

**RENATO DULBECCO**  
(1914–2012)

**INTERVIEWED BY**  
**SHIRLEY K. COHEN**

**September 9 and 10, 1998**

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**Subject area**

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**Abstract**

Interview in 1998 with Italian-American virologist Renato Dulbecco, who came to Caltech in 1949 as a senior research fellow at the invitation of Max Delbrück, joined the faculty of the Biology Division, and remained at Caltech until 1962. In this interview, he recalls his education at the University of Turin (MD 1936) in his native Italy, working with Giuseppe Levi and Rita Levi-Montalcini; his experiences during the war years in Italy; his arrival in the United States in 1947 to work with Salvador Luria on phage at Indiana University, where James Watson was a colleague; his meeting with Delbrück at Cold Spring Harbor; and his arrival at Caltech and eventual switch to the study of animal viruses. Discusses his work with western equine encephalitis virus, polio virus, Rous sarcoma virus, and his collaborations with postdoc Harry Rubin and student Howard Temin. Leaves Caltech in 1962 to join Michael Stoker at Glasgow University for a year, thence to Salk Institute for Biological Research, in La Jolla. Moves in 1972 to Imperial Cancer Research Fund Laboratories in London and works with Yoshi Ito. Focuses on breast cancer. Receives Nobel Prize in 1975 (with Howard Temin and David Baltimore). Returns to Salk in 1977. Recollections of Jonas Salk, David Baltimore, and Jacob Bronowski. In 1988, he succeeds Fred De Hoffmann as

president of Salk. Resigns in 1992 and divides his time between La Jolla and the Milan laboratory of Italy's National Research Council, working on breast cancer.

## **Administrative information**

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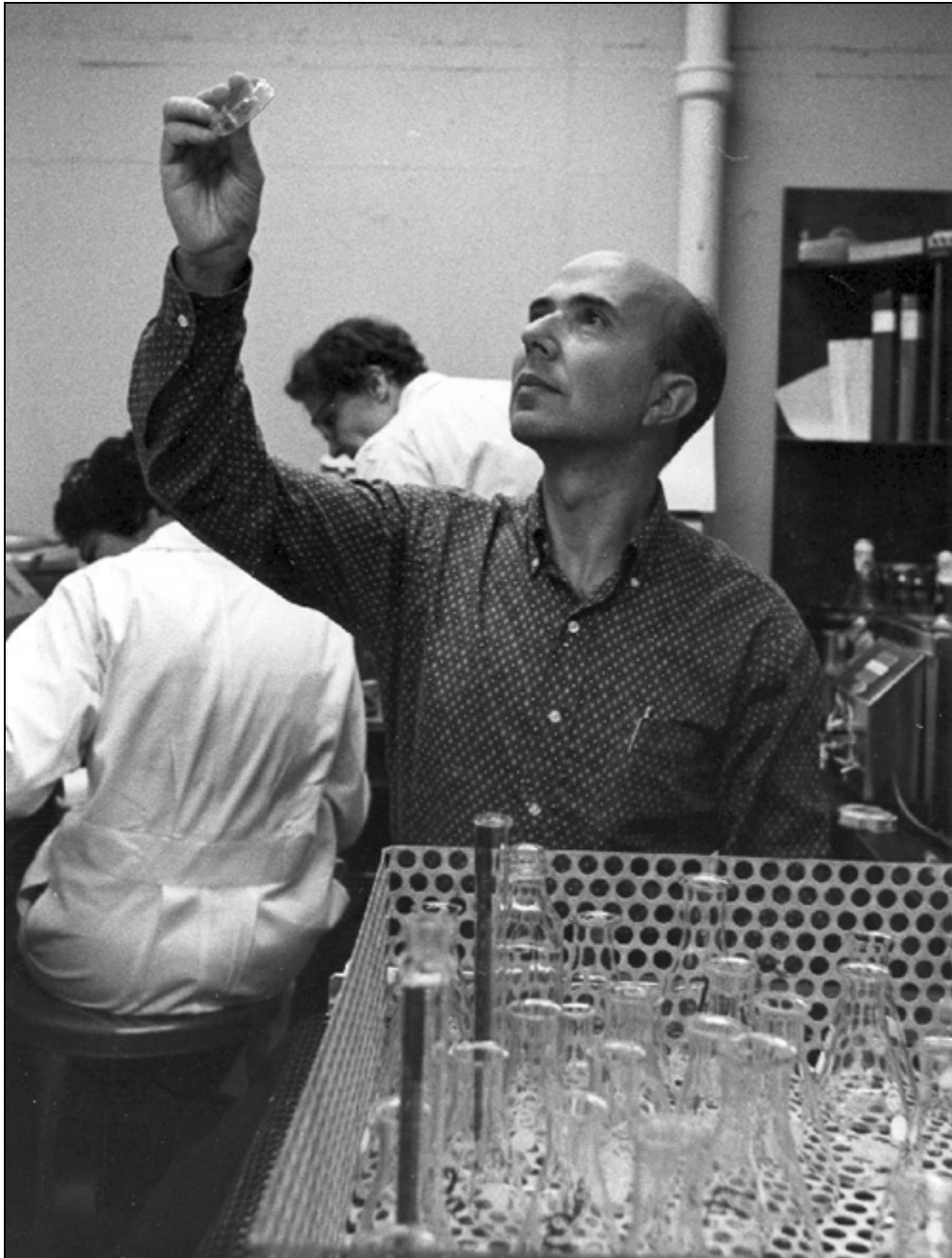
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Renato Dulbecco in Caltech lab, December 1961. Photo by James McClanahan.

**California Institute of Technology**

**Oral History Project**

**Interview with Renato Dulbecco**

**by Shirley K. Cohen**

**Pasadena, California**

**Caltech Archives, 2001**

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CALIFORNIA INSTITUTE OF TECHNOLOGY  
ORAL HISTORY PROJECT

Interview with Renato Dulbecco  
Pasadena, California

By Shirley K. Cohen

Session 1

September 9, 1998

Session 2

September 10, 1998

Begin Tape 1, Side 1

Cohen: Good of you to make this trip up from La Jolla. Perhaps we can start this interview with you just thinking back and telling me a little bit about your parents.

Dulbecco: My father was a civil engineer. He came from the north of Italy, near Genoa. My mother was from the south. My father, around 1910, was sent—he was a member of what was called the civil engineering group of the government. So he was sent to Catanzaro, which is the capital of the province of Calabria. In this territory there was an area highly damaged by an earthquake, which included a town called Tropea. Tropea now is very famous, of course, because it has a beautiful beach and is a touristy town.

Cohen: What year would that have been?

Dulbecco: Around 1910, 1911. He married my mother there, in Tropea. And they lived in Catanzaro for a few years. I was the second born—a boy was born before me, but he died when he was about a year old. He had meningitis, they tell me, which left my mother so desolate.

Then the war came, and my father was enrolled in the military, and he was sent to—we all went to Torino [Turin], in the north.

Cohen: You mean he wasn't a soldier who would go fight in the war?

Dulbecco: No, no. He was in Torino as an officer in the army, but they were making guns and things like that. So we stayed there for the duration of the war. And I remember essentially nothing about it.

Cohen: Well, you were just a baby, because you were born in 1914.

Dulbecco: I have some vague recollection of people queuing up for food across the street, and a few things like that.

Then from there, we went for a short time to another town in Piemonte—Torino is the main city in Piemonte—called Cuneo, which was about, I don't know, fifty miles away. We stayed there, not a long time. And then my father was sent back to Porto Maurizio for a brief period—where he had been born, actually. So we went there. He had a mother—his father had died—who was paralyzed by a stroke. We arrived there, and I remember my mother got a maid from her hometown to join us, so that she could care for this woman who was handicapped. We lived there for a long time. I got married there. We lived there until I came to the States, which was in 1947.

Cohen: But in the meanwhile, you, of course, were going to school.

Dulbecco: I went to the local grade school, the local high school, in Porto Maurizio, nowadays known as Imperia, which is a fusion of two towns, Porto Maurizio and Oneglia. That was a funny thing that Mussolini did. There happened to be a little stream going between the two towns, called Impero. So for some strange reason.... He was from Oneglia, or very close, and he knew about the area, and somehow he decided it should be united and form Imperia.

So I went to the high school, which is called *liceo* in Italian. There are two kinds: the classical *liceo* and a scientific *liceo*. I went to the classical *liceo*—the scientific one did not exist yet—and I finished there. I graduated when I was very young; I was sixteen, actually, which is two years early. That's because my mother, when I was a child, taught me to read, to count, and so on; it had nothing to do with me. [Laughter]



Then I went to the University of Torino. There was a difficult situation: I liked physics and engineering, my father being an engineer. I used to help him when he made projects, especially calculations for the reinforced concrete—which isn't really anything special but to me seemed a very important achievement. So I was inclined to go into engineering or physics. But my mother insisted I should go into medicine, because she had an uncle who was a surgeon in Naples, and she said that was the direction—

Cohen: Doctors are important.

Dulbecco: Doctors are important. So I went to the university and took my degree [MD; 1936].

It also was determinant for me, because in doing that.... I had always been very interested in research, in experiments, you see. When I was twelve, I built a radio for my mother; my mother liked opera, so I built a radio. I started with a crystal set, and then I built a real radio, with vacuum tubes. I used this knowledge to build a seismograph, because locally there was a station for earthquake detection.

Cohen: You did this while you were in high school?

Dulbecco: That was in high school. Probably it was the first electronic seismograph ever built, I imagine. [Laughter]

Cohen: Did anyone direct you in this? Or was this something you did by yourself?

Dulbecco: I did everything by myself. My parents helped me; they encouraged me; my father got me pieces. So I used this same approach when I had to build some kind of machine to start the heart pulsation, when I was in medical school, so that you could measure it without touching the heart. Of course, if I had been a good cardiologist, maybe this machine would have been developed. But there was nobody really interested in it at that time.

As I say, it was important for me, because in the first and second year you have anatomy, and the professor of anatomy there was a man called Giuseppe Levi. Giuseppe Levi was famous at the time, because he was an outspoken anti-Fascist. But on the other hand, he tried to live

with the system, because he loved to teach, loved his students. I remember when Mussolini decided that all university professors should swear allegiance to the regime: this must have been 1931. Levi was in a real dilemma. And we all knew this, in the school. He was obviously worried about this for quite a long time. And finally, we knew that he had decided he couldn't leave the school, so he would swear, no matter what. And he essentially explained why he did it; it was because he thought that the school was so important that he could not leave it. And even if he hated to [swear allegiance], he had to do it.

Cohen: His school and his students were more important than this.

Dulbecco: There was enormous applause from the students, who were very much with him.

Cohen: This was not the racial law yet?

Dulbecco: No, no, that was not the racial law—just general Fascism. The racial law came later.

It was important because, being interested in research, I became an intern in Levi's laboratory. And there was a laboratory and a desk—a place where I could work. He was interested in histology, in embryonic development. So since we were together the whole time in this laboratory, we knew each other very well.

Cohen: From what I've read, it was an honor to be asked to be an intern in Levi's laboratory.

Dulbecco: Well, it was very difficult—exactly! Anyhow, he selected his students. So that was very important, because Levi was a very inspired person. I mean, he had nothing to do with modern science. He was as far ahead as possible at the time, but still he was fairly behind, because his interest was essentially in histology and the cellular nature, trying to identify cell types, and no functional assays whatsoever. Anyhow, that was the state of the art at that time.

But he also was interested in tissue culture. And that was the thing that was important for me, because I immediately felt it was a really exciting idea. I read [Alexis] Carrel's book. You know, Carrel is the one who started this question of growing cells in vitro. So I had read his book, and I was very interested. So I learned about tissue cultures. I did some work on a variety

of things. But the important thing was Levi's personality, because he was highly encouraging and stimulating. On the other hand, he was critical to the maximum extent.

Cohen: I had the impression from this book I read by his daughter that he was not above shouting at times.

Dulbecco: I remember a funny thing in doing this tissue culture. One day, a strange pattern emerged that looked like a reticular type of cells. I went to Levi and showed it to him, and he said, "Ah, that's interesting." And then he said, "Well, you must not say anything to anybody, especially to somebody who is a good friend, because he's interested just in that. So you should keep this secret until you've really worked it out completely." [Laughter]

Cohen: This was typical?

Dulbecco: He was probably one of the broadest minded persons I can think of, in science and politics and things like this. But that was his style. [Laughter] Anyhow, it turned out to be nothing—it turned out to be an artifact—so the thing died there. Anytime that anybody went to him to explain something or say he'd found something, Levi had to look at the whole thing, and examine it, and ask lots of questions—and he'd say maybe it wasn't true because of this or that. But on the other hand, the criticism was very important.

Cohen: Good training.

Dulbecco: Very good training. He was inspiring and critical at the same time. Out of his laboratory essentially came the only three Italian Nobel Prizes [in physiology or medicine]: Rita Levi-Montalcini [1986], Salvador Luria [1969] [and Dulbecco, in 1975—ed.]. And certainly he had lots to do with that—not in the actual work that was done, because that was way ahead of the knowledge and thinking of the time, but in building up the personality.

I think those early years were very, very determining for me—as I am sure they are for anybody. When I was a young boy of eleven, probably, I decided to build this radio, and I bought a book, and I studied the book carefully, and I understood how a radio works, and so on.

And then I said, “I will build it.” And of course nobody believed me. But I did, you see. So these are things that leave a tremendous impression in the end, because you acquire confidence so that you’re not afraid of getting into things that nobody knows, nobody believes.

Cohen: But you also have to be in the right situation.

Dulbecco: Yes, exactly.

Cohen: Your parents had to go buy you the parts, and so on.

Dulbecco: Yes, parents are very, very important. And to me they were extraordinarily good.

Cohen: How was the life of the laboratory? I mean, I know how things are here [at Caltech]—its very sociable in the day, sociable at night. But were things more formal?

Dulbecco: Look, Caltech is a unique place. I’m sure there are very, very few places like Caltech, even now. The collegiality—people from various disciplines getting together, talking, and so on. This exists very little in other places.

Cohen: But certainly not there in those early years.

Dulbecco: Well, the Department of Anatomy is a big building. Mostly it was cadavers to dissect for students to learn the anatomy, and then there was a wing, and at the end there was a library and the laboratories. Rita [Levi-Montalcini] and I shared one of these laboratories, because we were the youngest in the group. But in effect the communication was between her and me—and Levi, occasionally. I did not know what the other people were doing. There was no tradition, you see. I don’t think there was any hidden purpose, or something like that; it was just the way things were done.

Cohen: So you were there until—

Dulbecco: Well, let's see. I graduated in 1936. And immediately I had to go into the army, because it was compulsory at the time. And I went to Florence, where there's a school for medical officers.

Cohen: You already had your medical degree?

Dulbecco: I had my medical degree, so I spent six months there. And then I spent two more years in the army, as a physician. That was before the war began. It was most interesting: there are countries that have compulsory military service, and lots of people think it's a waste of time. To me, it was not a waste of time, because I got to know people—people of a different class, different origins—that I would never otherwise have occasion to meet. That was very instructive just in understanding people. So it wasn't wasted time, for that reason.

That ended in 1938, and I went back to Torino. You see, in the meantime, I had shifted from the Department of Anatomy with Levi to the Department of Pathological Anatomy, because I thought for medicine that was more important. Because a patient arrives, there is an autopsy. You do the autopsy, or someone else does, and the physician there tells you what kind of diagnosis they had made and why. And now you can see whether the diagnosis was correct or not. So for medicine I thought [that was important]—in fact, I still think it is very important, although I don't think physicians do that anymore.

I wrote my thesis on the changes in the liver when there's an obstruction over the duct and the liver is destroyed. And I got the first prize, so that was very nice.

So then I went back to work in the Department of Pathological Anatomy. And that didn't last very long—

Cohen: Was Levi still there?

Dulbecco: This was a different department, but yes, Levi was still there. But then the war came, you see, and they grabbed me into the army again. And I stayed there until 1943, when the Italian Army went to Russia, to the Russian front. It was terrible. It was an experience, no doubt, but in the end only something like twenty percent [of the men] came back.

Cohen: Let me go back a little bit and ask you a question. At that time already, even Mussolini had to impose the racial laws. Did that in any way...?

Dulbecco: Yes, actually, that's an interesting thing. What happened was, essentially, we did not know—just vaguely knew—that if you were a Jew you could not be a professor at the university. It was something like that. But [I knew] nothing about the persecution—nothing, of course, about what was going on in Germany. That was unknown; nobody knew. Certainly, I did not know. Nor did my parents. My parents were very strongly against Fascism, so they were continually berating Mussolini. But this never came out. So obviously we did not know.

Cohen: But people like Levi—wouldn't he have lost his professorship?

Dulbecco: Oh, yes, sure, because he was a Jew. But I don't know exactly what his situation was. At that time, Rita had to hide in Florence, because nobody knew her there. And I was in the army. And there's a dramatic point when I became suddenly aware of this. It was when we were with this battalion of soldiers and [I was] the responsible medical officer. We were sent to Russia by train. We went through, I imagine, Germany, and through Poland. I know we were in Poland, because the train stopped in Warsaw. And then beyond Warsaw, at a certain point the train stopped in a station. It was a big station, lots of rails, and there were lots of people working there. Some men came, and I noticed one thing—that they had some kind of a yellow imprint or something. I knew a little German. And I said, "What are they doing?"

"Oh, there's a lot of work here."

I said, "Who are these people?"

"Oh," he said, "Those are Jews."

I said, "Well, why are they here?"

"Oh, they're here because they are our prisoners. Now, as soon as they are finished with this work, *kaput!*"

Cohen: They would be shot?

Dulbecco: [Silence] Just at that time, we had to get up into the train, and I explained this to the other officers in the battalion. And they couldn't believe it. They said, "That is impossible! You misunderstood." I said, "No, it's a very clear word. There's no ambiguity." Well, that was my turning point.

Cohen: Then you realized what was going on.

Dulbecco: And then I decided, OK, now I have to do my duty. Because, after all, these people I'm with are not Fascists; they're just like me. But then when I finally got back home, I was supposed to go back into the army and I didn't. Then I became connected with a group of partisans around Torino.

Cohen: Did you essentially have to run away?

Dulbecco: No. I had a period of rest.

Cohen: You were actually hurt when you were at the front.

Dulbecco: Yes, I had a dislocated shoulder. So I had a period of rest, and at the end of this rest period I was supposed to go back [into the army], but I didn't go.

In the meantime, I was married. And my wife's parents had a small farm in this area, about thirty, forty miles from Torino. This is an area that's hilly, all wooded, so it's a good place for partisans to hide. And in the beginning the only thing I knew was that I wanted to be out of the organization. There was one physician there, who really was very bad. So I decided, Well, I better help these people, and I became a physician for the village. Then I realized that if there were dental problems, there was nothing I could do, so I decided to learn to become a dentist—after all, I did everything in my life like that.

Cohen: Did you have supplies?

Dulbecco: Well, I could go to Torino, because I had a bicycle. I could bicycle to Torino—close to an hour's ride. The shops were still open, and I identified a place where there were dental supplies.

Cohen: Now this was still before 1945?

Dulbecco: This was 1943.

Cohen: So it was still the war years?

Dulbecco: Yes, 1943-44. And so I installed myself as a dentist, and I helped people there. I noticed that young people came, always belonging to the village. So I asked them.... I realized why they were partisans, so I became their physician. I helped them many many times.

Cohen: Would you go to them, or would they come to you?

Dulbecco: Normally they would come if somebody was wounded, to see what we could do. In the meantime, I continued to go to Torino, because I could still go to the university. Not to Levi's department, to the other place—the Department of Pathological Anatomy. During the war it had been bombed by the Allies, because nearby there was a factory [that made] ball bearings, and they were very important, of course. The Allies bombed the factory many times, and the bombs fell all around.

I remember I used to spend the night there. And the only place where I could spend the night was the morgue, where they'd keep the bodies. On top of the morgue, there was a bed. Usually somebody slept there just as a guardian. But there was nobody that time. Although the morgue was used, and actually there was an alarm connected to the various bodies, in case anybody woke up. [Laughter]

But then, in Torino, I got together with a group of people who wanted to rebuild the city and organize and so on. There were many political parties, and I became associated with a very small party, because I knew some people in it. It was all an underground set-up.



Cohen: You were doing many things. You were the doctor in the village. You were still doing some research at the university. And then you became involved in politics.

Dulbecco: Yes—in politics, in terms of looking to the future. A very good friend of mine had brought me into contact with the party, and he was also a physician. We decided we should have some kind of first-aid places throughout the city, because there was fighting. And through this underground organization, we succeeded in identifying such places. And I used to go, and there were women, and I explained first-aid techniques to them. I did that for several months. Then finally the final days came, and so this friend of mine and I went to the center of the city, to an old hospital which wasn't much used anymore. So we decided to set up our office there and wait.

Cohen: You know, this is interesting to me, because obviously everything you were doing was against the law.

Dulbecco: Yes, that's true. [Laughter]

Cohen: And yet you seem to be moving freely around.

Dulbecco: It's true. I had to be careful. I remember one day when I was at the hospital and the custodian, who knew me very well, came to me and said, "Two guys would like to talk to you." Now at that time, when they said two guys wanted to talk to you, that meant they were going to arrest you—they were police. But there was another door, and I went through the other door, into the main part, where there were lots of physicians in their white caps, and so on, and I mingled with them. And these guys couldn't trace me and finally must have left.

Cohen: But the people were against the government, so the people were sympathetic.

Dulbecco: Oh, yes. Essentially everybody was.

Cohen: So that's why you could do what you were doing.

Dulbecco: Exactly, yes.

Cohen: Nobody was going to say, “Come and get this man.”

Dulbecco: No. And that night, I remember this tremendous noise—cars, tanks, and so on. The Germans were retreating; they decided not to blow up the city—I don’t know why. And they retreated. And then the morning after, it was a beautiful day. And the streets of Torino were full of people—fantastic!

Cohen: They were liberated, when the Germans left.

Dulbecco: The most impressive thing was that evening. The town had been always dark. And that evening, on the main street, there were lights. Incredible!

Cohen: And that was when the Germans left?

Dulbecco: The Germans left, and then the Americans came, and you had to deal with the Americans. And actually, since I was part of this underground organization, automatically that became the control of the city; it took over as the city council. So we had to continuously report to the American authorities. But it was just a question of filling out documents. I stayed with the city council for two months. And then I said, “Well, I’m not made to be a politician,” and I went back to my work.

Cohen: And this group, I think from what I read, became the Communist Party.

Dulbecco: Well, my group was called the Movement of the Christian Left, which was kind of part of the Communist Party—a splinter group, with this Christianity attached, which Communism doesn’t have. That was important, because in Italy people are generally religious. But it disappeared. I left, and I know that the others all joined the main Communist Party. So that was the end of my career in politics. [Laughter]

Cohen: So in 1945 you went back [to the university].

Dulbecco: I went back. And Rita also came back to Torino.

Cohen: She was hiding in Florence this whole time?

Dulbecco: Florence, yes, working in a kind of laboratory in her bedroom, trying to do something, but she could not do much under those circumstances. But, you know, that keeps you going.

So I saw her, and she said, “Well, you know, that’s not a good place to work.” I knew that, in terms of the science. And she said, “Why don’t you come back to Levi’s [department], which has much better science?” And so that’s what I did.

Cohen: Was Levi back in his laboratory again, then? He must have been hiding during those years, too?

Dulbecco: Oh, yes, sure. He also, I think, went to Florence, because it was thought that if the Allies were coming from the south, as they did, then Florence would be easier, because [the Allies would reach it] sooner than Torino.

Cohen: But these people were able to hide effectively?

Dulbecco: Well, obviously, yes. Well, you know, everybody protected them; nobody was against them. That’s the difference. It was not Germany.

So I went back to work with Levi, especially doing tissue culture work, but that didn’t last very long, because, first of all, I was now interacting with Rita. That was very important for me, because Rita is a very wise person. And we became real friends. We talked continually about the future—what to do, what will come next, what science. And I remember, on the question of genes, we had a vague notion that there was such a thing as genes. At school, no one had taught us genetics. And there were also publications; they were all on histology, anatomy,

pathology—things like that, merely medical. So there was nothing that could direct us toward genes, but we knew something, and we were talking about this. And then she came with a proposal to try to visualize new methods for studying genes. And she said, “Since you’re good at mathematics, why don’t you enroll in physics, because that may be useful in this way of thinking.” So I did that. For two years, I was a student—

Cohen: How did you support yourself?

Dulbecco: I was an assistant, so I got a salary. I worked with the students, made practical exercises for the students.

Cohen: So she essentially said, “Go be a student again. Go learn physics.”

Dulbecco: Which I did. For those two years, I took courses. Since I’d already had some background in mathematics and chemistry and elementary physics, I could skip the first year and go directly to the second year. So I did the second and third year. At the end of the third year, a crucial event happened—and that was a visit from [Salvador] Luria. Luria had realized, at the beginning of the war, that the situation would be bad, so he left.

Cohen: He went to the United States.

Dulbecco: He left and went through Europe, and finally succeeded in getting away to the United States.

Cohen: So you had not met him before?

Dulbecco: Oh, yes. We had worked together [at Torino]. He was a year ahead of us, but I knew him.

He came to Torino to see Rita, especially, because he was a very good friend of Rita’s. And then Rita suggested to him that he should talk to me, because of these ideas and so on. So we talked, and Luria asked what I was doing. And I explained this idea to try to study viruses,

for their genes, with physical methods, especially radiation. And I was studying physics because of that. And he said, “By gosh, that’s what I’m doing!” [Laughter]

Cohen: And he was doing this at Indiana University?

Dulbecco: Yes. And so he said, “Why don’t you come and work with me?” Oh, immediately I said, “Sure I will!” That was in 1946. And of course they had to make some arrangement regarding my visa, which wasn’t easy. Then finally, I succeeded in getting everything together. So in the summer of ’47, I left. I left along with Rita, by pure accident, because she was going to Washington University in Saint Louis. She was an experimental embryologist and she had done nice things, so she went to work with [Viktor] Hamburger, who was an experimental embryologist there. We were on the same boat, so we went together. [Laughter] We were on a Polish boat called the *Sobiewsky*. As I say, again, you make a decision. It is not difficult for me to make a decision, even a very important one, when I’m convinced it’s the right thing. At the University of Torino I was an assistant professor, which in Italy is a life appointment, but I resigned and went [to the United States] in a totally uncertain situation. And it all worked out quite well; I was lucky. And after two years there, then Max Delbrück asked me—

Cohen: Let’s stop here. [Tape ends]

**RENATO DULBECCO**

**September 10, 1998**

**Session 2**

Begin Tape 2, Side 1

Cohen: In our last session, we discussed your life in Italy a great deal. And when we finished, you were just going to the United States. I would like to ask you a little bit about the atmosphere in Italy in the two years after the war, when people supposedly were resuming their normal life.

Dulbecco: Actually, in terms of the general feeling, the people in Italy rebounded immediately. It was an enormous change; I mean, it was a new country. I'll give you an example: There was a railroad bridge that had been destroyed, just south of Torino. They started working, and in a week—or ten days at the most—they built a temporary bridge, which meant the train could go again. I mean, things like that. The people were in a very positive mood. Of course, then the politics began. But in the beginning it was a wonderful time, I must say. Of course, for a scientist who worked in a laboratory, it was abysmal, because there were no facilities, nothing. And, of course, that was one of the factors in my decision to leave. But in terms of the general feeling among the people, it was a very positive time.

Cohen: And they were optimistic. They felt that they were going to get back to their normal lives.

Dulbecco: Exactly.

Cohen: And the physical destruction in Torino was not great?

Dulbecco: Well, there was physical destruction. As I told you, the place where I used to work was a big building—half of that was demolished. Across the street from the hospital, there was a six-story building which was demolished. There was a lot of damage, especially in that area, because, as I told you, the ball-bearing factory [was nearby]. But that was rebuilt after not an

especially long time. I think all that Italians need is to be pushed to the edge, you see, and then they react well. [Laughter]

Cohen: So, as far as the spirit of things went, things were OK. And then, of course, you were presented with this opportunity, and your work was very important to you. So you got a leave of absence?

Dulbecco: No, I didn't get a leave of absence; I resigned. I left. I didn't leave any door open to come back.

Cohen: And this was to go to Indiana University?

Dulbecco: Yes.

Cohen: And you didn't take your family with you at this time?

Dulbecco: No. I went alone, because I had a year's appointment. I didn't know whether it would be standard, and there was the question of the visa, and so on—it was very complicated. Actually, the question of the visa is another episode—which I think is a fantastic episode.

Before leaving, I went to the consulate many times. So they gave me something to take with me. And when the boat docked in New York, a young man came aboard to check on the people. And when I went there to present myself to this man, he studied my application very very extensively, for quite a long time. And then he wrote something on my passport and gave it to me, and he said, "OK, you can go." So I went down to the pier to look for my suitcase. And shortly afterward, I heard somebody running behind me, and I turned around, and it was this same guy, who came up to me and said, "Oh, give me your passport." So he took the passport, erased something, put in something else, and then said I could go. To me, it meant nothing at all. Actually, it was very important, because originally, you see, I was a teacher at a university—an assistant professor—and I was also doing research. And obviously he was weighing all these things, and at first he thought that fundamentally I was a researcher who came here to study. So he had given me a student visa, which would have meant that I had to leave the country after two

years. Then he changed his mind, realizing that that was unfair, that I deserved the other visa—which is a permanent visa—as a teacher. So he ran after me and gave me the other one. I don't know how many times something like this happened. It must have been an exceptional situation, to have a guy so conscientious that he would do that. Another guy probably would have said, "Well, OK, you're fine this way," and he wouldn't worry. I thought that was incredible.

Cohen: So, here you were in New York.

Dulbecco: In New York.

Cohen: Now, this was the first time you'd been to the United States.

Dulbecco: Yes, of course.

Cohen: How was your English?

Dulbecco: Very bad. [Laughter] I had studied, but.... Fortunately, there was a friend of a friend of mine, an Italian, who was in New York. He picked me up. Actually, he was waiting for me. I had to find a place to sleep. And he apologized to me, because it was the time of the World Series in New York, and it was difficult to find something, he said, but he'd find me something. So he took me to this big hotel in front of Pennsylvania Station. He took me to a place where there was a kind of sauna, a bath. Near it there was a big, big room, subdivided with movable partitions. And in each cubicle there was a bed, where people who were done with the bath, or whatever, went to rest. And that's where I spent the night, and it was full. Every bed was occupied. [Laughter] But it was nice.

Anyway, my train reached Bloomington—

Cohen: You left immediately the next day?



Dulbecco: Yes, I took the train to Bloomington. Luria had arranged for some organization, some ladies, to pick me up and help me get onto the train in New York. And then he was at the station in Bloomington. He had rented a room for me, and he took me there. And that was it.

So that started my life in the United States. [Laughter]

Luria was working on a phenomenon he had discovered, which was called multiplicity reactivation. Multiplicity is this: Phages are bacterial viruses. When you infect bacteria with these viruses, you can arrange the quantity of the two in such a way that there is, on average, one or two or three virus particles per [bacterium]. That's called multiplicity. Reactivation is this: If you take these phages and you shine ultraviolet on them before putting them into the bacteria, a large proportion of them become inactivated—that is, they cannot reproduce anymore. But if he put several of these phages, which by themselves could not reproduce, into the same bacterium—high multiplicity—then reproduction took place. And he thought that some kind of exchange and recombination was going on. So I worked on that and I found one thing; this gets into the mathematics. If you have an activation curve, a pure single activation curve, it should be a straight line on a semilogarithmic plot. Now, if you have a multiplicity factor, then they should be curved like that, because in the beginning nothing appears to happen, until finally—whatever mechanism is at work—activation continues. And according to Luria's idea that everything was based on recombination, then you predicted that the ultimate slope would be the same as for a single particle, that it was only displaced. But it wasn't—it actually turned out to be a lower slope. Which means that part of the genome could be dispensed with, but another part could not be dispensed with. Years later, this was understood. Because in order to have this reactivation, you need some activity, from genes or the virus itself. So this gene must be maintained. If it isn't maintained, then all the other damages persist, because they do not get repaired. So what you measure in the final slope is the cross-sections of whatever is needed.

Cohen: Did Luria have a very large group working on this?

Dulbecco: No. When I arrived there, he had on the top floor, under the roof, just one long room. In it there was a cubicle. And he sat there, in this cubicle, off this long room, and at the end of the room there were two desks. When I arrived, he gave me one desk, and the other desk was for a technician. That was all.

Later on came Jim Watson [James D. Watson, then a graduate student at Indiana University, later codiscoverer with Francis Crick of the molecular structure of DNA—ed.]. And he took the other desk.

Cohen: So you were a group of three—Luria and the two of you?

Dulbecco: There was a part under the eaves, where it was dark, and the microscopes were there, and I think finally somebody sat there also.

It was very nice, because we talked quite a lot with Jim. There had been an interesting experiment done by a Danish scientist named [Ole] Maaløe. The thing that impressed Jim was the fact that if you infect a bacterium with a phage which is marked in the DNA—because we knew that there were two components, DNA and protein—or in the protein, that the DNA would actually transmit to the progeny, whereas the protein would not. We were talking about this, and he saw that probably the DNA was important in transmitting characteristics.

Cohen: That really wasn't known at that time.

Dulbecco: No, not at that time. The two experiments of DNA were the experiment of transmission of bacteria to mice, and the DNA of bacteria could transmit the characteristic of virulence. But this was debated for a long time, because it was never pure DNA; there could have been a contaminant, and so on. And then the experiments of [Alfred] Hershey that showed with phage, again, that the phage transmits. But Maaløe did a number of experiments like that. I don't remember the dates—it may be that Maaløe did the experiment first. In any case, there was the experiment by Maaløe, and Jim was saying, "Well, you know, DNA...." And he was telling me, "I'm going to take my degree, and then I'm going to go to a place to study DNA." He already knew; fundamentally, the discovery of the role of DNA is his, really.

When I was in Bloomington, I decided to improve my knowledge. So I took a course in genetics with [Hermann J.] Muller. Muller is another Nobel laureate geneticist [1946]. I took the course together with Watson, and I remember that my English was very bad at the time. So there was a German woman, who took notes in German, and she passed me her notes in German. [Laughter] I remember the final test: Muller usually put the tests at the end in a pile, in order—

the best one was on top, and so on. And I remember that we were there, Watson and I, and we looked at the tests, and mine was on top. And Jim—he was very, very competitive. And he really suffered, poor guy, from the fact that he was below me. [Laughter] But we remained good friends. He's a difficult person—used to be. Nowadays he's better.

I remember doing two pieces of work there which were good and attracted lots of attention. When I was working on this multiplicity reactivation phenomenon: How do we know how many particles of phage, how many viral particles, can cooperate and be active in the same cell? Because there must be a limit; it cannot be an infinite number. Maybe we were using a number which was not adequate, and maybe we should cut down or increase and so on. So I worked out the mathematical system by which I could determine, measure the number.

Cohen: And that was really using your physics?

Dulbecco: Yes—well, at the time, that was very important, because that was the main weapon: statistics and mathematics. But it was an interesting experiment, a good experiment, done well: you know, by thinking about the problem, developing a model, and then testing it with the proper means, and so on.

I remember Luria asked me to give a seminar—a kind of informal seminar to a small group, where there was a professor of biochemistry. When I finished with that, [this professor] was very impressed and said, “Well, they should give a public seminar, not just to us.”

Then the other thing happened by accident. You know, accidents are wonderful in science, provided you can take advantage of them. [Laughter]

Cohen: If one notices them, yes, of course.

Dulbecco: And it was this: With phage work, we always have two plates for each point on an assay, to make sure that there is uniformity. I would sit at the bench and put the UV-irradiated phage in the two dishes, and put the two—one on top of the other—on the bench. And they stayed on the bench until I finished the experiment. Then everything got put into the incubator. One thing I noticed during the experiment with the phage was that in the end, when the plaques developed and I'd count, these two plates, the same pair, were always somewhat different.

Cohen: Even though you set them up the same?

Dulbecco: Yes. They should have been identical. This was not so—beyond statistics—and so it was certainly different. So I started wondering why. I thought, Well, maybe it was the way I put them in the incubator. Maybe I put one before and the other later, or one on top of the other. So I changed things around, but it was always the same. Then I remember one day looking at the thing. And on top of the plates was a big fluorescent light. And I said, “Aha!” I knew that something involved the effect of visible light on survival in bacteria. Someone had reported that. So I said, “It must be the light.” So we tested, and in fact it was the light.

Cohen: So the one that got put on top—

Dulbecco: Got the more light. And the one below got less. And then, of course, I started working to try to understand this, essentially—at least, which kind of light. So this was published in *Nature*. Again, this was very interesting, because also in bacteria reactivation occurs, as in phage, but in virus it had not been observed—it was the first time. And that told you something—that the effect must be related to something that happens in the genetic material of the virus. In effect it defined how the basic mechanism should be: effect of the light on the DNA damaged by UV. So those were the two main things that I did.

Cohen: This was in a one-year period?

Dulbecco: I stayed two years. After the first year, Luria gave me a promotion. I was still a fellow, but he doubled my salary so I could get my family to come. And they came after my first year. I remember, we lived in some kind of barracks that were remnants of the war—they were OK. The summer between these two years, and before my family came, we went to Cold Spring Harbor.

Cohen: It had already been organized?

Dulbecco: Yes. In the summer, lots of people went there. The phage group was the prominent one. That's where I met [Max] Delbrück [professor of biology at Caltech]. I had occasion to talk lots about science, because you were continuously doing experiments and then discussing them. And Max was always interested in anything, always trying to calculate a formula or explain certain curves, and so on. It was an exciting time. Max also gave me the feeling of the academic community in the States, which is very different from Italy. Here there's comradeship. In the evening, we had square dances; people had parties, and things like that. In Italy, the academic community is not like that.

Then, after the discovery of reactivation, I went to Oak Ridge to meet and talk about that. So Max asked me when did I want to go to Caltech. I remember receiving this letter from Max, and Jim Watson was sitting there. And I said, "What do you think, Jim? Do you think I should go there?" And he said, "Oh, absolutely. Caltech is the best place in the United States, so you should go there." So I went [1949, as a senior research fellow—ed.].

Cohen: But Luria must have been unhappy to lose you.

Dulbecco: Yes. Now they tell me—I never knew anything of that. But apparently there's correspondence between him and Max, in which he expressed irritation at Max taking away his people. I did not know anything about that. He didn't tell me anything.

Cohen: So you took your family. You were there two years in Indiana?

Dulbecco: Yes, two years in Indiana. So we drove west. I had an old car, which I had bought there, and we drove. I rented a small trailer, just a box, to put our few things in. So with that, we went across the United States. It was a tremendously interesting experience. Lots of adventures. And we made it safely. We camped all the way. I remember the last night—the last night we camped above San Francisco—Mount Tamalpais, where there is a state park. I remember talking to the ranger there, chatting. He said, "Where are you going?" I said, "Oh, I am going to Caltech." He said, "Oh, where they split the atom." That was its reputation.  
[Laughter]

We arrived. Here, for a while, I continued working with the phage, trying to solve the mystery of its biology.

Cohen: The group was not very big at this time at Caltech, was it?

Dulbecco: There was Seymour Benzer [then a research fellow in biophysics.—ed.].

Cohen: Did you know Seymour Benzer before this, or did you meet him at Cold Spring Harbor?

Dulbecco: No. Although he came from Indiana, too, but not Bloomington—he came from Purdue. So we became friends, but we didn't work together. For a while I worked entirely on my own, on phage, looking for something different.

Then there was this meeting, as you say, in 1950—

Cohen: Is this about the Boswell money?

Dulbecco: Yes, it was lots of money at that time—\$100,000. Caltech had received this money but did not know what to do with it, because it was for virus research. And it seems, from what I was told, that [Lee] DuBridge, who was Caltech's president, talking to Max, told him to try to organize something with this money, because Max was the one involved with viruses, you see—phage. And Colonel Boswell had shingles, and why couldn't we find a cure for shingles? You know, we had so many people working with viruses. And Max said, "Well, you know, these are different viruses from those that cause shingles." So they decided to try to make me do something in the field of animal viruses.

Cohen: That's interesting. You say this was at DuBridge's urging?

Dulbecco: That's the way I heard it. Max called Seymour Benzer and me to his office, explained the situation, and asked whether either of us was interested in getting involved with this. And Seymour said no, because he liked what he was doing; he was happy. But at the time, phage work didn't appeal to me so much. I needed something new, so I said yes. Also, because

with my background, I had an MD and viruses are a medical problem. Then, the other thing that I immediately thought was that to do anything in the field, you needed tissue cultures. And that I knew; I already had a background in that. So I said yes.

Then we discussed what to do. I said that I did not know anything about animal viruses, and if I was to do anything sensible, I should go and visit laboratories where they work with these viruses, in order to see what people do now—a base to start from. And they all agreed. And so I started on an almost three-month trip throughout the country, mostly in the east.

Cohen: Now, how long had you been in Pasadena by then? Not very long.

Dulbecco: Well, I must have been there two years by then.

Cohen: So you were well settled here?

Dulbecco: Yes. So I undertook this long trip to visit lots of places and learn about what people were doing—about the types of viruses one could use, their properties, and so on. And when I came back, I wrote a paper, saying that if we wanted to do some work in this field, the first thing to do was to develop a good system for assay of animal viruses. Because they used to have this method of progressive dilution and characteristics where a cytopathic effect was present or absent. But these were very rough ideas and not precise at all.

Max agreed to my plan, and [George] Beadle as well.

Cohen: Beadle would have been head of the Biology Division at that time.

Dulbecco: Yes, he was head of the division. So I said, “You know, the virus I need is the western equine encephalitis virus,” which was known to be pathogenic. And they were very worried about that, so they decided to send me to the second basement.

Cohen: Important things happen in the second basement. [Laughter]

Dulbecco: Yes. At the end of the corridor, there was a room by itself. So I was very secluded in there. Actually, there was an old man there, who was ready to retire. I don't know what position exactly he had—some kind of research associate, probably. He was very cooperative, helping me set up things.

Cohen: This was in the sub-basement of Church [Norman W. Church Laboratory for Chemical Biology]?

Dulbecco: No, the sub-basement of Kerckhoff [William B. Kerckhoff Laboratories of the Biological Sciences]. I moved to Church later, but in the beginning it was Kerckhoff. In the beginning, it was very difficult. Immediately I was thinking that my goal was to develop a plaque system like that of phage, because that is the way you can get a good assay. And for that, you need a uniform layer of cells. And there was no way to do that at the time, so I started trying to take small pieces of mouse embryos to make culture, using small pieces.

Cohen: One small piece in each petri dish?

Dulbecco: No, several. And that wasn't really good. And then, on my trip, I had to visit somebody—unfortunately I don't remember the name—who was also interested in growing cells. And he wrote to me and said that he had developed a method for making a “steak” of cells in petri dishes. He took the tissue, he put it in a glass tube, at the bottom of which there was a fine net, and then there was another tube in centrifuge. So this way the tissue was pushed against the net and broke into very minute pieces—single cells and so on—and he used that to start a culture.

Cohen: So he had many little dots to start with?

Dulbecco: Yes. But then, you see, they'll grow and fuse together when they grow. So I did that and it worked quite well. So I developed it, adapted it to my needs, and started experimenting. And I remember once I started that, maybe for a week or two, nothing seemed to happen. And then one day I took one of these cultures to see whether there were any of these plaques. And



for some reason, I put the culture in a tangent light, and I saw that it was full of plaques. They were not visible in transmitted light, like this. They needed defraction, or refraction, in order to be visible, because obviously when the cells are killed, they make very fine granules, which you see by the scattered light.

Cohen: The color is all the same.

Dulbecco: The color is all the same. So I remember, I went to Max and I said, “Can you come down?” And he looked at me and said, “Now you have something to tell me.” So I took him down and I showed him this thing. And he said, “What day is it? Be sure to remember.” But I don’t remember. [Laughter]

Cohen: But you knew it was important.

Dulbecco: Yes. So then we discussed it with this old man that was there to do something, because the plaques were very difficult to see. He suggested we use a lighter stain—that stains living cells but not dead cells. And so we added this to the medium, and we could clearly see the cells as—

Cohen: Oh, so this stained the living cells, and you could easily see it.

Dulbecco: —a red background, and these holes. So, for me, that was a great accomplishment and an important thing. I also remember that Max said I should give a talk to the National Academy [of Sciences], which I did. At the end of the talk, we were just outside, talking. There was someone, a very famous person [who had also given a talk], who works with plant viruses....

Cohen: Maybe the name will come to you.

Dulbecco: Anyway, he said, “I think that was the most important talk of the day.” So that was a nice compliment.

Cohen: About what year was this?

Dulbecco: The paper was published in 1952—the paper in PNAS [*Proceedings of the National Academy of Sciences*].

So that was the beginning. That put me in that field, and people started coming—postdocs, and so on—from all over the world. I concentrated, in the beginning, just on studying a little bit more about viruses—studying things like the role of antibodies in inactivating retroviruses, a variety of things. Then the people from the National Science Foundation came and said that I should try to develop a system like that for polio, because they were in vaccine development at the time.

Cohen: And there was money there. That was the March of Dimes.

Dulbecco: Actually, they also gave me useful information, because they told me that some people working with tissue culture found that you can disperse tissue with trypsin rather than use this complicated centrifugation method that I used. And I adopted that; that simplified things. So it was very useful.

Of course, people here at Caltech were very, very worried about work in polio.

Cohen: Let me go back a minute. When you were developing all of this, were you working essentially alone, or did you have a research assistant?

Dulbecco: No. I had one research assistant and no students. I had this old man who collaborated with me until he retired, which was soon after.

Cohen: This was the days before the big laboratories?

Dulbecco: Yes, exactly. And then, when this question of polio came up, I was still there.

Cohen: In the sub-basement?

Dulbecco: And Beadle said, “You know, you can’t work with polio here. You have to rent a laboratory outside.” So they rented a laboratory at the Huntington Hospital. At that time, Marguerite Vogt joined me. She was working with Max, and she came to be with Max.

Cohen: Who is this Marguerite Vogt—I see her name showing up in these things.

Dulbecco: She’s German. She’s the daughter of a very famous neuroscientist in Germany at the time. Both her parents were scientists. She was working in insect development for a while in Germany. But then she went to Paris—I think she worked with [Boris] Ephrussi. I don’t know how she got to Caltech; I think maybe through Ephrussi. Ephrussi knew Beadle very well, and he probably suggested her. In any case, she was working with Max on some problem that I don’t think she liked very much.

Cohen: She was a research fellow?

Dulbecco: She was a research fellow—she’s an MD, too. So, when I started working, and especially when polio came up—I don’t know how it came that Max one day asked me if I would like some help, an assistant, and suggested I ask Marguerite. And I said, “Oh, yes, sure.” We were very enthusiastic, because that was similar to the things she liked to do. So we worked together. Of course, we needed the cells from monkeys in order to do that. And we were equipped to do it. So we developed a plaque system which worked very well. Also, we succeeded in demonstrating two things: One is that if you want to have a pure strain, you have to pick one plaque, and it will give you a pure strain. And the second, that even by looking at different plaque types or size, and so on, you can get mutants. And I think it was this, especially the purification of the plaque, that was essential for the Sabin [polio] vaccine development. Because otherwise you use a system of enrichment but you always have mixtures. And it would have been impossible for him [Albert Bruce Sabin] to develop a vaccine without the means to really purify it with certainty.

Cohen: Of course, these were live viruses.

Dulbecco: Oh, yes, sure. So that was very, very useful.

Cohen: You must have been a professor by now. Is that correct?

Dulbecco: I'm not really sure. But I remember that when I developed this plaque assay for viruses, there was a visitor here from Australia, a virologist. He was somebody well known in the field. And he did not know about the plaques, and I showed him. He was very impressed. Then he went to talk to Beadle and told him how impressed he was. So this was one element. Anyhow, about that time they made me associate professor [1952], which was the beginning.

Cohen: Well, that was a permanent job.

Dulbecco: Yes, that was an important thing. Then they decided they could build a really good laboratory. And that was in the second basement of Church. And they built it in such a way that it was contained, so I could use any virus I wanted, and people would not feel threatened by it. So I started to get lots of good postdocs, students.

Cohen: And you still were using NSF money?

Dulbecco: Yes, for quite a long time. But then, when the switch occurred, I had a student as a postdoc here—Harry Rubin. Harry Rubin was a vet, who however was interested in research. He was also an All-American—he was a big guy. [Laughter]

Cohen: Caltech hardly had any sports, but anyway...

Dulbecco: Caltech had some team that used to fight with all girls' teams. [Laughter]

Cohen: You know, I've interviewed Herschel Mitchell [emeritus professor of biology]. And he told me he was the one who organized some of these things.

Dulbecco: Yes. But they always lost anyhow. [Laughter] [Tape ends]

Begin Tape 2, Side 2

Cohen: So you were working with Harry Rubin, who was a postdoctoral fellow.

Dulbecco: Yes. As I say, he was a vet. And for whatever reason, he was interested in viruses that cause leukemia in chickens. So he came here, and the idea to use chickens, of course, was not a suitable one—there was no way. In addition, we wanted to work with tissue cultures, but these viruses did not have any effect visible on tissue cultures. So we shifted to the Rous sarcoma virus.

Cohen: Now this causes cancer, doesn't it?

Dulbecco: In chickens, yes. At the time, I also had a student—Howard Temin. Howard Temin got to work with him, and they developed an assay system for this Rous virus which wasn't based on plaque formation but on the focus. They were made up of heaps of cells, quite distinct. So that was a useful thing. And they continued to work.

Temin was a very bright guy. He was interested more in the biology—How does a virus cause cancer?—and that became, in our group, the main thing: how does a virus cause cancer. And I remember that we talked a lot about that. One very important element—and this I really want to stress—was this: In addition to us working with this virus, with a good group, ten people, something like that, there was on the floor just above us a man named Jean Weigle; he was a Swiss. He was a physicist, actually, but like Max he had become a biologist. He was working with phage lambda, which is a temperate phage—a phage that establishes a relationship with a cell without killing it. But then after a while you can show that the virus is there, or at least its genes, because you can induce the release of virus—and actually this has been shown by André Lwoff in Paris—by simply shining a little white light on these bacteria, and they release the phage. So there was, therefore, something which told us that it is possible to have a permanent infection within the walls of the cell without the cell suffering from it.

You see, that was very important, because the essential thing in biology is the possibility of cross-fertilization. People who do different things, if they are there together, they talk to each other, they lunch together, and things like this. These things come up, and there's this cross-fertilization. I thought that was really a model that we should keep in mind. And in talking to our people, Howard would say, "Yes, there's no doubt. There must be something like this." And he tried to do an experiment to show that the Rous sarcoma virus persisted in the cancer cells, but nothing directly to show it. So finally he presented this idea as part of his thesis, as a hypothesis. And I remember that Max was on the committee. And Max wouldn't hear of that, you see. He said, "You have no evidence, therefore you cannot say that." He was very strict—too strict, actually.

Cohen: Ah, that was the physicist in him.

Dulbecco: Exactly. Anyhow, Howard got through very well. But Max would not accept it. [Laughter] Because there was no evidence. Anyhow, that remained in my mind as really the main model.

That was my model. But I was thinking: we know that this virus has RNA as a genome; how is it possible that the RNA persists in the cells? I didn't know any mechanism. So I thought, Well, if I want to look at the problem, I should look at the tumor virus, which has DNA rather than RNA. And at that time, people in Bethesda had discovered this new virus—polyoma virus—which causes tumors in mice. It seems that it was a DNA virus. So I asked them to send me a sample. They generously did. There was a good biochemist, John Smith, from Cambridge, England. We looked at this and we decided to see if it has DNA for sure. And we did, and we found that it was DNA. But first we had to learn how to clone the virus, to make an assay, and all this took time, but anyhow....

So we decided, Well, now we have to see whether we can use it in culture, because that was essential. So Marguerite would come to work and we would try with cells of various kinds. She was very good at tissue culture.

Finally we found that with hamster cells, once they're infected, after a while those cells become transformed, so there are foci in the cultures. So we had a system by which you could work. You could kill mouse cells so you could assay the virus by making plaques. And you

could transform cells, I could see, by working on hamster cells. So we had a good system, you see. And we started defining the system.

And then another accidental thing happened. There was a meeting in Texas—in Houston, probably—on viral DNA, or viral DNA was one of the topics. And they invited me to go there. In effect, I had nothing to say about viral DNA at that time, because—

Cohen: You were just starting to work on it.

Dulbecco: So I concentrated for a while on this particular thing. And I remember reading an article—by Jim Watson, actually, with somebody else—on polyoma virus DNA, I think. They had found that when they sedimented DNA, the sediment was in two phases, in two bands. And they suggested that the DNA must be present either as a single copy or two copies in the viral particles. I don't know why, but I thought that seemed unlikely. Why should a virus be in two copies in a particle? It occurred to me that it was funny.

So I decided to test it. First of all, I put the polio virus through the same experiment, and it did the same. There were two bands. So now we could proceed; at that time, somebody else had described the column for fractionated DNA—the Hershey column. So we said, “Well, let's set up a Hershey column.” Actually, my wife did that. She was a technician.

Cohen: What year was this now? Late fifties, early sixties?

Dulbecco: Early sixties. So she made the column; we put the DNA in the column; it came out as a single band. So there was a different explanation. So we started thinking what it could be. At that time, [Robert] Sinsheimer [professor of biology, 1957-1977] was here. He had shown that a virus, a phage, has a very small DNA, single-strand DNA, and it was circular. So I thought, Well, maybe that's the explanation. The virus has circular DNA, and sometimes the circle breaks and gives rise to molecules which are elongated. And so they separate in centrifugation, but the size is the same. So they come up in the column together.

Cohen: So you had one column with the circular and one with the broken—that is, straight—?

Dulbecco: No. In any preparation, there would be a mixture of circular DNA and straight DNA. And in the centrifuge, they would separate, because maybe the circular one has less resistance.

Cohen: I see. So it's really the same virus, but it has taken different forms.

Dulbecco: Exactly. Although they are different shapes, they would go together in the column, because that's based on the adhesion and the shape doesn't count. What counts is length. So we worked on that, and used DNase to see whether it could convert one to the other. It did. Anyhow, so I published and presented data at the meeting.

Cohen: This was the meeting in Houston?

Dulbecco: Yes. We had bad fortune in that particular case, because I wanted to have more direct evidence about the two forms. I had asked the electron microscopist here, who was just across the hall from me, whether he could look at the DNA, and he said he would. So I prepared my two samples. Then this guy had some terrible problems—personal problems—so he was never there, the thing was never done. So I couldn't do it, and that was a bit difficult. If I had done that, I would have seen that in fact my interpretation was only partly correct. It is true that it's circular, but the part that I thought was linear was not linear, because the enzyme cuts only one strand. One was circular, all twisted. The other was relaxed. So the twisted form ran fast in the centrifuge. The other didn't.

I remember there was a chemist here—[Jerome R.] Vinograd was his name. And he was interested in these things, and he was working, actually, with DNA, but he had not picked up the difference, and so on. But then when he saw my results, he pursued them and he succeeded in getting the electron microscopy done by somebody else. And he did find, in effect, that they were both closed, but one was supercoiled and the other was not.

Cohen: That's very interesting. How much did you have to do with the chemists here?

Dulbecco: Well, not terribly much—occasionally, as things happened. But I think that the really important thing here is, as I say, the possibility of extrapolating from one system to another,



getting everybody together—first in the lysogeny example, which was very, very important, and then the circularity of the phage of DNA. There's always a translation from one system to another.

Cohen: That's the strength here.

Dulbecco: That's the strength, exactly. You see, when I came to Caltech, remember, there was a sort of pride in the fact that there were no departments. It was the Biology Division, and everybody was in the same division—the neurologists, the plant physiologists, everybody was together. That has been the strength of Caltech. And at that time it was unique.

Cohen: It was unique, and also Beadle really believed in that.

Dulbecco: Beadle believed in that, sure.

Cohen: In your autobiography [*Scienza, Vita e Avventura*, Milan: Sperling & Kupfer, 1989], you have a very charming story of a relationship you had with Richard Feynman. This must have been about the same time.

Dulbecco: Yes. Yes, that was a time when things were moving fast. Soon after I came here, I actually took a course with Feynman, in quantum mechanics. It was something that was lacking in my physics preparation. Then, at a certain point, he wanted to do something in biology. And that was the time when RNA was a question mark—whether there was a messenger or some kind of connection between RNA and DNA. Nobody had proved anything at all. So I said, “Why don't you do an experiment like that? We could take phage, extract the DNA, infect the cells, extract the RNA, to see whether it hybridizes. Because that would mean that—

Cohen: There's some connection back and forth, yes.

Dulbecco: Some connection. Well, I started the experiment. [Laughter] I don't know; probably it was stupid. In order to have a good amount, instead of using the small samples you normally use for the phages, I used a flask with lots of bacterial phage, and so on.

Cohen: Did he actually come into the lab with you?

Dulbecco: He didn't touch things, but he was there. And I used one of those rotary shakers. I had not used it for a long time. And I used that one and made sure they're in the incubator. And then the following day, when I went to look, I didn't have any phage. I repeated the thing again, and it didn't have any phage. I thought the failure totally incomprehensible. In the meantime, see, that was not my main thing: my main thing was to work with the other virus, the polyoma virus. So Richard said, "I can see that you're more interested in the other experiment than in this experiment. Let's give up."

It was stupid, you know, because the problem was that this [rotary shaker] was going too fast.

Cohen: Now, in the book it says that you went to Max with this, and he was very discouraging.

Dulbecco: That's true. Max was very strict—very rigid, in a way. He didn't like imagination, I would say. You could have imagination if you had the proof. But without proof he didn't accept anything; he was excessive in this direction. So, yes, I discussed the experiment with him. And he said, "No, no." I don't know what reason he gave me that it wouldn't work. But it was a triviality, because the machine was going too fast. I realized it later, but by then it was too late. But on the other hand, I'm also glad, because if the experiment had succeeded, it would probably have put me in that direction. Because I don't mind changing from one field to another. I would have gone in that direction—a direction that was in a way interesting and new, extremely competitive, so it would not have been easy to make a real mark. Instead of staying in the field in which I was—a field that had been just explored and where there was more room, more possibilities. In fact, I think it was a good field.

Cohen: So actually, that was the only experiment that you tried to do that Richard Feynman was interested in.

Dulbecco: Yes. So, there were lots of people in the lab...lots of papers published. The main question, the main problem remained: What does the virus do when it goes into the cell?

Cohen: Tell me a little bit more about how the group worked. Did you have a seminar every week?

Dulbecco: Yes. We had seminars every week, and each of us discussed what we were doing. In addition, we were all together.

Cohen: You were all in the same lab.

Dulbecco: We spent our life in the lab, secluded in the lab where we worked.

Cohen: And on the weekends you went camping in the desert.

Dulbecco: Yes, that we did many times. That was another very good thing. During these camping trips, again, there was lots of discussion and talking about things. You see, you are navigating the unknown. Once you are in the unknown, you look for hints to develop and you see possibilities...where to go. Then you test them. But if you don't see the possibilities, you cannot do anything.

Cohen: And that's where you need the discussion.

Dulbecco: That is very important, helps enormously. You see, when I went down to La Jolla to the Salk Institute [for Biological Studies], that's what I always maintained—that the institute be built essentially [along the lines of] the Biology Division at Caltech, with no departments. Of course, there are groups, depending on funding, each has its own grants—that establishes some isolation. But when people are all together, you see—

Cohen: Do you want to talk about why you left Caltech? You were happy here.

Dulbecco: Oh, yes—I was happy. In effect, there were two reasons: One was that Jacques Monod came one day to see me, and he explained to me this idea of Jonas Salk's to have an institute for biology where people would have no teaching duties. Also Jonas of course had this dream idea that there should be a connection between art and science. And you wouldn't have to apply for grants, because the national foundation would give us a fund every year. They would get four or five of the best people existing in science to start it. They had some names, which, of course, were very good. So that was a very appealing thing.

The other thing was that I had some marital problems. I got divorced from my wife, and I married my present wife. And so I wanted a change of place.

Cohen: Did your ex-wife remain in Pasadena?

Dulbecco: For a while. Now she's back in Italy.

Now, on this question of teaching: we haven't yet talked about my teaching—only about my research. But at Caltech you could also teach. And I remember that after the plaque system had developed and I had done some work with these animal viruses, I remember one day meeting Beadle in the corridor. And Beadle said, "We think you should teach a course in microbiology."

Cohen: This was when you were a professor?

Dulbecco: No, this was before that. I immediately enthusiastically accepted, because that meant that they were considering me seriously. Of course, I did not know anything about microbiology. So what I did is for six months I really didn't do any more experimenting. I went to the library and spent all my time there, reading from the beginning—simple things to the complicated—the journals, to know what was going on in the field. Found some interesting things; identified some errors. Actually, that was a very exciting time, because there were these experiments with mice that had shown that there are certain bacteria that have two forms—one

form is pathogenic for a mouse and one is not. The experiment was famous. Anyhow, the experiment was to take fractions from these bacteria, put them into mice, and see which fraction preserved the difference between the two strains. And you could see that the fraction that kept the difference was DNA. But, as I mentioned earlier, that was debated enormously. There were lots of papers, about how pure the DNA was and so on.

So I decided to tackle that question in my course; that was one of the topics. Then, of course, came the experiment of Hershey, which I've also mentioned. It was a very, very hot subject. So, what I did was to look through the textbooks that were available. I found one which seemed to be suitable for a good introduction—

Cohen: Now, were these undergraduate students or graduate students?

Dulbecco: I think it was for anyone. Probably for undergraduates, but anyone could take it. I had graduate students as well. And that was a hard life. [Laughter] So I told the students, "You read this book. And that gives you background. But we are not talking about what is in this book. We're talking about what's going on now." And so I started discussing this question of DNA, the [Hershey] experiment, and how and why the objections were made. As the thing developed, there were new publications, I was up-to-date, so that we followed the thing completely to the end. And then we tackled other interesting subjects.

Cohen: How many students did you have?

Dulbecco: Twenty.

Cohen: Oh, a lot. For Caltech, that's a lot.

Dulbecco: And among the audience, there was Herschel Mitchell and his wife. And obviously—Mitchell never said anything—but really they had been sent by Beadle.

Cohen: Oh, to spy?

Dulbecco: [Laughter] Sure! Because how do they know that I was capable of giving a good course for a number of students like these—because they were very capable, well-prepared students. So, I seem to have been accepted. And I remember asking Ray Owen about—

Cohen: Now, he was the chair of the Biology Division then?

Dulbecco: No.

Cohen: No, he came after Beadle, I guess.

Dulbecco: Yes, after Beadle. Ray Owen knew about the course. And I said I thought that was the proper way to teach students. And he said, “Oh, absolutely—that’s the best way to do it. Because these students don’t need [to follow] the textbook—the background. They can read it; they don’t need it. They were smart enough. What they needed was this stuff that you couldn’t get in any other way. So that’s the way the course worked.

Cohen: Did you enjoy it?

Dulbecco: Oh, I worked very hard, all the time. Also, we had the lab for the course. So it was very, very hard. But I enjoyed it.

Cohen: Did you just teach it once, or did you teach it a few times?

Dulbecco: No, I taught it all the time. It became my course. Every year, I gave this course in the spring term.

Cohen: So, after you organized the course and you were teaching it, you did go back to your research?

Dulbecco: Oh, yes, yes. Because that was the main thing for me. But I kept up with the literature—because, you know, you can do both things. And then a major step was when they

made me professor. I don't know almost anything about that, except that somebody told me—I don't know who—that Beadle and the faculty were very uncertain whether they should give it to me or to Ed [Edward B.] Lewis [Thomas Hunt Morgan Professor of Biology, emeritus].

[Laughter] But I got it first.

Cohen: Now you were in a unique club. Did you actually get a PhD in physics when you went back to school?

Dulbecco: No. No, because, you see, then I came to this country. I was at the end of my third year. I would have needed one more year. But I thought it was more important for me to come here.

Cohen: So you are in a unique situation—with a few other people—in that you have no PhD. You have the MD. And you don't think that made any difference?

Dulbecco: No, because all my work was based on things which I did not learn in the classroom. And if I had been a PhD, it would have been the same. No, there is one thing—and I don't know whether it is a good thing or a bad thing. You see, on many occasions, if I had had a strong background in biochemistry, for instance, probably I would have taken a different direction—messenger RNA, maybe. On the other hand, if I had done that, I would not have taken the line which I took, which was maybe influenced by my background of being an MD. In fact, I think it's probably better. And also, as you said, very few people are MDs but lots of people are PhDs; most of them are. So in that area there's a tremendous competition, because they all have the same background. But I have a different background. And my background gives me a uniqueness, which can be a weakness or a strength at the same time. So, fortunately, I was able to take the advantage of strength rather than the weakness.

Cohen: Now, after you were teaching this course, did you have more to do with Beadle or with Max? I mean, how did this go?

Dulbecco: Well, you know, it's a funny thing: I never had anything to do with anybody for most of the time. Well, of course, with Max I worked, because it was a group. But then when I became independent, even Max—I didn't even know what he was doing. I know he started working with another microorganism. And Beadle, I hardly saw him—only a few times in my tenure here. I mean, even when I went to Salk I never knew who was the president, because I didn't care.

Cohen: As long as you could work, that was all you cared about?

Dulbecco: That's all! [Laughter]

Cohen: So you made the decision to go to the Salk Institute. Did they try and talk you out of it here?

Dulbecco: Not really, no. Also, they obviously recognized that I needed it. [Laughter]

Cohen: You felt it was time for a change?

Dulbecco: Yes.

Cohen: Let's finish your stay here at Caltech. You had several really influential people that you worked with—like Harry Rubin and Howard Temin.

Dulbecco: Well, lots of people. Actually, I tried the other day to put together names of people who were students. Howard Temin—

Cohen: He got the Nobel the same year you did [1975, with David Baltimore].

Dulbecco: Yes. And with David.

Cohen: Yes, of course.



Dulbecco: Jan [John W.] Drake. And I was thinking about what these people did. Jan Drake went to the University of Illinois, and now he's at the National Institutes of Health [chief of the Laboratory of Molecular Genetics, National Institute of Environmental Health Sciences—ed.].

Cohen: These are people who continued the work that they did in your laboratory?

Dulbecco: Well, not necessarily—this was for background. There were several medical students, physicians who wanted to do biology. Ed [Edward H.] Simon went to [Purdue]. Mike Fried is a very good scientist; he's now in London, at the Imperial Cancer Research Fund. I spent five years there.

Cohen: In between here and Salk?

Dulbecco: No, afterward—in 1972. He was a student here; he took his degree and then went to Salk. And then he continued to work at Salk, and then went to London.

Marcel Baluda. He is at UCSD [University of California at San Diego]. He was a very good student. I think he got very close to making the discovery of reverse transcriptase. I think if David [Baltimore] and Howard [Temin] had not done it at the time they did it, I suspect he would have done it.

Harry Rubin. Lee [Leland H.] Hartwell. He is the head of the cancer center [Fred Hutchinson Cancer Research Center] in Seattle. Klaus Bayreuther is in Germany. Gus [Gustave] Freeman became the head of the Stanford Research Institute. There was a lovely Finnish lady, Pirko Pohjanpelto. Lionel Crawford. John Smith—a very good biochemist. Roger Weil was a connection between me and [Jerome] Vinograd. He began with me, but then moved to Vinograd, and he was interested in the DNA work. Ernest Winocour, who is in Israel at the Weizmann Institute. And Michael Stoker, very well known in Britain. John Sharp, who went to Glasgow University as the head of virology. Eberhard Wecker is in Wurzburg, Germany, and is also the head of virology there. There's [Giuseppe] Attardi [Steele Professor of Molecular Biology]. He's still here.

Cohen: That was a good legacy for Caltech. So you decided to go in '62, but you didn't go directly to La Jolla, did you?

Dulbecco: Because there was no lab there yet. They had to build some temporary lab. So I went for a year to Glasgow—I worked in Michael Stoker's department. And actually there I did something interesting, because there was this dual life of the polio virus. It can either grow and kill cells or transform cells without killing them. And somehow, before leaving here, I had done an experiment in which I was looking for the multiplication of the virus. So we made these Hershey columns to measure the amount of virus, or DNA, present. I noticed that lots and lots of DNA came out. And I was debating why; there seemed too much for the virus. I can remember talking to Mike Fried about this, and Mike said, "But are you sure it's all viral DNA." I said, "Maybe we should check." So we did. And it turned out, actually, that it was not viral DNA. So the virus had, in effect, stimulated the cellular DNA to grow. So when I was [in Glasgow], I said, "Well, if the virus does this, maybe it also stimulates some of the enzymes required for making DNA." I did not know really which enzyme to do, but for some reason I thought, Well, why not start with something easy, which is thymidine kinase? So I did the experiment and it turned out yes.

Cohen: With what kind of DNA?

Dulbecco: Thymidine kinase, which is not in the main line of DNA replication, but it is one of the sidelines. And yes, I could show there that the virus markedly increases its production. Then when we went back to La Jolla, Lee Hartwell was there. And we decided to study several enzymes for DNA replication, and it turned out that they all increased.

Cohen: So what was your position this year you were in Glasgow? Who paid you for that year?

Dulbecco: Salk.

Cohen: So you were an employee of Salk already?

Dulbecco: While I was there, I was a fellow of the Royal Society. Because they had talked to Michael Stoker, and Michael Stoker—

Cohen: So it was like a sabbatical year?

Dulbecco: It was a sabbatic. I remember that the instruments they had were really primitive. To measure radioactivity, they had this machine that you had to put one thing in at a time, and wait and count.

Cohen: Why did you choose Glasgow?

Dulbecco: Because Michael Stoker was there. He was a good friend, and he was a good virologist. And he was interested in having me go there to bring in this new kind of virology that they did not have.

Cohen: So you spent the year there? And you enjoyed it?

Dulbecco: Yes.

Cohen: You were starting your life again, in many ways.

Dulbecco: And of course my wife is Scottish. So then we went also to visit people.

Cohen: So she was going home, in some sense.

Dulbecco: Yes. [Tape ends]

Begin Tape 3, Side 1

Cohen: We're going to talk now about your move to Salk, after you had your year in Glasgow.

Dulbecco: Then we went back. And at Salk there were temporary buildings—so-called temporary, because they're still there now, thirty-five years later.

Cohen: But the main building was not finished yet?

Dulbecco: No. So I continued to work essentially as I had here. I mentioned already that I had Marguerite Vogt, who came with me. And then Lee Hartwell was there, and a few other people.

Cohen: Did that cause hard feelings here, when these people left?

Dulbecco: Well, Lee wasn't here. He had been here briefly, then he graduated somewhere else, then he went to Salk. Marguerite, yes, she was here with me, and then she moved to Salk. As I said, we continued exactly as we had here. And the main direction was the one I indicated—namely, to try to find out how the viral genes could be.... First, whether they were present in the cells; at the time, we thought they were, but we had to prove it. So, together with Lee Hartwell, we explored how the virus affected cellular characteristics, in terms of multiplication—DNA replication. And so we discovered another enzyme which is induced—an enzyme more directly involved in DNA replication, which confirmed this general idea.

Then we tried to tackle the real problem. And the problem really was in the viral genes. You see, we had no hint of what viral genes would do, so that we could test them for function. So we decided that we should take a molecular approach. A gene is a piece of DNA. We would follow the piece of DNA.

And that was facilitated by the fact that we had quite a number of postdocs—really very good people. Some of them came from laboratories that were well ahead in molecular technology, and this was extremely helpful.

So the first thing we tried to find out was whether in these transformed cells, which seemed to have no indication of the presence of viral functions, whether the DNA of the virus was still there. And by that time, the technology of DNA hybridization had been discovered, and so we applied it—and indeed it turned out that even a long time after infecting the cell, viral DNA was there. That already was an interesting thing.

Then we decided to find out, since it was there, in what state it was there—whether it was free or integrated into the cellular DNA. And that was not an easy thing, with the technology of the time, because, you see, the DNA of the virus, the shape it had, somehow it wasn't easy to separate—to distinguish the DNA of the virus from the DNA of the cell—without a specific reagent, which I didn't have. However, I remember that I went someplace to give a seminar. I was talking to one person there, explaining what we tried to do. Actually, he told me that he had found—

Cohen: Who was this?

Dulbecco: I don't remember. He was studying the effect of radiation on cells. And therefore he wanted to see how many breaks are produced. Now, if you extract the cellular DNA with conventional methods, it's all broken up. But he had invented a method by which you would put the whole cells on top of a density gradient, suitable for DNA, but very alkaline. So that it would lyse the cell, and the DNA would get denatured, but it would remain essentially intact. And in fact that was true, because we tried it and it worked well. Then when we put viral DNA together, we could see that they were separated. The cellular DNA went down to the bottom. As I say, the difficulty with the viral DNA is that since it is circular and closed, then when you put in the denaturant it becomes very tightly coiled, and then it goes fast, you see, but not as fast as the cellular DNA. So the cellular DNA went much farther down than the viral DNA.

So now we had a test. So we did the experiment and the experiment turned out to show clearly that the viral DNA, for transformed cells, was integrated—came down together with the cellular DNA. I remember that at this point we decided we needed another test. We should take this DNA and put it in what is called a density gradient equilibrium, in order to see whether it was the real DNA. I mean, there could have been some contamination.

I remember I had to go to Cold Spring Harbor for one of these meetings, and I had to talk about our results. But the result of the experiment wasn't there, because it was done when I was leaving. So I agreed with [Joseph] Sambrook, who was doing the experiment, that he would send me a telegram. So I went there to start my talk. And when I had enough time to explain what we had done, just at that moment somebody came in with the telegram.

Cohen: How dramatic! They must have thought you arranged it that way. [Laughter]

Dulbecco: And the telegram said that it actually was confirmed. And everybody applauded—it was funny. [Laughter]

So that established the first point—that viral DNA is there in the cell, integrated in the host DNA.

Then we wanted to know about expression. As I say, genes we did not know, so we studied the messengers—because they express the genes and you usually know where they are. You can identify messengers, because they are RNA. And the messengers—again, I had people like Kim Oda, who is Japanese, who was very much interested in studying RNA. And somewhat later I had a student—Heiner Westphal, who had worked before with the hybridization. And I had a student from UCSD who was doing a thesis with me—Donna Lindstrom.

Cohen: So there was that cooperation between UCSD and Salk?

Dulbecco: Yes. I gave some lectures there, and then I could have students—and I had a few students. And at first Oda went to study the presence of RNA, specific RNA, and he found it. He found that there was always specific RNA in the cells, even when there was no sign. Obviously, some viral gene had to be active in order to have the transformation, otherwise there wouldn't be. So that was at least an assurance that there was.

Then Donna Lindstrom studied this in greater detail, because we knew there are these two phases—two possibilities: Either the cells are destroyed, so the lytic expression of the virus, or the cells are transformed, so the non-lytic expression. And she isolated the messengers from the two cell types, and she found that they were different. Which means that certain genes were expressed in the case of the cells that were lytic, and other genes were expressed when the cells were transformed. So again, it was encouraging to say that obviously it is the expression of some specific viral gene that make the cells transform.

There was a person from Wales, and he was interested in making hybrids between cells. So we said, “Well, why don't we make a hybrid between a normal mouse cell, which can undergo the lytic phase, and a transformed hamster cell?” Which means then what is needed for

lytic expression would be present in the hybrid. And they did. So again, confirming the idea of two kinds of genes—genes for lytic growth and genes for transformation.

Then at a certain point, I moved to London. This was in 1972.

Cohen: So for eight years, you were doing this work at Salk?

Dulbecco: At Salk.

Cohen: Now, is it true you did not have to go seek funds? Salk paid for everything?

Dulbecco: No, no. From the very first day I was there.... Actually, they did give me some kind of a fund, which I could use for getting postdocs, for helping with expenses.

Cohen: Set-up money. But it was no paradise of infinite money?

Dulbecco: No, no. I always applied for money for grants from NIH [National Institutes of Health].

Cohen: So it was like the rest of the world. But it was very pleasant?

Dulbecco: In effect, as I say, I continued my work as before; I was just in a different place. It was a nice place, but they didn't offer anything more than Caltech would have offered. In effect, the direction was already determined here at Caltech, and it was continued there, continually adding the new technologies—especially the technologies for nucleic acids.

Cohen: And your colleagues there?

Dulbecco: They were quite different people, because we started with—I had my group, which always was about ten people. And then there was a group in immunology. But at that time, there was no connection whatsoever between what I was doing and what others were doing.

There was a person who was interested in the origin of life. He was a good chemist and occasionally I talked to him.

Cohen: But the work did not overlap?

Dulbecco: No. Fundamentally each group was self-sufficient. Each one had a number of people—postdocs and so on. And they were so distant that there was no way to find any connection. You see, when I say it's good to have a variety of people, they cannot be *too* distant, because then you cannot interact. You speak a different language.

Cohen: But you would meet for lunch, eat together?

Dulbecco: Oh, sure.

Cohen: And, of course, you had the connection with UCSD, so there were some university atmosphere there.

Dulbecco: Oh, yes. So, as I said, I went to London and I had a postdoc for a while—

Cohen: Why did you go to London?

Dulbecco: Oh, we had a daughter. It was December 1970. And at that time we were worried about the state of young people in this country. My wife was British. So she especially felt very strongly that maybe we should leave the country; we cannot raise a child in this country.

[Laughter]

Cohen: So it wasn't for professional reasons.

Dulbecco: No, no, no—just for this reason. I talked to Michael Stoker, who had become the director of a large cancer institute in London [the Imperial Cancer Research Fund Laboratories]. And “Oh!” he said, “wonderful!” So he gave me a position there.



Cohen: Now you mentioned that this was an opportunity to work clinically with...?

Dulbecco: Yes, that's what I thought—that it would give me an added opportunity. And in fact that changed the direction of my work—toward cancer, breast cancer. That was part of the thing.

And so Yoshi Ito joined me there. We decided to continue the study of gene expression to try to identify genes more specifically, looking for mutants that would not transform. And we found something which was not really ideal, but really just was the right direction. He got the messenger for this particular gene and so identified this particular gene, which is the transforming gene. But as you were saying, I had shifted progressively away from that, especially when I got the Nobel Prize in '75. Then a fit of enthusiasm caught me, and I decided that I should work more directly for mankind: namely, to work on cancer—not cancer virus, but cancer. And I chose, as I said, breast cancer.

You know, one of the reasons was that Seymour Benzer's wife died of breast cancer. And we lived through that, because I was very close to him. A terrible thing. So that really pushed me in that direction.

Cohen: So you started to work on that in London?

Dulbecco: Yes, but still in an experimental way, not clinically at all; ultimately, I'm not a clinician. I continued to do this. Then I came back to Salk.

Cohen: How long did you stay in London?

Dulbecco: Five years. After the Nobel Prize, and things not being so bad in this country.

Cohen: Did you still have a home in La Jolla?

Dulbecco: No, I had cut my connections. But then I started again from the beginning.

Cohen: When you came back, you were president, or director?

Dulbecco: No, no. I essentially took back the same position I had before. I was rehired, so to say. Actually, when we were hired by Salk in the beginning, we received a letter of appointment which said that we were appointed for life and we could do whatever we wanted; it didn't always have to be with institute approval. So I could remain as a Salk scientist, according to the original letter. But I thought that was unfair. [Laughter]

Cohen: Let's go back. When was David Baltimore [Caltech's president 1997- ] there. Was he a postdoc in your group?

Dulbecco: Actually, he was not in my group. He had some junior position at Salk. I had been instrumental in getting him there, but I don't think he was in my group. He was independent. We weren't connected very much, but at that time he worked with polio virus, and the type of work he was doing had some relationship with ours, in terms of dealing with RNA, and so on. So there was some [interaction], not close but enough so that we could talk frequently, and so on.

I remember when he decided to leave. He came to me to tell me that he felt he didn't belong at the institute, that he really needed a bigger environment—which was true. [Laughter] So he went to MIT.

Cohen: He wanted more action.

Dulbecco: Yes, and also he happened to be at Salk at a bad time. The president of the institute was a man who used to be president of one of these rather large companies. And he was very extreme, ultraconservative. He took positions which were really—you wouldn't understand them. There was one episode: According to Jonas's idea of combining the arts and science, at a certain point we had the new building and there was an exhibition of paintings—contemporary artists, not classical. It was interesting, and that's what you wanted in a place like that—something contemporary. Well, there was a painting of a naked woman with her hand like this, and this guy said that this was obscene, because the woman was masturbating. And he decided that there should be a guard where this painting was, to prevent young people from seeing it. I

mean, absolute craziness! And you know, David has always been a very forward-looking person, and that made him absolutely mad. And it made everybody mad, but some more than others, obviously. [Laughter]

Cohen: Now, was [Jacob] Bronowski still there?

Dulbecco: Bronowski was still there. Yes, that's another complicated story, because Bronowski was very ambitious, and he wanted to be the director of the institute, or president, or something. Jonas was the director nominally, but in effect nobody was directing. So Bronowski got the position of vice director, or something like that.

Cohen: So there was a director, and then also a president?

Dulbecco: Yes. The president was an administrative president. But Jonas Salk was directing the scientific side, and of course he didn't direct anything, because everyone was directing themselves. But, you know, we didn't care. And Bronowski was supposed to promote the humanities, and he brought in some number of interesting people for a while. But the thing didn't really work out. And finally even his position was abolished. And he didn't really like that, but nevertheless he bounced back, because he was a very capable guy. And so finally he died [1974] and was never replaced.

Cohen: So it became just strictly scientists—they didn't even try.

Dulbecco: No—even now. Now the only thing that's in the direction, not of the usual humanities but of thinking and so on, is Francis Crick, because he is interested in the problem of consciousness, which is a very tough problem. And you know, he collaborates with somebody here at Caltech—Christof Koch [professor of computation and neural systems]. So that's really the only way for the science connection to art to be solved. You know the neuroscience; you know the mechanics of the brain. And here you have the product—art and literature and so on. And what's this in between? In between, there is this process of consciousness, which connects

the one to the other. There's no point to try to connect this with that if you don't have the bridge. So the important thing is to study the bridge. And we hope that this will work out.

Cohen: Sounds like a harder job than viruses.

Dulbecco: Oh, it is very, very hard, there's no question.

Cohen: But, of course, [Roger] Sperry [Caltech professor of psychobiology, d. 1994] already earlier was interested in something like this, wasn't he?

Dulbecco: Sperry, yes, especially in his later years, he was interested.

Cohen: But he got involved with religion, too.

Dulbecco: Yes. He got into philosophy, you see—that's the problem. It is so easy to become a philosopher rather than a scientist.

Cohen: So your five years in London were good? You enjoyed those years?

Dulbecco: Well, good in the sense that it exposed me to a different world, because England is completely different from the United States. Scientifically, it wasn't too much. Also I had to commute—take a train in the morning and take a train in the evening—and this is disruptive.

Cohen: Not like walking over to your office. Scientists live very luxuriously in California.

Dulbecco: Yes, I know. Paradise. [Laughter]

Cohen: So you came back. But now you had the Nobel Prize. Now you can talk about where you did that work—at Caltech, at Salk? What is your feeling about this?

Dulbecco: The feeling is this: If I had not been at Caltech, I would not have done it. That's certain, because it was the interaction with the phage group, in various ways, as I pointed out. One, because I knew, from conversation with people who worked with it, lots of the details that were at that point available. And that was something that led to that particular hypothesis, and so on. Then there were connections with people—the presence of people like Sinsheimer, who studied the shape of the DNA. It was the fact of having found that DNA was circular, which I learned here, that was a very good inducement for the idea that there should be an integration, because of the circular form. If you want to integrate something easily, just one break is enough for the integration.

And the interaction with people. For instance, Howard Temin, a very, very nice young man—we shared lots of ideas, and it was very nice. You have an idea, but to have somebody else who has similar ideas is a very encouraging thing. Of course, there was the quantitative method we developed here for assaying viruses and measuring transformation and so on. So the basis, without question, was here. And when I left, the thing had reached the point that we just continued. The direction was already there. Adding new things as the technology developed, because I had people who came who had the experience with technology and who used it.

Cohen: And you really attribute that to the interaction with many people who are thinking all the time.

Dulbecco: Yes. It's a wonderful place for research. While I was here, I didn't think about anything else. I didn't have to worry about who the president was, who directed the department. I knew who they were, but it didn't matter, because they left me alone. There was no politics involved. You see, at Salk, there became lots of politics. Salk brought together people who did not accrue spontaneously but were taken from here and here and put together, and each one had developed his own entirely different way of how you should run a place. So there was quite a lot of disagreement on this. Soon, after a year, we decided we didn't need a director, and Jonas resigned as director. And so there was a council, and then we determined the scientific direction of the institute. And so we had a new chairman every year. I remember one year I was chairman, in a big room with a table. And I was sitting there, and there were four or five other people there. And it was such a hassle—insignificant things, and people arguing. And at a

certain point, I got really mad and I hit my fist on the table and said, “Let’s stop this nonsense!” And it started trembling. There was an earthquake—the strongest earthquake I’ve been in in the area. [Laughter] And at this moment! [Laughter]

Cohen: That’s like the telegram you got at Cold Spring Harbor!

Dulbecco: I was actually calming down all these guys.

Anyhow, it was difficult. Also, Jonas’s position was very difficult. You see, he was really not a scientist, he was a physician who had developed this vaccine. But it wasn’t a scientific feat at all. And sometimes people argued with him. And people told him, “You think you’ve done a great thing. It’s not science.” Poor guy! Well, all this type of thing did not facilitate, did not create, the right atmosphere. If you talk about things constructively, that’s the important thing.

Cohen: I don’t know—it continues even now. You know, young people I think feel very pressured to build up their group and succeed in such a—

Dulbecco: Well, pressure—even then, everyone felt pressure that you had to do something. We knew we were here not to waste our time. No, no, I think that’s good. You have to have pressure.

Cohen: Well, I think everybody was ambitious, and I don’t use that word in a bad sense.

Dulbecco: No, exactly.

Cohen: So, when you were back at Salk, did you become president, or director?

Dulbecco: Then I became president. That was a situation where the president was Fred De Hoffman. He was an Austrian, a physicist who worked on the atom bomb, and he had started a business in San Diego—quite good, it went fairly well—based on developing atomic power stations. He became president. He was a very good fund-raiser for the institute. Not a fund-

raiser in the way David [Baltimore] is a fund-raiser. But he did well and could go ahead without problems for all these years. He was president for quite a long time. Anyhow, finally, it turns out that he developed AIDS. Because he thought he had some problem with his heart, so he went to some place in La Jolla, where they gave him a [heart] test. These tests are so often false positives, and he was positive—I bet he was false positive. Anyhow, he decided to have a bypass. He went to Harvard, I think, to have this operation, and they gave him a transfusion and the transfusion gave him AIDS.

So finally, around 1988, it affected his brain, and he couldn't really be functional anymore. So they convinced him—probably his wife succeeded in convincing him—to give up. And they needed somebody to step in and so they asked me. So I was there first as a temporary president. Then they decided I wasn't doing too bad, so I could be president, not temporary president. [Laughter] So I stayed while they were looking for somebody more permanent. This happened in 1992.

Cohen: So you were president from '88 to '92.

Dulbecco: Almost five years.

Cohen: Did you enjoy it?

Dulbecco: Actually I did like it, yes. I liked it because the institute was in very bad shape from the point of view of the morale of the faculty, because De Hoffman, really, wanted to do everything himself. And several people were ready to leave and actually had already made arrangements to go—and the people who were left seemed to have been destroyed. So I worked very hard at convincing them to stay, and I succeeded. And then, in order to be sure the faculty had its say, we set up a structure—there is an academic council elected, and it has the power to decide every academic affair.

Cohen: So there had never been anything like that?

Dulbecco: Nothing like that. And the council remains straight ahead. Of course, everything has to be approved by the president, but he's not the one who determines the things. So the faculty was happy about that. And they have stayed, in spite of lots of variations and bad experiences subsequently.

Cohen: And then did you have to raise some money? Did you do that also?

Dulbecco: Well, I tried. You know, you don't raise money; people give you the money. Unless they want to give you money, you don't raise it.

Cohen: I always had the feeling that there was this big social scene in La Jolla. Did you get to be part of that?

Dulbecco: La Jolla's a strange place. It's not a place for that. Even the symphony, which you'd think would be something, went bankrupt two years ago.

Cohen: With all those rich people.

Dulbecco: Exactly. It's terrible. In this respect, it's a very bad place intellectually.

Cohen: So then you retired in '92.

Dulbecco: I'm not really retired. [Laughter] I'm half-time. They want to keep me there.

Cohen: So you have your laboratory still?

Dulbecco: No. I tried for a year, because I commute between La Jolla and Milan now. You know this quest of the Human Genome Project? We were certainly one of the people who promoted it and said it should be done. In fact, I am the [first one to propose] it: in an article in *Science*, ["A Turning Point in Cancer Research—Sequencing the Human Genome," *Science* 231: 1055-1056, Mar. 7, 1986], where I said that we had to start to find the genes, and so on.



So when this happened, in Italy the head of the local medical research council contacted me, saying that if I was willing to go there and be the coordinator of the project, he would fund the project for general resources. And I thought, Well, it's a good idea. But I said, "I'll do it part-time, not full time." So I have arranged part-time at both places.

Cohen: So when do you go? A specific time?

Dulbecco: No. Whenever I feel that I'm needed, either here or there, I go. Usually I stay about two months here, two months there, and so on. Every two months, we change. Not that rigid—sometimes maybe two and a half, sometimes a half. It depends on what's going on. If there's a meeting here that I want to attend, I come here. And on the other hand, if there's something there that requires me to stay a little bit longer, I stay a little bit longer.

Cohen: And how long have you been doing this?

Dulbecco: Five years.

Cohen: How do you find Italy again, after all these years of not living there?

Dulbecco: Oh, the problem with Italy is politics. Politics is impossible. And the politics dominates everything. Now, lately things have improved, because there have been changes in the government, especially since there have been a group of judges who decided it was time to stop all the illegalities that were going on all over. And they started this action, which was very drastic, and lots of people were put in prisons. So that was a very sobering thing. Big people, big names are often indicted, usually because of pay-offs on a large scale and things like these. So nothing was done. Even now, in the universities and so on, people are not appointed for what they're worth. They're appointed because they have friends. But as I say, two years ago, a new government was elected. And that election was much better than previous elections, because of the repercussions of all these negative things. They changed the electoral system, which was originally totally based on parties: you elected a party, not the individuals. Now, instead, eighty percent are individuals elected, and twenty percent are the party.

Cohen: More like our system.

Dulbecco: Yes—it should be a hundred percent [individually elected]. This creates problems even with twenty percent.

Anyhow, so there's a leftist government. The left is reasonable, and they have done quite well. Now Italy is qualified to become a member of the new Europe, and the currency will become the euro. And all this stuff will require tremendous changes. And the minister of research in the university is a sensible person who has made many changes in the right direction. They're not entirely solving problems a hundred percent, but certainly they're important contributions. So things are moving forward.

Cohen: And what do you think of the genome project? How is it going?

Dulbecco: It's fantastic. There's been great success. They've done more than we expected. Now comes the difficult phase of the project. The genes are known; those that are unknown, we know they can be found. There's no problem now. But the important thing is to know what they are doing. And that's the hard part.

Cohen: Well, it sounds like you have a very nice life.

Dulbecco: I can't complain. [Laughter]

Cohen: So, looking back, it was OK?

Dulbecco: Yes, it was OK.

Cohen: Is there anything else you'd like to discuss?

Dulbecco: Do you have any other questions?

Cohen: Let's see. Looking back at influential people in your career?

Dulbecco: Well, influential people. First of all, Giuseppe Levi, as I described, because he was the origin. And Rita Levi-Montalcini, because we were good friends and we influenced each other in a very positive way. Luria, Max Delbrück. These were really the crucial people.

Cohen: And you certainly spoke very highly of the people you worked with here.

Dulbecco: Oh, yes. They were very important. And all those who came when I was at Salk; many of them were also very important.

Cohen: And the point you made, which I think is very interesting, that it's important to be with interesting people to do the work. A person doesn't work alone. So you enjoyed your years here at Caltech?

Dulbecco: Oh, yes, sure—hard but enjoyable. Because, as I say, Delbrück was a very difficult person, very demanding.

Cohen: Can you describe a little bit how it was working with Delbrück?

Dulbecco: He put me a test often, because I came from Italy, with an MD for a background. So he wanted to make sure that I could do what I was supposed to do. And so I had to give seminar lectures. I remember once he asked me to . . . . [Tape ends]

Begin Tape 3, Side 2

Cohen: We were talking about Max.

Dulbecco: Well, first of all, I had a graduate student here. He was working on this phenomenon of photoreactivation. In photoreactivation, there's a chemical reaction involved; then if you

interrupt the light, you get an effect which is beyond the amount of light you give, because the reaction starts and then continues for a while. And so he made a thesis—and I suggested it—just on that, on the effect of the interruption. Well, [laughter] Max one day came and sat down, talked to both of us. And then he asked me, “What is the basis of this experiment?” And I had to go and write all the equations on the blackboard to see how you could get this light phenomenon, and so on. So, OK, I knew that. Of course I knew—I had done the experiment—but he wanted to see that I knew. That’s good. Another time, he asked me to lead a kind of seminar in an area of physical chemistry, which of course wasn’t my field. And I prepared myself very well. And then I went into the lecture hall, and there was the professor of physical chemistry! Max had asked him to come, so that he could determine how good I was. [Laughter] And the professor concluded that I did a good job.

Cohen: So he was always testing?

Dulbecco: Oh, he was always testing, always testing.

Cohen: Was he that way with everybody?

Dulbecco: Probably. I bet he was, yes. Also, as I say, it was not easy for him to accept ideas that were not really absolutely anchored in solid reality. When Jim Watson was here, we had some conversation about molecular biology. And we thought that the time had come to start a new chapter in biology called molecular biology. And we went together to talk to Max, to explain this thing. And he said something like “There is no molecular biology and we know nothing. There’s absolutely no point in wasting our time.” And that was it. [Laughter] You see, he was so stubborn in this way.

Cohen: But yet he really was much appreciated by his group.

Dulbecco: Oh, he was wonderful, because—in effect, he was almost like Levi. You see, Levi was encouraging but very strict. And he wanted to have evidence. Because it’s so easy otherwise to have an idea.... I always said that in science the ideas are the easy thing, the

difficult thing is to prove them. Max was like that—but to a very extreme point, because of his origin. And in a way that wasn't bad, because none of these things prevented people from doing what they wanted to do. And on the other hand, maybe he made them think, to be sure. So you need a person like that, absolutely.

Cohen: Do you keep in touch with the biologists here now at Caltech?

Dulbecco: No. What I'm doing now has become concentrated on breast cancer. And we are interested in the genes, the change and evolution of cancer that takes place. In fact, I do that in Italy, because in Italy it's easier. I can get surgical material. You see, pathologists there can be accommodating. Here they are very strict before they hand over pieces that are suitable for molecular analysis.

Cohen: Do you have a laboratory in Milan where you do this work?

Dulbecco: Yes, but it's not my laboratory. It's a laboratory which was there already, and I kind of became attached to that.

Cohen: I see. Is it at the university?

Dulbecco: It's the National Research Council, which has lots of laboratories throughout Italy.

Cohen: So what are you looking for, in this breast cancer work?

Dulbecco: Well, I wrote in this paper in *Science* in 1986 that my justification, my reason, for saying that we should have a genome project was because it was clear already that cancer is a very disorderly process. And what counts is not—well, it's important to know how it happens, and this we know perfectly well. But it's important to know what are the final changes in the genome—which genes are altered, in the sense that either they are overactive or underactive. It is impossible to think of developing a rational therapy for cancer unless you know these things. You have to know which gene is overactive and to fight, and which one is underactive and to

boost up. Now our knowledge is at the point where we can actually learn that. And there are several projects doing that. We also do it, a small part maybe, somewhat differently from others. It's a very difficult thing technically, you see, because cancer—when you talk of cancer, maybe you think of a lump or mass. That's not cancer. Cancer cells move around and mutate. So, if you want to study cancer cells, the first problem is how to get them. Because the original mass, if there is one—sometimes there is, sometimes there isn't—is almost irrelevant, because that's the beginning. The cells that migrate out of that mass—that's the crucial thing. And you cannot get many, you can get very few, then you must examine all the RNAs in order to find which genes are active and which are not active. So technically, it's a very difficult problem.

Cohen: I see. So are there people who are working on this all the time in Italy? And then when you go, you join them?

Dulbecco: Yes, there's a group there. Actually, before there was this genome project, people did what lots of other people around the world are doing: to try to find new genes to map. But this is a thing of the past. And just last year, we made an agreement so that we work together with the people at the Cancer Research Institute, which is in Milan. It's a big place. And they have lots of breast cancer; they operate on a thousand or two thousand a year. So material is available. And the people are understanding. The pathologists there, they can say, "Well, we don't really have to have a hundred percent of the tumor for our use; we can take ninety percent and give you ten percent, without touching it." That's the important thing. Of course, the pathologist has a tremendous responsibility, because he has to make the diagnosis of severity, and how bad the disease is. And if he gives up a piece, maybe that piece was the one that contains the clue. But on the other hand, you know, it can never be perfect. Even with all they're doing, they can never look at a hundred percent. So reasonably, they can give us ten percent.

Cohen: They won't do that here, in this country?

Dulbecco: No. Here, they take it and fix it. And then they examine it, and what's left they give to you. But this way you can't analyze it anymore, because once you fix it, then the RNA is

damaged. And that's a problem. And there are very few cells. And then you have the problem [of getting] as much as possible, all the RNAs from a few cells. And this is not an easy thing. But overall, things are improving.

Cohen: So you really do most of your research in Italy.

Dulbecco: Oh, yes. I don't do any here. The reason is simple. Here, to do research, I would have to organize a lab, which I don't have, and I would have to apply for grants, which takes time. And if I don't have a group, I cannot get a grant. Whereas in Italy, I have a group—it's not mine, but it's there—and I collaborate with them. And on funding, it's easier, because I can get some private money. And there are banks in Italy that belong to foundations, and these are foundations whose purpose is to do benefit. So I can convince them to give me money for this type of research. It belongs to their mandate, and they give it to me. So I can get enough money to do this work.

Cohen: How has the Nobel Prize helped you?

Dulbecco: It's been very important, especially in Italy, because there are very few. So we have to take advantage of that.

Cohen: Are there any other honors you've gotten that are particularly important to you?

Dulbecco: Oh, I don't know. I think that probably what struck me the most was when I got an honorary degree at Yale [1968]. The motivation was very, very nice. It accentuated my contribution and my role in biology—said I was like a new Christopher Columbus in the field. [Laughter]

Cohen: And that was before you had the Nobel Prize.

Dulbecco: Yes. You know, when you get any kind of prize it's always pleasant—or any recognition. But on the other hand, I've had enough of it. [Laughter] I'm not looking forward to more. I'm happy with what I have.