NIDDK

Oral History Project

Interview with Dr. Griffin P. Rodgers

Conducted on August 15, 2019 by Kenneth Durr

KD: This is an interview with Dr. Griffin P. Rodgers for the NIDDK [National Institute of Diabetes and Digestive and Kidney Diseases] Oral History Project. Today is August 15, 2019 and I'm Kenneth Durr. Dr. Rodgers, thank you very much for taking some time to talk today.

GR: Thanks for coming in and visiting with us.

KD: I want to go clear back and start from the beginning. You grew up in New Orleans. I understand that had something to do with your interest in science.

GR: It did. I was born in New Orleans and raised in New Orleans in the '60s and early '70s before I left to go off to college. It is said that one can live in any city, but New Orleans is the only city that lives in you and that has a lot to do with the influence on me in terms of going into math and science, STEM disciplines as we understand it. My father was a high school science teacher, my mother was a public health nurse, and they at an early age instilled in me a love of science. Medicine and serving others were important principles. Through, it was called then an elementary school, I guess it's called middle school now, and then subsequently in high school, that love of math and science persisted. So I was pretty much sold on a career in medicine at a very early age.

KD: Medicine more than research? You wanted to be a doctor?

GR: Medicine more than research. There was great interest in the field of medicine and learning what I could, and I thought that would be a practical application related to my love of both math and science. But something happened during high school which

tweaked that a bit and I actually got more interested in a subspecialty in medicine, and more importantly doing research in medicine, and that was three good friends in high school who—this was now in the late ‘60s, early ‘70s—had sickle cell anemia. Back at that time there was very little that you could do for individuals who suffered with that condition. When I say suffering, I really mean suffering. They would have these periodic bouts of just excruciating pain, oftentimes requiring emergency room visits and hospitalizations and intravenous fluids, and pain medications to get that under control. Oftentimes their anemia would be more profound, requiring a blood transfusion, and of course they had infections and had to be treated with antibiotics at the time. Essentially, that’s all we had in terms of treatment at the time. One of my friends passed away when I was still in high school, I believe in 11th grade, and the other two passed away while I was in college.

Somewhere during that time while I was still focused on a career in medicine, in fact I had actually gotten accepted into medical school straight out of high school in several combined programs, I decided to consider what is necessary to subspecialize in blood diseases and focus on research, particularly in this area, to see whether there was something I could break beyond.

KD: What are the odds that you’d have three friends that had sickle cell disease?

GR: Sickle cell disease is a genetic disease. It is oftentimes common among African Americans or people of African ancestry. The prevalence seems to be higher in the South because of the slave trade and the expansion of the population in that region. Growing up in the late ‘60s and early ‘70s, in the still segregated South it was more likely that people would come in contact with my race and ethnic group. On the surface you would say it’s probably not that common, but actually the odds were stacked in favor of having friends and acquaintances that have that disease.

KD: You went to Brown with the intention of becoming a doctor, pre-med.

GR: Yes. This program allowed people to be accepted, it was called an accelerated medicine program. It allowed us the opportunity to get accepted not only as an undergraduate, but at the time it was a six-year program allowing one to get a Masters of Medical Science, and then they had a reciprocal relationship with several of the other Ivy League schools. You could do the last two years at Princeton. Others were Harvard, Yale and University of Pennsylvania where you formally received your M.D. Fortunately after the first year I was there they had an attractive sufficient number of clinical faculty at Brown, so they could offer a full experience, and you could actually get your M.D. from Brown. The program moved from a six-year program receiving a Bachelors and a Masters to a seven-year program receiving a Bachelors and an M.D., but I opted to also get a Master's Degree, so I was able to get three degrees.

KD: You were thinking of becoming a scientist at this point?

GR: Yes. In fact, my focus of my Masters, I worked with a fairly preeminent hematologist who had done outstanding work in the late '60s and early '70s in New York, Dr. Herbert Lichtman. He worked in the area of sickle cell disease, and I was already trying to execute this plan. Unfortunately, there are not a lot of people in sickle cell disease in Rhode Island, which is the opposite of what I told you what my experience was in New Orleans. However, there was no deficit of people who were of older age in Rhode Island, so my thesis was to work on red blood cell function among octogenarians. That got me acquainted with the research method, working with red blood cells, and the like. And I learned quite a bit from Dr. Lichtman in terms of the process, the rigor and the importance of reproducibility and the conduct of science during my graduate training.

KD: You worked with a gentleman named Dr. Galletti as well.

KR: Pierre Galletti was my science advisor. Dr. Galletti was from Switzerland and he was a major figure in the medical device instrumentation industry. He developed an artificial kidney, an artificial lung, and he actually merged them together. In my first year as an undergraduate I worked in his lab on a system called an artificial Klung. This was done in

an animal lab and it simulated the effects of the lung and the kidney, so it filtered and it also oxygenated the blood. My role on his research team was to collect blood samples before they went into this device and then after they came out to see the effect of his novel device. It was very large. I couldn't see how it could be used, but now with miniaturization it certainly is possible. It leads me to something that hopefully we'll conclude on and that is developing artificial organs to treat patients that have the kinds of diseases that NIDDK is responsible for [researching].

KD: You have the benefits of having worked all around blood every way you could.

GR: That's right, exactly.

KD: At some point you got an M.D. from Brown?

GR: Yes, 1979. I was in the fifth graduating class.

KD: Where did you get your clinical experience?

GR: After I completed that, I was accepted at Barnes Hospital Washington University School of Medicine in St. Louis. I went there to do a residency in internal medicine and was offered the opportunity to become the Chief Medical Resident at Wash U as well. That was from 1979 to 1982, and I had a great time at Washington University. In fact, they wanted me to stay there to do my fellowship training in hematology, but I opted to follow the advice of others to leave St. Louis and to actually come to Bethesda.

KD: So going to the hospital and working in a clinical setting didn't change your mind about doing research.

GR: No. It actually inspired me. There were quite a large number of patients in St. Louis with various blood diseases, and I developed an affinity for working in those clinics in addition to my general internal medicine clinic. At that time I was able to take on a large

number of patients that had sickle cell disease, so I was still very much inspired to follow that path that I had set out on high school.

KD: Did people tell you about NIH and NIDDK in particular?

GR: Yes. While I was in my second year of my training. Then one begins to think about what one is going to do after their last year. The options existed to do hematology training at a number of places. One of my mentors at Washington University was a Dr. James Gavin who himself had worked in the intramural laboratory at NIDDK—for one of its precursors—we had gone through the evolution of several different names. Dr. Gavin worked in the lab of Dr. Jesse Roth, who was a former NIDDK scientific director. Working in his laboratory he discovered the insulin receptor. This was really critical to the understanding of the pathogenesis of diabetes, so this was very high on his [Gavin's] list.

Dr. Gavin was an assistant professor at Washington University at the time and he says, "Griff, you should go and consider Bethesda, Maryland, and doing some training at the NIH. I'm not sure whether they're doing sickle cell disease research, but it's something that you should consider. It's a great place, and I'm sure you'll have a great time there."

In fact, Dr. Gavin is really one of these mentors—there are a number of pieces of advice that he gave to me over the years that I followed assiduously. One was when I was at Brown and looking at residencies. I met with him among other people. He took a half a day off and cancelled his clinics so he could take me around and introduce me to various people. While the places that I did interview for were considered some of the better residencies, this was the first time that had I actually had experience where someone was looking at me and thinking about my career trajectory.

At the end of the day as I was off to the airport he said, "You really should consider this place." So when I came I said, "Look, I followed your advice." As I was leaving I turned to him, and said he told me to come here. This is more or less what got to me and a few

other things. The third piece of advice that he gave me, he said, "You should learn to play golf." He was a great golf player, and he wanted someone to play with. Now that was something that my wife wasn't that excited about because it typically would get me away from her for four or five hours at a time, but I followed that piece of advice as well.

KD: You followed Dr. Gavin's second piece of advice and ended up here. Tell me about the interview, what your impressions of this place was.

GR: I came here my junior year. Of course, we didn't have the Internet back then, so I had to go to the library at Wash U and read through and see who at the NIH was doing research in sickle cell disease. Then I made a few phone calls to the National Heart, Lung, and Blood Institute and I spoke with Dr. Clarice Reid who was the head of their blood division. And she says, "If you'd like to come to the NIH and work on this, the person that you should speak to is not at NHLBI, he's actually at NIADDK, it's Alan Schechter." He had published a two-piece review article in *The New England Journal of Medicine*, as it turns out, just a month before, and he was already envisioning how one could attack this disease. Dr. Schechter came at this disease as someone who had a biochemical perspective. He worked in the laboratory of chemical biology under the lab chief who was one the four intramural Nobel Laureates who worked with Chris Anfinsen.

When I set up the interview, as was standard back then, before you talk to the person that you are coming to work with you have to speak with the lab chief first to get his or her approval that this person is appropriately vetted, I'd like him to come, now you can talk to the person you want him to work with. So in my interview with Dr. Anfinsen—I had read that he was a Nobel Laureate. I tried to read up on how he received it and why, so I could sound intelligent when I spoke to him about protein folding. We met in his office and after about the first ten minutes I got a good feeling that things were going well. And he says, "Griff, this is great. I think you should come here. Don't look at those other offers that you have." He says, "By the way, let's go down to the cafeteria and maybe we can talk more over coffee." And while I was there, I said, this is great. This is the first Nobel Laureate I ever met. As we were sitting there, coffee in hand, he says, "Have you

got two bucks I can borrow from you. I want to buy some cigarettes?" My whole opinion of a Nobel Laureate, this guy asking me for money, how can I say no. I said, "Sure, here it is." I have to say when I came back, he remembered, and he offered to give me the money back. I said, "No, please keep it. I have a story to tell for the rest of my life."

I later met with Dr. Schechter and we clicked immediately. He was working really more on sort of the basic biology and trying to understand the molecular and cellular pathophysiology of disease. I told him I'd really like to work on that, but I'd like to expand that somewhat to work in addition on some of the more clinical aspects of the disease. So when I came to join his lab in '82, I continued as a collaboration of work that he was doing in some of the basics, but also looked to expand the lab into projects involving clinical research as well.

KD Had Dr. Schechter made some important findings about sickle cell disease at that point?

GR: He absolutely did. Most people thought that sickle cell disease, as the name implied, was a problem when red blood cells lost their oxygen, as they're supposed to as they deliver oxygen to the tissue. The thought there, and this was something that was initially argued by Linus Pauling and others, was that when the red blood cell gives up its oxygen and picks up carbon dioxide from the peripheral tissues that unlike people with normal hemoglobin, people with sickle hemoglobin, their red blood cells would begin sickle, and it was that sickling process that caused obstruction to blood flow in the small vessels.

It was. Dr. Schechter's idea and actually other people in our intramural program, Dr. Bill Eaton and Jim Hofrichter, that suggested that it wasn't the sickling per se, but it was actually the state of hemoglobin. It gets to be a little bit technical, but the state of the hemoglobin, the mutation in sickle cell disease causes a substitution for what's called a hydrophobic amino acid valine in position 6. It substitutes for glutamic acid. And as a result of that substitution this hydrophobic valine causes an interaction with an adjacent hemoglobin molecule upon deoxygenation, and that causes these hemoglobin molecules to bind to one another almost like Velcro. A process gets set up where these long strands

of polymer form and it's actually the polymer that's inside the cell. Think about it as reinforced steel inside of a cell. As they elongate, they begin to change the shape of the cell so that at very extremes you see the sickling of the cells, and that's what people were seeing under a microscope.

Dr. Schechter's and [Dr. Constance Tom] Noguchi's contribution, and Dr. Hofrichter's and Bill Eaton's contribution was finding that it's not actually the sickling of the cell per se, but it's the biophysical characteristic of the polymer, whether it's either a polymerized form or a non-polymerized form, that determines the underlying pathogenesis of the disease. So the goal now was, instead of developing something that could unsickle the cell or desickle the cell, one is looking at potential chemicals, and this is where his chemistry background came in, that could disrupt that Velcro binding, that binding of neighboring deoxygenated hemoglobin molecules that would lead to the depolymerization of deoxy sickle hemoglobin and thereby stabilize the disease. That's what I came to work with him on.

He had a great model of explaining it, and explaining it in those terms actually offered alternative targets in terms of getting at the underlying pathogenesis of the disease. For example, they learned that the rate at which this polymer occurs varies with the 32nd power, the intracellular hemoglobin polymerization concentration, which means that if you could overhydrate the cell in some way you can dilute out that concentration and thereby greatly perturb the rate at which polymer forms under deoxygenated conditions.

Now the challenge was to try to figure out drugs that could cause red cells to swell. In fact, people from Boston and others showed that was actually a viable approach. They proved the concept—it was somewhat untenable how people had to go about doing it. They had to drink several gallons of water a day along with something called DDAVP, a vasopressin analog, which caused their total body water content to increase. The red cells act like small—as the concentration of free water increased on the outside that would swell the cells. Then you start to think about other things that could affect that as well.

KD: What year is this?

GR: We're now talking about 1981, '82. Dr. Schechter's idea came out in '79, '80, '81. I arrived in the lab in '82, so we're now looking at proof of concepts of this theory that people here and other people around the world were actually embracing now.

KD: You were working with Dr. Schechter and he was the one who came up with that insight.

GR: That's right.

KD: Tell me how you came up with your research plan and the decision as to what to do next?

GR: We were working on that concept that he had and trying to look for circumstances that would either support or reject that hypothesis. Anything that would swell the cells would be favorable, anything that would dehydrate the cells would be unfavorable, and that would be reflected by changes in their overall clinical and hematologic status. There were certain populations who had the same disease, but their disease seemed to be more attenuated, they had milder forms of the disease. During that early time between '82 to '85, we began to show that people that had a second condition, alpha thalassemia, which is a very prominent disease or condition among African-Americans and other groups that had high prevalence of sickle mutation, that seemed to attenuate the disease, and we figured out how that worked. It still worked through the same mechanism of polymerization.

Interestingly, we found that people that had a second mutation causing a high level of another type of hemoglobin, fetal hemoglobin, also had an attenuation in their disease manifestation. There weren't many people in the U.S. with this, but it was quite prevalent in Saudi Arabia and in India, and other places in the Middle East that in addition to having sickle hemoglobin, they also inherited mutations that led to high levels of fetal hemoglobin. And that's what really was sort of the backdrop was for the work that I did in the late '80s, to see whether you could use a drug that might stimulate the expression

of fetal hemoglobin among people who had low levels normally, it normally is between one and two percent in everyone, but if you could get that up to 10 or 15 to 20 percent with a drug or some other pharmacologic approach that might attenuate the disease in the same manner that we saw in those populations that had their normal levels were in the range of 20 to 25 percent.

KD: To get to the fetal hemoglobin, was that a matter of looking through literature or talking to people?

GR: It was looking at these various populations that had been described. For example, the people that were in the Middle East in particular, as people were going out doing surveys to actually determine the origins of the sickle mutation, they were finding that it did exist at least in old world Africa, in three predominant sites. Of course, countries didn't exist thousands of years ago. They were sort of artificial based upon where there were mountains or rivers, or other geographical demarcation zones.

But in general, it was found that with the knowledge that we gained from so-called DNA haplotypes or restriction enzyme polymorphisms, RFLP, which is really the basis for all of the legal aspects of genetics in which you can use people's DNA to move them in or out as suspects or looking at Ancestry.com and these other groups that can tell what the linkage is with you and your family, they're all based upon the concept of haplotypes or RFLPs. That work was discovered by a prominent hematologist at the University of California at San Francisco, Dr. Y.W. Kahn. He worked on sickle cell disease and thalassemia disease, so he applied that knowledge initially to doing prenatal diagnosis. He came up with this concept of haplotypes.

Getting back to Africa, they found there were probably three areas in Africa where the sickle mutation arose thousands of years ago. There was something that existed in the region around Senegal, the Central African Republic and also in Benin, which is in the middle. As it turns out the people who were in Benin, in spite of what the name sounds like, they actually had a more severe type. The people who were from the Central African

Republic haplotype had a more intermediate type and the people from Senegal had a milder form of the disease. What distinguished those three groups, as Dr. Kahn and others later found out, was that the people from Senegal had modest elevations of the fetal hemoglobin level.

Now with this in hand, people went to areas of the Middle East in the ‘70s to begin to explore this. One of the people who published a lot of work on this was a fellow named James Bowman. James Bowman was the father of Valerie Jarrett, the former advisor to President Obama. She’ll tell you that she was actually born in Iran and moved around in places because her father was a molecular geneticist surveying and understanding the origin of these various hemoglobin mutations. People were moving into the Middle East, particularly these large oil companies and they wanted to make sure that they had a healthy population to do what’s needed in terms of drilling for oil and things like that. So there was a lot of money going into geneticists and others who could screen the population for the presence of certain diseases that might make them great candidates to work with.

He actually determined that in Saudi Arabia and some of the other Middle Eastern countries there was a fairly high prevalence of the sickle mutation, actually slightly higher than what was seen in Africa. But he and his group also found that what distinguished them was they also had fairly high levels of fetal hemoglobin. When you look carefully, it turns out when you go to India because of the trade between Indians and Saudi Arabia, that same haplotype. So these people from Saudi Arabia, the Middle East and India actually had a very mild form of sickle cell disease, in general, and what distinguished them was this high level of fetal hemoglobin. This is the backdrop to the study as we get into it.

In India, the prevalence is actually so high that there are more people in India with sickle cell disease than anywhere else in the world. One would think this is a disease exclusively in Africans, but that’s not the case. It actually exists in portions of the Mediterranean, Southern Spain, Italy, Greece and other places, but large pockets of India and also in the Middle East.

High levels of fetal hemoglobin protects the disease. We know it protects it now because it acts in the same way that swelling the cells and developing a chemical that could interfere with the polymerization does. Nature really developed the best way of doing that in the form of maintaining a high level of this type of hemoglobin which normally gets turned off at the time that we're all born. Because of these other mutations they have a persistent high level of expression. That sets the stage for, can you develop a drug or something that might be able to achieve that same objective pharmacologically in people that have low levels, people who are from Beninian haplotype or the Central African Republic haplotype and somehow induce that, turn it back on, and that was the goal.

As I got here there was a group in the Heartland Blood Institute who started working on this using 5-Azacytidine, which at the time was known to potentially reactivate genes that had been turned off due to chemical changes that occurred in a certain part of the gene that controls the gene expression. More precisely, methylation of the promoter element seemed to turn off the genes. If you could demethylate it, and 5-Azacytidine was a drug that causes demethylation, maybe you could reactivate the gene and turn it back on. And it turns out that was the case.

Scientists always argue about mechanisms. Some people felt that well, that could be one explanation, but another thing could be that, like all chemotherapy, it first causes some toxicity to the rapidly divided cells, and then when you withdraw the drug and you give the cells a chance to recover maybe that's what's turning on the genes. That led us to actually consider this drug Hydroxyurea because it's a form of chemotherapy. It works on rapidly dividing cells. It doesn't have the same toxicity profile that drugs like 5-Azacytidine does.

That was the basis of our work in the late '80s and early '90s that using this drug in about 70 percent of hospitalized patients we could turn on their fetal hemoglobin to modest levels and the longer you gave it to them, the higher their values would go. Subsequently our work was replicated by groups in Seattle and Harvard and Johns Hopkins, and that

led the NIH to fund this fairly large study of a cooperative randomized clinical trial, which tested whether the drug would have a benefit.

The study was stopped a year early because one group, which was blinded at the time, was doing much better than the other group, and that group was the Hydroxyurea group. Then three years later, the FDA approved it.

KD: That was in 1990?

GR: In 1990 our paper came out. In 1995, this large randomized trial showed that hydroxyurea was beneficial, and in 1998, the FDA approved the drug as the first drug that was approved to treat adult patients with sickle cell disease.

KD: Had you done your own clinical trial before the 1990 paper?

GR: We had. We were looking at a number of other agents and smaller subsets of patients to determine whether they might have some role. For example, we thought that since the problem in sickle cell disease was fundamentally that these cells, because of the polymer content, had a difficult a time negotiating the small arteries, arterials, capillaries and venules, maybe if we gave a drug that could dilate the vessels that might improve the blood flow, so you could get the cells through the microcirculation and back on the oxygenated side so that polymer would be removed. In that circumstance that trial used the eye as an example to directly measure that. We showed that certain types of drugs, specifically calcium channel blockers were actually quite efficacious in these patients. This has been replicated by other groups. We did clinical trials going into this.

KD: You must have been very encouraged when you read that there was going to be this very large trial.

GR: Absolutely. We collaborated with the people at Johns Hopkins. In fact, we had the benefit of being here in the intramural program so that you could actually bring people into the

hospital without concerns about their insurance. They could be hospitalized for extended periods of time. In fact, patients in our initial trial were in the hospital for three or four months as they were getting the drug, we knew that they were taking it, so drug compliance wasn't an issue, and we could then modify the dose and gradually escalate it and look for side effects.

So what our trial was able to do was not only show that it worked, but we could define what the starting dose should be, the average dose, and what the maximum tolerated dose was. That information was used to support the large cooperative clinical trial that NHLBI supported.

KD: Did the success of this trial come to the FDA's attention? Is that how this happens?

GR: It was after this large cooperative trial, so-called the MSH, Multicenter Study of Hydroxyurea was ongoing. It was stopped prematurely because the Data Safety and Monitoring Board, who looked at the data, periodically noticed that among the patients in one arm -- of course it was blind at the time -- the group receiving let's say Treatment A required fewer blood transfusions. They seemed to have less pain. They seemed to have fewer hospitalizations. Their blood values were actually increasing compared to people who were receiving Treatment B, which turned out to be the placebo arm. Their thought, which I think was appropriate was since you're already seeing an effect and it seems to be non-random, which is statistically significant, was we should stop this trial, that it would be unethical to keep this group of patients who don't seem to be benefiting at all on whatever they're receiving because you can stop the trial, figure out, sort out who is getting what and then offer what seems to have been given to Group A to Group B, and that's what happened. That was published in 1995. Then the FDA, after thinking about this, finally gave approval in 1998.

KD: This is a pretty big deal.

GR: It's a pretty big deal. It turns out that when our study came out, before he was a famous author on the *New York Times* Best Seller List, Malcolm Gladwell was a science writer for the *Washington Post*. He actually published our results on the front page above the fold about this hydroxyurea work. He and this other guy Warren Leary of the *New York Times*, [and] another science writer at the *Los Angeles Times* covered this as front-page stories, so it did make a bit of a splash. At that time, we had a limited number of patients, but we were excited that we had something of a 70 percent response rate, and that was, after it was replicated it vaulted us on to the NHLBI's attention that funded this multi-center trial.

Our result of about a 70 percent success rate ultimately was replicated in a larger trial, so about 70 to 75 percent of adults on the drug seemed to respond. The other 25, 30 percent still for unclear reasons, you know that they're taking it, in our setting they knew they were taking it, when you give patients drugs on an outpatient basis you don't know what the adherence rate is, but since it came out to be the same as ours we assumed that most of them were in fact taking the medicine. At least having an unambiguous confirmation here at the NIH set the stage for developing the right dose and the maximum dose, and parameters that were to follow, and that was exciting.

KD: This was pretty good for your first project at NIH. Tell me about the people that helped you. Who was in your lab and how was it structured?

GR: I worked with Dr. Schechter and a colleague Dr. Noguchi and we were able show in the lab this effect that we had in terms of increasing the fetal hemoglobin, what the molecular and cellular effects are in terms of inhibition of formulization. I also worked with Dr. Arthur Nienhuis who was at the National Heart, Lung, and Blood Institute. While most of his work was actually in basic molecular biology, he was quite accustomed to doing clinical trials and setting up appropriate clinical trials. What I tell people is that I have a foot in NHLBI and NIDDK. In fact, both of the institute directors at that time claimed me as their own. Dr. Gorden was the Institute Director at NIDDK and he knew that I was here doing this work. Dr. Claude Lenfant, who was the Institute Director of the Heart,

Lung, and Blood Institute at the time, was certain that I had worked in the Heart, Lung, and Blood Institute. He was saying this was work that was being done in their intramural program. That withstanding, Dr. Nienhuis taught me a lot about the conduct of clinical trials, safety issues, how to recruit patients for the trial and more.

I started off more with the project and that ultimately led to a program in terms of the clinical aspects of sickle cell disease. We shortly thereafter showed [results] in another piece in The New England Journal that if you add a drug, recombinant erythropoietin, you could actually synergize the effects and get higher levels of fetal hemoglobin in these patients. Doing those clinical trials was a great start to my career.

KD: At this point you've been at NIH for about 15 years. Is that about the time you became a section chief?

GR: Our programs are reviewed every four years, quadrennially. It turns out, in 1990, when that paper came out, I was put in and received tenure. In 1994 after my review, I did some additional clinical and some basic work, and I was put in to become a Section Chief. I was still in the Laboratory of Chemical Biology, and by this point, Dr. Schechter was not a lab chief. When I came to work with him, he himself was a Section Chief, but about a year later, Dr. Anfinsen left and he then became the Lab Chief. So from 1984 to 1994, I got tenure in about six years and then for the next four years I was a section chief. Then in 1998, I was granted my own lab, my own branch. At that point I physically separated from the laboratory that I was in, Dr. Schechter's lab, and I began to recruit people to expand the program what I thought the next step should be in terms of sickle cell disease clinical research.

KD: Is this the clinical and molecular hematology branch?

GR: Molecular and Clinical Hematology Branch, that was 1998. The person who Dr. Gavin worked with was Dr. Jesse Roth. He was a Branch Chief. He subsequently became the Scientific Director of the Institute. In 1990 when I received tenure, I was the very last

candidate that he brought on under his wing as a tenured scientist. He subsequently left and Dr. Allen Spiegel became the Intramural Scientific Director. That's important because in 1999, one year after Dr. Spiegel had put me in to become a Branch Chief, he actually became the Director of NIDDK. He succeeded Dr. Phil Gorden. That was in 1999.

KD: Putting your new branch together was an opportunity to build something entirely new. What did you do differently?

GR: Traditionally laboratories at NIDDK studied basic and translational research whereas branches were focused mostly on clinical studies. That, somehow, 20 years ago, began to be a little bit less clear cut. Even in this Laboratory of Chemical Biology where I worked, I did a lot of clinical research, I did basic and translational work. I thought that calling it a branch would be true to the historical perspective of focusing more on clinical work but supporting that with basic studies as well. So I went about hiring people in my branch as tenure track investigators to take up some of the clinical work that I had envisioned, which would be the next step in this moving forward.

KD: What were those hires?

GR: The first person I hired was a fellow named John Tisdale, who was actually one of my fellows when I was an attending in the hematology branch. I hired John with the idea to develop a bone marrow transplant program to treat patients with sickle cell disease. Up until now that wasn't available. While most of the patients that had been treated with bone marrow transplants who had sickle cell disease were pediatric patients who had not yet suffered all the end-organ complications of sickle cell disease that would occur after 20, 25 or 30 years, since our focus was on adults, the goal was in my mission statement to him to develop a regimen that could be safely applied to adults who had suitable bone marrow donors for them to transplant.

He took that on first in animal models, rodents, subsequently in primates before we then applied this to humans, and he developed what's called a non-myeloablative transplant regimen, which was actually quite unique. Instead of using high doses of chemotherapy and radiation to completely wipe out the bone marrow and then transfuse the patient with the bone marrow and hematopoietic stem cells from an HLH compatible donor, the goal was to make a little space in the bone marrow, not completely ablate it. So mini-transplant, or non-myeloablative, there are a number of terms for it.

But it was really based upon the observation that in a number of these kids who had undergone full ablative transplantation with sickle cell disease, most of them continued years later after they were cured to show a hundred percent of their cells in their peripheral blood were of donor origin. A small number of them, as it turns out, after a number of months to years, their own bone marrow started to come back. So they had elements of both donor marrow function as well as recipient, their own. That state is called mixed chimerism. You have a little bit of this and a little bit of that.

Unlike the patients who had a hundred percent donor cells in them, the patients who were about 20 percent recipient, 80 percent donor, or 60 percent, or 70 percent donor, and 30 percent recipient, they seemed to be cured as well. So that raised the possibility that maybe you don't have to exactly wipe out the entire bone marrow. Maybe you can use less intense regimens to open up some spaces where you can put these donor cells, because it seems like they can live together quite well in this state of mixed chimerism. He was able to test this hypothesis in a transplant rejection-prone model in mice and then subsequently apply this to this non-human primate, and actually showed that it worked, which ultimately led us to move forward with this clinically.

The reason that you don't want to use high doses of radiation and chemotherapy, because after 20, 25, 30 years of sickle cell disease and all the damage it does to the organs, the lungs, the liver and many other organs, the heart, this high dose of radiation and chemotherapy could be the straw that broke the camel's back. I shouldn't say that, but it could tip people over the edge and cause partial compensation of these organs that were

severely damaged to then be fully damaged. So we estimated that the likelihood that adults with sickle cell disease, particularly the severe patients that we often were referred, could result in a 20, 30 percent mortality at a hundred days. Usually the hundred-day mark is when people begin to count whether the transplant was successful or not.

In doing this non-myeloablative approach, as it turns out, in the first 30 patients that we transplanted, all but one survived. The one who passed away, passed away from a condition unrelated to the transplant itself. When we expanded that to 50 to an excess of 60 patients, it turns out there's a 95-percent disease-free survival and about a 98 percent overall survival. So these are results that were similar to what you see in kids. As it turns out somewhat unexpectedly, the beauty in this regimen is that most people who get an organ transplant, bone marrow or kidney, or liver, you have to give them anti-rejection medicine. That's one of the downsides. So yes, you have a new kidney and you don't have to be on dialysis anymore, but for the duration you're going to have to take a medicine to keep your immune system from rejecting what it still sees as a foreign tissue.

With this regimen we're able, after a year or 18 months, to get them all off of anti-rejection medicine. So this is a gold standard for organ transplantation to both successfully get in the organ as well as not requiring immunosuppression, which has side effects, as you can imagine.

KD: So it sounds like this project is still underway.

GR: It is, but we're now about to move onto the next phase. It's quite effective, 75 to 80 percent effective in adults. Just two years ago, in 2017, the FDA extended the approval of the drug for infants and kids. Kids respond even better, but we realize that it's not a cure. These transplants actually seem to cure the disease, but unfortunately, only about one in four potential patients have a full sibling match. So while it is a cure and it has a high cure rate, it's not going to be effective in everyone. The actual cure would be to take their bone marrow cells and peripheral hematopoietic stem cells and modify them in such a

way that you actually correct that initial genetic defect, so-called gene therapy of the disease.

KD: Yet to come.

GR: Well it actually is happening. The guy who works with me is working actually with a company that has developed a new beta globin gene that has inside of it not only the normal beta globin, sickle globin, but it also has another mutation that if it ends up getting next to a sickle hemoglobin that's starting to polymerize it actually goes in and it causes a disruption in that to occur. So you melt away existing polymer, so that you both increase normal hemoglobin that can deliver oxygen. But if there's still some residual sickle hemoglobin in there it accesses an anti-sickling agent in a sense. Based upon the results that John has gotten with transplantation, they quickly contacted him to see if whether he would be interested in applying what he's learned in the transplant world to this gene therapy.

That work was actually just reported on 60 Minutes about four months ago. Dr. Collins was quoted that he's optimistic and he dared to say the word "cure." But he said this is a cure. That's good if you have access to this company's proprietary compound. I thought a while ago when Dr. Tisdale and I were working on this that if you can pick out the kids at high risk from the time that they were born, if you get a couple that are at high risk for having sickle cell disease, and if you were able to collect their cord blood at the time of birth and then freeze it away using the correct practices, then eventually you can actually take that cord blood, manipulate it with gene editing technology and then ultimately give that cord blood that's now edited back to the child without doing any manipulation, because it's their own cord sample.

About 15 years ago we began a cord blood program here to collect. This was before CRISPR-Cas, the gene editing technology was available. We anticipated that eventually it would be available. So now we have collections of cells, we're now working also with people in Northern Virginia to do this. We think when it's ethically and scientifically

justifiable we'll be moving forward. We're doing preliminary studies to test it right now, but this might be really the cure that could be more widely applied.

KD: We've taken the science right up to the present day. There's this whole other track of the administrative side. When did you get a sense that you might be tapped as Deputy Director?

GR: I didn't until the time I was asked. My Scientific Director at the time who thought enough of me to move from Section Chief and have me start my own branch, in 1998, the very next year, he became the Institute Director. Because he was now freeing up his position as the Scientific Director in early 2000, and the person who was his Deputy Director at the time was someone who wasn't a scientist, he was a businessperson, he was about to retire. So Allen turned to me and said, "I would like you to consider moving into the administrative track. You could either considering doing the position that I had, the Scientific Director, or because this person will be retiring in a year you could wait and become a candidate for the Deputy Director slot." I said, "You know what, let me wait a year. The research is doing well." So in January 2001, I became the Deputy Director of the Institute.

KD: And you got an M.B.A. as well?

GR: The person that he had that was his deputy was a businessperson and he was managing a lot of the budget and financial aspects of the work. Dr. Spiegel confided in me and wanted me to take over that aspect. I said, "I'd love to do that, but I don't have any business experience per se, finance, accounting, and the like." It turns out that they had just started a program in Johns Hopkins, a Master's of Business Administration focused principally on the business of medicine and science. It wasn't one of these executive programs where you get a degree in 18 months, two years. It was actually a full program and every part of it was focusing on either medicine or science, in accounting, finance, negotiations of legal aspects, economics. It all centered around case studies that dealt with the business of medicine. So after three years I was able to get that M.B.A., and

that's what I started doing as a deputy, managing aspects of the budget and other things at the Institute. I'm someone who believes in continuous learning. In fact, in 2017, I went back and I got a degree in law as well.

KD: I want to talk about becoming the Director, but I don't want to miss how you and Dr. Spiegel split things up. It sounds like his intention was for you to take care of some of the nuts and bolts.

GR: That's right. We actually split up some of the scientific aspects of it. This is a very large institute dealing with diabetes and endocrine disorders and inborn errors of metabolism and congenital defects. We also have digestive disease and nutrition, obesity and liver disease, and then we have kidney and urologic and hematologic diseases. Each of those organizations expect you to attend their national meetings and meet with them regularly. At last count we had about 68 different advocacy groups, three Celiac disease advocacy groups, Inflammatory Bowel Crohn's and Colitis Foundation. There's not only the American Diabetes Association, but also Juvenile Diabetes [JDRF, formerly the Juvenile Diabetes Research Foundation], and it goes on and on. There were about 68 at last count. He wanted to divvy up the scientific aspects of this as well, so we developed a nice way of managing that. Then I had my own areas that I focused on like the budget, and we have an intramural program not only here, but we have one out in Phoenix. So several times a year I would go out and manage certain aspects of what was going on out there as well.

KD: How was the transition to becoming the Director?

GR: In 2005—I was Deputy from 2001—now about four years later Dr. Spiegel told me, "Griff, I'm going to be looking at," he tends to speak in paragraphs, he's so brilliant, "I'm looking at another opportunity that I would consider to be my final push." And at that time he was offered a number of positions. The one that he chose finally was to become the Dean at Albert Einstein School of Medicine.

He told me that he was looking at positions, considering positions. Ultimately in 2006, he had accepted a position to be the Dean at Albert Einstein College of Medicine. Upon him accepting that position I was asked by the Director, Dr. Elias Zerhouni to step into the company of the Acting Director, and I continued to be the Deputy Director as well and did that for a year. After a national search, which was co-chaired as it turns out, by Dr. Francis Collins, who was then an Institute Director, and Dr. Tony Fauci, I was offered the permanent job on April 1, 2007. I told Dr. Zerhouni, and I still joke with him, "I know you picked that date because you could always say 'I was just joking.'" It was April 1st. I've been the formal Director since 2007, now a little bit beyond 12 years.

KD: When you came in, when you started in this formal position, what did you want to change, what did you want to do more of? How did you see NIDDK moving forward?

GR: This was an organization that historically did extremely well. I learned in business that there are generally four types of businesses in a situation where a new director or CEO comes in. There are start-ups. This obviously wasn't a start-up. It had a rich history. There are organizations that were turnarounds that started off going well, but you had to completely put it in a different direction. There were areas that you just had to realign some of the minor aspects of it to keep it on its ongoing successful mission. Then there are very successful organizations, which I think this is. There you want to put your own stamp on it and really continue to do more of what you had been doing historically. That's how I view this.

So I set in motion, after talking with a number of people, five objectives that I tried to accomplish. The most important thing was we wanted to maintain a bigger connection to our investigator-initiated portfolio. In terms of our budget, we have 85 percent of that budget that goes extramurally out to individuals at universities, medical schools throughout the country, and a small amount of money internationally. We wanted to make sure that people with great ideas could succeed in applying to our institute and consider this a place to have a viable research career for their entire career.

We wanted to make sure that there were exceptional training and interning opportunities. We wanted to make sure that we get cutting edge clinical research that would have a beneficial and demonstrable effect on people's lives. It was important that we consider in both the clinical trials and in our early scientists and our established scientists that we make sure that we were an institute that was diverse and inclusive, particularly given the kinds of diseases that we were responsible for, as they disproportionately affect women and certain under-represented groups. We wanted to make sure that not only did the patient population that we recruited for our clinical trials reflect that diversity, but also the individuals who would actually be performing those studies. Our principal investigators and their supported staff also felt that NIDDK was a local home for them as well.

Since we're a publicly funded institution, we wanted to make sure that the results of our trials, be they positive and negative, were immediately spread in a way with public education and awareness, and outreach. Not only to the public, but also to practitioners and the policymakers who ultimately decide what our budget is going to be, we wanted to make sure that our outward face in terms of both the Internet, and increasingly, social media, reflected the things that we were doing and achieving with this public support.

KD: Speaking of public support, did you have to testify before Congress and things like that?

GR: Yes.

KD: Tell me about the first time you did that and what you learned.

GR: I came into this job on April 1, 2007 and I think the first committee [hearing] that I attended was only about two weeks later. It was the Senate Appropriations Committee. At that committee [hearing] we were all asked questions. We testified along with Dr. Zerhouni, who was the [NIH] Director at the time. Senator Daniel Inouye from Hawaii was on that Appropriations Committee and I remember this very distinctly. We had set up a program in Hawaii to train the next generation of biomedical researchers at a college level. Then that spilled over to looking at feeder high schools in the Hawaiian Islands that

could potentially bring these talented kids ultimately to the University of Hawaii as college students. Then from there they might expand to get graduate degrees or medical degrees, or other affiliated STEM degrees.

Senator Inouye turned to me and said, [paraphrasing] "I'm very much aware of this program that you're doing, but I would like you to consider expanding that somewhat to the American territories that exist in the Pacific Islands because these are a lot of places where people just don't have these opportunities." So, hearing his remarks, we set up a program very quickly in Guam and then in American Samoa, and in Saipan, Palau, and the Marshall Islands and others. In fact, just earlier this month at the University of Hawaii, because I happened to be in Honolulu attending another meeting, I recognized the person who was very helpful, now it's ten years in action, who set up that program and expanded it so greatly. Senator Inouye is no longer alive, but a representative from Senator Schatz's [and Congressman Ed Case's] office, as opposed to a local representative, sent representatives with proclamations because they were so impressed with how the program was going.

I've testified at different times to the House as well as to the Senate.

Every two years there is a special committee that I testified to, its actually the Aging Committee [hearing before the Senate Special Committee on Aging], which is co-chaired by Senator Susan Collins and more recently, on the Democratic side, Senator Casey from Pennsylvania. It's set up specifically [to talk about] for a pool of funds called a Special Diabetes Program to focus on Type 1 diabetes. The second time I testified—it's every other year—the other people who testified with me, it was an interesting group. On my right-hand side was Mary Tyler Moore, then I was here, and next to me was Sugar Ray Leonard, and the person at the very end was Nick Jonas. There must have been maybe 500 people all in this room. Of course, they were all there to see Nick Jonas, especially these kids. All of these senators showed up and they all wanted his autograph. Of course, they said they wanted this for their grandkids. It was the first time someone from *Rolling*

Stone magazine took a picture. Actually, I have it here on the wall. So I appeared in *Rolling Stone* magazine. I said, "Life can't get any better than this."

We were very successful during that time. Senator Collins asked me, "When are you going to be able to develop an artificial pancreas so that these kids won't have to prick their finger and go through the kinds of very tedious and arduous painstaking way of managing their diabetes?" I said, "We're going to work on this." This was maybe around 2011. In 2016, the FDA approved the very first [hybrid] artificial pancreas. Now there are several others under FDA consideration for approval." So we've been able to stimulate the biotech industry to move very quickly in this phase, and we're developing other things that make life living with Type 1 diabetes much more manageable. Those are very exciting.

KD: The artificial pancreas? Did NIDDK help fund the research?

GR: It's funded through the Special Diabetes [Program] allotment that we get. In fact, most of the major, the early work on the various components of the artificial pancreas – which consist of a pump to continuously deliver insulin and then bolus certain levels at the time of a meal. It consists of something to continuously measure glucose as your pancreas does, and then some device, a Bluetooth device that detects those changes and then signals the insulin pump to either increase or decrease or bolus the appropriate level. All of that fundamental work was funded in the early stages by NIDDK, and then it was in many instances taken over by private industry. Two things that you might hear on television, there is a system of continuous glucose monitoring called the Freestyle Libre that Abbott puts out that doesn't require a finger stick at all. You don't have to calibrate it. This is something you take your smartphone, put it next to it and it tells you what your blood glucose level is. The early funding was done through NIDDK.

There is an implantable device called the Eversense that can stay in place for several months at a time and you can get the same information. That was also funded [by NIDDK], a different type of hormone. Not only does your pancreas make insulin, it

makes something called glucagon, which if your blood sugar gets too low the body kicks in glucagon. We worked with chemists to develop a more chemically stable agent that has a longer half-life, shelf life, so you can actually put it in the pump as well, so have a bi-hormonal pump. I can go on and tell you about many of those. This work with industry, in my mind, was greatly assisted, I think, not only because there's a general interest in this, but by some of the business training that I was able to obtain.

KD: Talk about some of the bigger issues. There were some clinical trials going on.

GR: A major one in the diabetes phase is the Diabetes Prevention Program [Outcomes Study]. At the moment there are about 30 million Americans with diabetes, most of whom know that they have it, but some don't or are unaware. There are another 84 million Americans that have what's known as prediabetes. Their blood sugar levels are not normal, but they're not quite yet high enough to categorize them as having frank diabetes. But they're on the cusp and sometime within the next five to ten years they're at high risk of developing type 2 diabetes.

This Diabetes Prevention Program was set up to answer a very simple question: If, for example, you were to treat these individuals with a lifestyle intervention to get them to lose about five to seven percent of their weight through diet and exercise, would that be enough to greatly reduce, compared to the standard instructions, the rate at which people go on to develop diabetes? We had a third arm to this trial, [a drug] called metformin, which is a standard pill that one uses to treat patients once they have a diagnosis. After three years it became clear that metformin reduced the conversion to diabetes by about 31 percent with this lifestyle intervention resulting in about 58 percent reduction in the conversion. We went on to extend that study, a new Outcomes Study, with a later follow-up. Even at ten years, the benefits were durable. There were demonstrable, statistically significant results with [more in the] lifestyle group [and metformin] of patients who still either had pre-diabetes or the blood levels went back to normal [compared to the placebo group].

I guess we were wise enough to know that other things that are at high risk of putting one in this category of pre-diabetes [converting to diabetes] includes women who have had a history of gestational diabetes, which includes the same ratio in ethnic groups that are at a high risk for diabetes, but it also includes people over 60. So, working with our colleagues in the aging institute, we tried to over-sample for people who were 60 or older at the time of randomization. The reason, as it turns out in hindsight, that was a good thing, was that while overall population, about 58 percent of the people responded to the lifestyle. If you look only at the people who were 60 or older at the time that they were randomized, they had a 71 percent reduction in the rate of transformation to diabetes. It was funny because people said you're never going to get people over 60 to exercise, and even if you do, they're not going to sustain it. Well, both of those things have proven to be not correct.

With this one-on-one counseling it required six sessions and then a boost every month after they had gone through the formal sessions. It was a very expensive enterprise with one-on-one. There's no way that you can make a dent when there's 84 million people at risk. So we figured we'd try to scale this up in a way that, instead of doing this one-on-one, we'd do it in a group setting and we chose the YMCA as a venue to do this. You might ask, why the Y? Well it turns out there are 2,600 YMCAs in this country [at the time] and the average person lives about three miles from a YMCA. So we thought this would work and we could scale it up and you would have a great way of starting to achieve that. And it turns out the benefits that you saw in a Y setting, getting group counseling, could achieve similar weight reduction as we saw with one-on-one counseling.

Now you're making it cost-effective and the fact that we're able to get a lot of people at the age of 60 or older, Medicaid and Medicare services, or CMS looked at this and said maybe we should offer this as a benefit for people 65 or older. Just last year it became an approved benefit. So anyone who's 65 or older [with Medicare] who want to be tested if they have pre-diabetes then they would cover this service. It's very unusual to have a clinical trial result, in relatively short order, about 15 years, to actually make this a policy. That's one of the things I'm proud of.

KD: Speaking about reaching lots of people, where did the idea of your radio show come from?

GR: About 12, 13 years ago, locally there was a radio station that decided that they would host an event at a local hospital that's now closed, called Providence Hospital, and it was called "Take Your Loved One to the Doctor." A lot of people, particularly in urban settings, particularly men, don't like to see a doctor. So this was used as an occasion every year to encourage people, they do different types of screening there, and they asked me and several other people to come and host a radio show where people can call in and ask questions. They knew that at the time—I was the Director of the Institute—with diabetes, obesity, and kidney disease, there would be a lot of interest in calling up and saying, "Doctor, I have heartburn, what should I take for it and what does it mean?" So I did that and that went pretty well.

They asked me the next year, but rather than having a local radio personality they actually had someone who had a national spot, a fellow named Tom Joyner, who has a fairly large reach. And that went well, and he said, maybe you could consider doing this not just locally, but on a national scale. So about 10, 11 years ago we set up a program with him and we went to the radio stations initially here in Washington then we expanded to Baltimore and Philadelphia and Richmond. The goal initially was just to do those areas because I could use this venue to try to recruit patients to come to the NIH to get involved in clinical studies. Then we expanded that even more to Atlanta and places in the Midwest. Then over time, we actually expanded it to another personality who's in 41 markets around the country.

So what started off just here in Baltimore and Washington with maybe 10 or 20,000 listeners, is a program that's now in 41 markets with 60 million listeners on a weekly basis. And I expanded it to go beyond what we do in this Institute. I have other co-hosts from other institutes like Dr. Fauci, for example, who will talk about HIV and people from the Office of Research on Women's Health talking about that aspect, complementary and

alternative medicine, bioengineers coming in and talking about loose sensors, smart watches and Fitbits, and things like that. I've also opened it up for celebrities [to discuss their health concerns]. I was able to get Sugar Ray Leonard to talk about diabetes. I was able to get Sean Elliott the former basketball player who was on the San Antonio Spurs, he had a kidney transplant and he talked about kidney transplants.

More recently I've collaborated with Barbra Streisand. That's gotten a lot of likes and hits because she's very interested in the fact that heart disease affects women differently than it affects men. She actually set up a foundation to do educational awareness around this. She came to visit NIH and I mentioned some of the reasons that women had it different is a lot of those women had diabetes. Pre-menopausal women generally benefit from the estrogen effect, so their disease is not—it is several years to a decade before they start having effects. But with diabetes, you erase all the beneficial effects that you have due to estrogen. I made her aware of that and so she agreed to partner with me. We did a month-long series on heart disease in women, particularly those with diabetes.

That's grown and it gets a lot of listeners. Of course, with social media, we just don't have it on the radio now, it's on the web, it's on Twitter, and other places where you can see it.

KD: You've talked about reaching out, and I want to wrap up by looking inward again. The older scientists that I've talked to say at NIDDK you can do anything. There's not necessarily a discipline or a science that holds it all together. Having been here and having held it all together, what do you think the glue that is keeping this institute coherent?

GR: I don't want to argue with the great scientists that you talked about. I would differ a little bit. There are areas we focused on that are absolutely clear to our mission. We have an intramural program that focuses on liver disease, diabetes, obesity, kidney disease and others. We have basic scientists who actually support some of the research moving into that, maybe what they're expressing is we have people who do basic work in structural

biology, for example, without an obvious connection to the clinical arena. So they seem to be outside of what our disease mission is, but their work is so fundamental and so impactful that it has changed how we think about it. It turns out that it has that application that was unanticipated before.

I would say the glue that keeps things together, this is something I inherited so I think I can't take credit for this, is that this is a place where people like to work. Year after year in terms of ranking, in terms of global satisfaction, employee engagement and other things we tend to rank one among all the large to medium size institutes at the NIH. There is something called the FEVS, the Federal Employee Viewpoint Survey that ranks things in various domains and we tend to do quite well. As you leave you'll see our picture from 2018. We're about somewhere between five to 10 percentage points above everyone else. In fact, people think that the best institution as they look across is actually NASA where it always tends to be the number one ranked institute. But if you look at our numbers as an institute compared with theirs as an agency, we actually outperform even NASA.

People like to work here, and I think it's not the satisfaction, it's engagement, that people feel like they're family. Even our outfacing elements—we try to make sure that people realize the importance of their work and what effect this has on the American population. So we're ranked it turns out in the top three of mobile devices for our website, for example. Except for Social Security and the IRS at the time of taxes, we actually get more hits on our website, particularly now with our mobile sites than any other services that the federal government ranks.

With that regard in terms of personal engagement, its actually reflected by the fact that we have a fairly long turnaround. People stay here 30, 40 years. There's one employee that works here who turned a hundred last year and he's actually worked with the federal government with our institute now for 65 years. Next year we will celebrate our 70th anniversary and 65 of those years he's been with us. He has been a federal employee for I think 70 years because he was with the Coast Guard for five years before he came to us.

KD: Herb Tabor.

GR: Herb Tabor, exactly. I think he reflects the same sentiment of people who have been here for 60 years like Marty Gellert and Gary Felsenfeld, and others. This is a place that people enjoy working here.

I think the mission focus, even people doing basic science, they interact a lot with the more clinical people to understand how they connect. The basic scientists work hand in glove with some of the clinical people to expand their work into the clinical arena. I think that's the special sauce or the glue that keeps it together.

KD: Well, thank you for keeping it together for 90 minutes. It's been a good discussion. Anything else we should talk about?

GR: Thank you. I think we covered most of the areas.