The Nobel Prize

Marshall W. Nirenberg is best known for his work on deciphering the genetic code by discovering the unique code words for the twenty major amino acids that make-up DNA, for which he won the Nobel Prize in Medicine or Physiology in 1968.

Nirenberg was the first government scientist to win the Nobel Prize. The National Library of Medicine and the Office of NIH History has amassed a collection of correspondence, laboratory administrative and research materials, and publications that documents Nirenberg's career as a researcher in biochemical genetics at the National Institutes of Health.

Dr. Nirenberg is featured in The Profiles in Science web site of the National Library of Medicine celebrates twentieth-century leaders in biomedical research and public health. Students appreciate the history, and share some of the excitement of early scientific discoveries in molecular biology. The National Library of Medicine is digitizing and making available over the World Wide Web a selection of the Marshall W. Nirenberg Papers, for use by educators and researchers.

In 2007, the Archives and Modern Manuscripts Program, History of Medicine Division completed a Finding Aid to the Marshall W. Nirenberg Papers, 1937-2003 (bulk 1957-1997). Individuals interested in conducting research in the Marshall W. Nirenberg Papers are invited to contact the National Library of Medicine.

The NLM digital materials and references provide the background for the series of six interviews conducted with Marshall W. Nirenberg, Ph.D., by Ruth Roy Harris, Ph.D., between September 20, 1995 and January 24, 1996.

The "Harris Interviews" took place in Nirenberg's laboratory on the campus of the National Institutes of Health (NIH) in Bethesda, Maryland. Harris also conducted several supplemental interviews, both by telephone and in person, with individuals either involved in the breaking of the genetic code or personally acquainted with Nirenberg: James Pittman, Joan Geiger, Philip Leder, Thomas Caskey, Sidney Udenfriend, and Perola Nirenberg. Interviews with Pittman and Geiger are now in the Marshall Nirenberg Collection at the National Library of Medicine (NLM). Notes from other interviews are held at the Office of NIH History.

A number of individuals and institutions worked on editing the interviews for clarity and content: Sarah Leavitt, Victoria Harden, Caroline Hannaway, Alan Schechter, Robert Balaban, and Alan Peterkofsky. Caroline Leake, Katrina Blair, and Mary Alvarez provided administrative and technical assistance. In 2008, Deborah Kraut edited and formatted the interviews to correspond to the NLM digital materials.

Each Section begins with the NLM digital summaries summaries and references. Additional references, when appropriate are added:

From NLM "Profiles in Science"

http://profiles.nlm.nih.gov/JJ/Views/Exhibit/narrative/codeoflife.html

In October 1968, Nirenberg received the news that he had won the Nobel Prize in medicine or Physiology, an honor that he shared with Robert W. Holley and Har Gobind Khorana for their collective efforts in deciphering different aspects of the genetic code.

DK: Recommend an excerpt from the NIH Record at this point.

Harris Interviews – Tom Caskey

Tom Caskey, who had been a postdoctoral fellow, working in the Laboratory at the time that Dr. Marshall Nirenberg was awarded the Nobel Prize for Medicine or Physiology.

RH: You were present when the Nobel Prize to Dr. Nirenberg was announced. Would you please describe what happened, the reaction, and what you saw and heard?

CASKEY: Oh, it was a fantastic day. I had come in early to work, which was my habit, and somehow I had missed the radio announcement; so I was working in the laboratory when my wife, Peggy, called and said that she had just heard on the news that Marshall had been awarded the Nobel Prize for his work on the genetic code. So, immediately the word spread. There was no formal announcement out of the NIH at that point; it was just on the news. Of course, we contacted Marshall. Marshall had also heard it on the news. He had not been formally contacted by the committee at that point. So we started getting ready for his coming into the laboratory. We were getting ready for a party.

I remember this famous sign that was made and hung in the hallway. If you remember, poly-U was the RNA that was the very first polymer that decoded phenylalanine as the coding segment. So we wrote out a string of U's, "UUUUU are great," and we had a big banner that hung in the hallway. Eventually Marshall came into the laboratory about mid-morning, and we were, of course, celebrating and having a good time laughing and joking with him when about that time the formal phone call came through. —

This is the way I remember it--He was formally told while he was in the laboratory by the

Nobel committee or a representative of the committee that he had been awarded the Nobel Prize. We were drinking champagne out of beakers. There is a photograph of Marshall with the phone in his hand and the beaker which was holding champagne, or did at one point hold champagne, and that was, in fact, the actual call. That photograph is not in any way staged; it is accurate. So that was the excitement of the early morning.

Then I remember that there was a press conference that was to be held over in the Administrative Building, I think Building 31; so we left the Clinical Center. By then, of course, the crowd was pretty great. It was family up there. There were little kids and wives and husbands; and so a few of us accompanied Marshall over to the press conference. I will always remember this one reporter, who, I think, was not very informed, asking Marshall as we went up on the elevator, "What would this do for male baldness?" (Laughter) I kept thinking that there still is a disjoint between major discovery and the public's understanding of what's going on here. But we went from there to a conference room, and Marshall was interviewed by news reporters and gave his accounting of the history of it.

That afternoon and evening we went out to Marshall's house. Everybody went. I mean, it was wives, children, the whole deal, and we had a celebration at his home. I am trying to remember whether that was late morning or evening. I can remember being at his house with everybody so excited and with little kids running around, and Perola's hosting this disjointed group of people who were just happy over the day's events.

Then, I think, later that evening we moved to this restaurant on Wisconsin Avenue, and we had, more or less, a banquet that evening. Again Marshall and Perola were there. Now the children were gone, and it was mainly scientists that evening. Round after round of scientists got up and made very nice comments about Marshall's history at the NIH and the development of the project.

<u> 1995-1996 – Harris Interviews</u>

Marshall Nirenberg (MN): When you get the Nobel Prize, they call you from Stockholm and tell you. But before that, before you go to sleep—and this had been happening for a number of years—the night before they announce it, reporters call you because they seem to know who is in the running. They want to know where the person will be so that if the person wins the prize, they can get an interview. So some reporters

had called me the night before, and they had called me on previous years as well. But I didn't really think about that very much.

When the people from Stockholm called me early in the morning, they woke me up. At first I thought it was a joke, that some of the boys in the lab were just pulling my leg. But then it became clear that it wasn't a joke.

Ruth Harris (RH): It is too bad that your parents didn't live to see you win the Nobel Prize.

My parents had both died by then. Actually, my mother was a patient in Building 10 around 1960. She had cancer, and she was being treated there. I saw her every day. This was before the work on the poly-U came up. This was in the early phase of the work when I was working alone on protein synthesis, and I thought I was using nucleic acids to direct protein synthesis. I think that we had just found that a contaminant in ribosomal RNA would stimulate amino acid incorporation. I told her I was on to something big and important, but it was hard to explain the magnitude of the work. I really thought that it was terrific. She understood that this was important, and I worked on it almost all the time. I would take maybe an hour or so a day to come down to see her and to be with her. Occasionally we would go out for a drive. She died in Building 10. It was just before all these things took place. My father died before the poly-U finding, or maybe just afterwards. He never really understood it. I don't remember the precise dates.

My parents knew that I was working on something that I thought was very important and very exciting, but they never knew that it developed into deciphering the code. My father would have loved it. He was always interested in science, and he would have been extremely interested. I wish that he had lived a little bit longer. Actually, his brother, my uncle, and his wife came to Stockholm, and my sister also came when the Nobel Prize was awarded, but my parents had died by then.

Apparently my father stopped in to see Dr. Stetten soon after I began working here and wanted to know if he thought that I would be able to make a living as a biochemist. My father knew me pretty well. I was never interested in money basically, and he thought that I would do best maybe in an academic setting, so he simply wanted to reassure himself. I was very embarrassed when I found out about it, to tell you the truth, but it was important for him to know that at least I wouldn't be a total failure.

RH: What did you do that day?

When they announced the Nobel Prize, the boys from the lab just spontaneously came over to the house and had a party to celebrate there. That afternoon I had to leave to go to Philadelphia to accept a medal awarded by the American Philosophical Society. So I had to leave early to make that trip.

MN: The boys arranged a lunch at one of the local restaurants, so we had a party there.

There were people calling that afternoon from all over congratulating me. You receive

many telegrams of congratulations and telephone calls as well. But then I had to attend this event in Philadelphia, so we took a plane to Philadelphia.¹

The Ceremony in Sweden

RH: Tell me about the Nobel Award ceremony in Sweden.

MN: They do it very beautifully in Sweden. They plan a week of parties. The parties go from embassy to embassy. Then you also give a talk. I gave a talk at Uppsala. Then they have a big dance as the final event. They have this marvelous dinner and dance after the award ceremony in the Town Hall. The Town Hall has this tremendous room that has mosaics in gold. The whole room glitters and glistens, and it is a very festive occasion. The diplomatic community attends the awards ceremony as well as scientists and some visitors.

The entire audience is all dressed up, Perola in a long formal gown and I, in white tie and tails, as well. Since many of them are diplomatic people, they all have medals and decorations of all kinds. It was a glittering audience. The chair of my department from Michigan was there. I was surprised to see him. He was a visitor in one of the Swedish laboratories. There were some other people who were visitors also, on that occasion. I wish I had taken many more photos, to tell you the truth.

Afterwards they have a wonderful dance that goes on until the wee hours of the morning and in which Swedish college students join in. Apparently it is a prized thing in the colleges to get to attend. I think that invitations are given out on the basis of what they do to help. I don't know if they serve as waiters or waitresses, or something of the sort during the banquet, but the mixture of college students is the thing that really carries it because it's a very festive occasion. The men wear these little caps that you sometimes see in Swedish films. They still wear those little caps as a routine thing.

Meeting President Lyndon Johnson

RH: After winning the prize, you and Perola spent around an hour with President Lyndon Johnson. Can you recall what you talked about?

MN: Yes. He wanted to know what I did. So I told him what I did. We went down with the Robert Marston, the director of the NIH and with Wilbur Cohen who was, at that time, head of HEW [Department of Health, Education and Welfare, now the Department of Health and Human Services]. I started to tell the President what I did, and I saw something like a glaze come across his eyes. I just don't think I got through to him at all. We talked. I don't remember exactly what we said, but we talked. Then I explained some of the things I did, and then Wilbur Cohen said some things, and Robert Marston said something. 34

Marston came to be head of the NIH as a total unknown. Nobody knew of him. He was an M.D. who had had administrative positions of various kinds. He left here as a virtual hero because he was not reappointed by Nixon. Nixon or the White House had told him to reduce the amount of money requested for medical research, and he did not comply. Instead of following these orders, when congressmen asked him, "How much money do you think you'll need for medical research in the country?" he told them what he thought. As a result of his noncompliance, he was let go, and he was a hero when he left here, I must say. He then became president of the University of Florida. I went down there one time and gave a talk. He was a terrific individual.

While we were down there at the White House, Johnson walked over to the Lincoln desk, that massive, beautiful desk, and started to rummage through the drawers while he was cursing under his breath. It was obvious that he was looking for something. Finally, he found something and he pulled it out and gave it to Perola. It was a medal. When we looked at it afterwards, it was in a beautiful case. This was a medal that he was supposed to present, I think, to the President of Mexico because a week or so later there was some kind of joint American-Mexican endeavor that had been instituted between the two countries. It was obvious that he couldn't find what he was looking for, and so he just pulled out whatever he had and gave it to Perola. That was funny.

While we were there—this was during the Vietnam War—the White House was a nerve center. Every few minutes some young man would come in with something typed on little squares of color-coded paper, and he would show them to the President. It obviously

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was a message coming in from some place. We were late in getting to see him because

apparently he had had a meeting with one of the generals just before our meeting, and

things were not going well in Vietnam. This was a time of great trauma for him and for

the country as well. He was a very impressive individual. I must say that he was

tremendous in size and a tremendous force of personality.

RH:

Did you have to return that medal?

MN:

No, we still have it. We still laugh about it.

The Impact of the Prize

RH: Can you tell me what the impact was at the NIH of your being the first Federal

government scientist to win a Nobel Prize?

MN: Perola says the Nobel Prize never really changed anything, and I just wanted to

say that, yes, it changed things in small ways but not in large ways because I tried very

hard to maintain things as they were. ⁵ I didn't want to make any major change. I wanted

to continue doing research as I had been doing it, and so the continuity of the work was

the strongest agent that kept things going the way they were going. I wouldn't say that my

life changed in any very large way. In minor ways, yes, but not in major ways.

My own thought is that the NIH is loaded with terrific, really good people. There are many people who deserve the Nobel Prize. It is a shame that only relatively few people are given the prize because there are more deserving people than there are actual recipients. So I think prizes are good because it is some kind of feedback for the people although that is not why people work at all, certainly not why I work. My own personal view is that I am somewhat retiring and shy. Award ceremonies are not the kind of situations that I relish.

In answer to your question, I don't know what effect it had upon the NIH. I think it must have helped its prestige. There are four other people who were at the NIH who have received the Nobel Prize, and they deserved it. ⁶

It is strange about prestige. Let me say something about the NIH. I have always considered it a privilege to work here, and some people have asked me why I stayed. I can tell you why. I received offers of positions from most major universities and other research institutions around the United States. Invariably, the salary was higher, there was more space, certainly more prestige, in some cases even more people, more positions connected with it. But I stayed at the NIH because I think it is the best research institute in the United States. It is probably the best research institute in the world. It does not have the prestige I think that it should have because, as I said before, each laboratory is a department by itself.

In each laboratory you have a head of a laboratory who would ordinarily be a professor in a department. If you had a single department that had some ten laboratories that had ten people who are good scientists in it, it would be equal to or better than any other department of that kind in the United States. But it doesn't. So what people compare actually is a single laboratory, which is a single individual and the people that work with that individual, by and large, and maybe a few other independent investigators, but there is only one laboratory. There is the Laboratory of Molecular Biology in the Institute of Arthritis and Metabolic Diseases that is set up like a university department. Because of that, I think, the NIH does not have the prestige that I think it deserves.

I have always thought that by staying here, I have saved perhaps a third of my time that would ordinarily be devoted to getting grant money, by writing grants, which is laborious. In universities that is about the amount of time that people use just trying to get money to do research and then more of their time teaching. They are lucky if they can spend 50 percent of their time doing research. Here you are free. Maybe 10 percent of your time is spent on doing things that are needed to validate your research, such as writing annual reports or being reviewed—things of this sort. Basically I have gained time.

I always asked myself two questions when offers like that came in: one, would it improve the research that I do; and two, would I be able to do any more research and would it be any better? In very few cases, I found the university to be equal. I would have been part of a department. I would have interacted with very good people, which is advantageous. But I have never found a place which I thought was a better place than the NIH. For all its faults, because it does have faults, it is a marvelous place to do research.

RH: How did the organization of the NIH affect the work that led to the Nobel Prize?

MN: It is absolutely clear—there is no question about it—that I couldn't have done the work anyplace else except the NIH because I couldn't have gotten a grant to work in the field of cell-free protein synthesis because I had no experience in the field. Nobody would have supported me, given me funds, to do research. So it is fortunate that I was here and I did it here because I couldn't have done that work any other place. After a way had been found to decipher the code, then people would have supported me, but not before. So I feel very fortunate that I was here and that the NIH supported that kind of work.

Right now it is very difficult to get grants and it has been for quite a while. Only one out of ten grant applications is funded, a terrible percentage (only ten percent). It is very difficult to get the money to do research outside. I have always felt fortunate because I was able to change fields whenever I wanted to. I was able to go into neurobiology. If you are in the extramural program in a university, you have to get permission to do this kind of thing and it is very difficult to change fields. You have to have experience before you will be funded in any field. I always felt fairly comfortable in doing risky research here.

Basically, what I have done throughout the entire time I have been at NIH is extremely risky work. I have done pioneering work in neurobiology as well as in protein synthesis. I always felt glad that I was at the NIH because I felt that in the long run I didn't think I could fail. But in the short-run I could certainly fail, and so I felt lucky and fortunate to be supported by the NIH.

The footnotes that appear below will be placed in a separate digital file for linkage to this file.

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¹ Interview with Tom Caskey by Ruth Harris, 20 February 1996, interview notes at the Office of NIH History, NIH.

² Wilbur J. Cohen (1913-1987), Secretary of Health, Education and Welfare in 1968, graduated from the University of Wisconsin in 1934 and played a major role in establishing the United States Social Security System and other government health and education programs.

⁴ Robert Q. Marston (1923-1999) received a B.S. in 1943 from the Virginia Military Institute, an M.D. in 1947 from the Medical College of Virginia and a B.Sc. from Oxford University in 1949. He served as director of the NIH from 1968 to 1973.

⁵ Perola Nirenberg said that she noted no special changes, other than that the couple moved to a larger house. (Interview with Perola Nirenberg by Ruth Harris, 15 December 1995, interview notes at the Office of NIH History, NIH).

⁶ Hyperlink to the Nob el NIH page