

NCI Laboratory of Molecular Biology
Oral History Project
Interview with Dr. Benoit de Crombrughe
Conducted on November 6, 2008, by Jason H. Gart

JG: My name is Jason Gart and I am a senior historian at History Associates Incorporated in Rockville, Maryland. Today's date is November 6, 2008, and we are in the offices of the National Institutes of Health in Bethesda, Maryland. Please state your name and also spell it.

BD: Benoit de Crombrughe. That is B-E-N-O-I-T. The last name is spelled D-E capital C-R-O-M-B-R-U-G-G-H-E.

JG: Terrific. I want to briefly describe the interview scope. Established in 1970, the Laboratory of Molecular Biology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, commonly known as LMB, currently has among its ten groups four members in the National Academy of Sciences. LMB has trained many other prominent scientists and its research has contributed to both basic science and to novel applied cancer treatments. LMB has initiated this oral history project to capture recollections of prominent scientists currently and formerly associated with the laboratory. You were born in Belgium?

BD: Yes.

JG: What year and then also the town?

BD: I was born in Bruges in 1935; 26 February 1935.

JG: What was the town like? Was it small—large?

BD: It was a town of only about 100,000. It is an old medieval town and I grew up in fact partly there because during World War II my family used to live in the house of my grandmother. At the beginning of the war my grandfather was still alive also. He was a Chief Judge in that town. I grew up also outside of Bruges in the countryside, in the family house, which has remained in the family for several generations.

JG: Explain a bit about your family background. You mentioned that your grandfather was a Judge?

BD: Yes.

JG: What did your parents do?

BD: My father was a lawyer and he was also a banker. He was the president of a local bank in Bruges. My mother had seven children and she was raising her children.

JG: What were some of your interests as a child?

BD: One of my interests fairly young was to play soccer. [Laughs] I remember leaving school before the time that school got out to go with some friends of mine to play soccer. I did that probably for about six months until we were found out by our teacher. It has always been the sport that I most relate to. Otherwise when I was in middle school I had a classical education which at that time was Latin and Greek. I had Latin for six years and Greek for five years. There was math; but there wasn't much science. I remember my physics teacher was not very good at doing experiments, and after many unsuccessful ones he got discouraged, and he was just reading nice novels to us.

JG: Were there any teachers that were particularly influential for you?

BD: Yes. I think the teacher which I thought was my best teacher was in the last year of high school. He was a history teacher but also taught Latin and Greek. He was very good at teaching history and giving broad overviews connecting history and art and literature of the different periods. Somewhere in the middle of the year, we had a very small class, maybe twenty people, we had a trip to the South of France and to Italy to see Roman ruins, to see the Renaissance paintings and the Renaissance buildings, and then we went to the South of Italy where there are some beautiful Greek temples. He was a great teacher in opening our minds to large concepts, large avenues, large vistas.

JG: And what was his name?

BD: His name was . . . He was a monk because I was in a small school which was run by monks, a Catholic school, and his name was Father Lambert—L-A-M-B-E-R-T.

JG: Do you have memories of the Second World War and its impact on Belgium?

BD: A little bit. I remember that my grandfather died during World War II and there was a huge funeral because he was very well known in the town and what I really remember most was when the Germans were fleeing at the end of the war in 1944. They were just trying to take everything with them and it looked like an army that had accepted defeat.

JG: You attend the University de Louvain?

BD: Yes.

JG: Did your parents encourage you to go into the sciences?

BD: No, not really. Both on my father's side and on my mother's side men were mainly lawyers. I have a brother who is a lawyer. I do not think there was much interest in science in my family. I remember that my father was an amateur-botanist. He was very interested in collecting plants and he used to plant a lot of different species of mostly pine trees because they grow very well there..

JG: This was just as a hobby?

BD: This was a hobby for him.

JG: That is very interesting. Okay, walk me through your formal education?

BD: So after high school I thought I may be interested in math and maybe would become an engineer. Since my math background was not very good there was a special school to learn more advanced mathematics. I did that and after a while I thought that this was not really going to be for me. So then I went into medicine thinking that it would be an interesting career. At that time it was more sort of idealism, to try to treat patients, and to be very frank, to do something different from the rest of my family. No one in my family had ever gone into medicine.

JG: What about your siblings? What were your brothers and sisters doing?

BD: I had a brother who was older than me and went to law school. My family was a very conservative family and my two sisters unfortunately did not pursue formal university studies. They went to some social school. This was in the late 1950s.

JG: You graduate in 1961?

BD: That's right.

JG: Talk a little about the training you received and what it was like to be there.

BD: Okay. It was the usual training I guess. In the early years anatomy and physiology and histology—which I was not really terribly interested in. I found it very static. I had a pretty good teacher of biochemistry, when he was there, which was [Christian] de Duve. He was a cell biologist, who received the Physiology/Medicine Nobel Prize in the 1970s. He was traveling a lot, and so we had other people teaching also, but he was the better teacher. He was an inspiring teacher although I think my interests in science were not yet very strong. I had to decide about the kind of medicine I wanted to do. After I went to medical school I did an internship and then a residency also, and it was at that time that I really decided that I was going to go into research to try to understand the causes of human diseases. The most interesting branches of medicine at that time were hematology and endocrinology. There was a little bit more biochemistry and a little more understanding about the mechanisms of the diseases especially in endocrinology, and I was not really interested in hematology because I thought that it was at that time still very descriptive cellular biology. Cancer was so difficult, almost impossible to understand, so I was interested in endocrinology. In fact, I had spent some time already during my medical school years in a lab of endocrinology working on iodine metabolism in the thyroid.

JG: You mentioned a moment ago that you decided you did not want to be a physician.

BD: I told myself, “Am I going to prescribe insulin for the rest of my life to patients which have diabetes?” It was a very simplistic view. I told myself I did not want to do that. I want to get more experience in research.

JG: Describe how the Universite de Louvain influenced your career. You mentioned the Dr. de Duve?

BD: Yes. It was, except for the biochemistry classes, a very clinically oriented training. The professor would bring a patient in the classroom, and discuss his or her disease. I thought internal medicine was more interesting in general because at least people were trying to think about what the origins of the diseases were or the rationale for the treatment that could be found for some of the diseases. I had a fairly old professor who was well known in endocrinology, especially in diabetes. I think he was one of the first ones to have injected insulin in patients, of course many years before I knew him.. At the time that insulin was discovered I think he knew [Frederick G.] Banting and [Charles] Best personally.

JG: You mentioned that your internship, or your post-graduate work, was at Laboratoire de Pathologie Generale?

BD: Yes.

JG: What was that like?

BD: That was interesting. I was already working in that lab during my medical school years. I would go to the lab in the evening and do work in cardiac physiology in rabbits and then later on I became interested in the thyroid and I published a few papers about iodine metabolism.

JG: These were your first papers?

BD: Yes.

JG: You become a Fellow at the Belgium American Education Foundation.

BD: Right.

JG: Talk about how you became connected with that?

BD: I think it was through the Laboratoire de Pathologie Generale. It was customary also for people to spend at least a year in the States just to learn more about what was going on in specific areas of medicine. Having done some work in the thyroid I had become familiar with some of the literature in this field. So I applied for a fellowship to the Belgium American Education Foundation and that is how I came to the NIH the first time. I came to the Clinical Endocrinology Branch of what was then called the Arthritis Institute [National Institute of Arthritis and Metabolic Diseases]. Ira [Pastan] was there also at

that time but I worked with Harold Edelhoch, a physical chemist. For the first six or more months I worked together with a well-known British scientist who was a visiting scientist at the Clinical Endocrinology Branch. She was already a fairly senior scientist at the time and had been probably one of the first women in biochemistry in England. Her name was Rosalind Pitt-Rivers. She was a direct descendant of the two [William] Pitt's who had been prime ministers in England in the 1800s. She was a very interesting person. She had discovered one of the thyroid hormones, triiodothyronine, which is given to patients all over the world. It was fun to work with her and it was really my first exposure to a more exciting type of science. The sort of things that I was doing in Belgium was interesting, but it was not terribly exciting in any sense.

JG: You mentioned that it was customary for someone from Belgium to go to the United States.

BD: Right. That is how I got into that Fellowship. It was a reasonably prestigious Fellowship because there were about twelve of us each year from the entire country who would be selected to go for studies and training in the U.S.

JG: The Fellowship was for two years from 1963 to 1965?

BD: Right.

JG: This is your first visit to the United States?

BD: Right.

JG: What were your impressions of the U.S. in the early 1960s?

BD: Everything was new to me of course. I came to the NIH in September of 1963. In November the President [John F. Kennedy] was assassinated. I felt that was a big shock to me also that something like that was possible. I had never heard anything like that, certainly never in a small country like Belgium, where there are always governmental coalitions, and so people from different political parties have to agree and to compromise. To me it was a big shock especially because Kennedy was revered by young people like me and in Europe he was considered an exciting new person. It was a somewhat similar situation as the one we have now with the campaign and the election of President Barack Obama which is exciting for so many young people, even for not so young persons. So the assassination of Kennedy was a big shock.

JG: How did you hear the news?

BD: I rented a room in a house very close to the NIH campus and the lady of the house told me after I had come back from the lab. It was a Friday I believe, a Friday around five or six o'clock, and I heard about it. In fact I wanted to go to the Naval Medical Center because they were telling over the radio and on television that the President's body was

going to go to the Naval Medical Center and I even tried to go there but I could not get even close of course.

JG: What was the pursuit of biology like in the early 1960s here at NIH?

BD: I came to work in a very prestigious NIH branch or department—the Clinical Endocrinology Branch where top people in the thyroid field pursued their research projects which was very focused on the thyroid. My project in Harold Edelhoch's lab was also focused on the thyroid and on a particular protein in the thyroid gland where the synthesis of the thyroid hormones takes place. It was an exciting period because there were lots of very good people and Rose Pitt-Rivers was one of them and I worked with her. I was really exposed to real science here with sophisticated centrifuges for example. It took me a little while to adjust also because initially I had thought about research that was more closely related to medicine but I saw those people, very smart people, who were doing very, very basic research and I found it very interesting.

JG: What was NIH like at the time?

BD: There was lots of great science including the discovery of the genetic code by [Marshall] Nirenberg and others. There was discussion about polypeptide hormone receptors. There was also a good amount of work in bacterial genetics. NIH was smaller and so one knew more people and I knew a lot of people that I am still friends with. There was a very

good friendship between the different postdocs especially those coming from Europe and so it was really nice to work here.

JG: When did you learn about the discovery of the double helix by Watson and Crick?
Would it have been in Belgium?

BD: Yes. It must have been in Belgium. In some of my classes there might have been some talk about the double helix. At that time, I probably did not understand much about the implications of the discovery.

JG: You mentioned that while you were a Fellow you met Ira Pastan.

BD: Right.

JG: What were your impressions of him at that time?

BD: Ira was a young faculty member in the Clinical Endocrinology Branch. He was doing very good work. He was interested in polypeptide hormone receptors on the surface of cells more particularly in thyroid receptors. I found his work very interesting. He was a hard worker. He was very dedicated and very focused.

JG: How so?

BD: Everybody respected him because he was very dedicated and wanted to do very novel and ambitious work. His lab was very productive. I did not work with him the first time I was here because I was with Edelhoach and more closely related to Jack Robbins and Ed Rall, who recently passed away, the two heads of that branch. Ed Rall became the scientific director of the Arthritis Institute. I went back to Belgium after about a little less than two years. During this time at the NIH I also met Emma my wife who is from South America.

JG: Was she also at NIH?

BD: No. She took courses at Georgetown University.

JG: You returned to Belgium?

BD: Returned to Belgium.

JG: You become a physician at the Central Military Hospital?

BD: That's right. Because of NATO agreements military service was still compulsory for essentially all Belgian males above the age of eighteen. My work at the Military Hospital was not a full-time job. I was able to do some work in the lab in Louvain to complete some work I had started at the NIH. I also finished training in Internal Medicine.

JG: Compare and contrast what it was like being in the United States and then returning to Belgium.

BD: Yes. I was fairly rapidly offered a faculty position in Belgium but I felt I had insufficient training in research to be a fully independent and successful investigator. At the same time I was also not envisioning a research career to work on the thyroid protein that I had focused on during my time in Harold Edelhoch's lab for the rest of my life. I certainly would have liked to stay longer at the NIH or in the United States but I really had to go back to perform this military service. I could not escape from that. If I stayed in the United States as a person from Belgium I was concerned I might be sent to Vietnam so I thought it was better to do my military service in Belgium. I certainly was not in favor of the war in Vietnam. I remembered very well what the French had done there and that was very influential in my thinking about the Vietnam War. They lost the battle of Dien Bien Phu [March 1954] and they had to leave Indochina. They had been the colonial power for a long time.

JG: Right, in Indochina.

BD: In Indochina.

JG: When you came to the NIH were you politically active in protesting the Vietnam War?

BD: No. I had discussions with a bunch of people but no I was not politically active.

JG: You returned for your military service?

BD: Right, and did some more work there.

JG: Then you come back on another Fellowship—the Eleanor Roosevelt Fellowship of American Cancer Society.

BD: Yes.

JG: You come back in 1968?

BD: Yes.

JG: What was different? How was NIH different in 1968?

BD: NIH was not terribly different. The growth occurred more in the 1970s and 1980s. I mean this building was probably built in the late 1960s and we were still in Building 10. I went to work with Ira. His work and his approaches were much to my liking. Ira had done groundbreaking work and discovered cell surface receptors for polypeptide hormones. Since cyclic AMP was thought of as a second messenger for a number of polypeptide hormones in mammalian cells Ira was interested in how the hormones were working inside cells. I wrote an Eleanor Roosevelt Fellowship application which was

mostly about cyclic AMP and the second messenger hypothesis and so Ira's lab sounded like a very good lab to work in. In fact we worked in bacteria. It was a good modern way to understand what cyclic AMP was doing at the gene level. We used the so-called *lac* operon of *E. coli*, the genetics of which had been extensively developed by the French Nobel laureates [Jacques] Monod and [Francois] Jacob and by other bacterial geneticists, to demonstrate how a specific group of genes was regulated. It was exciting. Very quickly I understood that this was a terrific project to work on.

JG: What brought you back to NIH?

BD: It was a combination of things. One thing was that I felt I needed additional training in molecular biology and genetics. Even though I wanted to do research as my principal life occupation, my research training, which was very good and very rigorous, had been in protein chemistry, and I did not think that was the sort of work that I wanted to spend my life on. I wanted something a little broader. The work that I did then with Ira really influenced the rest of my career. I am still working on the control of gene expression and the transcriptional control of cell differentiation. My work on the *lac* operon in Ira's lab and somewhat later on the *galactose* operon in *E. coli* influenced the rest of my career.

JG: Did you apply for other Fellowship positions besides the NIH?

BD: I applied for a few other Fellowships but I was not selected for the other ones. I got the American Cancer Eleanor Roosevelt Fellowship which for some reasons was

administered in France and I was supported by my previous professor of cancer pathology who was an internationally recognized cancer researcher and clinician.

JG: When did you start thinking that you would like to stay in the United States?

BD: There was really a succession of events. I got a job here. The Fellowship was for one year and then Ira gave me fairly rapidly the equivalent of a faculty job. My wife is from South America. She really liked it here also and then we had children fairly soon. I still had an open appointment at the Louvain Medical School in Belgium, which I never took, but it remained open for a few years. They told me, "If you want to come back you will be welcome." In fact, I remember having spoken with de Duve when he came for a visit here at the NIH and he told me, "Do you want to come back? I think it would be a good idea." I felt the door was open. I never really thought about taking the ECFMG [Educational Commission for Foreign Medical Graduates] exam which is for medical graduates from all over the world to continue their medical education in the U.S. I was still a little bit in the situation of should I look for research which is closer to the clinic, closer to patients, to actual medicine. My decision to stay in the U.S. came slowly, my work was really very interesting, it was also the beginning of recombinant DNA.

JG: Ira sets up the Laboratory of Molecular Biology. How do you get involved?

BD: I was working with him first at the Arthritis Institute and then at the Cancer Institute where he initially was the head of a section. Ira was then offered to become a Lab Chief

of a new laboratory at the Cancer Institute. Moving with him was almost a natural continuation of my situation in Ira's lab. I felt at the time that Ira's lab would continue to be highly successful.

JG: Describe Ira and then also describe Dr. Max Gottesman.

BD: Yes.

JG: What type of scientists are they?

BD: Right. Ira was a very productive and very rigorous scientist. That first year, when I came back, Howard Varmus and Bob Perlman were in the lab and the cyclic AMP project was developing rapidly. It was a very exciting time. Ira wanted to work on things which were very new and I can remember how he clearly differentiated himself from the work in the Clinical Endocrinology Branch which was mostly related to the thyroid. "Would there really be earth shattering discoveries made in the thyroid?" He did not think so. He was interested in the cellular events and signals triggered by polypeptide hormones and their receptors. You could feel that he was a very ambitious scientist. He wanted to really go forward and he was very rigorous. He knew the rules of how not to cut corners and how to generate very solid data and how to test intelligent hypotheses. It was exciting.

Max joined the Laboratory of Molecular Biology from another Institute at that time, at the same time as Sankar Adhya. I think Susan Gottesman came somewhat later. Don Court also. They were bacterial and bacteriophage geneticists. In Max one could sense a person who had intense satisfaction in thinking and discussing genetic experiments. He clearly has a brilliant mind. He and the other geneticists would spend a lot of time in front of a blackboard trying to figure out or explain their experiments and elaborating the best hypothesis which accounted for their results. The design of their genetic experiments, which was based on selecting for specific mutant phenotypes, was crucial. However, I felt that my approach, based on my previous training, should be more biochemical but this approach was very complementary to that of the geneticists and I gained a lot training in genetics and appreciation for the power of genetics by my interactions with them.

JG: How did you see your career progressing?

BD: I thought the prokaryotic system was very good, it was exciting and had been rewarding. I got some terrific papers published in *Nature*. But my medical background drew me to systems that were closer to animal biology. I thought the molecular biology of bacterial operons was a wonderful experience but I thought that for me it was a step

JG: What was it like to be published in *Nature*? This was the first time?

BD: Yes.

JG: And that is a very prominent—

BD: Yes. That is considered a very good journal. I did not realize how much you get recognized by other scientists and so you are very happy that your paper gets published in *Nature*. The recognition comes more slowly. So I thought first of all, the NIH was a good place to work, and I got recognition for the work I did in Ira's lab. At the same time I had some questions about becoming a full time bacterial geneticist. I thought, probably naively, that what was most interesting to me was going to come out of studies in animal cells and that at some time the genetics of animal cells or of entire animals would also be possible and one would be able to do very good work in that area.

JG: Speak a minute about the recombinant DNA controversy. How did it impact the laboratory in the 1970s?

BD: I do not think we got terribly involved in the actual controversy. I personally felt it was a bit political, that a number of scientists felt they had to take a principled position to make sure the scientific community and the public in general had to become aware of potential dangers of recombinant DNA. Maybe I was pretty excited about the obvious exceptional benefits of recombinant DNA. With my colleagues, mainly Bruce Howard, we were the first to clone a small piece of cDNA for a collagen gene in Ira's lab. Everybody was getting there and there was a sense that this was going to be very interesting and very

important to be able to understand the regulation of mammalian genes and so the first thing to do was to make a cDNA. It was a very exciting period.

JG: You become the Chief of the Section of Gene Regulation at LMB in 1976.

BD: Right.

JG: Then you leave in 1987?

BD: Yes.

JG: Walk me through those ten years and some of your significant research projects.

BD: I first continued to work on another bacterial operon, the *E. coli galactose* operon in collaboration with Sankar Adhya, Richard E. Musso, and Roberto Di Lauro and also with Ira at least initially. We obtained some very interesting results that showed a novel type of control of gene expression which consisted of a mechanism using two different promoters, one of which was controlled by cyclic AMP while the other one was not and was repressed by cyclic AMP. Later Ira and I and others were looking for a eukaryotic gene system that could be regulated. It was the beginning of recombinant DNA and there was a lot of excitement to isolate eucarytic cDNAs and genes and their regulatory segments. Ken Yamada and Ira had observed that the levels of the extracellular matrix protein fibronectin was strongly decreased in fibroblast, which were transformed by the

Rous sarcoma virus (RSV). This sounded like a nice model to study the regulation of the fibronectin gene in normal and transformed cells so we set out to clone a fibronectin cDNA and the fibronectin gene. In reality we ended up cloning a collagen gene, which was equally downregulated in RSV transformed cells. Since many of the coding sequences or exons of this gene had exactly the same size this led to the hypothesis that this gene or its ancestor had been assembled by amplification of a single short exon. This also accounted for the highly repetitive nature of the collagen polypeptide.

Then in the early 1980s I felt that it was time for me to take a sabbatical and I went to work at the Pasteur Institute [Institut Pasteur] in Paris. It was not a very productive year scientifically for me but it was interesting to be in a French lab, my mother tongue is French. My kids went to a French school and so it was useful also for the family. It was also useful for me because I met French scientists. I was offered jobs while I was in France and I traveled a fair amount in Europe. Then I came back. I continued to work on another collagen gene and tried to work hard in trying to figure out how this collagen gene was regulated in Rous sarcoma virus transformed cells. I spent a fair amount of time, several years probably, and people in my lab in particular, trying to understand this regulation but we never got anywhere.

JG: What is that like? Do you consider that a failure or did you still learn something significant that made it successful?

BD: We learned mainly by hindsight that it was not such a terrific project after all for a number of reasons. My sense was that it took several years, maybe 1985, until we knew that it was not going to be a good system, that I needed to look for a better system to study the regulation of eukaryotic genes. Up to then my work was very exciting. I had worked on the bacterial *lac* operon and then the *galactose* operon and then we switched to use recombinant DNA to clone a collagen gene starting with a cDNA and determined the structure of the gene and proposed how by evolution the whole family of collagen proteins had evolved. We tried hard to understand the regulation of the gene we were studying, we even did some genetics, but did not succeed probably because the system was not clearly defined and because the downregulation of collagen genes in cancer cells was a secondary event in the neoplastic process. That was about the time I was starting to look for jobs outside the NIH.

During the Reagan administration there was often a hiring freeze for civil servants. Whenever you lost a position it was difficult to regain the position. I felt that it was about time for me to become a department head. I looked at a few places and decided in 1986 to accept a Chair position at the M. D. Anderson Cancer Center in Houston and it took another year before my family and I moved. Maybe there was some disappointment with the system that I was working on and that I was looking for a next step in my career.

JG: How had NIH changed between 1963, when you first arrived on the campus, and 1987 when you left to go to Houston?

BD: Between 1963, when I worked as a postdoc in a rather small lab on the major protein of the thyroid gland, and 1987 there had been a tremendous growth in the knowledge base in the biomedical sciences brought in part by recombinant DNA. Oncogenes were discovered by Harold Varmus and Mike Bishop. NIH became much larger. Ira's lab was much larger also but there was a very good exchange of ideas and information. Overall the NIH was always a terrific place to do science. For instance the journal clubs were always very good and we learned a lot of things in the journal clubs. I had joint lab meetings in the early 1980s, together with Ira, it was very exciting to have that the in-depth analysis of results. There were also lots of seminars on the NIH campus. Ira had at that time started to switch to immunotoxins and one could feel that it was really going to be his work for the next ten, fifteen, twenty years. He is still working on it. The difference was that the lab was much larger and there were many more people. In the early 1970s for instance probably more than half the people in Ira's lab were working on prokaryotes and the rest on eukaryotes.

JG: The vegetables and the animals?

BD: Yes. The vegetables and the animals. But even after Max left—and soon after Max left Don Court left also to go to Frederick [Maryland]—the vegetables were still very strong. But I had already decided that my work would continue in eukaryotic systems. I felt also it was time for me to have the opportunity to put together a department. That is something that I wanted to do at that time.

JG: How did your years at NIH impact your time at the University of Texas? Were there things from Ira and Max, their style of management, for example, that influenced you?

BD: Yes. Certainly from Ira you could see that science had to be outstanding. I certainly took that with me. Thanks in part to the people I was fortunate to hire my department turned out to be a fairly successful department. What I learned from Ira was to get a department where real basic science was going to happen and we tried to hire very good people, new people with new ideas, so that was very important in terms of organizing. From Max I learned how much research has to be fun and that it was very important that the people in the department would interact well with each other.

JG: Do we have a few more minutes?

BD: Sure.

JG: Speak about the responsibilities that you have to younger scientists. How do you balance the need for them to be both creative and then also skeptical in their research? How do you train them?

BD: I think I would put the emphasis on creativity, on new exciting ideas. Of course be rigorous about your results and make sure that all necessary controls are part of each experiment is essential. For new faculty that aspect was essentially a given. We had regular blackboard discussions with the faculty where controls of experiments were

always an important part of the discussion. This aspect had also an important part in journal clubs where important papers providing new insights were analyzed in depth and where the conclusions of papers were always very critically examined. We tried hard to encourage the young people to be part of our discussions in journal clubs. I think this was at least occasionally successful.

JG: Two last questions. First, what are some of your hobbies outside of science?

BD: So we did something crazy, my wife and I, in the early 1980s, when I was still here. We bought an old farm house in Tuscany and we slowly restored it and so I have spent probably every summer since then in Tuscany. Now I am growing olive trees there and am getting olive oil. It was a family project, in fact. The kids were coming, they brought their friends. I also read a fair amount mainly history books and sometimes very good novels.

JG: That is very nice. The last question is if you had one piece of advice, one lesson learned that you would like to pass onto a future scientist or researcher working ten or twenty years out what would that be?

BD: Be ambitious. Try to make a big discovery. Do not work on trivial things. Work on difficult projects. Be patient, it takes time to develop a difficult project. Find the best collaborators you can find, the ideas of others will enrich your project. Have fun in your work. Research in biomedicine is among the most exciting careers there are. It is a very

exciting way of life. You also have to adjust to the times and use as much of the new methodology as needed. Some of these methodologies at least in genetics allow one to examine some functions of all the genes in the genome in a single experiment. But despite these new broad technologies the work has to continue to be hypothesis driven and one should try to understand the molecular mechanisms involved in cellular processes. The fun part of science is to think hard and formulate an exciting hypothesis and design experiments that will test your hypothesis. Many very, very important and unexpected things will still be discovered.

JG: Thank you very much.

BD: Thank you.

[End of Interview]