in infectious disease and then in pediatric hematology oncology. Then, I worked in the laboratory of a very distinguished investigator, a man named Stuart Orkin where I got an NIH K08 training grant and was worked in his world for nearly five years. The award was intended to transition me to set up my own career, but it was always in this context of addressing very interesting research questions that I, at first, was clinically oriented but learned the immense value of basic science in that the transition from discovery to utility was always unpredictable. So remember I said I went to medical school thinking I was going to do something in public health and primary care, most likely involving Third World medicine, particularly in lower middle income countries for children and nutrition. But over the course of the early phase of my medical education, and particularly that first year of the family exposure to pediatric cancer and the terrible loss of my brother, there was no question that I tacked towards pediatric oncology and that was what I was going to go do. That experience put me on a trajectory, which was further defined by events unfolding at that time. Simultaneously, that was 1981 and AIDS wasn't even described until the middle of 1981. And then when it started to break in children in 1983, then it was very clear that there was a fascinating and challenging problem. And so I did quite a bit of work in pediatric AIDS for the first few years of my career.

So to me, again, in considering life choices, sometimes there's almost a sense that they're made for you. And that's the way that I look back at how I got started and why I am where I am. I can look back at my life and see there were all these different currents. Again, maybe it's my personality, but I'm rarely at a point where I ask, "What do I do next?" I mean, it was just very clear what the next steps were. I needed to do this, or I was going to pursue interest in that. For me, opportunity came knocking and I felt I could move towards something where one could really make a difference and there was a tremendous opportunity for discovery.

And it was during my time at Children's as a resident where I came in a lot of contact with people like Samuel Lux and Stephen Sallan and the heads of the hospital, Mary Ellen Avery and then David Nathan; in that rich environment, I got bitten by the research bug in the sense that I saw all these cases, and I wanted to continue to help them. But we had to figure out what's the underlying basis for a given challenging disease? What do we need to do? Research is really what drives those changes, just not empiric rolling the dice, per se. So in that regard, my time at Children's was really formative in shifting me from a public health implementation orientation to real hardcore science. Whether it was basic laboratory or translational or now epidemiologic. Those were the interesting questions. And to me, follow, go where it's interesting.

HWT: You've anticipated almost my next question. I wanted to ask you when you started out, what you knew and what you didn't know, and what the interesting questions were, and what you pursued. Do you have anything to add?

SC: I think that the interesting questions can change. And there are some scientists, and some of my colleagues who I have tremendous admiration for who have spent 30 years studying something, trying to solve a particular problem. I guess I'm a little too restless. I think what I find intellectually satisfying is addressing and challenging what needs to be answered. But I don't necessarily stay with that. So you know, when I came out of my residency, I was going to be doing pediatric HIV. And then I did molecular immunology of rare pediatric immune deficiency and the complications of cancer, trying to use these as models to understand how and why kids got in trouble when they were given chemotherapy, things that we saw on the floor. So that's where I worked for a good period of time. When I came to NIH in 1991, I started working on pediatric HIV in immune-compromised hosts and infections in children. But by 2001, with the advent of the genome and the opportunity to look at variation in the genome, the interesting questions were still there, but not really realizable because it's so hard to put together large enough sets of these rare diseases to go to more common problems of breast cancer and prostate cancer. So my career has seen shifts based on what are the available opportunities, and most importantly, what are the really interesting questions that are emerging from the science?

I followed this principle as a resident in Children's Hospital and this as a laboratory fellow with Stuart Orkin – and Stuart was quite a remarkable, different kind of mentor. [He] was always, what's the next question? It's not just theoretical thing, I'm going to solve this, or I want to call myself something. Stuart would say, "Don't worry what you

call yourself. Go follow your nose to where it's an interesting question." He was the kind of person who you never met with in his office. Never. Maybe five times in five years. But you'd talk with him at the bench all the time. You'd show him something and you'd end up having a half hour discussion. And you would write on the little mats that we were doing our research. And everyone would save those because these were these "transcripts" of the master speaking. That was a kind of enthusiasm and an interest in what's the question at hand, or what's the next pressing question. And those kinds of experiences and coming in contact with those types of people were really formative and I think sort of brought out my kind of personality and my proclivities in science. I am forever grateful to a whole group of people when I was up at Harvard. And I had some colleagues who were at other institutions who I collaborated with at a distance who were marvelous mentors as well.

HWT: Anybody you care to mention or talk about?

SC: Outside there was a marvelous person at the Scripps Institute, a man named Bernie Babior, who I collaborated with very closely. He passed away a number of years ago. He was almost a family member, and it was sad when he was elected to the National Academy of Science because he was very sick. He came to Washington and his wife came and stayed with my wife and I. It was a wonderful celebration of his career. And he had a big effect on my career as he taught me an awful lot by telephone and fax. Science can be learned in different ways. It's all about observing and about looking at things and processing and rethinking things. It's not a great metaphor, but it's not dissimilar to what

Dwight Eisenhower as a general said: “The best-laid plans are fine before you start the battle. But the minute the battle starts, most of those plans go out the window and you have to go with what’s in front of you.” And I think that science has some very strong parallels of what’s the data in front of you? What’s the next question that you can do with that data? Or what do you need to go get? Or what do you need to do differently? Or how do you revisit that particular problem in a different way to try and solve it?

HWT: Wonderful. You know, I wanted to ask about technology, for obvious reasons. And you’ve already mentioned the advent of the genome. So I always ask what technological advances drive science? You know, because there are so many. But let’s talk about that a little bit, and then we can weave it into the rest of the conversation around your work.

SC: Sure.

HWT: But I want to know, you know, your field seems to be inseparable from advances in genetic research.

SC: Right.

HWT: Can you talk about the Human Genome Project and what it’s done for cancer research?

SC: Sure. I mean I think I’ll go back to when I was a postdoc with Stuart Orkin. We would make our own enzymes for doing laboratory work. And sequencing was done with these

complicated gels that you could do one or two a day and get a little bit of information. It was very exciting. And you know, it was always a question of how do you get more information? How do you take it to the next level? And technology was limiting in that. And I remember when PCR (polymerase chain reaction) was discovered. The first grant I got, I bought one of the first machines and I still have that over in my laboratory. I have a wonderful senior technician who regularly asks, "When are we getting rid of this?" I always answer, "You can't. This is history." This Perkin-Elmer machine, it's like having a Model-T Ford. You don't get rid of it. (*laughs*) We don't use it, but it sits there and reminds us of how far we've come.

So I think the progression of the technologies advanced to the point of what then enabled the genome project to really take off in the late 1990s was all of a sudden transformative. There was this whole new world of saying, all right, instead of asking a question about one particular place in the genome, we can now look across a genome in an agnostic manner. It was the shift from genetics to genomics. And with that, as we put together these maps, or as people put together these maps, you could compare them between people and see that there were millions of differences for each person. Representing still a small fraction of the total amount of DNA. But those differences may be really informative. We know about them from severe catastrophic diseases like hemophilia or sickle cell anemia or cystic fibrosis. But a lot of the variation is tolerated. But it just subtly turns you one way or another. But this notion of what your individual carburetor is set for and how well you will and will not handle stress is that it can lead to diabetes or to breast cancer or to heart disease really was something that was very clear to me that that

was a question that was going to take an awful lot of effort and advanced capacity to do it at a scale that we hadn't thought of. So that was really very exciting. And you could see where we were going. It also meant we hard to work in teams. And the question is, how were we going to get there? And it was going to involve the use of technology, and more importantly, the scientific know-how to put together large data sets. Instead of just looking at one or two individuals or sets of samples, we needed hundreds to thousands. And that's where in 2001 I started to have contact with the man who was the founder and director of the division that I now direct, Dr. Joseph Fraumeni. And Joe Fraumeni was a very visionary scientist who created the first cancer maps, did a lot of the family syndromes with Bob Miller. But he had this idea that if they do enough large studies and you collect the specimens, the technology will catch up. And indeed, that's what happened.

So in 2000 or 2001, I started spending a lot more time talking to Joe Fraumeni and people here in DCEG than I did in the Pediatric Oncology Branch. And you could see, well, they had large collections of men with prostate cancer and controls. Or they had cohorts where they could pull these things from. And so I started to attack and do my work and really pursue questions there. And a lot of it was how do we set the technology in a reliable and valid way that allows us to say we have comparable measurement for each individual? That means we can put the data together and say, all right, we can see genetic variation is important for this disease. And in another place, for another disease. So it was, to me, a very exciting time when I learned an awful lot on the fly from people like Bob Hoover, who was one of the greats here in DCEG, and Peggy Tucker and Joe Fraumeni. And

certainly colleagues who were still here who I collaborated with like Nat Rothman and the late Sholom Wacholder. These were people who all of a sudden presented me with a whole new discipline that I needed to master to be able to take the science that seemed most interesting at that time. And that's the way, at least, scientific discovery in my life has gone. But again, there are others who have a very strong focus on trying to understand the conundrum of sickle cell or cystic fibrosis. I have tremendous admiration. But that's a different kind of patience and a different kind of focus.

And so I feel very blessed to have come to the intramural program where one can do those kinds of things and make some of those shifts. What I'm doing now, I would have never imagined I could have done 20 years ago, or 25 years ago.

HWT: Well, let's go back a little bit. Say, 25, 30 years ago. So you joined the NIH in 1991, correct?

SC: Yeah.

HWT: Okay. And of course you joined to study oncology and infectious diseases, as you've been talking about. And then your interest changed in every way that you have described the drivers of that. Is there anything else you want to add, though, about your work in the 1990s? Because I don't want to miss out on a whole decade.

SC: I think it's interesting how I came here. Because in 1980, 1979, my brother was diagnosed with a synovial cell sarcoma by Al Rabson, who was a legendary pathologist at NCI. And Phil Pizzo, then a very young investigator in the Pediatric Oncology Branch took care of my brother for a year. Steve Rosenberg was my brother's surgeon. He was the newly minted head of surgery at NCI. So I obviously kept some contact with them. But in 1989 and 1990, I started to see Phil Pizzo at meetings, and he invited me to a position in 1991. And it wasn't a question. It was like yup, you're coming. I need to just come when I'm ready, when I finish some of the things in Boston. My wife and I have four kids and they were anywhere from one to seven at that time. And my mother, father were here. You know, having grandparents nearby was a major attraction, especially in light of the loss of my brother. We were raising four kids on our own without nannies or anything in Boston—pretty crazy, huh?

And one of the really seminal moments in my recruitment to NCI was when my father, who was at NIAID for 50 years, sent me to speak with Tony Fauci, the NIAID director, five or six years. On a Saturday morning when I was down here, looking and trying to figure this out, he called up Tony and said, "Would you talk with my son Stephen?" So I went over, and I saw Tony for a highly informative half hour discussion. And it was very interesting, because he really characterized better than anyone I know the case for the future of the intramural program and why coming to the intramural program is so exciting. The opportunity to work in a very supportive and intellectually exciting place, and to be able to take your science where you need to take it at the time that you see you need to do it. That you're not encumbered by grants. You're not slowed down. And in

fact you can, if you have the initiative and the abilities, you can build what you need to to address the big questions. And you can change the questions you want to address in the intramural program. And he said, “When you’re on the outside, it’s much harder to do that because you’ve got to have grants, and you get sort of pipelined into these things.” I’ll never forget him telling me that. And he said, “You know, this is a great place if you really want to do science and you’re going to pursue where it is. It’s not to do just the same thing.” And you know, those words really resonated and were very important in my decision to come. Because there I was at Harvard. I had a K08 grant, and things were looking good. They wanted to promote me to assistant professor. And I thought, oh, this is great. And a lot of my friends there sort of said, “You’re crazy.” And I said, “No, I’m going to a good place.” You know, it was 31 years ago. I haven’t left. And things have transpired have been very satisfying and very productive. And you know, I don’t look back with a second of regret.

So when I came down, I was in the Pediatric Oncology Branch. And I was doing a fair amount of clinical research while I had a small laboratory. And it was really in 1996-’97, when the genome really started to have legs, that I started to shift, so that by 1999 and 2000, I was really thinking about these larger, more thorough and more satisfying studies that would require large populations. So I made that shift. And some of my colleagues thought I was crazy to do it. I had a site visit in 1998 where they said, “Keep doing the things you’re doing. That’s great. Why do you want to do this other stuff with the genome?” You know, there were people who were interested in what I was doing in a more molecular way. And I’ll never forget. I have kept the report close at hand and it just

makes me smile each time I read it. And I'm glad I didn't listen to them. I made the changes, and my career has been, I think, far more productive and satisfying and probably more important in the impact of things I've done by following and pursuing what were the pressing questions that were emerging out of new technologies and scientific opportunities.

HWT: So you've mentioned the name Phil Pizzo a couple of times. Do you have a story about him you want to share?

SC: Yeah. I mean, Phil is a truly remarkable person. He's a true clinical scientist and was here at NIH for a period of time as head of the Pediatric Oncology Branch. And he was the one that started Camp Fantastic. So when I came down in 1991, by 1993, I would go to camp with him for a couple of the seven days of camp. I couldn't possibly get permission from my wife to vanish for a week with four young kids. (*laughs*) But he ran the summer camp, and he had this incredible sense of humanity in him, in treating and understanding each and every child as a remarkable person. I'll never forget some of the things that he said, you know, and I've parroted, I've said the same thing that he said. He said, "You know, some of the most remarkable people I've met only live to be ten or twelve. But during that time, they had a remarkable effect and a terrific capacity to see truth and see the essence of a situation." And that's very true. And I had that same kind of experience of being around kids, whether it's in the wards or at camp that you just marvel. I mean, you feel privileged to be in their presence in the face of just horrific circumstances. You know, very, very poor prognosis cancers still going on and wanting to go swimming and

play games and do things with other kids. There is humanity there. I don't understand why they have to go through that. I mean, that's more of a religious and philosophical question that continues to disturb me. But it's really inspiring.

And so Phil was really one of the first people to not only characterize that, but to live that in a way that, a good mentor does things that you admire and that you want to imitate. And that's one of the things about Phil. His humanity was remarkable. He's brilliant. So he's here and I come down and after about four years, he goes up to Boston Children's to be head of the hospital, but he's now retired after serving for ten years as the dean of Stanford Medical School. And I stay in touch with him from time to time. I don't have to have conversations with him every six months. But whenever I see or have a conversation with him, it's filled with wonderful sort of exchange of ideas and thoughts. And his wisdom and his insights are really quite something. So in that regard, he was a different kind of mentor. I didn't have as many deep-seated, what I would call intellectual, conversations about science in the same way with Sam Lux or Stephen Sallan or Stuart Orkin or Ken McIntosh at Harvard. I mean, they were people that, they looked at the data and this is what's next, this is how you interpret, this is good, this is bad, this is what needs to be redone. So in that regard, there are different kinds of mentors that sort of contribute to what one would call the complete person. And you know, I feel very, very fortunate to have worked with Phil.

And when he left, he very kindly said, "How would you like to take on Camp Fantastic?" And I've done that since 1995. Now I have a terrific young guy who's a pediatric

oncologist, Jack [Shern], who is taking it on. Because all good things need succession. Jack is now starting to run the camp and it will be marvelous under his leadership. I'm getting a bit old to chase the kids as much as I used to, so.

HWT: So, a couple of follow-up questions. One, I'm wondering if you can describe the NCI when you first arrived 30 years ago, you know, and talk about how it's evolved.

SC: Well, when I arrived in 1991, it was in a very interesting place where much of the element of the Yellow Berets and the whole idea of the intramural program of the NIH was undergoing real transformation. You know, during the 1960s and 1970s during the Vietnam War, the best and brightest came here in lieu of being sent to Vietnam and did research. And there's so many chairmen of departments and Nobel laureates like Harold Varmus and the like. There was this sort of intellectual excitement. And I came down from Harvard in 1991 and I would say even to this day, probably the most exciting intellectual environment to be in is Harvard. It's just the sheer number of talented people up there. It's a crazy place. I wouldn't want to be a young investigator, because then you get your ulcers. I'll tell you a story about that in just a minute.

But it really taught me, you know, it gave me a sense of what science can be, and the excitement of science. And here in 1991, there was sort of this transition. The Yellow Beret program was basically over. You had many of these marvelous, brilliant people staying on. But the next generation coming in was starting to shift. And so the question was really what was going to be the future of the NCI? And it was also quite heavily

engaged in HIV work. Appropriately so, with people like Bob Gallo and the like who were doing it. So there was a sense of some transition going on. And I think the leadership of Harold Varmus of NIH in trying to really codify what is an intramural investigator, the Bishop-Calabresi report, really changed the place and gave definition and boundaries to what the intramural program could or couldn't do. And watching that, and one of the advantages I had, unlike I think many of the people from my same generation who were coming, I had experienced NIH before. I'd grown up on the campus and I'd seen people like Jim Wyngaarden and Don Frederickson, former directors of NIH as friends of my parents or the father of a schoolmate. Don Frederickson's son was my classmate for several years in grade school. I'd play on weekends there. So I saw them as people, but I also heard their comments. And so I could make personal connections, or at least understanding how and why some things were changing. And so in that regard, one could see that the NCI particularly was changing. And I think between Harold Varmus and the appointment of Rick Klausner in 1995 or 1996, really put it back on an academic trajectory of really academic excellence and codifying in a much more rigorous manner. That's not to say there wasn't great science going on. But when I first came, it wasn't clear. And you could hear that from the senior people. And of course, I had the advantage of going to dinner every Saturday night at my parents' house, and my dad's friends with all these other people from other institutes, just hearing the background gossip and commentary was very helpful to better understand the evolution of the NCI. And through a couple of its directors it has really been able to repurpose itself. And more importantly, get back on track. And we saw that in the19'90s with Rick Klausner. And then certainly when Harold Varmus came and was the director in 2010. And I think Ned Sharpless, who

just left, you know, the last twelve years have been a great run at the NCI in my mind. There were some issues in the aughties [2000-2009]. I think Andrew von Eschenbach, as very kind a person as he was, I'm not sure his vision was for this kind of scientific excellence at a research level that needed to take place. He had more practical implementation goals. While his ideas were noble, this is a research institute, okay? That's first and foremost.

HWT: You mentioned definitions and boundaries of what the intramural research area could and could not do. Can you give me any specifics?

SC: Sure. Well, until, when I came for the first four years, I was like senior staff fellow, or medical staff. It was a position that didn't really have a definition in terms of a progression, a structure of what was next and how would you get tenure. That wasn't really well-defined. So the Bishop-Calabresi report, which was relevant to particularly the NCI—there was another report, I'm blanking on it, for NIH—defined what does it mean to be an intramural investigator? What are the different levels, and how do you go from one level to the next? And how are you resourced, and how are you reviewed? So there was a kind of rigor that provided an expectation. So someone that was here would know the ground rules. And it was getting away from, oh, it was more the old boys club. Oh, we like you and you stay, or no, we don't like you, you should go somewhere else. You earned your spot. You earned your capability of staying and having the trust of the public to continue to do terrific science.

And that changed in the19‘90s. And I think much of that really, I think many people are part of that, but I would give a good proportion of that responsibility to Harold Varmus and his envisioning how and what way science can be done at NIH.

HWT: What was the response of the staff?

SC: I think for the most part it was, thank God, now we have clarity. We know what the next steps are. We know what it takes to get tenure. We know what a board of scientific counselors does. You know, academics have to prove themselves and they have to have both constructive criticism, but they also have to be evaluated to be sure they’re doing the right things. Not that there is a science that has to be done. Like the NIH in the late 1980s had a challenge with Bernadine Healy, who came in well meaning, but she wanted there to be certain pillars. We were going to focus on certain things. Basic science, and I mean, the research entity, you can’t do that necessarily. You can do that in a commercial, pharmaceutical house. And they clean shop every two or three years. They change directions. But not in the academic. There are things that people did 15, 20 years ago that are now coming to fruition in the clinic. And you have to be very open-minded and recognize that you don't know exactly where the next really important thing is going to come. You know, we learned about the BRCA mutations in breast cancer in 1991 and then19’94. It wasn’t until five years ago that we had drugs for those particular types of breast cancer. You know, 25 years of real research it took. And it’s not like someone said, “Oh, I’m going to solve this problem tomorrow.”

So in order to be the best possible institution, there has to be an academic set of expectations and criteria for evaluation. And for the most part, I think that works very well here, but there are times when it is clear that we suffer a little bit from the mindset of Lake Woebegone where everybody's a bit above average, and for the most part, that's okay. (laughs) But at the same time, you want institutionally to be consistent and top notch. Afterall, I mean this is the taxpayers' money. You want to be solving the problems that are going to be of interest to the taxpayers, whether it is one rare disease or a major public health menace, like COVID-19.

HWT: As you were giving me an example regarding, say, breast cancer research, I couldn't help but think of the vaccine for COVID, and the miracle of the last couple of years based on several decades of intense research.

SC: Yeah. No question of what Barney Graham did. And part of Barney Graham's career was trying to figure out a conundrum that had challenged my father with RSV. So my father was a mentor to Barney. (laughs) So it's interesting to see how that plays out.

Just as an aside, my father was the first person to describe coronavirus in 1966 in the United States, with Ken McIntosh. And the original paper describes eight individuals from whom they got three isolates. Well in those days—I don't want to get in too much trouble—my mother, my brother, myself, Ken's wife, Al[bert] Kapikians's wife, and two or three other family members were the people who had the swabs. So for one of the original coronaviruses, there's a 37.5 percent chance it came from a member of the

Chanock family. (laughs) That was the coronavirus in 1966. The Australians had described it in 1965. So, you know, science was very different in those days.

HWT: Amazing. What a story. (laughs) So, I'm wondering if you could, thinking back, in particular to the 1990s, before we move on past 2000 and talk about all of the work since that time, can you take me through an average day, if there was such a thing?

SC: Oh. (laughs) It's hard to say that there was an average day. Because I was trying to balance a laboratory program where I had a technician and several postdocs. And I was in the clinics doing both infectious disease and oncology. And it's not like, you know, a young child with a bone tumor is having a problem and you can say, "Oh, I'll see you tomorrow," or, "Wait till next week." You get called and you've got to handle it. So there was a sense that, I don't think, you know, the best of intentions, I used to keep file cards in my pocket and would write down the things that I'm going to do in a quasi-schedule. Maybe 10 percent of the time was I anywhere near able to get all the things done in the schedule that I thought I was going to do. It was the nature of the beast. You were on the hot seat. And it was the fun of it, but it was also just crazy. You work very hard and for me it was also a very strong personal sense of commitment. You know, I was coming back to working on the ward that my brother was on. And I would go to visit the ICU where my brother died. And I felt that, you know, it was my imperative to do the best that I could so that somebody else didn't have to experience what I had experienced as a sibling. Or as a parent. Or, most importantly, as a patient. So you did what you had to do. And if it meant going the extra mile, I mean, at that point we lived very close to the

campus. With four kids, my wife and I would have dinner and put them all to bed. And at ten o'clock, I'd go back to the lab, from ten to one. Because that's when I was able to have quiet time to think. Because otherwise it was just, you were on the hot seat. It's like being a coach on the sideline of the football game. You can't sort of say, "Oh, well, we have five minutes to think about what we do next." The game is going on. It's bang, bang, bang.

HWT: That's a good analogy. Can you describe your lab during that time?

SC: Sure. I had a lab on the thirteenth floor with a couple of postdoctoral fellows and a technician. It was a classic NIH single investigator, where we were asking very particular questions related to how, in what way, parts of the body would fight infection. What are called neutrophils or white blood cells. And trying to use molecular biology to understand them. And it was very exciting. It was productive. And from an academic point of view, just continued on that. I mean, I could have gone elsewhere as I had offers and grants to be an associate or full professor, at one or another universities.

And so the laboratory environment was a place to sort of see mechanism. And I liked that. But I wasn't cut out to do only that. I had to see the patients. You had to go back and forth. And NIH enables you to do that. And my laboratory was 50 feet from the clinic. So I can run back and forth. But I was running back and forth.

HWT: Incredible. So is there anything you want to add about the 1980s? Your schooling? Your time in Boston at Children's Hospital? Or in the 1990s.

SC: Well, I'll tell you one other story that's of interest to Camp Fantastic. So in like 1988, I got a call like the night before I had to do this. So Steve Sallan, who was head of pediatric oncology had been invited by Paul Newman and his Hole in the Wall Gang Camp leadership to come down to his house in western Connecticut to plan a camp for kids with cancer. And Steve at the last minute couldn't so he called me and said, "Chanock, you want to get up at six tomorrow and do this." And I said, sure.

So I drove down and spent one of the most memorable days of my life in the living room of Paul Newman with four or five other pediatric oncologists from Sloan Kettering and from Brown and from Yale. And we planned and explained what needed to be in place to take care of these kids. Because no one had set up a camp like that. And it was really very interesting. Because he had several of his friends who were really interested. And Paul Newman every half hour would offer us, "You want a beer? You want a beer?" We were doctors trying to do serious work and not going to drink a beer at 2 or 3 in the afternoon, particularly if we were to say something intelligent,. So we spent literally ten hours planning the thing. And had this big chalkboard, writing all over it. Very animated. And he says, "All right. We're going to go do dinner."

So we go to his favorite Italian restaurant in town, and we eat dinner and he's telling stories. Couldn't be more charming. Then all of a sudden, the whole building starts to

shake. And there's a helicopter coming that comes to pick him up because he has a NASCAR race the next morning, God knows where. So he leaves us all. And he says, "We'll be in touch."

So he leaves. And then, oh, about three weeks later, his lemonade and cookies and all this stuff just starts pouring into our house. Like once a month you get these, a big package. And this is before any Amazon. So this is like really exciting to my wife and kids. (laughs) And I stayed in contact with the people in his group.

So when I came here, Phil Pizzo was like, "Oh, I know you already have that experience. You know what you're talking about." And that's why he wanted me to engage in the camp here as soon as I arrived in 1991.

HWT: That's a fun story. What a character!

SC: Yeah.

HWT: I also wanted to ask you, however, you mentioned Harvard is just this incredibly stimulating place but you wouldn't want to be a young investigator because of the ulcers. Do you want to elaborate there?

SC: Yes. It's a very stressful place because it's a Darwinian aspect to it. So I'll tell you a story. So I was there until 1991. And I go to a meeting, I think like in 1993 or something,

the American Society of Hematology. And three of my colleagues, who have all done incredibly well. Two of them are members of the National Academy of Sciences now, but this is back in 1993. So it's in Nashville. So we go to the airport. And there are four of us. And they're waiting for their flight to Boston, and I'm coming back to Washington. So we go get something to eat at a barbecue place. You know, that's when you're in Nashville or Memphis. And I'll never forget, each of the three of them, one says, "Oh, I've got to take my medication because of my ulcer." The next one says, "Well, I just got scoped and I'm starting my medicine next week." And the third one said, "Well, I have my endoscopy in six weeks." And I just sort of said to myself, yes, I don't have an ulcer. (laughs) I made the right decision to get out of there.

HWT: Yeah. That's a bit of a sacrifice.

SC: I'm not going to name names. But they all know exactly who they are. We've told the story over and over. (laughs)

HWT: That's a bit revealing. So let's talk about, you know, sort of the last 20 years. I want to begin by asking you to talk about your work as a tenured investigator in the Genomic Variations Section of the Pediatric Oncology Branch at NCI. However, there's a lot to talk about over the last, I mean, sorry, yes, the last 20 years. So I'm going to start there. But I also want you to be able to—and I'm perfectly happy to, I'll be asking you about every role, in other words. But if there's something that you consider the most important place to begin over the last 20 years, feel free.

SC: I was in the Pediatric Oncology Branch until 2007. But by 2001 and 2002, I was clearly headed towards asking the bigger questions in epidemiologically, rigorously defined studies. And that was the realm not of the Pediatric Oncology Branch but here in the Division of Cancer Epidemiology and Genetics with Joe Fraumeni and Bob Hoover and Peggy Tucker and Nat Rothman and others. And so I had my appointment, but I ran a big facility for them here starting in 2001. So I was really split. And my own individual research shifted towards these kinds of things central to DCEG.

So it was a natural progression that by 2007, when I went to Joe Fraumeni and said, "Well, how would you like to have a program to follow up on these things? The Laboratory of Translational Genomics." And he said, "Great." And so I formally moved over in 2007-2008. But I would say the six years from 2001 to 2007, I was scientifically transitioning. I was spending as much if not more time talking to people in DCEG than I was to the Pediatric Oncology Branch and CCR. Then my branch chief, Lee Helman, a wonderful guy, saw that and was very supportive. And again, Lee is a little bit older than I am, and had been in the intramural program. And understood how things had been redefined in the 1990s and wanted to see me succeed, and was incredibly supportive and very generous. And again, what's a pediatric oncologist doing thinking about breast cancer and prostate cancer? Well, that's because where the studies were big enough and mature enough that we could make the first methodologic studies, and more importantly, the first real observations. So that's one I attacked over time.

I would say in the Pediatric Oncology Branch, it was a very vibrant place. And I kept saying, "Well, we have to think about these things in pediatrics. But the numbers are much smaller." So it was clear that I wasn't going to be able to address the questions only in pediatric oncology. And my final point, I think, is not only did Lee and others recognize that, but I think Joe Fraumeni, a very softspoken, brilliant person, was like, okay. He's going to come here in the fullness of time. Later in talking with Joe, he said, "I knew you were going to come over. It was just a matter of when." (laughs)

HWT: He was a visionary, you said.

SC: Very. Very, yes.

HWT: So what were your initial goals before we move on from the Cancer Genomics Research Laboratory. What were your initial goals and how did they evolve? I mean, you're describing that. But getting a little bit deeper into that. also, what did you accomplish when you were there?

SC: Well, in the Pediatric Oncology Branch, I was doing a lot of molecular studies of people that had inherited defects in a gene that would lead them to get infection. And if we understood something about that, could we figure out how to protect people or have better therapies during chemotherapy or radiation therapy and cancer. So I did a study where we got together like 150 individuals with this rare disease, chronic granulomatous disease, that others at NIH had been studying for years as well. And tried to ask the

question, can we look at genetic variation to predict who's going to get what outcome? So I published a paper back in 1998. And it was in a rare disease. And I knew that I couldn't get large numbers.

And that's when the conversations started with Joe Fraumeni and Sholom Wacholder and Nat Rothman and others. Like, "Well, we can get you 10,000 prostate cancers." And the numbers are very different. So I said, well, if we're going to understand common variation, which all of us have, we need numbers. It is the differences that makes you different, why you look different and have different characteristics, such as disease proclivities and outcomes. How and what way do we characterize that variation? And then how do we apply it in well-designed studies?

By 2000-2001, I could see that we needed to do very large studies. And Joe would say, "Well, what's large enough for you?" I said, "Whatever you say to me, Joe, I want twice that." He would laugh and say, "Well, I can get you certain things. And then we just have to build those resources." And now we've gone from studies with 200, 500, 1,000, that right now we're doing a big breast cancer study with 350,000 cases, and 350,000 controls led by Montse Garcia-Closas, a longstanding colleague and superb deputy director of DCEG. And the statistics and the capacity to have stable observations and get a more comprehensive landscape analysis is transformative. So we could see that back at that time, but it was going to take years to evolve that. And to me the question was where could that evolve? You know, I could have remained at the Pediatric Oncology Branch, but there was nothing I could do to change recruitment and access to adequate sample

sizes for what the size required. And that's why the steady transition to work with people in DCEG was very clear as the way forward.

HWT: Okay. And then you were also co-chair of NCI's Genetics, Genomics and again, it's a difficult word for me—

SC: Proteomics, yeah.

HWT: Thank you. Proteomics faculty. Can you talk about that? And that was for five years, correct?

SC: Yeah. That was part of an approach when everyone was keen on a second phase of formalizing what the intramural program would look like. Making it more academic. So the idea was what's in a faculty? A faculty is usually a group of people who have common interests who come together, share their ideas and are sounding boards. In the early 2000s, that's one of the things that evolved at the NCI, having these faculties but they petered out over time. But that's okay, because I think they were the, sort of the seed, the fertilization for collaboration and team science. And when I started to work with DCEG, it was quite transformative. Because Joe Fraumeni had a very different way of thinking about things. And DCEG is a community really of team science, where you have people with different expertise that all come together. It's not like in a laboratory where somebody could work on cell lines or sequence something or manipulate something. This isa very important distinction. I'm not in any way downplaying that. But to address the

role of genetic variation and how we could study that or not study it really depended on epidemiologists, statisticians and geneticists and coming together. And the culture of DCEG was very different. And it's a culture that I actually have really come to embrace and enjoy very much, the team science ethos. So the collaborative network puts you in contact. I mean, I have 71 principal investigators here, and I published with just about every single one of them at some point in the last eight years. And having contact, we all work together. And we don't have individual things that people go off into corners. We fund and make programmatic decisions as to what scientifically is best right now. Where can we go? What can we do? So to me, that's really a very exciting part of the environment. And Joe Fraumeni had really fostered that approach. And Sheila Zahm as deputy director has been instrumental in effecting this along with Bob Hoover and Peggy Tucker. The list of others can go on and on. But this notion that building the resources and knowing that the time will come to be able to use them was quite visionary. You don't see that in many places. And again, the intramural program can do that, knowing that there's going to be a day to be able to use these things. And you can't get grants to do that easily on the outside. My moving over here was like a kid a candy shop. I was like in a Godiva chocolate shop. I love chocolates so it was like, wow, keep going until I get a bellyache. (laughs)

HWT: It sounds like it was a very natural progression, for sure.

SC: Yes. You know, again, it really, it was where the science was going and where the opportunities were. And still are.

HWT: And so, you were also then made, so you were director of the Laboratory of Genetic Susceptibility, LGS.

SC: Yes.

HWT: So can you talk about when and why that was set up, and your work as director?

SC: Well, that was set up in 2013 when I became director because I had set up the Laboratory of Translational Genomics in 2008. And there's a practical thing that's very important. I can't give myself money. As the director, I oversee the budget of DCEG. And so the Laboratory of Genetic Susceptibility does things very similar to the Laboratory of Translational Genomics. Virtually no difference in the work that's done. But I needed to have a separate small entity that's well carved out, adequately but not liberally funded that someone else oversees and that I get reviewed. I had my review last week, it went very well. But to me, it's an important element to lead a group, particularly where team science interactions and collaborations are crucial, is that I need to have a reputation based on my scientific productivity and scientific capabilities reviewed like everybody else who I oversee the reviews for here. And so LGS was basically set up for that reason. The people in LGS talk with the LTG, the Laboratory of Translational Genomics people with great regularity and sharing things. So nothing special other than I think the practical, institutional funding issue there, okay?

HWT: Thank you for clarifying that. So I have a question for you that's probably a little broad and a little technical. But I'm looking for some examples. So I read that LGS scientists continue to identify to loci within the human genome that are associated with cancer risk. So I'm looking for examples.

SC: Yeah, I mean, so the LGS, is not your usual lab, so to speak. And there are no real usual labs in DCEG. I'm very involved in kidney cancer and one of the central people is a terrific senior investigator in one of the branches here named Mark Purdue. I work very closely with him, and we're in the process of analyzing new data to try to map what are the susceptibility regions of the genome for people getting kidney cancer, the seventh leading cause of cancer in the United States. And then I'm very interested in trying to understand how and why each of these regions contribute to kidney cancer as a way to understand kidney cancer and how it develops. So that's been a themes for the last 20 years is identifying and then characterizing how susceptibility regions actually work. From 2001 to 2007, it was very early in the characterization. We barely knew what variation looked like, what was its scope and how is its distribution by populations.

But by 2007 and 2008, we started to see the enormous number of variants in the history of the human genome and as the technology came into focus with what are called the SNP chips, it gave us the ability to perform genome-wide association studies, agnostically looking across the genome. And we've done a tremendous number of them, and we've identified probably 75 percent of the regions known to be associated with cancer risk, identified either directly or in collaboration with international partners from

DCEG. And I've been a big part of many of those, and I've actually led a number of them. In the first publications back in 2007, I was senior author on those. And so in that regard, if we break it into two parts, one is the discovery to figure this out with these large sort of complexes studies called genome-wide association studies. And then you figure out all right, you have a marker but there are a lot of other markers. How do you figure out which one is the real one? And then how does that work? Does it turn something on or off? Does it get in the way of something? Note that this is a much slower and more laborious science. And that's takes us back to holding more conversations about collaborations with people in CCR and other institutions where we collaborate with friends, you know, at Harvard or Penn or in Europe or in Cambridge. Sadly, many lab scientists have yet to see the value of pursuing these findings.

But I think the key thing is that we want to understand is what is the complex nature of cancer etiology. Every cancer that we know, there are very few cancers that you can say is due to one thing, okay? A small fraction of cancers are familial, but most breast cancer in the United States is due to many different factors, both genetic and non-genetic exposures/lifestyle. The lifestyle for women. You know, do they take hormone replacement therapy? What about their weight? Do they smoke? Do they drink? These are all important factors. And what we've learned over and over is you find something and then you address a particular question and then it leads to another question. So what's the interaction between what you see in genetics and in lifestyle, and how that's really, to me, the future is how you merge those two. What is it about one particular woman versus another woman who changing her lifestyle would make a big difference in reducing her

risk for breast cancer. Okay? Those are the kinds of questions that clearly need to be addressed with very large studies. And very good small ones as well, so that we can do this. And how is it different by different population histories? We know the different incidence and distributions of types of breast cancer in women of African ancestry versus Asian versus European. So as we go along, yes, we answer some questions, but we now raise new questions. And they become more and more comprehensive. And be more accurate and precise so that we can really bring this to the clinic. There will be a day when hopefully all women will be screened with their genetic proclivity, known as a polygenic risk score, to breast cancer, along with certain things that may allow them to say, I'm going to make certain decisions. I can eat a certain way, or I can live a certain way. Or, in other circumstances, I'm very high risk, so I need to do everything I can to get myself on the lower end of the curve of breast cancer risk, okay?

HWT: I have kind of a related question. It's an ethical question in terms of knowing, you know, with the advent of the Human Genome Project, and you know, I actually had an opportunity to interview Dr. Lee Hood for another project a couple of years ago.

SC: Sure.

HWT: Fantastic. You know, but there are these ethical questions about knowing, you know, and maybe that's an aside conversation. I'm just curious what your thinking is. You know, in terms of knowing your susceptibility. And then we have the insurance industry, or you know, who gets that information beyond the individual.

SC: Oh, absolutely. You know, modern genetics and genomics are coming front and center to all sorts of ethical issues. I had an experience years ago. I had to go downtown to Congress, this is like oh, in 2003 or 2004 or 2005, I can't remember exactly when, and talk in front of a group of congressmen and staffers. And the issue, so I used the example, I said, "Well." There were mainly males sitting there. One versus the other. "The person on your right has three times the risk of prostate cancer than you do on the left, a Democrat to Republican." And they kind of said, yeah. I said, "Well, that's what the data's telling us."

And a very conservative gentleman said, "Well, that's the most unamerican thing I've ever heard, Dr. Chanock." He said, "We fought a revolution to give everybody equal opportunity. You're telling me your genetics are important."

I said, "You bet. It's not political heredity. It's just the basis of genetics."

And he said, "Darn it! That's really fascinating." And you'd think that they would then say, well, maybe universal healthcare should be the way to get around this. But nope, that's not the conclusion that many have come to. I've always personally maintained that what we learn from the genome may someday drive us to that. But I like to quote Winston Churchill in his famous comment about Americans: They usually get it right, but after exhausting every other possibility. (laughs) And I'm afraid with healthcare, that is

our destiny. But maybe I'll get fired for having said that. But that's okay. "C'est la vie," [that's life] as the French would say.

But I think that again, the ethics of what you learn from people's genomes is a very challenging issue. And I've been involved in lots of ethical debates and discussions. Published on this and gone to meetings. And different populations with different histories have very different views towards this. This is highly understandable. For instance, I have had very strong collaboration with German collaborators and their perception of the sanctity of genetic information is particularly sensitive. And in this country, with individuals of Native American background, similarly very sensitive. We can't do certain studies because they're just too nervous about us having the federal government know their genetic information. And you have to appreciate the context of where and how that opinion has arisen. So I can tell you, I've had very interesting experience. I've been, for quite some time been interested in radiation in genomics. And we'll talk about Chernobyl. But for seven or eight years, we've proposed a study in Japan at the RERF, the Radiation Epidemiology Research Foundation, which is the big center that follows all the survivors of the atomic blasts in Nagasaki and Hiroshima. And the NCI and the program that I direct has close ties. People going back and forth. The exchange of academics and publishing a lot of papers, looking at the epidemiology. But I wanted to ask this question, what's the effect on the second generation? And they've collected 1500 families when they have these trios. And myself and the branch chief, Amy Barrington, have been there. We have these regular calls and we're now just starting to move towards doing a kind of study, partly because of the results that we found in Chernobyl that were

negative, so to speak. Children born to those people who cleaned up at Chernobyl don't have increased genetic mutations in their genome, in the Chernobyl de novo mutations.

But in Japan, it's very complicated and it's politically a very sensitive subject. And I've gone there and met with the leaders of Hibakusha, the group that are the survivors. And the sensitivities are very great. And it's taken literally years to get our investigators to the point of having the confidence to be able to raise this with the survivors. And one understands just—one can appreciate, I don't think I can ever understand, I can appreciate just the depth of mistrust if I were a survivor of, say, the Hiroshima blast, of authority, particularly Americans. You have to, in a very fundamental level, it really is, it's been fascinating, illuminating, and extraordinary part of my career to have now moved into some of these very delicate political situations where science and politics collide. And that said, a very important thing, that we have to have the science be right and do the science for an appropriate reason that could have real implications, whether or not someone wants this. So going back to the Japanese, the Japanese government was very worried about my coming. And one of the times I went, I had to meet with people in the embassy, the American Embassy, because they were very concerned that the Japanese didn't want us to do this study to find something. Because if they did, then that meant that 150,00 Japanese, the children of the survivors, would all be followed for the next 40 years, or 50 years. And that was billions and billions of dollars. And was that necessary? And so you can sort of see the political tectonic plates shifting. And above, these scientific opportunities of the advancement in sequencing technology and be able to address these questions and say yes, there is or is not a transgenerational effect of

moderate to low amount of radiation exposure. And we answered that question in Chernobyl and we hope in the next three or four years, we'll be able to do that in Japan. But just the sensitivities are just so heightened.

HWT: I can imagine. Go ahead. Sorry.

SC: I'm finished. Go ahead.

HWT: Sorry. I can imagine also among the Navajo in the Southwest, with all the nuclear testing. That's a huge, huge issue, and cancer rates have become really high.

SC: They're not as high as you think. We have done those studies as well. We're part of that. I mean, one of the things of the division in the last, since becoming division director, I've learned a tremendous amount. We have fabulous people here, but we do science that's often unpopular. The people's science and figuring out why a chemical may or may not cause cancer in industry, in vested interests, and politicians don't like that. So we get lots of letters. I have gone down to meet with congressmen, testify, and things like that because they don't like our results. You know, the science is the science. I always try and work in the comment, "Well, I don't like cancer. But I can't tell you, I can't ignore that one in three Americans are going to get cancer. And if you are unfortunate enough to have a particular type of cancer, that's what you have, I can't pretend that it doesn't exist. Or that there's no risk. Because there it is. And there are agents that are responsible or contribute to people having many of these cancers. And so we have to understand those."

But that's not always a popular idea, particularly when it touches on certain industries. They get very upset about this. You know, get all sorts of emails and letters written attacking us.

HWT: It goes back to what you were saying about the public good. I have a question for you. So we're about ten o'clock for me, one o'clock for you. Do you have a hard break at 15 after? I do have some more questions.

SC: I do. I do have a hard break.

HWT: Okay. So I'm going to lay out what I have so you know. I have just three broad categories. One, I still want to talk to you about your roles as director. In particular, acting director and of course afterwards. I want to ask you about the impact of your work, how you feel about that in total. I want to ask you a few COVID-related questions just in terms of the reaction as a director there. And then just a few questions tied into mentorship and things of that nature. So, let's start with, so let's try to keep it on track because all of those questions are important. Let's start with your role as director. Think about both successes and highlights or your team, or setbacks that you've experienced and what you've learned. Anything of that nature.

SC: I feel very fortunate to be the director. It's the best job in the world. I've been offered and recruited to other things and no, I made it clear that I am not interested. Because this is director of a program where there's a tremendous range of science going on. There are

just marvelous and incredibly talented people here. But we also have the capacity to collaborate with hundreds of people outside. And so the team science is just not here, it's in these big consortia for breast cancer from around the world, or from pediatric cancer or what have you. So I'm very excited and love my job. And I have to say that I feel very fortunate to have been appointed to a position that Joe Fraumeni had set up. And the way I would describe it is, it's like being appointed the director of the Metropolitan Museum of Art. I didn't have to go build a whole new wing and raise a lot of money. I get to polish the marble. I get to work with a very solid foundation.

And the people who are here, from the junior to the senior people are just outstanding. I learn from them continually. And they educate me, because I'm not formally trained in epidemiology, but I've learned an awful lot. So much so that I can jokingly say like that Holiday Inn Express commercial. You know, I've slept in it so now, I'm here long enough that I have pretty good intuition about epidemiology. But I also think that it's the kind of environment where you want to continue to learn and exchange ideas. And in that regard, it's an awful lot of fun. I have a great time coming to work. I get to see all sorts of science. I wouldn't give it up for the world. It's one of the best scientific positions that I can vision anywhere. You know, there's a certain amount of administration, but it's to make the science happen. So I like that.

And with that comes mentorship. I mean, in the last eight and a half years, I've had that opportunity to hire a whole group of people and know that at some point I'll step down. I won't do this forever. You know, a lot of energy and a lot of excitement and it takes a lot

out of you. Ten years from now, I can't imagine being in this position. Or five years? Who knows? I'll have to make the decision as we go along. But I'm so confident with the next generation of people we've been able to recruit, build and mentor through our ranks, as well as hire from the outside. This place is in great shape and will continue to do great work for the next 20 to 30 years. When we tenure someone, they often stay here for 20 to 25 years. So it's a big decision. Because they can't get funded and supported on the outside in the same way they can here. Lots of our disciplines, like in radiation, epidemiology or occupations are just not funded by grants. Because some of the studies are 30 and 40 years old and have to be that way. It's just a marvelous place. So I'm really enthusiastic about the next generations and seeing how they've moved into scientific leadership and shown how their excellence and their capabilities are realized on a daily basis. So it's a very dynamic and I find it very enthusiastic and inspiring place to be.

HWT: I was going to ask you about mentorship. I'll just ask you one quick follow-up question, which is what—I hear about mentorship a lot in interviewing people at the NIH and other scientists elsewhere. It's fascinating to me that mentorship seems to be a part, so much, it's integral to the scientific community. Would you agree with that?

SC: Absolutely. And mentorship is done in many different ways, in different manifolds. We're not a set of individual laboratories where you train someone into sort of the—here it's more like you're in a medieval guild and you come and you learn to do shoemaking or you do glove making or whatever. I'm thinking of sort of Elizabethan times. And then you get to be good enough and you go off, or you stay as the master builders and

continue to do it. You learn by doing research on the spot. So we'll have 130 trainees at any one time, and we have so many terrific trainees. We can't keep them all. But the reassuring thing is you look out on the maps, and you see these people doing well in other places. And we can claim partial credit for their success because they trained here with us. And there's a lot of satisfaction with that.

HWT: Can you talk about the total impact of your work? I know that's broad.

SC: The total impact. That's an interesting question. I go to sleep at night most nights thinking that I've done the right thing. Sometimes I wake up in the morning thinking gee, I need to do this, or this needs to change, or what about such and such? But I think the impact of my work is not only in characterizing and trying to understand the relationship of the genetic variation to cancers and other diseases and their outcomes. But along the way, we've found some very unusual things. This whole world of genomes going awry and falling apart with age, we were the first to describe that in 2010 and 2012, what's called genetic mosaicism. And now clonal hematopoiesis, which is one of the big, exciting things. It's all derived from work that we had distilled from our big studies in 2008, 2009 and 2010. So I feel a tremendous satisfaction in seeing these things. And it's not—I go back to my father. My father was the kind of person who was more interested in what the science was and what comes next than whether somebody gets the credit. You know, I'm less interested in saying, oh, Chanock published that in 2010, everybody should be saying that's the greatest thing. No! It's incredibly satisfying to see that people are doing many things derived from or based on that. That's the way science works, you

build on the shoulders of others. Some are giants and some are not, and there are a few Lilliputians out there who focus too much on self-aggrandizement. You have to live with that.

But I know, I mean, I was raised and I was educated by the Quakers here at a Quaker school for fourteen years. And George Fox, the great Quaker, said you judge a person by the imprint that they leave on the earth when they go. And I feel quite confident I've left a very good imprint. How big? Well, that's an ego question and not one that I want to spend a whole lot of time thinking about. I just know I've left an imprint and I think it's a good one. And I have things to imprint tomorrow. (laughs) So I go on.

HWT: Wonderful. So a few COVID-related questions. So first of all, I want to ask you what your response to COVID, to the pandemic two years ago, was in the early parts. The first month of shutdown, just before that time, and also how—

SC: It was terrifying. It was terrifying. And I have to say I grew up in a house where my father for years had worried about this. And a lot of his colleagues who had written books that now everybody is holding up, from Robert Webster's 1995 book *Flu Hunters* and things like that. People could see that this was coming down the road. And I'm inherently conservative about my own health. So my wife and I and my four kids, now five grandchildren, we've all tried to be as careful as we can. During the time, I actually had a personal newsletter with about 250 friends and family where I would write about what I would see and do. But I had to do that at a personal level because the NIH and HHS and

the government were in real tumult over the political approach of the Trump administration and downplaying and doing, saying all sorts of crazy things.

But it's been very disruptive. And I think it really has scarred a lot of people but the staff in our program are resilient. We were on mandatory telework for two years. And it's remarkable what we've been able to accomplish during that time. But it comes at a price. And I think we're going to learn more what that price is over time. Just the sort of mental health aspects and how it changes the ways we interact with each other. I mean, we learned how to do Zoom, like you and I are doing. There are a few good things. But it's been a challenge. You know, I don't want to go through it again. And you know, you respond, and you do things. Back in March and April of 2020, I got very involved because I have a son who's a very successful major league baseball agent. He lives in Beverly Hills. He represents 40 top major league baseball players. He knew my father, his grandfather, very well. So with him we wrote the plan that the major league baseball used in 2020 to go back to work, for them to go. And so on the side, I still consult with them. And I'm going up in a couple of weeks to New York to give a lecture. But I'll go to major league baseball the day before and spend an hour or two with Dan Halem and Rob Manfred. Because they're interested in what we know and what we're thinking about the future. And how do they run major league baseball, what do they do in baseball parks, etc. So you know, when given lemons, you make lemonade. You know, you make the best of it. And felt that it was really important to get some things out on the field so Americans could feel proud again and have something to look forward to. We were all getting sick of Netflix and Amazon Prime.

HWT: How true. I just have two more questions. And I'll ask one, we'll see if we get to the next one. COVID has of course had a disproportionate impact on marginalized communities here and you could say worldwide in terms of vaccine distribution. Can you take a moment to talk about health equity and also plans at the DCEG?

SC: Well, I think, thank you. We'll go a couple minutes over. This is a key issue. I think that in the midst of COVID was the public horrific event of George Floyd's murder and several other activities in the Black Lives Matter movement which really crystalized over a matter of months the length of the issues of the disparities and health equity in this country that have not been solved. And we've had very, very serious and extensive discussions across our workforce, and remain clearly committed to diversifying our workforce and taking our questions to many different corners of different populations in the U.S. and around the world. And I think that's been eye-opening. And for epidemiologists and geneticists, it's central. Once the conversation started, it's obvious, that's what we need to do. We need to look at what's common, what's different, how to use it, what to do with it. What can we take that we've learned to apply and be for the public good? And the public good is just not the general, but for certain groups. For certain people who have certain kinds of backgrounds. We know genetics are important to a point. And then the question is access. How do we understand breast cancer incidence in the United States, where there are major observed differences between African American women and women of European ancestry. Some of that is access to care, what time they come. You know, I can remember some of this goes back quite some

time. In pediatrics, for instance, kids with leukemia, higher risk of leukemia, kids of Hispanic and Puerto Rican background, because they would come to the doctor at a much later stage, so their leukemia was more advanced. And that was identified 30, 35 years ago. And now we know the genetics of that, of what contributes to that. But it's not one or the other. So I think the context of how we do science, coming back to these ethical and political issues, becomes all the more compelling. And it's much more a part of our mindset. And I envision the mission of our program going forward, we've gone through this strategic planning exercise, is to really, to pivot a certain amount of our activity towards disparities and equity. Because we have the expertise to be able to put together these more complex matrices, to understand how the socioeconomic together with the genetic and the environmental all work together. And that's a big part of our future.

HWT: I'm just going to throw this out there. It's probably too late. But I wanted to ask you about the future of personalized mRNA cancer vaccines. Because that's been in the news.

SC: It's an intriguing idea. It could work but has a long way to go before testing. The coronavirus is very different. You needed antibodies to a particular protein. So you got the mRNA in, the host system then creates enough of that antigen and you make the antibodies and then you're protected. Cancer's a bit more complicated. I think a lot of the things with CAR T-cells and immunotherapy are very exciting. And I still think we're early in that. And I think as we go deeper in our understanding the kinds of basic research that goes on as well as population science and epidemiology, and genetic is going to be crucial to do that. I have a hard time imagining how a single mRNA is going to solve a

particular cancer. Unless we know enough about what's that event that we're trying to prevent or we're trying to overcome. It's not a generic—breast cancer doesn't occur because of one thing. It occurs because of a number of different things. And in each person, there are different sets of those things that appear to be operative. So you're going to have to have multiple mRNAs. I mean, it's an interesting question. It's worth looking at. But I'm not counting on it changing anything in the next five years.

HWT: Okay. Well, thank you for going over. I really appreciate your time. It's been fascinating. And a pleasure. And we'll be in contact.

[End Interview.]