Hohman, Robert 2020

Dr. Robert Hohman Oral History

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This is an oral history with Dr. Robert Joseph Hohman about his career in the National Institute of Allergy and Infectious Diseases (NIAID), on February 26th, 2020, at the National Institutes of Health (NIH). The interviewer is Dr. Victoria Harden, Founding Director, Emerita, of the Office of NIH History and Stetten Museum.

Harden: Dr. Hohman, would you please state your full name, that you know this interview is being recorded, and that you give permission for the recording.

Hohman: My name is Robert J. Hohman. I know this is being recorded, and I give you permission to record it.

Harden: Thank you. You were born on the 4th of July, 1953 in Pittsburgh, Pennsylvania, the middle child and only son of Robert Francis Hohman and Ruth M. Hohman. Your dad was a distribution manager for Park Davis Pharmaceutical Company. Tell me about your growing up years through high school, especially about any family members or teachers who influenced your decision to go into science.

Hohman: We moved around a lot because at that time, my father was a distribution manager for Park Davis, a pharmaceutical company. For the first, second, and third grade, we lived in Pittsburgh. Fourth, fifth and half of six, in Buffalo. The other half of sixth and seventh in Minneapolis, and then back to Pittsburgh for eighth through high school.

Harden: Were you interested in science at this time?

Hohman: I liked science. And unlike today, where you take kids around to visit colleges, we didn't do that. When I was in high school, my parents said, "I guess you're going to go to college." And I said, "OK." I liked chemistry, so I thought that I'd study chemistry. And then there was the question of where to apply. We lived in Pittsburgh, so I applied to the University of Pittsburgh, to Penn State [the Pennsylvania State University], and to Indiana University of Pennsylvania, because that's where my sister went. I got into all three but decided to go to Penn State because it was about three hours from home and I'd never been there. The other two were more familiar. The first time I stepped foot on a university campus was when my parents dropped me off at Penn State, helped me move in, and then left. It's very different from the way we do it now. I started in chemistry, but then I decided that I would like something a little more biological. I thought about going to go into medical technology, but finally I decided on microbiology, so I became a microbiology major.

Harden: Was there any teacher who encouraged you in microbiology?

Hohman: Yes, there was a young assistant professor at Penn State at that time in the microbiology department. His name was Paul Kolenbrander [Dr. Paul E. Kolenbrander]. He was studying a bacterium, *Arthrobacter crystallopoietes*. I had him for a couple of courses, and he was by far the best professor I ever had. When I was a senior, I did a research project under him with the electron microscope (EM), and that's an interesting story.

This was in the early seventies. I was in the microbiology department, and I really wanted to learn how to use an electron microscope. I asked the person who ran the EM if I could do a project using the EM. He said, "No, because it is very expensive, you're a stupid undergraduate and you'll wreck it." I kept pestering, and finally he told me that if I learned how to use an EM, I could do a project. So, I took a course in the Geology Department, which also had an electron microscope. The entire grade in the course was based on a project. Almost all students were geology majors, and hence were using the EM to analyze rocks. However, since I was in the micro department, I decided I'd take pictures of a virus.

I talked with a professor in the microbiology department who agreed to give me some herpes virus to analyze. The standard way to prepare a sample was to take a copper EM grid and coat the grid with a plastic called formvar. The sample is applied and stained with a negative stain. I took some very nice pictures and wrote up a great report on what I was seeing. Resolution of EMs in the 1970s was nothing like today, but even so you could almost see the capsid structure of the virus. I received an A in the course and subsequently the next year, I returned to the person running the EM in the microbiology department and called him on his offer to allow me to do a senior project on the EM if I learned how to use one. After all, I did get an A in my course.

Paul Kolenbrander agreed to sponsor me for my senior research project, which was taking electron micrographs of cell surface rings during replication of *Ar throbacter crystallopoietes*. The pictures turned into my first scientific publication, it appeared in the *Journal of Bacteriology*. Initially, the manager of the micro department's EM had not liked me too much, but eventually we got to be okay. At the end of the semester, I proudly showed him my report on imaging herpes viruses. All of the sudden he started laughing hysterically. As it turns out, there was no virus on the grid. My "herpes virus" was, in fact, holes in the formvar coating I applied to the grid. I had taken pictures of the holes in plastic. The geology professor, well versed in EM of rocks but not biological material, didn't know the difference. That was my start in biotechnology.

Harden: But the geology professor let you take pictures of a virus as far as he knew?

Hohman: They were inactivated. Yes.

Harden: But even so, they weren't rocks.

Hohman: They weren't rocks. He was a nice guy. I said “Look, I'm in the micro department. I want to do something micro related.” He said, “Sure. Knock yourself out.” The idea was just to learn how to use the scope, which I did.

Paul Kolenbrander, who directed my undergraduate research, came to NIH in 1978 and joined the Dental Institute [National Institute of Dental and Craniofacial Research] where he had a long and productive career studying oral biofilms. He retired in 2009 and passed away in 2017. Paul was awesome and largely responsible for getting me interested in microbiology.

Harden: You came to NIH in 1975, when you finished your undergraduate work. Before we get into what you did exactly, tell me how you found and landed this job in Earl Stadtman's [Dr. Earl Stadtman] lab in Building 3.

Hohman: That's also an interesting story. I've been really lucky throughout my career and often seemed to be in the right place at the right time. I was a senior at Penn State. I had never heard of NIH, don’t forget, this was back in the days before the internet. We had a two-liter fermenter for growing up bacteria that I ran a couple times. This was all before molecular biology, so there was no cloning and over-producing proteins – therefore we needed lots of bacteria for doing whatever anyone in the lab wanted to do. I was graduating from Penn State with an undergraduate degree in Microbiology. I applied to the Ph.D. program University of Hawaii in Medical Microbiology, and I was accepted with full support. My future was set. I was graduating from Penn State in March, and my plan was to stay at Penn State over the summer, because living at Penn State without needing to go to classes is like living in a country club. They have pools, tennis courts, two golf courses and lots of bars. I was planning to stay at Penn State over the summer and then go to Hawaii in the fall to graduate school. But lo and behold, just before I graduated, a professor from the micro department came back from a trip and said, "I was at NIH. They're looking for somebody to run a fermenter. Since you have some experience, do you want to apply for the job?" I said, "No." I wanted to play at Penn State and then go to Hawaii. But then I said, "Well, where is NIH?" He said, "It's down in Bethesda, Maryland."

My sister is three years older than I am, and she was a schoolteacher working in College Park. I didn't have any money then, but I thought that I could go down to Bethesda and spend a day or two with her if I took this interview. So, I came down for my interview in Dr. Stadtman’s lab. Mike Poston [Dr. J. Michael Poston] was the scientist running the lab, and I interviewed with him. That was the best interview I've ever had, because I was really relaxed since I didn't want the job.

He showed me the fermenter that they had, which was a 500-liter behemoth – I was used to a 2-liter fermenter. Not only was it huge but it obviously had been put together by a plumber, not the fancy computer-controlled instruments we have now. There were at least twenty valves you had to open and shut in the right order to get this thing running. Mike asked me, “What do you think of that?” I said, "No problem - a piece of cake."

I immediately forgot about the interview and enjoyed the weekend with my sister. The next week they called and said, "You got the job." Well, damn, I didn't want the job. But I took it anyway. Also, I really didn't know anything about running this big fermenter. I thought I'd work in the Stadtman lab for the summer and then leave, but I never quite got around to leaving.

Harden: Why not?

Hohman: I started in March 1975. Earl's lab was really exciting, and it was an awesome place to work. His decades work on glutamine synthetase was in full swing and there were lots of really smart people in the lab doing very interesting research. So, I liked D.C. and NIH – and loved the Stadtman lab. One day over the summer I went to Earl and asked, "Is there any chance I can go to graduate school while I'm working here?" He said, "No, not really, there’s no mechanism to do that." And I said, "Well, okay, in that case I'm going to be leaving in the fall." And he said, "Well, let me see." As it turned out, Earl was on the faculty at University of Maryland and taught a course in bacterial metabolism. They let him have a graduate student, so I was able to take courses at Maryland and do my research with Earl. At the time NIH didn’t have a mechanism for dealing with graduate students and I was Earl’s first.

Harden: And you could also continue running the fermenter.

Hohman: Yes. I took courses during the day at Maryland and ran the fermenter during the evening. When my classes were completed, I conducted my thesis research with Earl at the NIH.

Harden: You also worked with a number of other investigators in his lab. I'm thinking of Sue Goo Rhee [Dr. Sue Goo Rhee] and, and Terry Stadtman [Dr. Thressa C. Stadtman] as well. What did you do with them?

Hohman: Earl was studying glutamine synthetase. Sue Goo Rhee was studying the other enzymes of the glutamine synthetase cascade. I would grow up one or two 500-liter batches of *E. coli* a week. Once a week, Earl's technician Polly Smyrniotis [Pauline Smyrniotis] and I would purify glutamine synthetase. We would start with anywhere from three to six kilos of frozen *E. coli* paste. We would purify the glutamine synthetase, and then we'd give the rest of the extract to Sue Goo Rhee, who purified the other enzymes in the cascade.

Harden: After two years, while you were enrolled at the University of Maryland to get your Ph.D., you added a biochemistry to your focus on microbiology and immunology. In his own oral history, Earl Stadtman said that your Ph.D. work, "made a rather significant contribution to the field of immunochemistry and polymeric 2 enzymes." Would you talk about this work?

Hohman: The Stadtman lab was a very physically oriented, biochemistry lab. There was Sue Goo Rhee, Charles Wang [Dr. Charles Wang] and Boon Chock [Dr. P. Boon Chock], who were studying the kinetics of the glutamine synthetase cascade. Ann Ginsburg [Dr. Ann Ginsburg] was studying the physical chemical properties of the enzyme. Andy Shrake [Dr. Andrew Shrake] was a postdoc in Ann's lab and is largely responsible for my passing my physical chemistry course at Maryland. Rod Levine [Dr. Rodney L. Levine] joined the Earl's lab a couple of years later. Rod and I ended up sharing the lab for a brief period.

I was interested in immunology, so I wanted an immunological focus to my thesis project. However, since the investigators in Earl's lab were physical chemists and biochemists, there was no one in the lab that could mentor me in immunology. I looked up and searched out Henry Metzger [Dr. Henry Metzger], a world-renowned immunologist who was just a couple of buildings away on the NIH campus. I explained the situation and asked him if he would be willing to take me under his wing and help with my thesis project. Henry told me he would be happy to help, and we started what turned out to be a very important (for me) relationship. Many people focus on the budgets and availability of state-of-the-art research resources when they talk about the advantages of working at the NIH. While this is true, I believe the true value of working at the NIH is the large number of really smart scientists with very interesting research questions. In addition, most everyone at NIH is very collaborative and loves to share ideas and expertise. I was extremely lucky to have two of the best mentors at NIH during my training – Earl Stadtman and Henry Metzger.

Earl and I came up with this idea to make antibody against AMP [adenosine monophosphate], the post-translational modification that regulated GS [glutamine synthetase] catalytic activity. Glutamine synthetase is made up of twelve identical subunits. Each one may or may not have an AMP group attached to a specific tyrosine residue. Hence, each molecule of glutamine synthetase has from zero to twelve AMP moieties, called the state of adenylylation. We would adjust the state of adenylylation of the enzyme by controlling the growth conditions of the *E. coli* in the 500-liter fermenter. By controlling the source and concentration of nitrogen in the growth medium, we control the state of adenylylation of the enzyme. However, that was a crude way of controlling the state of adenylylation and didn't always work as we wanted, in which case we'd end up with 500 liters of *E. coli* with the wrong state of adenylylation. I chemically coupled AMP to BSA [*bovine serum albumin]* and used that as an immunogen to make antibodies in sheep against AMP. The antibodies had a high affinity for the AMP moiety of adenylylated GS but did not recognize glutamate synthetase at all. With Henry Metzger's help, we conducted some immunochemical studies on adenylylated GS.

In addition, we used the antibodies to fractionate glutamine synthetase based on its state of adenylation. This allowed other investigators in the lab to study a GS preparation with a more tightly defined state of adenylylation.

Harden: When you received your Ph.D. in 1982, you went to the Institut Pasteur in Paris for two years as a postdoc. I have several questions for you about this period. To begin with, why did you choose the Institut Pasteur?

Hohman: This is how I got to Institut Pasteur: as I was finishing up my Ph.D. in Earl Statman's lab, Georges Cohen [Dr. Georges N. Cohen] was a world renowned biochemist and worked in France at the Institut Pasteur. He and Earl Statman were close colleagues and friends, and in fact Earl's interest in nitrogen metabolism (i.e. glutamine synthetase) began when Earl spent a sabbatical in Georges lab at the Institut Pasteur some years earlier. Georges was working on aspartokinase / homoserine dehydrogenase, which is one protein with two enzymatic activities that catalyze two consecutive steps in a reaction chain. Earl's work while in Paris got him interested in nitrogen metabolism. When Earl came back to NIH, he wanted to work on nitrogen metabolism but did not want to directly compete with Georges. He ended up working on glutamate synthetase. Earl tells the fascinating story of the early days of glutamine synthetase that deserves to be read [Earl R. Stadtman, "The Story of Glutamate Synthetase Regulation," *Journal of Biological Chemistry* 276 (2001): 44357-64].

While I was at NIH working on my Ph.D., I'd see all the foreign postdocs who would come and live here for a couple of years and I thought, "Oh, I'd really liked to do that." As I was finishing up my Ph.D., Georges Cohen, who was a Fogarty Scholar, came to the NIH for a 6-month sabbatical in Earl's lab. I worked with him, and we got to know each other. Before he left, he asked me what I was planning to do after I graduated. I said, "I want to go to a foreign country to do a postdoc. I don't care where, but it has to be someplace they don't speak English because I want the whole experience." He said, "How about Paris?" There were certainly worse places to go! That's how I got to go to Paris.

When I got there in 1982, I couldn't speak a word of French. I figured I'd learn French just like the way people from other countries learn English, immersed in the language. In the lab, I worked for Michel Veron [Dr. Michel Veron]. Michel, who had been a student of Georges, was starting up his own lab with his graduate student Jean de Gunzburg [Dr. Jean de Gunzburg], and me. These guys were both French, but they spoke English as well as I did. I liked talking too much to speak French if they could understand my English, so we spoke English all the time in the lab. About once a week they'd say, "We're not being fair to Bob. He's not learning a word of French," which I wasn't. They would then say, "We're going to speak French." They'd start talking in French and I'd ignore them. After five minutes or so, they would back to English. After four months, I still could not speak a word of French which I realized wasn't ideal so I enrolled in *Alliance Française* for a couple months, and I got to the point where I could speak a little bit of French. In order to learn to speak a new language, you have to get over this fear of sounding stupid, which luckily happened rather quickly with me. I was then able to make progress.

Harden: French is hard.

Hohman: French is hard, and I'm not very good at languages. But what I did once I started learning a little bit was to get on a train and go out of town, out of Paris a couple of hours, because too many people in Paris speak English. So on weekends, I would get on the train and just go for the day and try to speak French.

I need to take a second and give a shout-out to the French. They get a bad rap for pretending not to understand Americans speaking French unless it's spoken with a perfect accent. When I speak French, to my ear I have a perfect accent. However, when I listen to a recording of me speaking French, my accent is quite horrendous. I can be speaking French to my good French friends with my "perfect" accent and they really can't understand. All the time I was in France learning the language people, for the most part, tried really hard to understand me.

A good example of this was when I almost got myself into big trouble while trying to use my newly acquired French in the lab. Jean de Gunzburg [Dr. Jean de Gunzburg], the graduate student in the lab, was working on a project with Nicole Guiso [Dr. Nicole Guiso], a researcher in another lab down the hall. Part of the project was making antibodies in a rabbit, which Jean was doing. He left on vacation for a couple of days and told me that he told the animal caretaker to contact me if anything came up with the rabbit. As luck would have it, the rabbit died, and the caretaker asked me what he should do. I walked down the hall into Nicole's lab and in my perfect French said, "Jean's rabbit died." There were five or six people working in the lab and there was a collective gasp of surprise and horror. Nicole said, "OH MY GOD, THAT'S TERRIBLE." I said "yes, it's sad but these things happen and it's no big deal. We can deal with it later when you're not busy– no big hurry". It was then I noticed everyone looking at me rather strangely and seemed very disturbed by my attitude. I shrugged and went back to my lab to continue working. About 10 min later Nicole, came down laughing and told me everyone thought I said, "Jean's father died" rather than "Jean's rabbit died", and they were most put off by my cavalier and totally uncaring attitude I showed over the death of Jean's "father."

Harden: Ultimately, you became fluent in French.

Hohman: Ultimately, I became fluent, but that was mostly after I met my wife and we moved back to the US.

Harden: Tell me about meeting your wife. I think she was also a scientist—a geneticist maybe?

Hohman: Yes. Marie-Christine was a graduate student studying the molecular biology of blue-green algae. After I was at the Institut Pasteur about 6 months, I came in from lunch one day and found a young French woman putting her samples in my freezer. She left, and I asked my boss, Michel, "Who's that?" He said, "That's Marie-Christine Rebiere [Dr. Marie-Christine Rebiere Hohman]. She works down the hall with Madame Stanier. Her freezer died and I told her she could store samples in your freezer." It was a big, long hall. There are three labs. There was mine, and then another, and then Madame Stanier's. I started scoping out where Marie-Christine was working. She didn't like me at first, so I tried to be nice. One day, I had an American friend visiting me. We were in the hall talking and she walked by. I said, "Hi." She just kept walking, and I said to the guy, "I'm going to end up marrying her." And he said, "Well, you've got your work cut out for you."

One day, after a couple months of trying to be nice, when she walked past me, I said, "Hi, M. C." M. C. for Marie-Christine. Many French people have two names and the French absolutely do NOT use nicknames. She said, "What did you call me?" I said, "I called you M.C." She said, "My name is Marie-Christine." And I said, "Well, that's too hard for me to pronounce (it really is), so from now on you're M. C." She stomped off, but that at least got her to notice me.

Harden: You eventually won her heart and hand.

Hohman: Right. We came back to the U.S. in 1984. She worked at NIH for a couple of years as a postdoc with Tom Kindt [Dr. Thomas Kindt]. And the rest is history. We got married and have three boys.

Harden: I believe the first one arrived around 1988.

Hohman: That's correct. His name is Julien.

Harden: Now, before we get to your work at Institut Pasteur, I noticed that you were there in 1982, '83, '84, at the beginning of the HIV AIDS epidemic. Luc Montagnier's lab at the Institut Pasteur was working on the cause of AIDS. My question is, were you aware that this was going on? Did you know any of the people in Montagnier's lab and what they were doing? And if so, could you comment on it?

Hohman: I didn't know any of them. I arrived in Paris March 1982, and I heard about AIDS by the end of 1982 or early '83. I received a letter from a friend in the states who was working in office in DC. She said, "I don't know if you've heard but there's a disease that men are getting—really healthy men who get sick and die, and we have no idea what it is. I have a guy in my office. It just happened to him." That was the beginning of AIDS, at least from what I heard. But at the time, I wasn't aware of it enough to know who was working on it. I also didn't read French, so it took me awhile to catch on.

Harden: But there wasn't a lot of talk.

Hohman: There was talk but remember, I didn't speak French, so I spent most of my time focusing on my research and enjoying Paris. There is a lot to enjoy in Paris.

Harden: Let's come back now to your own work. Tell me about your personal research during this time in Paris.

Hohman: Michel Veron, my boss, was studying various aspects of cellular differentiation in in the slime mold *Dictyostelium discoideum*. It's an amoeba, a single-cell eukaryotic organism, and it normally lives in the forest and feeds on bacteria and decaying organic matter on the forest floor. This unicellular growth phase lasts as long as conditions are favorable. However, when amoebae run out of food, they become "aggregation competent" and one of them gives off a pulse of cyclic AMP (cAMP), which acts as a chemoattractant. Neighboring amoebae sense this signal and migrate up the gradient of chemoattractant; they then give off their own pulse of cyclic AMP and momentarily become refractory to the attractant. As the amoeba collect at the site of the original pulse they coalesce into a multicellular "slug" containing between 10^5 and 10^6 amoebae. The slug is capable of migrating as one multicellular species. Eventually the cells of the slug differentiate into either pre-stalk or pre-spore cells and form a small fruiting body consisting of spore cells on top of stalk cells. The spore cells are resistant to adverse environmental conditions and germinate into new amoeba when conditions improve. *Dict yostelium discoideum* is thus a simplified model system for studying cellular differentiation.

Harden: Interesting.

Hohman: Prior to my arrival in the lab, Jean de Gunzburg extracted the protein from the ameobe and identified three cAMP binding proteins. My project was to pick one of the proteins, purify it to homogeneity, identify its function and characterize the protein. My protein ended up being s-adenodyl-l-homocystein hydrolase which I purified and characterized. My experience at the Institut Pasteur proved to be invaluable from a scientific, personal, and cultural perspective. I encourage all young people coming through the lab to consider working abroad if at all possible.

Harden: In 1984, you returned to NIH for a second postdoc with Henry Metzger in his Chemical Immunology Section, in what was then the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases. In 1986, that Institute split into two, and Dr. Metzger's section came under the new National Institute of Arthritis and Musculoskeletal and Skin Diseases, and he also served as Scientific Director for the Institute. Would you comment on Dr. Metzger and his philosophy of science during a time when there was a considerable disagreement between whether you should emphasize basic research or applied research?

Hohman: Like I said, I was really lucky at this early stage in my career to have two of the best mentors ever at NIH, Earl Stadtman and Henry Metzger. They were both very similar, in that they believed that it was very important to be rigorous. One way to achieve this was to design experiments that would *disprove* your hypothesis rather than only conducting experiments to prove it. Henry was somebody who if, for example, published something and two years later, somebody published a paper that didn't agree with his findings, he would call the person to try to figure out how they could resolve the different interpretations. Henry was an M.D., but he hadn't done any clinical work for a long time. His interest was IgE receptor signaling on mast cells. Pretty much everybody in his lab was doing basic research on IgE receptors. At the time I was in the lab, Henry's time was completely taken by basic research. Earl Stadtman's lab was similarly focused on basic research.

Back then, the pharmaceutical/biotechnology industry was just starting to become respectable. Many scientists at NIH were under the impression that R&D or applied research was for scientists who couldn't land an academic position.

Harden: Would you expand on your work on the IgE receptor?

Hohman: It was known that mast cells are triggered to release histamine and other mediators of allergy when IgE receptors on the cell surface bind to an allergen, thus resulting in aggregation of the IgE receptor on the cell surface. Any method for aggregating cell-surface IgE receptors, including antibody against the receptor, is necessary and sufficient to activate the mast cell. Henry Metzger was interested in studying the mechanism by which aggregation of IgE receptors on the surface of mast cells results in activation of the cell with release of mediators such as histamine. What Henry really wanted was a cell-free preparation, a membrane preparation, with IgE receptors so that he could aggregate the receptors and study initiation events, in other words, what is the very first step in the activation process.

Henry was convinced that the best (and maybe only) way to accomplish this was to develop a cell-free system for studying the very first steps in mast cell activation in a synthetic membrane preparation. Many people had tried for a long time to develop such a system but had no luck. Henry didn't give up easily, so he had a large portion of his lab working on the problem. I arrived to the lab about the same time an M.D-Ph.D. named Steve Dreskin [Dr. Stephen C. Dreskin] was doing a fellowship, and we both decided to try to develop a cell-free receptor preparation that exhibited the first steps in mast cell activation when the IgE receptors were activated. As a first step, we decided to try to develop a simplified mast cell preparation. We took two different approaches. I purified a protein called alpha toxin from *Staphylococcus aureus*. This toxin would poke holes in the cells large enough to allow free exchange of small molecules between the buffer in which the cells were suspended and cellular cytoplasm, but small enough for the cell to retain all of its proteins. These preparations underwent one of the earliest events in activation, hydrolysis of membrane phospholipids. By the time I completed my postdoc, I had published the purification protocol for alpha toxin and conditions for optimal permeabilization and began to characterize factors influencing IgE receptor-mediated activation of the permeabilized cells.

Steve Dreskin worked on another system called cytoplasts. He developed a system using cytochalasin B to produce small membrane vesicles surrounding cytoplasm. These cytoplasts, when activated by aggregating IgE receptors, hydrolyzed membrane phospholipids similar to intact cells. By the time his fellowship was finished, Steve had produced and characterized a truly cell-free system for studying receptor-mediated activation.

The three years I worked with Henry were awesome. Henry had many of the same attributes as Earl Stadtman: They both loved science, training the next generation of scientists, and doing everything possible to make sure their trainees were successful. This attitude is reflected in the relationship between Steve Dreskin and me. In effect, we were competing with each other to achieve Henry's Holy Grail – to develop a cell-free system for studying receptor-mediated activation of mast cells. In other labs, this could lead to unproductive conflict, but in Henry's lab it was natural for Steve and me to work closely together and help each other out. Steve Dreskin and I remain close personally and professionally to this day, over 35 years later.

Harden: In 1987, you accepted a position as a special expert in Mike Kaliner's [Dr. Michael A. Kaliner] Allergic Diseases Section in the NIAID Laboratory of Clinical Investigation, and you stayed until 1992. Tell me about your research there.

Hohman: Basically, I continued the same research that I started with Henry. Mike was an M.D. He and Dean Metcalf [Dr. Dean P. Metcalf] ran the Allergy-Immunology training program. Mike and Dean had lots of clinical fellows coming in for the research part of their fellowship, and what Mike wanted was a basic research person to help interface with the M.D.s, to help them with their research. That was me. But I also continued my own work on receptor mediated activation of mast cells.

Harden: Okay. How was it working with the young M.D.s? Did you have to teach them a lot about the science?

Hohman: These folks were really, really smart. They had not had much research training, but they were smart, hardworking, and they caught on very quickly. It was a lot of fun working with them. One of my fondest experiences was the opportunity to work with Prescott Atkinson [Dr. T. *Prescott Atkinson],* who was assigned to work directly with me on my research projects. Prescott was a really interesting character. When he was younger, Prescott was in the Navy and flew Orion P3 sub hunters. This was during the height of the Cold War, and the U.S. would use these big, 4-engine propeller planes to track Soviet subs. As you can imagine, Prescott has many stories from back then. After his discharge, Prescott went on to get a M.D., Ph.D. and was accepted into NIAID's Allergy/Immunology training program. Prescott had a very successful career at the NIH and went on to the University of Alabama and is currently a professor there. We have stayed in close contact over the years. One more fun-fact about Prescott, he is an avid amateur fossil-hunter and has specimens displayed in museums in the US.

Harden: And it goes the other way to a certain extent. I mean, you may not have had clinical training, but as a really smart person, you had learned a fair amount of medicine.

Hohman: As I mentioned before, the best thing about NIH is that there are lots of smart people with really cool things going on. Although I have no medical training, it was always fascinating to watch the research being conducted in the labs being translated to clinical research taking place in the NIH Clinical Center. It was also interesting to see how everything becomes much more complicated once you move from the research lab to the clinic.

Harden: Now I'm going to step sideways and observe that in 1988, your first child was born, and the other two were born in '92 and '95. In today's world, there is considerable concern about work life balance. Did becoming a father have any impact at all on your science?

Hohman: Not on my science but on my wife's science. When we first came to NIH in 1984, we were both postdocs working in the lab. When kid number one came along, Julien, we decided that two people in the lab was going to be one to many. She ended up staying home for a couple months with the baby, and then she got a job as a research reviews editor for a scientific journal. It was called the *New Biologist*. When the second child came along, Steven, in 1992, they discontinued the journal, so she got to be a mommy for a while. Number three, Thomas, was born in 1995. Around 1997 Marie-Christine began what turned out to be a very successful tutoring business. Since then, she's been a tutor for math and science, mostly for high school calculus.

Harden: In 1992, you left NIAID to enter the private sector as Director of Biochemistry at Oncor, Inc., a biotech company located in Gaithersburg, Maryland. Would you begin by telling me something about Oncor, and then give me your impressions of how working in the private sector compared with working at NIAID.

Hohman: By 1991, I decided, okay, now I'm a big boy. I've have a kid. It's time to get a real job. I looked around, and I had a couple offers. One was the work with Max Cooper [Dr. Max D. Cooper], at the University of Alabama, where my buddy Prescott worked. I also received an offer at the University of Texas Medical Branch in Galveston. These were both academic positions and awesome opportunities. Then I received a call from Oncor in Gaithersburg, MD. Oncor was started by Steve Turner [Stephen C. Turner], who was the founder of one of the very first biotech companies. In 1976, Steve founded Bethesda Research Lab, BRL. Later, BRL was bought by Dexter Company and then by Life Technologies and then by Invitrogen.

Steve started by selling water saturated phenol. Don't forget, in the mid 70s, we MADE all of our reagents in the lab. The field of molecular biology was just getting off the ground and one of the reagents we needed was water-saturated phenol. Phenol is really nasty, and it's smelly and very dangerous to handle. He started BRL by producing and selling water-saturated phenol, but then restriction enzymes came around in the second half of the 1970s. BRL was one of the first companies that produced and sold restriction enzymes—manufactured them and sold them to academic and biotechnical labs. James Watson, of Watson and Crick, would visit Steve from time to time just to see what he was up to.

After Steve left BRL, he started Oncor. But let's take a step back. Steve wasn't a scientist. He was a music major from Stanford University, and he had perfect pitch and could play any tune or song from memory. Steve could have made a career as a pianist. He had a keyboard and computer at his house and he could play any instrument from this keyboard. He would make multi-track music recordings, playing each instrument from his keyboard. The guy was really, really creative.

When he decided to start a company, he first talked to a professor at Georgetown. He said, "I'd like to start a company. What can I start?" And the professor said, "molecular biology." Remember, there were no such thing in the mid-70s.

After BRL grew and was sold, he started another company, Oncor. He found an academic researcher who had some DNA probes for fluorescence *in situ* hybridization, called FISH. Steve decided that Oncor would be a FISH company. Then he said that it would be really cool to be able to use these probes in a clinic for diagnosing illnesses that normally a cytogeneticist has to perform. We made DNA probes, labelled them with fluorescent molecules. Steve realized that these FISH probes might have commercial potential as a diagnostic tool. In order to get them into the clinic, each one had to pass strict regulatory control from the FDA [U.S. Food and Drug Administration].

I started in '92 when we were still making probes and trying to figure out which one would be the first to take to the FDA. We subsequently decided on a probe for HER2/neu, which is a prognostic marker in breast cancer. Normally, if a woman has breast cancer and the HER2/neu gene is amplified—meaning that you have multiple copies of the gene—that's a poor prognosis. Therefore, HER2/neu provides an independent negative prognosis in breast cancer. However, it is also the target for Herceptin, the breast cancer drug developed around the same time by Genentech. Herceptin only works on breast cancers that are HER2/neu amplified. We were excited as our FISH probe could be used to identify women who would benefit from Herceptin.

Oncor essentially bet the ranch on getting HER2/neu through to the clinic. Oncor was a small company, and this process was complex, time consuming and very costly. And in the meantime, we had to generate some revenue because we were spending tons of money on the clinical program. To help generate cash, I started a Research Products Division. We had developed products for apoptosis and protein oxidation, PCR, DNA methylation and several more. The research products business was profitable and provided some income to support the clinical program. Around 1998 Oncor sold that business to Intergen Company, at the time the world's largest producer of bovine serum albumin (BSA), so they could focus of getting Her2/neu through the FDA. Intergen had relationships with many pharmaceutical and biotechnology companies, but no R&D, and in fact none of their employees had a Ph. D. or similar degree. The idea was to use their contacts to build up sales of our research kits. When Intergen Co. acquired Oncor research products division, they needed to integrate the two companies. I agreed to stay for one year to integrate the two businesses. After the year was up, I was recruited back to NIH.

Harden: As you were rising through Oncor and into administration as Vice President for Research and Development, I wondered if your French connection from your time at the Institut Pasteur helped in the acquisition of Appligene.

Hohman: Appligene. That was a really good story. Steve Turner, the CEO of Oncor, was looking to get a foothold in Europe so they could sell our products, and we could sell their products here in the US. There was a small research products company in Strasbourg, France, called Appligene, and he thought maybe we should buy it. In 1994, he was scheduled to go over to meet with the management of the company and the bankers from Paris that were helping fund Appligene. About two days before he was to leave, he said, "Oh, geez, I can't go. Can you go for me?" I said, "Sure, I'll go, but tell them it's me coming and not you because they're expecting the CEO." He said, "Sure, no problem. I'll tell them." But he never told them.

I arrived in their office in Strasbourg, France, a Tuesday morning, bright and early. There was a conference room, and there were three or four senior managers from Appligene and three bankers who had come all the way from Paris to meet the Oncor CEO. Strasbourg was a four-hour train ride from Paris. When I walked in, they said they could speak some English and then said, "Hello Mr. Turner. So happy you came all the way over here to see us." And I thought, "Uh, oh." Then I said (in English), "So Mr. Turner didn't tell you? I'm Bob Hohman, the vice president for R&D. Steve Turner couldn't make it."

They all became very angry and started talking to each other in a very agitated French. They were saying things like, "Who does this guy think he is? We came here to speak with the CEO, NOT him." I let them go for a while and let them continue to say unkind things about Steve, about me, and about Oncor. And then I started speaking in fairly good French. They stopped and they said, "Did you understand us?" I said, "Uh huh." And one person said, "Why didn't you tell us?" I said, "I was having way too much fun." Then we got to be friends, and we ended up purchasing Appligene. Since I was the only one at Oncor who spoke French, I spent about one week a month there in 1995, the year kid number three was born.

Appligene was an awesome experience for me and I really enjoyed all of the trips I got to take to France. Once I even got to fly over on the Concord which was an out-of-this-world experience. Several years after we purchased Appligene, we took the company public on the French stock market. I got to talk up the company to French investors, which was quite a challenge given my proficiency, or lack thereof, in formal French. Since I learned French "on the job" it was every-day conversational and not formal. However, I wouldn't have given it up for anything.

Harden: You talked about how Oncor Research Products was bought and became Intergen, at which point you became Vice President and General Manager in order to help them get themselves up and running through the transition. But then you decided to come back to NIH. Tell me about this transition.

Hohman: After a year with Intergen, I decided it was time to move on and decided that I should maybe look around for another job. I was in my late 40s and thought it was a good time for one more transition. One day, when I was unhappy about something at Intergen, I saw the ad for the Chief of the Research Technologies Branch at NIH, and I applied. As you know, job searches at the NIH tend to take a lot of time and it took several months for NIH to get back to me. By then, I had cooled off and almost refused the interview. I finally decided to take the interview and it started really well. I really didn't want the job, so I was very relaxed – much like my first interview at NIH when I was graduating from college. As the interview progressed, I realized that they were talking about an awesome job and then I had to scramble to show my enthusiasm. I ultimately was offered the job and was fortunate to spend 20 years in one of the best jobs at the NIH. During this time, I had 4 Scientific Directors, Dr. Thomas Kindt, Dr. Kathy Zoon, Dr. Hugh Auchincloss (who was Dr. Fauci's Principal Deputy Director and was the Acting Director of the DIR after Dr. Zoon retired) and Dr. Steve Holland.

Harden: But they brought you in, if I understand correctly, as the Associate Intramural Director for the Development of Research Technologies as well as the Chief of the Research Technologies Branch (RTB). They obviously thought very highly of you.

Hohman: The job has two main responsibilities, managing the Research Technologies Branch (RTB) and helping the DIR [Division of Intramural Research] evaluate and access new enabling technologies. I was lucky that during my time at Oncor I was able to comprehend the difference between basic research and applied/R&D type research. I learned at Oncor that it was critical to hire a particular type people for R&D. Being located in Gaithersburg so close to the NIH, I received many job applications from postdocs looking for a position in Biotech. It took me a couple of mistakes with hiring decisions at Oncor to realize that we could have a really talented scientist who was great at doing research but that he or she would not do so well in a R&D setting. This is because when you're doing research, there is the excitement that makes you want to design an experiment, run it, analyze it, and go wherever those results take you. But when you're doing R&D in a company, you can't go forward from wherever you are. You must go backward from an end point. You goal is to develop a particular kit or test, and if something really cool happens, you can't go off and study it because that's not the goal. Some people really enjoy doing R&D, and some people don't. At Oncor, I got pretty good at figuring out who was going to work out in a R&D environment. Working in the Research Technologies Branch at NIH is more like working in a R&D outfit, because it's applied research. Your job is to help people get their job done, not to do your own research.

Harden: That is especially interesting to me because it was also the philosophy of Bob Bowman [Dr. Robert Bowman] in his Laboratory of Technical Development [1949-1994] in the National Heart, Lung, and Blood Institute [NHLBI]. He really wanted to help people do their research, not do his own, and that was most unusual to many people.

Hohman: It is unusual. The people now in the Research Technologies Branch, instead of learning everything there is to know about, say, Ebola as a biological system, they learn everything, for example, about electron microscopy. These days, technology is complicated enough that we really need people who are dedicated to individual technologies. And I will add that there are some people at academic institutions like NIH who will say that if you're really good, you will be a PI [Principal Investigator] running your own lab, and anything else is second, third, or fourth class. Some scientists say that in order to get somebody who's good at working on a technology, they will also have to be doing their own research or else they're not going to be any good. That's so wrong. The people in the RTB are very smart, capable scientists. They just enjoy working on a specific technology and developing new applications as opposed to basic biomedical research. The fact is, a successful institution needs a diversity of talented scientists.

Harden: When you first arrived back at NIH, what were your goals for the Research Technologies Branch and for technology in general at NIAID?

Hohman: Back in 2000, when I started, the RTB consisted of several sections including flow cytometry, confocal microscopy, and protein chemistry, and they all reported directly to the Scientific Director, Dr. Thomas Kindt. He realized that to be successful, the RTB needed to be clear on its mission, have access to the state-of-the-art technologies needed to conduct cutting-edge research, recruit and retain highly skilled scientists to transform new enabling technologies into applications useful to investigators, and dedicated management that could be held responsible for making it happen.

Dr. Kindt was willing to dedicate resources to making this happen, and I thought it would be an exciting challenge. Just to brag a little, the RTB has gone through three reviews from the NIAID Board of Scientific Counselors (BSC) and we have received a rating of "Outstanding" (the highest possible rating) each time.

Harden: Your branch expanded from those sixteen people to sixty. What spurred this rapid growth, and what sort of skills did you need in your expanding workforce?

Hohman: The size and scope of the intramural program grew, and new enabling technologies were developed. For example, when we started the RTB in 2000, the first human genome was still being sequenced. The first one took 13 years and cost three billion dollars. We now can sequence a human genome in a week for several thousand dollars. There have been similar advances in other technologies including light and electron microscopes, flow cytometry, mass spectrometry, data science, and information technology. These advances have spurred the development of applications that allow us to do things we couldn't have imagined 20 years ago. These technologies require very complex and expensive instrumentation, and even more importantly, talented scientists to turn these technologies into applications for investigators.

A good example of how the RTB grew is our confocal microscopy facility. In 1999 the RTB purchased a confocal microscope (Leica SP1) and hired Owen Schwartz [Dr. Owen M. Schwartz], an experienced scientist, to operate it. Back then, the state-of-the-art with confocal microscopes was using fixed tissue and imaging with two colors. Fast forward to today. The facility has five Ph.D.-level scientists, one dedicated solely to image processing and analysis – eight confocal scopes and a variety of other microscopy systems. In addition to the scopes, the facility has four advanced workstations for image analysis. Rather than simply imaging fixed samples in two colors, we now can image live animals in multiple colors. We can also quantify the movement of individual cells in living tissue. These advances in applications are due to advances in a number of fields including lasers, optics and computing power.

We also experienced considerable growth when we started the RML Technologies Section (RTS) around 2005, which at the time consisted of facilities for EM, genomics, and flow cytometry. The genesis of the EM facility was a PI, Claude Garon [Dr. Claude F. Garon], whose research was based on EM analyses. He had a couple people working with him. Another PI, Jim Musser [Dr. James Musser], started a small genomics facility in his lab in the early 2000s. Around 2005, Claude retired and Jim left the NIH, and we decided to incorporate the two groups into the RTB so all DIR PIs could have access to this technology. While we were at it, we added Aaron Carmody [Aaron B. Carmody] to the RTS to provide access to flow cytometry technology. Lastly, several years ago we incorporated the Visual and Medical Arts Unit (VMA), run by Anita Mora [Anita Mora], into the RTS. Incorporating the VMA into the RTB proved to be a great move. Their main function is to communicate very complex research through image and video communication, and Anita and her group are second to none in their ability to communicate complicated scientific concepts. The RTS has proven to be a very wise investment and provides critical technologies not only to RML PIs but the entire DIR.

Harden: Right. I recall that there was an electron microscopist involved at RML back in the ’80s when Willy Burgdorfer [Dr. Willy Burgdorfer] was working on Lyme disease. His name was Alan Barbour [Dr. Alan G. Barbour].

Hohman: RML has always been at the forefront of EM. Currently at RML, Beth Fisher [Elizabeth R. Fischer] runs the EM facility with state-of-the-art SEMs and TEMs. We had one of the first cryo-EM [cryogenic electron microscope] systems in the country and have just received approval to purchase a second one. Cryo-EM technology has revolutionized the field of structural biology and now investigators can have structural information at a resolution that rivals Xray diffraction in a fraction of the time. In fact, the discoverers of cryo-EM recently received the Nobel Prize in Chemistry in 2017

Harden: Before we go back to RML, tell me about how your division supported NIAID’s biodefense research initiatives.

Hohman: As part of the country’s response to the Anthrax attacks following the terrorist attacks in 2001, NIAID decided to construct two laboratories dedicated to research on biodefense and emerging and reemerging diseases. When Building 33 [Building 33 is the C. W. “Bill” Young Center for developing new and improved diagnostics, vaccines, and treatments for diseases caused by infectious agents that may intentionally be released into civilian populations] opened in 2006, we outfitted it with a multi-photon confocal microscope and a cell sorter inside a BSL-3 [Biosafety level 3] laboratory. There are very few such installations anywhere. We had to solve a number of technical, physical and safety issues but reasoned that the “Infectious Disease” institute really should have these resources available in a high-containment laboratory. These instruments have proven to be especially useful during the current COVID-19 pandemic. The same time NIAID was constructing Bldg. 33 in Bethesda, we built a BSL-4 facility at RML and outfitted it with a couple of flow cytometers. Aaron Carmody, who provides access to flow cytometry technology at RML, is qualified to work in the BSL-4 lab and operates the instruments. It is difficult to get the service technicians from the companies that make these instruments to enter the BSL-4 lab, so when something breaks, Aaron gets instructions from the vendors and then fixes the problem. He’s getting quite good at making the repairs.

Harden: I did not realize that RML had a BSL-4.

Hohman: The BLS-4 was authorized after the 9/11 attacks as part of NIAID’s Biodefense program. In addition, RML has BSL-3 laboratories. Speaking of biodefense, various RTB personnel have clearance to work on select biological agents that may pose a serious threat to the public, livestock, or crops. If an emergency should present itself, RTB staff can drop what they're doing and work with the experts on the organism and ensure that investigators have access to state-of-the-art technologies in high-containment facilities including flow cytometry, electron microscopy, confocal microscopy or genomics for whatever should be needed. Therefore, while providing enabling technologies every day, RTB staff can immediately pivot in the case of a national emergency.

Harden: Wow.

Hohman: And actually, many of the coronavirus pictures you see in the news come from RML. They were taken by Beth Fisher and her group, and then they were colorized by Anita Mora and her group in the RTB’s Visual and Medical Arts unit at RML.

Harden: Tell me more about establishing the Research Technologies Branch at RML, especially the challenges of guiding it through what was apparently a turbulent change in senior management.

Hohman: There was turbulence, but I can’t talk about the details. RTB had four units at RML at the time; genomics, electron microscopy, flow cytometry and visual and medical arts. We were forced to make some management changes, which was especially challenging given that I was based in Maryland. Thanks to the character of the Section leaders and everyone in the RTS, the group pulled together and the RTS is now much stronger than ever.

Harden: You developed a web-based portal first at NIAID called myRTB.gov. And then you wrote an open-source version called LabShare [LabShare.nih.gov] so that other NIH institutes could use it. I looked at myRTB.gov, and I was impressed at how easy it was to use for someone new to it—my definition of a great site! Tell me about developing it and how much it's used.

Hohman: First of all, it was developed under my watch, but the work was done by some very talented software developers in collaboration with many people in the RTB. Twenty years ago, when we started the RTB, the total number of RTB staff was much smaller than today – around 14. The head of each section managed the logistics of their section however they wanted. For example, Owen Schwartz, Chief of the Light Microscopy Section, had one person (Owen) and one scope. He had a paper notebook and investigators would write down their name to reserve the scope. Owen's group now includes 5 Ph.D.-level scientists, 8 confocal and 8 wide field microscopes. Clearly, he needs something more than a notebook for managing the section.

Kevin Holmes [Dr. Kevin L. Holmes], who ran the flow cytometry group, is another example. The flow cytometry group has always been one of the most heavily used. Kevin had a rudimentary app for scheduling time. I called it the "Rolling Stones concert ticket model" for making reservations. Every Tuesday at 9:00 am, investigators would call to reserve scopes two weeks ahead of time and it was first come, first serve. If people got stuck in traffic and arrived at their phones a couple minutes late, all the reservations would be already filled causing much stress and anxiety. Once again, when the RTB was small this was almost workable, but as we grew, we clearly needed another solution.

By the early 2000s, we realized that a flexible system was needed to manage all functions of the Branch including appointments, requests, communications, data storage, and billing. It was a complex problem as each section of the RTB is quite different and therefore has its own specific requirements for managing the section. Some sections, like genomics, electron microscopy and mass spectrometry, are project or sample-based while others, like confocal microscopy and flow, are appointment-based. Therefore, whatever we developed had to be flexible enough to handle this diversity. We conducted a survey of available solutions, and there was nothing available that was suitable for our needs, so we decided to develop a flexible, custom solution and called it MyRTB. We have been developing, evolving, and updating MyRTB over the past 15 years or so and it now is an integral part of the Branch.

Back in 2005, when we were equipping Bldg. 31, I began a very fruitful collaboration with Sam Michael [Samuel Michael] from NCATS [National Center for Advancing Translational Sciences]. We needed to install a liquid-handling robot inside a BSL3 lab, and since Sam was in charge of automation for NCATS I asked him for help. The system worked very well, and we continued to collaborate until I retired. Sam was an awesome collaborator; he was always anxious to help out, even if there was nothing it for him. He reasoned that we all worked for the NIH and if he could do something to help, he was all in. I got to re-pay the favor several years ago when Sam was looking for a solution to manage their laboratory and administrative functions. Somebody suggested he look at MyRTB and Sam contacted me. Suhas Sharma [Suhas Sharma], the developer in charge of MyRTB and the development team, demonstrated the app to Sam, who decided it was a great platform for managing many facets of NCATS including managing proposals, projects, publications, laboratory instrumentation, supplies, and service contracts. NCATS also uses the system for other functions including assay design and sample management. At the same time, other Institutes began to express an interest of using MyRTB to manage their facilities and we renamed the collaborative development effort to LabShare when it is deployed to non-RTB facilities. Since everyone would have to customize the app to some degree, we wanted to capture everyone's modifications and improvements so we all could benefit. Along with Dr. Hugh Auchincloss [NIAID Deputy Director and Acting Scientific Director] I developed a short Memo of Understanding (MOU) to facilitate the interactions. In addition to NCATS, the MOU was signed by facilities in NCI, NIAMS [National Institute of Arthritis and Musculoskeletal and Skin Diseases] and NEI [National Eye Institute]. Sam Michael was an awesome collaborator, and because of his leadership and active participation we were able to add many new features that are available to any facility at the NIH.

Harden: Is it linked to any of the patient data information in the Clinical Center?

Hohman: No. We are not a CLIA [The Clinical Laboratory Improvement Amendments of 1988] facility. CLIA regulations include federal standards applicable to all U.S. facilities or sites that test human specimens], and therefore our work cannot be used for treatment decisions for patients. Since the vast majority of our work is for basic research, the overhead of becoming CLIA certified is not worth the investment. We do work on patient samples, but only in a research setting.

Harden: Another data sharing program you started was called *projectHEDWIG*. Tell me about it and what it provides.

Hohman: At RML we now have several electron microscopes, including one (soon to be two) cryo-EM systems. These scopes take tens of thousands of pictures and collect over one petabyte (one million gigabytes) of data per year. These photos need to be cataloged, stored, analyzed, and shared with investigators. Some of these data collection experiments will take several days, so you want to be able early on to see if this is working and, if not, you want to shut it down, because the scope is too valuable just be running if you're not getting good data. As with MyRTB/Labshare, Sam Michael and NCATS have been very important collaborator, and imaging scientists from the National Institute of Standards and Technology (NIST) are also collaborating on the project. When completed, project HEDWIG will be available for use by any facility at the NIH.

Harden: You also established an accounting system to provide a transparent view of resource utilization and establish the NIAID Staff Scientist Promotion and Tenure Committee.

Hohman: We track resource utilization through MyRTB. To access any of the resources, the user must "register" with their contact information, name of supervisor and CAN [Common Accounting Number]. When a reservation is completed for an appointment for a microscope or flow cytometer, or a request to run samples for genomic, or mass spec analysis, the requestor's budget is automatically charged a small fee – about 10% of the actual cost. This makes it possible for DIR leadership to see who is using the resources and also to help make decisions on funding, purchasing new instrumentation or adding additional personnel to the RTB.

As for the new Promotion and Tenure (P&T) committee, there are relatively few types of positions for Ph.D.-level scientists at the NIH. The majority are either Principal Investigators (PIs) or Staff Scientists. A PI runs a research program (the NIAID DIR currently has about 120 PIs) and a Staff Scientist works for a single PI and supports their research program. Staff Scientists are recruited, retained, and promoted based on the research they conduct. The P&T [Promotion and Tenure] committee that evaluates Staff Scientists relies primarily on metrics such as the number of first and last author publications in high-quality journals, invitations to speak at national and international meetings and letters of recommendation from scientists in the field who are NOT collaborators. While this works very well for Staff Scientists conducting research, the system is not at all appropriate for scientists involved in R&D-type projects such as vaccine development or scientists in the RTB who provide access to technologies for the entire DIR as opposed to conducting their own research. Shortly after I arrived at the NIH in 2000, I could see that various labs, including the RTB and the VRC [Vaccine Research Center], were having trouble hiring Staff Scientists because a lot of the expertise that we needed came from industry R&D programs, not basic research environments, and therefore candidates didn't have a huge CV.

The NIH didn't have a hiring model appropriate for these individuals. My SD [Scientific Director], Tom Kindt, encouraged me to get together with the DIR's personnel experts to suggest an alternative. We formed a new designation called a Core Staff Scientist. This designation applies to a Ph.D.-level scientist whose job is not performing basic research. Instead, it may be making peptides, operating microscopes, mass spectrometers or running genomics core facilities or writing clinical protocols. We formed a separate committee to evaluate these scientists, and I was the chair of the committee. The committee makes hiring recommendations to the SD and reviews all Core Staff Scientists every four years, just like the standard Staff Scientists. Core Staff Scientists are evaluated on the impact are they having on the DIR's research agenda. Also, Core Staff Scientists tend to work for multiple PIs, so it's a very different set of criteria for revaluating their performance. And letters of recommendation can be from people they work with because we tell Core Staff Scientists, "You're supposed to be working just with the DIR." Therefore, it's not fair to say, "We want you to work only with the DIR, but by the way, you need to get letters from people on the outside." This program has been very successful in that we've been able to recruit scientists with important skills whom we could not reach with other mechanisms. There currently are approximately 40 Core Staff Scientists in the DIR and VRC and they are driving many of the DIR's applied research programs.

Harden: It's interesting that NIH in general is flexible enough to permit this kind of change when many bureaucracies become rigid and aren't able to change.

Hohman: Yes, we were very lucky to have support from the SD and some very good people in the DIR who made a good case to Building One for us to try this new designation. That was over 15 years ago, and the Core Staff Scientist committee is still going strong, and the group of Core Staff Scientists are making very substantial contributions to the DIR.

Harden: What I am hearing you describe is how you were able to rationalize critical resources within the Institute. I assume that you employed a lot of your private sector experience in doing it. Now I want you to tell me about how you began to outsource things, to outsource the generation of transgenic mice, for example.

Hohman: At NIH, lab space is one of the rarest and most precious resources, so it's important to manage space requirements. In addition, outside vendors are constantly springing up that can provide many technologies that previously could only be done in an academic lab. I constantly evaluate the portfolio of our technologies, and in discussion with the section chiefs and PIs we decide what to outsource and what to keep in house. In general, we only run projects in house if we can add value. Added value usually comes in the form of closely working with an investigator to make sure the entire data collection process, from experimental planning to sample preparation to data collection to analysis run smoothly and efficiently. This can be difficult to achieve via outsourcing.

You asked specifically about generating transgenic mice. When I started at the RTB back in 2000, we had a facility for generating transgenic mice up in Fort Detrick, and there were problems. We were spending a lot of money, about $400,000 per year, and PIs were complaining they weren't receiving the mice they asked for. As it turns out, we were generating fewer than 10 mice per year. We just didn't have the right system to make it work. NCI [National Cancer Institute] also had a large, efficient transgenic mouse facility in Fort Detrick and agreed to produce transgenic mice for about $7,000 per mouse. We outsourced the technology to NCI and our backlog soon evaporated. We were able to serve all investigator's needs while at the same time saving considerable money – we spent $70,000 for ten mice from the NCI, compared to $400,000 for operating our own facility.

As for interacting with other Institutes, the NIH Intramural program is large and diverse, and for the most part each Institute develops their own resources that are available only to members of that Institute. There is a constant push to combine all resources so everyone can use them. While this is an admirable idea, the logistics tend to become very complicated. I found over the years that having bilateral relationships is much more effective. As I mentioned before, we've worked very effectively with Sam Michael at NCATS, and we've worked closely with Jim Cherry [Dr. James M. Cherry] at the NCI on a variety of technologies and projects including transgenic mice and technologies that were important to several investigators but not required by enough investigators to warrant the investment by NIAID. We also have very productive bilateral relationships for sharing technology with NHLBI, NIAMS and NIDDK [National Institute of Diabetes and Digestive and Kidney Diseases]. For example, NHLBI has a very expensive (around $1 million) 3D STED [S timulated emission depletion] microscope that we need on occasion. Rather than purchase one ourselves, we give them some money every year to help pay for the service contract and scientists from our Biological Imaging Section have access. Dave Garboczi [Dr. David Garboczi], the chief of our Structural Biology Section, has a similar agreement with NIDDK for using Xray crystallography instrumentation. We help them pay for the service contract on the instrumentation and in return Dave Garboczi and his team have access. We gain access to a million dollars' worth of instrumentation and NIDDK gets help paying for service contracts. Another example is our agreement with NHLBI. The RTB has one of the few Edman sequencing systems on the NIH campus. While Edman sequencing has largely been supplanted by mass spectrometry, there are times when Edman is the only effective technology. The NHLBI has a mass spectrometry setup specifically designed to accurately measure the mass of intact proteins. We have a limited need for determining protein mass and the NHLBI has a limited need for Edman sequencing. Rather than each of us developing our own expensive system, we share these resources. These arrangements not only allow us access to instrumentation but, equally important, allows us to share techniques and best practices. The cost is minimal, and benefit is enormous.

As for other outsourcing opportunities, when it came to knock-out mice, we didn't have the space or the facility or the people to generate knock-out mice here and setting up a facility would have been cost prohibitive. We outsourced the generation of knockout mice to a company in Australia, of all places. We told them the gene we needed knocked-out or knocked-in and they would send us the mice. This was a very long and expensive process and in general took from one to two years to receive the modified mice. Several years ago, a new technology came out, CRISPR-Cas9 [CRISPER= Clustered Regularly Interspaced Short Palindromic Repeats; Cas9= *CRISPR*-associated (Cas) protein 9], which allows us to produce modified mice in months rather than years and we have moved the technology back in house and is now supported by the DIR's Comparative Medicine Branch. Thus, we outsource or insource technologies depending on what makes the most sense in terms of cost and performance.

In another example, several years ago there was a burst of interest in yeast two-hybrid screening. The Scientific Director at the time was Dr. Zoon [Dr. Kathryn C. Zoon]. She asked if we should set up a yeast two-hybrid screening facility. I thought, "Great. We know nothing about that." In addition, we didn' t have the necessary space or instrumentation. As it turns out, Myriad [Myriad Genetics, Inc.] was using the technology for their in-house discovery program. We set up an IDIQ (Indefinite Delivery/Indefinite Quantity – we only pay for what we use) contract, and for about $12,000, they ran the whole experiment and sent us the results, which is much cheaper than what it would have cost if we had to build up a facility and do it ourselves. Equally important, interest in the technology only lasted about two years so we merely did not renew the contract and had no expensive facility to dismantle.

Harden: Since you have had considerable experience with both private sector and federal employment, would you compare the strengths and weaknesses of the way the programs run? And then tell me why you decided in the long run to stay with an NIAID despite all the restrictions that federal employees have to deal with.

Hohman: That's a really interesting question. Some people who work at NIH a long time tend to think NIH is a big, bloated bureaucracy and that institutions on the outside are run much more smoothly and efficiently. I have worked in small companies and in larger companies, and every place has its own set of frustrations. They're not the same frustrations, but they're pretty comparable in degree of frustration. Given the resources and outstanding scientists that we have here at NIH, I've become a lot more patient with some of the nonsense that we have to put up with because there's nonsense everywhere and once you get past it, NIH is an awesome place to work. This is the third time in my career that I've worked at the NIH. The major draw for me is all the smart people who are here and how much they really like working together and the fact that you can get lots done. It's a really exciting place to work.

Harden: Those are all my questions. Are there other things you want to get on the record before we stop?

Hohman: Thanks for asking. I'd like to give a shoutout to the current DIR leadership, specifically the Director, Dr. Steven Holland and the Deputy Director, Dr. Karyl Barron. Running a facility like the RTB is impossible without the strong support of DIR leadership, and Drs. Holland and Barron have been outstanding bosses and mentors. They are both MD-researchers and since I have a Ph.D., their perspective on clinical research has been invaluable. They have always been there when I needed them, and the recent successes of the Branch are due in large part to their involvement. Steve Holland had an appreciation for the role of state-of-the-art technologies in biomedical research and would go out on a limb to approve early-stage technologies that showed promise. In addition, Steve made sure these enabling technologies were available to all DIR investigators, which was made more difficult by the wide geographic distribution of DIR labs, from Bethesda to Hamilton, Montana. Dr. Barron was the Deputy Director for all 20 years I was in the RTB. She knew the DIR better than anyone, was a critical ally and advocate and was invaluable in helping me navigate the intricacies of a large, complex organization. As I reflect on my time running the RTB, I realize even more how important it was having these Steve and Karyl for bosses.

I would also like to mention training. NIH has a very important training mandate and the RTB enjoys the opportunity to train the next generation of scientists. During the summers, we mentor and train very talented high school and college students. Some return for multiple summers. The experience helps the students decide if a career in science is right for them, and it's interesting to see them develop their ideas over the course of the summer. This program is especially important out at RML. Unlike the DC area where there are multiple opportunities to be introduced to biomedical research, the opportunities in the Bitterroot Valley are more limited. Beth Fischer and colleagues at RML have been very productive in launching local kids into very successful careers in biomedical science.

Twenty-three years ago, scientists at RML (Anita Mora, Beth Fischer and Katherine Tilly) began a program called *Biomedical Research After-School Scholars* (BRASS) in the Bitterroot valley. This program was designed to introduce middle school students to the exciting world of biomedical research and consists of five sessions covering hematology, genetics, cancer, infectious diseases, and animal research. Each two-hour session is designed to be highly interactive, with RML scientists providing background on the topic, followed by several hands-on experiments designed to increase the student's understanding of the topic using the scientific method. The program encourages participation by a diverse group of students, particularly minorities, females, and economically disadvantaged students. In addition to being a valuable learning experience for the students, postdocs from RML participate in the program, which provides them with valuable teaching and mentoring experience. The BRASS program has been very successful and has provided the opportunity for local students to pursue a career in science. I can immediately think of two examples.

Bryan Hansen was born and raised in the Bitterroot Valley and participated in BRASS in 1997, which piqued his interest in science. He became a high school student intern at RML in 2003 and enrolled in college in 2004. While in college, he was a summer intern in RML's Electron Microscopy Unit, was mentored by Beth Fischer, and became a post-baccalaureate trainee after graduation. He became a permanent member of the Unit in 2010 and has had a remarkable career. Bryan has become highly skilled in all aspects of electron microscopy from sample preparation to data collection to image analysis. He has also developed considerable computational skills and is interfacing directly with software developers on a highly automated and efficient data processing application. Clearly, none of this would have been possible without the BRASS program and mentoring he received at RML.

Another successful graduate from the BRASS program is Forrest Hoyt. His father was a smoke jumper, and Forrest attended his first few years of elementary school in a one-room schoolhouse in a remote location on the Idaho/Montana border. He eventually moved to Corvallis, with a population less than 800, in the Bitterroot valley not far from RML. Forrest participated in the BRASS program in 2004 and 2005 and became interested in science. He was a high school intern in the EM Unit until he graduated in 2009. After receiving his degree in Biochemistry from Montana State University he returned to the EM Unit as a post-baccalaureate trainee for one year and then enrolled in a Master's program at the University of Glasgow. Upon completing his degree, he returned to the EM Unit and became a permanent member in 2019. Forrest has developed outstanding computational skills and has become the lead microscopist in the field of EM structural biology.

Bryan and Forrest are prime examples of the importance of the training programs at RML. These programs not only provide the opportunity for students to become familiar with biomedical research but also provides the RML with a pipeline of highly skilled and dedicated local scientists. The success stories like Bryan and Forrest require a concerted, coordinated, and long-term training program that starts in middle school and continues through high school, college and graduate school.

The NIAID has another training program called Introduction to NIAID Research Opportunities (INRO), which focuses on underrepresented minorities. The program consists of a three-day introduction to biomedical research conducted at the NIH for highly qualified college and graduate students. The students then have the opportunity to participate in the summer intern program as well as opportunities for post bacs and post docs. The RTB plays a very active role in this program and routinely accepts several students both in Bethesda and RML.

One INRO success stories is Danielle Hewey, a member of the Navajo nation who grew up with her grandparents in New Mexico and slept in a shed without electricity or running water. She graduated from Fort Lewis College in Durango, Colorado, and her advisor encouraged her to spend some time off the reservation. She attended INRO in 2015 and was granted a post bac position in the EM Unit at RML, where in a short time she became a talented microscopist and completed projects for investigators across the DIR. She received a prestigious award for full scholarship and attended physician assistant school in Western Michigan to complete her professional ambitions of providing medical services back to the underserved communities on the Navajo reservation. Danielle currently is back in New Mexico providing health care for the Navajo nation. She gives presentations on her personal career path and general opportunities for college programs targeting Native Americans for pursuits in science at high school, graduate, and professional school levels.

Having labs in Bethesda and RML provides interesting opportunities for trainees. Michael Walker came to the RTB Bethesda in the summer program when he was in high school. He initially thought of majoring in Biomedical Engineering, so we placed him in the confocal microscopy facility working with Owen Schwartz. After spending a summer at the NIH, he decided to major in Molecular Biology, so we switched him to the Structural Biology Section headed by Dave Garboczi. When he graduated, he did a one-year post bac in the Genomics Unit out at RML, and then entered a Ph.D. program in Molecular Biology at Penn State University and will be graduating in 2021. Michael's experience in multiple environments enabled him to decide which field of science he wished to pursue.

While we are all very happy when we help someone figure out which area of science interests them the most, not everyone who spends a summer at the NIH decides to stay in science. Some students decide that biomedical research is really not the career for them, and that's OK. One very talented high school student who thought he wanted to become a physicist decided instead to get a degree in Finance. Another extremely bright student, who happened to be the valedictorian of her high school class, thought she wanted to attend medical school, but after a summer at the NIH she decided to major in business. In both these cases, the students have graduated and are very successful. The point I want to make is science is not for everyone and I have no problem if, after spending some time at the NIH, they decide to pursue other careers. I take satisfaction in helping the young people decide which career is right for them.

When I recruit people, especially people who are earlier in their career, I say, "If you come here, we have all these resources, we have all these smart people, and you are limited only by your ability. And I think that's one of the really cool things about NIH."

Harden: What does the future hold for you?

Hohman: I just retired, two months ago, so we're going to do a lot of traveling. I'll be doing some consulting. Also, at least for now, I'm a volunteer at NIH, and I am still finishing up some of the transition.

Harden: But you plan to stay in the area.

Hohman: Yes. We'll stay in the area, at least immediately. We're in no hurry to go anyplace else.

Harden: Thank you so much for a wonderful oral history.