Dr. Alan Peterkofsky
Oral History Interview B
April 11, 2023

Higingbotham: Good afternoon. I am Haley Higingbotham, the Assistant Archivist of the Office of NIH History and Stetten Museum. Today is April 11, 2023. This is the second part of our oral history with Dr. Alan Peterkofsky. Today we'll cover the first part of his career at the NIH. Thank you for joining us, Dr. Peterkofsky.

Peterkofsky: Okay. Well, we left off the last time when I was talking about my PhD research, and I'd like to pick up at about that point. Towards the last part of the year 1958, the decision was made that the five graduate students at the Public Health Research Institute should defend their thesis work at New York University. Of the five students, three of them were men who were mentored by Dr. Efraim Racker. It was me, and then there was Harvey [S.] Penefsky, who was working on the way that that ATP was synthesized by mitochondria, which was a very active program in the Racker Lab; Dan Levin [Daniel H. Levin] who was working on some metabolic enzymes; and me, working on photosynthesis. Then, there were two women who were the graduate students of Dr. Sarah Ratner, who was the deputy chief of that laboratory.

So it was an interesting mentality dealing with defending your thesis at New York University. The idea was to have the students demonstrate that they were ready to accept academic positions at universities and create their own research program. Typically, what's involved in doing that is that you write a grant application and compete for funding to support your research. The way that was devised for students to demonstrate that they were academically competent was for them, as part of the oral defense of the thesis, to also submit to the faculty at New York University four proposals for doing research projects. The requirement for doing that was to write a proposal that was clearly independent, never done before, and in order to do that, you had to be absolutely certain that nobody had published that idea before. There was a lot of activity in biochemistry during those years, so we would put together our four ideas and write them up. All the students would spend every day going to the library and checking the newest literature to make sure that your idea hadn't been published that day. There was a lot of anxiety there, and in fact, one of my ideas during the period of presenting these proposals was actually scooped, and I had to come up quickly with another idea before the examination. One of them, apparently, turned out to be an idea that the chairman of the biochemistry department liked, and he actually put one of his postdocs to work on that proposal, which put him in a really good mood when it came to defend my thesis work because he was thankful that I had provided one of the ideas for him to work on. So that was pretty good.

At the defense of the thesis, there was a committee put together and, of course, the chairman of the biochemistry department, Severo Ochoa, was sitting in command of the meeting. He was a guy who was caught up, as many biochemists were, in the excitement of what was going on in biochemistry and molecular biology. During that period of time, he had decided to have a major focus in his laboratory on determining how ribonucleic acid was synthesized because that was one of the major features of the new field of molecular biology. He had gotten into his laboratory to pursue that idea a woman scientist from France whose name was Marianne Grunberg-Manago. She eventually discovered an enzyme that would synthesize RNA from the

precursor ribonucleotides. They named that enzyme polynucleotide phosphorylase. I had an opportunity while we were students, because my wife was also working in that laboratory, to interact with her and it was sort of interesting. She had a new baby, and she would come to the laboratory with her baby carriage. People would have a lot of fun visiting with the baby as well. That was good. Eventually, Marianne Grunberg-Manago went back to France and pursued her independent studies, and eventually, she became well enough known as a figure in molecular biology that she started a program that was called the Summer School in Molecular Biology. It turns out that the first summer school that she organized in 1966 was held on this beautiful Greek island, and I was really very lucky that she invited me to make a presentation at that summer school. I'll have something to say about some interesting stuff at that summer school maybe a little later in this talk.

So there was also at the oral examination Efraim Racker, who was my mentor, and he was actually in a very active position in terms of job hunting himself. It turned out that about a year after I came to the NIH, he appeared there, spending a sort of sabbatical there in the laboratory that I would spend a lot of time in, so I got to see more of him. He eventually came to accept a position to found a biochemistry department at Cornell University, and he left the Public Health Research Institute to go there. While he was spending his sabbatical at the NIH in the laboratory of Leon Heppel, who was the head of one of the labs that I would spend some time at, he convinced Leon Heppel to go with him as an associate to this new biochemistry department at Cornell. That was an interesting development there.

Another person who was in the committee was Charles Gilvarg who was the advisor to my wife doing research there. Because of my wife's relationship with him, he was very sympathetic to supporting me. At the examination, Dr. Gilvarg was recognized as probably the most brilliant mind in the biochemistry department. He had a reputation for being very complex in terms of his questions and very challenging, so when it was his time to question me during the oral examination, he put together a very complex set of questions and that I was totally incapable of answering. I saw that every person on the committee also looked very perplexed and couldn't understand what he was getting. So, eventually, he was very nice, and he explained what he was after and confessed that it was rather a challenging question, so I got by with that.

The other person who was on the committee was Dr. Ratner, who was the advisor to the two female graduate students. She was a very interesting person. It was clear from her treatment of students that she was quite a feminist; she only had women as post-doctoral candidates. She only took women as graduate students. The two women graduate students were her students, and they were working on the methodology to synthesize the amino acid arginine. Sarah Ratner’s background is that she had come from Columbia and done her PhD work with Sidney [C.] Rittenberg, who was a major figure in the early use of heavy isotopes to study metabolism. She had worked with him and knew a lot about the use of tracers to track the way metabolic processes took place. It was very interesting, and they very competent people.

The crew managed to get me through, and it turns out that all the five students passed their oral examinations, and we were pretty exhilarated about that. Then, the next step was to go on to various new occupations. It turned out that Harvey Panefsky stayed in the Racker laboratory, and even when Racker moved to Cornell, he took Harvey Panefsky with them. Panefsky became quite famous because he developed a unique assay for determining how ATP is synthesized biochemically, and the assay that he developed became known as the

Panefsky assay, so he was well established in his reputation. Dan Levin went on to a position at MIT. One of the other women, whose name was Barbara Petrack, went on to do a postdoctoral period with Fritz Lipmann who was a Nobel Laureate, and I had occasion to have an interaction with Fritz Lipmann during the course of my subsequent work as well, so I saw her after that. It was an interesting trajectory of the various groups.

The next thing was: What am I going to do when I finished my work? The general decision and advice that I got was go to NIH. One of the driving forces for going to NIH is the alternative if I didn't go to NIH; I had been having a student deferment from going into the army up until that point. The deferment ended, and I was eligible to be drafted. One way of dealing with that question was get a commission in the Public Health Service and serve my time at NIH. We got to work on managing to get me a commission in the Public Health Service, and then the question was: Who would I go to work with at NIH? The advice I got from some of the contacts I had at NIH was that the most exciting investigator at that point was a scientist whose name was Gordon Tomkins. Everybody seemed to feel that he was on a trajectory to do great things in his career, and he was also a very magnetic personality. I got in touch with Gordon Tomkins and proposed that I would love to come to his laboratory. And he said there was only a possibility that he would be able to accommodate me because he had one position that was occupied by a scientist, whose name was Victor Ginsburg. Victor Ginsburg at that point was on a sabbatical in Europe, and Ginsburg loved being in Europe and was talking to Tomkins about, well, maybe he wouldn't come back. He'd stay in Europe because he had an offer for a position there. Tomkins told me that if Victor Ginsburg didn't come back, I could take his position. I was hanging on a thread there waiting for the decision by Ginsburg, which turned out that he was going to come back. So what to do?

The backup arrangement that Racker helped me with was to get a commitment to go to the laboratory of Herbert Tabor. We made the arrangements, Tabor took me as a candidate to come as a postdoctoral fellow in his laboratory, and that decision was made that I would come there at the beginning of June. We had a June 1 date for me to leave the Public Health Research Institute and go to NIH. Beverly was a student at New York University in the Gilvarg laboratory. With that understanding that we would leave, both of us, on June 1st to go to NIH, Gilvarg, her mentor, was very understanding and got her to write up the work that she was doing in his laboratory on a transaminase protein and submit it to get a master's degree, which she did very successfully. Then the question was: What was Beverly going to do when she came to Maryland? She wanted to continue her studies. An arrangement was made for her to go as a research assistant and student in the Heart Institute, in the laboratory of Sydney Udenfriend, who had just recently started a cooperative program with the George Washington University biochemistry department whereby students of his could work and do research in the Heart Institute laboratory of his and take courses at George Washington University and get a PhD degree that way. We're all set to go June 1st to the NIH. Beverly in the Udenfriend laboratory, and Alan in the Tabor laboratory. We set about getting an apartment and furnishing the apartment and getting our furniture moved there, and we're all set.

Then, it turns out that at about that time – a couple of months before then – Racker, in anticipation of losing his three students, had accepted a new student, a woman by the name June [M.] Fessenden from New Zealand, to continue the studies that I was doing on photosynthesis. Because of that, when it came close to June 1st, Racker said, “You can't leave. You have to stay and help June Fessenden get comfortable with doing the work that you were doing to carry on.” There was a delay, and Racker contacted Herbert Tabor and said, “Sorry, Alan can’t

come on June 1st. Give him another month, until July 1st." The consequence was that Beverley went to NIH on June 1st, and I stayed in New York for another month. Then when it came to be close to July 1st Racker said, "We gotta do some more experiments, so I'm going to call Tabor and ask him to delay your arrival for another month." That was now August 1st, scheduled to come. And this went on forever. It was a delay until August 1st, and then a delay until September 1st. Eventually, I was let go so that I could come to NIH on October 1st.

Higingbotham: Oh, wow. That's quite a delay.

Peterkofsky: Yes. It was a distressing situation but that was the understanding that I had. He was my boss, and he made the ultimate decision. I eventually came to NIH in October 1st of 1959.

I thought it would be useful in order to get a perspective to talk about what was going on in the world of molecular biology about that time. The discovery of Watson and Crick in 1953 about the structure of DNA resulted in an enormous stimulus of activity that was focused on how was DNA made and how was RNA made and how was protein made. There was this new field that emerged, and as I indicated a little while ago, the Ochoa laboratory at NYU that I would go and visit—for my coursework and visiting Beverly, who was in that department—was focused with Ochoa and Marianne Grunberg-Manago working on how was RNA made. Eventually, Marianne Grunberg-Manago discovered this enzyme that they called polynucleotide phosphorylase that made RNA. Eventually, Marianne Grunberg-Manago came from the Ochoa laboratory at NYU to spend some time at NIH working in the laboratory of Leon Heppel, where I saw her and interacted with her again. It turned out that while she was in the Heppel laboratory, she was the person who made this polynucleotide using her polynucleotide phosphorylase. And she made this polynucleotide called poly U, which Heppel supplied to Marshall Nirenberg when he did his most famous early experiment showing that poly U was the vector that could be used to synthesize polyphenylalanine. That was the beginning of the solution of the genetic code, so that was very interesting.

At the same time that the workers in the Ochoa laboratory were working on how RNA is made, Arthur Kornberg was working on how was DNA made. He was a noteworthy person. He also actually had graduated from the same college, City College of New York, that I went to, so we had something in common. He had, shortly before I came to NIH, moved from NIH to Washington University, where he pursued studies on how was DNA made, and they discovered an enzyme that they call DNA polymerase that was able to use precursors to make DNA. As a result of the recognition of the studies Ochoa on RNA and Kornberg on DNA, they were jointly awarded the Nobel Prize in 1959. That Nobel Prize turned out later on to be very controversial because the way the prize was described, it was for studies of the synthesis of DNA and the synthesis of RNA. It turned out that this enzyme, polynucleotide phosphorylase, that was alluded to be the enzyme that made RNA was actually not an enzyme for synthesizing RNA. It was an enzyme for degrading RNA, and it turned out that the enzyme that Kornberg discovered and described and purified for the supposed synthesis of DNA, didn't actually synthesize DNA. It was an enzyme for repairing DNA or degrading DNA. The prize was not taken back, but it was evaluated as an incorrectly described prize. Eventually, other enzymes were described that actually synthesized DNA. It was called DNA polymerase number two, number three, and for RNA, RNA polymerase, rather than polynucleotide phosphorylase, but it was an interesting kind of thing. It was just indicative of the excitement and the ferment that was going on in the field of molecular biology.

Higingbotham: That's all really exciting. What were y'all focused on at the Tabor lab? You joined the same year the Nobel Prize was won [by Ochoa and Kornberg].

Peterkofsky: Yes. Eventually, I got another aspect of molecular biology that I'll talk to you a little bit about later on. Let me see what else I wanted to talk to you about. In October, I went to the NIH, working in a laboratory in Building 4 on the first floor, where there was the Tabor laboratory. The project that I was given by Dr. Tabor was to study an enzyme called histidase. Histidase had been described previously in a paper by both Herbert Tabor and colleague of his named Alan [H.] Mehler as an enzyme that degrades histidine by clipping off an amino group to form ammonia and a derivative that was called urocanic acid. The project was to study the mechanism of this degradation of histidine by this enzyme. There was a mentality by a lot of biochemists in that area that you had to purify an enzyme before you could study the mechanism. There was a sort of mantra that people [attributed] to Arthur Kornberg, and also Efraim Racker, that people have repeated over and over again. That mantra was, "Do not waste clean ideas on dirty enzymes." That was written in many books, "Do not waste clean ideas on dirty enzymes." The orders that I had was, you could think about doing studies on the mechanism of this reaction, but you must purify the enzyme a lot before you could do that. What I was expected to do was to struggle from bacterial extracts where the enzyme histidase was only a trace protein to purify it away from all the other proteins. So that was, in those days, a very challenging thing to do. Fortunately, at about that time, another scientist group in the [National] Cancer Institute, by name Herbert [A.] Sober and Elbert [A.] Peterson, had developed this procedure for using a derivatized form of cellulose, that was called DEAE cellulose, as a way of fractionating proteins, which was useful to some degree. I was doing that kind of stuff.

Tabor was a very hands-off person. He would leave me alone to try to manage to get purification. My typical interaction with him was that once a week, he would pop into the laboratory, and he would say to me, "Alan, how many fold?" which meant: What kind of progress have you made in purifying the enzyme? I would give them a report about a little bit of progress, but it was very difficult and rather disheartening. At some point in time, after several months, I was able to get something like an 80-fold purification of the enzyme, but it was hardly what you would call a pure enzyme at that point.

I decided that even though Dr. Tabor was quite resistant to my trying to do any meaningful mechanism experiments, I would go and do it anyway. He was not happy, but I did it. I started to do some experiments with radioactive components—experiments that involve exchange of ammonia, which was a product of the reaction into histidine, or hydrogen, which was also one of the products—and discovered that I could see an exchange of both hydrogen and ammonia. And, actually, I saw that I could get hydrogen exchange but not ammonia exchange, and also the product of the reaction, which was urocanic acid, was able to show exchange. In order to do these kinds of experiments, I had to use a scintillation counter that detected radioactivity. There was a primitive scintillation counter that was in the laboratory of another scientist in another building. His name was Yale Topper. I asked his permission if I could use this primitive scintillation counter, and he said, "We're really very busy with it, but you could use it at night." So I would have to do my experiments in Building 4 during the day, and when I wanted to make measurements, I would have to go in the evening to Building 10 to do these experiments in this scintillation counter that allowed me to get these exciting, early results. Based on that I was able to convince Tabor to actually order a more modern scintillation counter, so it was one of the early

scintillation counters that came to Building 4 as a result of my experiments. In any event, the results of the experiments led me to propose a mechanism for the histidase reaction that I published. As a result of that, I think the word caught around NIH that I was a reasonable researcher, and I developed a reputation at NIH as a competent researcher.

It turned out that that the other major scientist in that group, who was a person who actually had described that histidase reaction with Herbert Tabor, was a scientist whose name was Alan Mehler. Alan Mehler was a very interesting guy, and while Herbert Tabor tended to be rather remote in his interaction with me, Alan Mehler developed a very close interaction with me. I would see him essentially every day and spend sometimes hours talking to him about science, and he was very good. I became both a scientific friend of his as well as a family friend of his. He, in addition to being a research worker in the laboratory, was also extremely interested in education, and he spent part of his time in the evening teaching disadvantaged kids in a Black community in the area that was called Ken Gar. He tried to recruit me to also go in the evening to teach these disadvantaged kids, and he was not happy when I declined that invitation. In any event, it didn't destroy our interaction.

He was also a person who was very active in in the beginning of this organization that was called a Foundation for Advanced Education in the Sciences [FAES] that started in 1959, the year that I came to NIH. He was successful in nominating me to go on to the Board of Directors of the Foundation for Advanced Education in the Sciences that we called FAES. Eventually, I became first the secretary of the organization, and then I rose to become the treasurer of the organization. Then eventually, I became the vice president of the organization, and eventually I became president of the FAES and spent numerous years involved with that organization. During the time that I was there in that organization, I became involved with developing and managing the Health Insurance Program at FAES that became a pretty important feature of scientists who were visiting NIH because the government health insurance was only available to government employees, but not available to visiting scientists. We developed this program that covered health insurance for essentially all of the foreign, visiting scientists that came to populate the NIH, and it became a very important feature of living and working at NIH for this group of young scientists. Now, it's a very large program that I believe covers insurance for something like 2,000 scientists at NIH. That was a real achievement.

Alan Mehler was also very interested in educating both people that he interacted with as well as his family. He had a son, his name was David, who eventually became an attorney and worked as a public defender in Washington, DC. A lot of his experience as a public defender was that he was acting as the advocate for young juvenile delinquents who had committed crimes, and he was so impressed with the problems that these kids faced, he came up with this idea that he could solve their emotional problems that led them to get into trouble by teaching them to play chess. It was a really unique idea. The consequence was that he gave up being an attorney, and he started a group that eventually became known, and very well known, as the United States Chess Foundation. It still exists today, and he is the director of the chess foundation. It's been pretty well documented that it turned around the lives of a lot of young people. He's made a really important contribution. Alan Mehler had another child, a daughter, whose name was Louise who was very bright. She actually spent one of her summers when she was a high school student working in my laboratory, and we coauthored a paper that made her and her father very proud.

Higingbotham: Oh, that's nice.

Peterkofsky: Yeah. Louise eventually got an MD degree and went to California. Unsurprisingly, she also felt like a public-spirited person. She spent her medical career helping disadvantaged people to solve their issues with respect to health care, and she had a husband who was very interested in preservation of historic properties in California.

Higingbotham: They all seemed really interested in community service.

Peterkofsky: Yes, he had an interesting kind of influence on his family as well as other people as well.

Higingbotham: Yeah, I see that we we've been talking quite a bit. Do you want to bring it back? I think I saw that you had a journal club with Heppel.

Peterkofsky: That's an interesting thing. Well, in the Heppel laboratory, which was on the ninth floor of Building 10—and I was working in the Tabor laboratory on the first floor of Building 4—there was this journal club that took place every day of the week. It was scheduled to start precisely at 11:45 in the morning and stop at precisely 12:30 in the afternoon. Tabor and me and a couple of other postdocs would make the trip from Building 4 to Building 10. Every day we started at 11:30 precisely out of Building 4 to arrive at the 9th floor Building 10 before 11:45. There were about 25 people who participated in this journal club. It turned out that about that time in the history of that journal club, that originally was started by some senior scientists that included Leon Heppel and Bernard Horecker and Arthur Kornberg, that they would present their analysis of papers that were published in the *Journal of Biological Chemistry* and have a discussion of that while postdoctoral fellows would be expected to sit and listen to them, but not to participate as active presenters. At about the time that I came, there was a liberation so that postdoctoral fellows like me were allowed to be active participants at journal club, so we would do that at about that time. The *Journal of Biological Chemistry* was published once a month as a sort of a slim journal compared to what it is today where it's published every week as a big, thick thing. We were able to essentially, over the period of one month, discuss all the important papers that were published in the *Journal of Biological Chemistry*. It's a very interesting kind of activity and very educational and helped us to become very critical of other people's work.

Higingbotham: Very interesting. Is this journal club where you had a connection with Herbert Weissbach?

Peterkofsky: Well, Herbert Weissbach is the character that came to influence my life a lot, because Herbert Weissbach had been my friend and also classmate at City College of New York. He had come to the NIH earlier than I did because he came directly from City College to work at NIH, whereas I went to the Public Health Research Institute. About the time that I came to NIH, Weissbach had already gotten his PhD degree in that cooperative program that I described with George Washington University. Then, he went to do a postdoctoral experience in a well-known laboratory at the University of California that was run by a famous scientist whose name was [Horace A.] Barker. While he was in this laboratory and in Berkeley, he discovered what was described as the coenzyme form of vitamin B-12. He was very excited about this, and he got permission from Barker when he left the laboratory to come back to NIH to continue working on this coenzyme form of vitamin B-12. After I

had been at NIH for about a year, Weissbach returned. He was my friend and got in touch with me and told me about his exciting findings in California and said, “Let's work together on working out how it's made.” I told Tabor about this offer of my friend to collaborate with him, and Tabor was very much opposed to this. He indicated that if I wanted to be a successful scientist, I should always work by myself the way he did. I did not take his advice and began to work with Herbert Weissbach on that.

Weissbach was installed in a laboratory actually very close to where Beverly was working in Building 10. I began to split my time working in Building 4 on the histidase problem and in Building 10 with Weissbach on the mechanism for how the coenzyme form of vitamin B-12, was formed. We did a lot of work together and published a whole bunch of papers that were very well recognized, and we discovered that the coenzyme form of vitamin B-12 involved a reaction with ATP to transfer the adenosine fragment of ATP to vitamin B-12 to form what was described as adenosyl B-12. The products of that reaction were the three phosphate groups of ATP that were split off as a single form called tri-polyphosphate. It turned out that there was another scientist at NIH working in the Mental Health Institute named [S.] Harvey Mudd, who was studying the way a derivative of methionine called adenosyl methionine was formed, and it turned out it was a similar kind of reaction. That methionine interacted with ATP to transfer the adenosyl group to methionine just the same way that we had found that the identical group of ATP was transferred to vitamin B-12. In his case, instead of resulting in a cleavage of the three phosphates of ATP to form tri-polyphosphate, it was a sequential loss of one of the phosphates and then the other two phosphates, but it was very similar action and very interesting. That was an exciting period of time.

Then, it turned out that in 1961, my friend Alan Mehler, who I had developed a very close relationship with, had gotten an offer to go to leave the Arthritis Institute [National Institute of Arthritic and Metabolic Diseases] and move to form a new section in the Dental Institute [then National Institute of Dental Research]. The Dental Institute was in a period of rapid expansion. They had had a new building called Building 30 to house an expanded Dental Institute, and he was offered and accepted a position to form a section there. He asked me if I would come to work in that section as a permanent scientist, so I left my commission as a Public Health Service officer, accepted his offer, and went to work in the Dental Institute and Building 30. It was an interesting new experience. The chief of the laboratory in the Dental Institute that was called the Laboratory of Biochemistry was a very fine man by the name of Frank [J.] McClure, who had a historical reputation in that he had been one of the early workers that demonstrated the benefit of adding fluoride to water to protect your teeth. He was still living in that old age of fluoridation, and I had only a minimal interaction with him, but he would periodically—because he was a friendly gentleman—come by and ask me how my work was going. I had developed this stock answer to him of saying, “Dr. McClure, I'm working very hard, trying to find a problem that I can get my teeth into.” And he really liked that. That was sort of funny. That is about all I had to do with Dr. McClure.

After I transferred to the Dental Institute, I continued my studies of histidase and also on the coenzyme form of vitamin B-12, but Alan Mehler was very interested in doing a transition to the field of molecular biology. He decided that he would encourage all the people in his group to be working in molecular biology, and he wanted to have a focus on the first steps in protein synthesis. The first steps in protein synthesis were to attach an amino acid to an enzyme that was called an amino acid activating enzyme, and then transfer that amino acid to a small RNA molecule that was at that time called soluble RNA, but it's now called transfer RNA. He set up a

program of getting big amounts of E. coli extracts and fractionating the RNA into multiple species, because there was at least one transfer RNA that was specific for each of the 20 amino acids. There were also at least 20 amino acid activating enzymes, one for each amino acid, so it was a big, big field to be working in.

Eventually in getting acquainted with the field, it turned down that these small RNAs, that were called soluble RNAs, had about 100 nucleotides and had this unique feature of having some of the bases modified, many of which were modified by having methylation of a nucleotide called methylated bases. I decided that I would focus mainly on studying what the significance of methylated bases in RNA were, and I started to ask questions about that. It turned out that one of the former professors of mine at City College of New York was now at Columbia University, and he was working in the area of molecular biology. He described a mutant of E. coli where it was possible to manipulate them by starving the bacteria for the amino acid methionine, which is the methyl donor for methylated bases. If he starved those, then they would continue to produce RNA, and then those features would lead to an accumulation of RNA without methyl groups. It allowed a study doing a comparison of RNA that was fully methylated, compared to RNA that was partially methylated. I got that mutant from Dr. [Ernest] Borek and began to study these features of RNA that was either fully methylated or only partially methylated and was able to then ask questions about whether the RNA was active. The answer was that yes, these RNA species that were deficient in methyl groups could actually still accept amino acids from amino acid activating enzymes. I [then] was able to ask the question of whether one species of RNA or one amino acid differed from the species of another amino acid in the content of methylated bases. The answer was that they varied specifically for which species of the bases they were. And then I studied the effects of different agents on the activity. In one of the studies, I was able to show that an activating enzymes from another species could differentiate between methylated and unmethylated bases.

There were a lot of studies that I did, and because the work that I was doing was in this very popular area now of molecular biology, I was able to get highly recognized scientists like Christian Anfinsen, who won a Nobel Prize on the basis of his studies on ribonuclease, to communicate some of my work to the prestigious *Proceedings of National Academy of Sciences*. There was a time that it turned out that Fritz Lipmann, who also was a Nobel Laureate and then at Rockefeller Institute, had one of his postdoctoral fellows working on exactly the same problem that I was working on – what is the significance of methylated bases – and he got in touch with me and asked me to come to Rockefeller to have a meeting with them. I told him about my results, and he said that I had scooped him and gotten the answer to the same question that he was asking. He was gentlemanly enough to be a sponsor of a paper that he submitted to the *Proceedings National Academy of Sciences* on my behalf. So things were going really quite well while I was pursuing this work.

The thing that happened then was that Alan Mehler in 1965, which was after I came to the Dental Institute, was recruited to become a professor at Marquette University. He asked me to come with him to become a faculty member there. Of course, I liked Alan Mehler very much, but Beverly had just at that point completed her PhD degree, and she was actively looking for a position at NIH and was opposed to my going. I declined the offer to go with Mehler to Marquette University. And the consequence was when Alan left, he left me with some of the people who were supposed to be working with him – he had a technician, whose name was Celia Jesensky, who became my research assistant and worked with me for many years. She was very good. She eventually got

married to an Indian scientist at NIH and eventually moved to the University of Texas, but we work together for many years.

Up until the time that Alan Mehler left the Dental Institute, I had been working by myself. I interacted with people, but never supervised anybody else. But he left me with a research associate, who had come to work with him. I inherited this guy who became my first postdoc, his name was [J. Donald] Don Capra. He was a very smart guy but really didn't know anything about how to work in the laboratory because he had come as a graduated MD, who then had a residency in medicine. His arrival at NIH was his first experience in science, but he was very good and a very quick learner. He eventually went on to a very successful career and became the director of the Oklahoma Medical Research Foundation. He kept in touch with me over many years and told me that he learned the basics of doing science, where it was important to know that every experiment you set up should have control. The mantra of doing a control that he was telling his students in the future was, “Just remember with and without.” And he said he owed that slogan of “with and without” to me. I was very appreciative of that.

The project that Don Capra worked on with the methylated bases and RNA problem was to determine whether there was any difference between normally methylated and methyl-deficient RNA on coding. For that, we started a collaboration with the Marshall Nirenberg laboratory to determine coding properties of these different species of RNA, and we were able to show successfully that you could differentiate normal versus special methyl-deficient RNA with coding. It was the first introduction to interacting with the Nirenberg laboratory.

Well, it turned out that in 1967 Nirenberg was promoted to become chief of his own laboratory. The consequence of that was that he now had positions and space made available to him, and he was very receptive to the idea of my moving into his laboratory. He approached the scientific director of the Heart Institute, his name was Robert Berliner, to introduce the idea of my coming to the Nirenberg laboratory as the section head. I went to be interviewed by Robert Berliner, and I made three conditions of my coming as a section head to the laboratory. One of them was that I would be able to hire my own postdocs, and he agreed to that. The second was that I would get a red parking permanent that gave me preferred parking, and he agreed to that. The third was that I would be able, when I was ready, to go on a sabbatical to someplace else for a year, and he agreed to that. As it turned out, I never did it.

Higingbotham: But you had the option.

Peterkofsky: Yes, I had the option. It turned out that then I came to the laboratory. I think I've pretty much exhausted my time allocation. I'll stop here and continue at another time.