



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

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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

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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]

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.