Roland Berger

Personal Details	
Name	Roland Berger
Dates	1934-2012
Place of Birth	Paris
Main work place	Paris
Principal field of work	Human cytogenetics

Interview	
Recorded interview made	Yes
Interviewer	Peter Harper
Date of Interview	19/04/2005
Edited transcript available	See Below

INTERVIEW WITH DR ROLAND BERGER, 19 APRIL 2005

PH = Interviewer (Peter Harper)

RB = Roland Berger

PH **It's Tuesday 19 April and I am talking with Professor Roland Berger at Hôpital Necker in Paris.**

May I ask first of all how did it happen that you became interested in both medicine and in genetics?

RB In medicine, it is a very old story. When I was very young I decided to become a medical doctor, very young, perhaps after a disease, I don't remember. And for genetics it is more recent. I was an intern in medicine at that time and I read by chance a paper on the double helix and it was fantastic for me.

And I asked people, where can I go to learn medical genetics and here it was not so accessible.

PH Was this soon after 1953?

RB It was. I met Lejeune for the first time in 1960 and some people told me that a young investigator named Jerome Lejeune had discovered Trisomy 21 in mongolism and I went to Lejeune and I asked him to learn to work, and he started something.

PH Were you at that time in training as a paediatrician?

RB Yes.

PH Here at Necker?

RB No it was at Hôpital Trousseau where the lab was, Turpin was there and Lejeune too.

PH Because afterwards some parts of Trousseau came to Necker.

RB Yes.

PH So did you then leave clinical work for some time to do full-time research, or did you combine the two?

RB No no. I combined it for a few years, because in France we have the internship. Internship is a good formation for clinicians and it was difficult to become intern at that time because of concourse, and when you have the possibility to spend four years of formation, serious formation in medicine it was ridiculous to me. So I spent four years in paediatrics and more so in general medicine, combined both aspects and after I went to regional hospitals.

PH May I ask, did you then also do courses in formal basic genetics as part of this work?

RB You mean the formation, the training?

PH Yes.

RB It was in Faculte des Sciences I learned the basics with a man, a very good professor. I have a problem with the names. He died recently. He was a formal geneticist. Very good as a professor, but it was only for one year and after I followed formation in biochemistry and in cellular physiology and so on.

PH Yes. So did you have contact with people like Ephrussi, L'Héritier?

RB L'Héritier no. He was retired, no. He was still professor of genetics when I started in the Faculty of Sciences.

PH And Malécot, he would have been earlier?

RB He was in Poitiers or . . .

PH Oh I see. Not in Paris?

RB At that time he was not in Paris.

PH And here at Necker, so your research was based in the lab at Trousseau?

RB No no, we started at Trousseau and then after we came here.

PH So here already would be Maurice Lamy and Jean Frézal, and Jean de Grouchy perhaps also.

RB Yes

PH So was your research entirely with Jerome Lejeune or did you have much interaction also with the others?

RB Only with Lejeune. Jerome Lejeune was a good friend of De Grouchy. They were very good friends and ate their dinner together every Saturday, but there were no laboratory links.

PH So do you think this was partly because one group had come from Trousseau already formed, or was it more the philosophy?

RB No I think that geneticists, medical geneticists, didn't believe too much in cytogenetics and Lejeune was a little . . .

PH I can imagine.

RB A little tough so to speak. Probably the characters were not in good agreement.

PH Yes. I can imagine, because apart from Jean de Grouchy the others were not so much interested in cytogenetics.

RB No. In France it is curious, but that is due also, it seems to me at least, that Jerome Lejeune would keep the cytogenetics in his hands. He was decided not to share cytogenetics with other people except De Grouchy, and this was a problem. It was a misunderstanding between the other people, but it was difficult to understand that when you are young and when you are coming in a lab.

PH And also if there are these difficulties between senior people it makes it very difficult for a young person, because it is easy to be caught in the middle so to speak. May I ask was Professor Turpin also at Necker or did he retire?

RB Yes he came here for quite a few years.

PH So at the time you were working with Lejeune, Professor Turpin had mostly retired?

RB Almost yes.

PH Almost.

RB And Lejeune became professor in 1965 as far as I remember.

PH Was he professor of basic genetics or of paediatrics?

RB No, basic genetics. Turpin was a paediatrician only and Jerome Lejeune had the chair after that, fundamental genetics was the name of it.

PH But it was here based at Necker?

RB Yes and he had two organisations, here and the old Faculty of Medicine in Paris in second arrondissement.

PH Can I ask then, reading and looking at the papers it seems to me that at the time you started, Trisomy 21 was discovered, but you were very much involved in all the subsequent discoveries of chromosome abnormalities is that correct? Cri-du-Chat?

RB Yes Cri-du-Chat, I wrote the first case in the lab of the translocation, familial translocation of a child with Cri-du-Chat.

PH So may I ask, when you were working with Jerome Lejeune, were you given a specific project, or was your remit to prepare chromosomes on everything interesting?

RB No, it is complicated because we were very few when we started. There were 3 people, Lejeune, Mary Martineau, perhaps you know her?

PH I don't know her, no.

RB When she was unmarried she was Mary Hayes. She was a student and she learned cytogenetics in Lejeune's lab when I came. There were 3 only and a technician and we were obliged to be interested in everything, so I participated in the constitutional abnormalities and for my MD thesis. Lejeune proposed to me to be interested in leukaemia and I started, my MD thesis was on leukaemia.

PH So at this point the Philadelphia chromosome was already known?

RB Yes.

PH But there was at this time no banding.

RB No.

PH Did you find any great new changes in leukaemia or was there nothing until banding came?

RB OK. The problem was difficult because we were not certain; we have a Trisomy 6 which was really recurrent in leukaemia but it was impossible to say it was an 8 at that time and the problem was that people in France, and also in all countries I suppose, were disappointed by the study of chromosomes in leukaemia and in solid tumours, because they were unable to find something consistent as the Philadelphia chromosome was, and if you look at the literature at that time, many people said all chromosome abnormalities are secondary, even without significance, and even people who later said it was important but you can find . . .

PH At the time.

RB Yes. It's written in papers.

PH I have read.

RB So this was a problem, but we believed that because of the existence of the Philadelphia chromosome there was something to understand. This is the reason why I continued with this work.

PH After Trisomy 21, which was the next constitutional abnormality to be found?

RB As far as I remember, Lejeune and Turpin, but I was not involved, published the twins with discordant phenotype but I was not involved and also the Robertsonian translocation.

PH With Down's?

RB No I suppose without; it was a British group.

PH Yes I think it was Polani.

RB Yes it was Polani.

PH By the way Polani is still living. He is more than 90. I have visited him.

RB He is still present?

PH Very much. Very. So the first one that you found?

It was a Cri-du-Chat, '63 I remember and also the monosomy 21, we had a case of monosomy 21 which was the start of a big theory on the type and counter-type.

PH Yes, anti-mongolism. So with the Cri-du-Chat can you give me an idea how did you find this patient and what was it that made people, you know, look at chromosomes?

RB No, it was children sent to the lab because of mental retardation and some physical anomalies, malformations also, and Lejeune saw the first case probably alone and he was interested by the cry. And he told us that he saw a child with a curious cry resembling a cat cry. And the second and the third case came from this idea that mental retardation plus special cry should be a syndrome. The theory of Lejeune was to ascertain the existence of a new syndrome we must have three patients.

PH Yes, that is probably quite sound.

RB His attitude. So we had three and the third was the result of a maternal translocation. It was the first translocation resulting in deletion.

PH And the first and the second case then, had they already had their chromosomes examined, or did that wait until you had all three patients.

RB No, they were examined in Lejeune's lab.

PH But it was thought that it was possibly coincidence until you had

RB Three.

PH Three yes. That's very interesting. So that was 1963 and then remind me then which were the other main constitutional findings after this?

RB The deletion of the long arm of the chromosome 18.

PH Was that also first described from Necker?

RB Yes. It was interesting because the phenotype was so obvious when you knew it. I remember I saw a child who was a mosaic and recognised the thing. I kept seeing the child. The paediatrician was.....

PSH very impressed.

RB ....with me because I saw the kid.

PH With that, and because at this time already Trisomy 18 was known, did this influence Lejeune's ideas on the imbalance with monosomy and trisomy, in the same way also as for 21?

RB No I don't think so.

PH Can you give me an idea as to how the technology you were using had changed, because talking for instance with Marthe Gautier, the original techniques, I mean everything was very primitive.

RB Yes, very primitive.

PH To me it is amazing the quality of preparation with such very basic equipment.

RB Yes it was funny, because Marthe Gautier, maybe she told you, was the main person involved in the culture. So she introduced fibroblast culture in the lab. And Lejeune curiously was reluctant to introduce blood cells and with Mary Martineau we had problems because everybody started with blood culture and Lejeune said 'No' and once when he was absent at a congress, we tried to with Mary Martineau.

PH And did you succeed?

RB Yes, yes.

PH What did he say, was he pleased?

Oh he said, I can improve your technique!

PH This was something someone else told me, he always, if there was some new technique, he always had to make some alteration himself so that it worked better. I think it was Marie-Odile Réthoré. But in my mind I was wondering did it really work any better because he did something, or not? It seems unlikely.

RB No, when I met him very soon after, he was starting to write his book which appeared five years later, I don't remember

PH Now which book?

RB 'Les chromosomes humains', and he was absent for a long time because he was travelling in every country, he was engaged writing the book and so on and the technician, Mary Martineau . . .

PH OK Yes.

RB No he didn't participate in the technique, once or twice. The difficulty we had with the fibroblasts because we had a cock.

PH In Trousseau. Did it come to Necker also?

RB Yes

PH I heard from Marthe Gautier about the cock.

RB It was terrible! She was expert in getting, yes she was very good.

PH So was Marthe working with Lejeune and Turpin at the time you began your studies?

RB Yes, but she left afterwards for many reasons. There were problems.

PH It does not surprise me and I have not asked about it, but if I tell you my impression, I get the picture of Jerome Lejeune as a very strong character, probably not so well disposed towards strong women and then equally I get the impression from Marthe Gautier of two very strong characters.

RB Yes maybe, but she was probably disappointed because of the attitude of Lejeune and Turpin. She was considered as a technician, a good technician but probably she was angry. But she is, I think she is very honest.

PH Very. I am sure, but she was already an experienced worker when she came to work back at Trousseau, so I can understand and it occurred to me it's a little like the situation of Rosalind Franklin.

RB Maybe

PH I think in those days it was very hard for women, very hard. So to return to the abnormalities which you were involved with. You had the Cri-du-Chat. You had the partial monosomy 18. Which other conditions especially did you contribute to?

RB In the meantime we had clonal evolution in leukaemia, in the Mongol child. That was in also '63 with the acquisition of supernumerary chromosomes; as you know now that is considered not a mechanism of acquisition normally and we tried to find ourselves cases such as this one, someone had published but it was de Grouchy who tried to study clonal evolution in CML patients. Otherwise we have a separate Trisomy syndrome, trisomy 18

PH May I ask was this mosaic or full trisomy 8?

RB Both I think. And we had also the ring 13.

PH Yes. Was that the first ring identified do you think?

I don't know but it was perhaps the first syndrome, not the first case of ring, and also the ring 18, I don't remember exactly.

PH Can I ask you there, it's a little unfair to ask you these questions so suddenly, the ring chromosome 18, was the phenotype similar to what you had seen with the monosomy?

RB Not entirely.

PH That's interesting.

RB You know perhaps, at that time Lejeune was interested by the ring

PH I didn't know.

RB I forget their names, L'anneau Möbius, and it started with that gene. The rearrangement of the ring from this Möbius ring.

PH Was Lejeune always very interested in the underlying theoretical aspects of these chromosome changes?

RB It's difficult to tell. He was interested at first in the mechanics, non disjunction, segregation, but after the banding era he was no more interested in cytogenetics, and I don't know if people told you, his mood in the lab, it was very difficult for some people because he was enthusiastic against the Pill and then abortion, and if you didn't follow him you were an enemy and I refused, perhaps I was the only one, to sign against the Pill and abortion, because it seemed to me that it was not correct or responsible for the chief of the lab to ask people to sign an engagement.

PH Absolutely not.

RB And also because, in my opinion at least, I don't wish abortion on every woman, but sometimes it is a necessity. So starting from that later I was considered as an enemy and my situation was a little difficult, so that is the reason why I left as soon as I could, but the last time the bands he learned he read in Nature, first in the lab since we received the journal, the paper of Yunis, Claude Yunis?

PH Yes.

RB And the bands with the heterochromatin and not all chromatin with the R bands, after they were named R bands. And he asked Dutrillaux to try to reproduce these R bands in the lab in the faculty, not in the hospital.

PH So was Bernard Dutrillaux working in the faculty?

RB Mainly. Not entirely but mainly and it was secret. We were not aware and during the sixties, it was ridiculous. So it was not so . . . And after, Dutrillaux was in charge of the bands and they were introduced in the routine lab and Lejeune was less interested. He was more interested in the structure of molecule with models to try to find the treatment for mongolism and he spent all the morning, he was only in the morning in the hospital, in the afternoon he wasn't in, with this model. I was always on my microscope and I didn't see the model and once he called me "Come and see my new model". And I saw the carbon which was pentavalent and I said I don't know carbon with five. Oh he was furious. So he was not competent enough in chemistry and so his idea was not good. He tried to treat Fragile X also, but it was also a little ridiculous.

PH **One thing which I was hearing a little this morning, was the effects of these problems on the wider community of cytogeneticists across France, because Simone [Gilgenkrantz] was telling me that until this time, people would come from the other cities in France to learn and to exchange ideas, but when this problem about signing something arose, it created this big division, not just in Paris, Necker but in France generally.**

RB I am not sure. I don't know but I am not sure. You see the problem, perhaps you met Andre Boué.

PH I meet him on Friday.

RB They were involved in the study of the abortus and they were supported by the paediatrician Robert Debré, who was a big paediatrician at that time but outside the influence of Lejeune, completely outside, and people were very long starting this prenatal diagnosis because they were afraid.

PH Of course.

RB You know when I would leave the lab, Lejeune's lab, I was in the CNRS, the Centre Nationale de Récherche, and I had to write to say I want to go, and I was allowed and I found great difficulty because people were afraid. They were not being complete with Lejeune, even here where my professor told me that I must leave Lejeune for more than10 or 20 years. I cannot be in, I cannot support you. It was ridiculous. And I succeeded. Somebody told me ask François Jacob for advice and opinion. So I went to François Jacob and he told me he was not interested in human chromosomes, but perhaps he could find a lab for me and he sent me to neonatologists where were Alexander Minkovski . . .

PH I know the name.

RB And Minkovski accepted, welcomed me in his lab and when I saw the authorities in the CNRS I said I wanted to leave Lejeune to go to Minkovski because I had the right to do so. The answer was fantastic. It was "Be cautious. It will be considered as a political action." It's ridiculous. I cannot believe that it is so in UK?

PH No.

RB It's impossible, but it was done. So it explains the climate

PH It does not make for a happy atmosphere in the lab, does it.

RB At the time Marie-Odile Réthoré was happy, because she believed every single thing Lejeune said.

PH Can I ask, Jean de Grouchy, he was from Necker from the beginning and so was he always in a separate group from Lejeune, or did they join groups.

RB No, they were separate groups. The heads met every week for lunch, I met de Grouchy, but I never worked with his team, never.

PH So this was a separate cytogenetic lab, because his work was mostly cytogenetics?

RB Yes. Only.

PH So did they share any facilities or was it . . .

RB No they exchanged techniques probably and some ideas, because Lejeune was very inventive at that time, at the beginning that is. More, probably more than de Grouchy. But de Grouchy travelled, spoke very good English as you know, he travelled. He knew everybody. He was a good, nice person, very pleasant and so on, so he had many good relationships with people of all walks. So he had probably a relationship with other labs in USA and perhaps in Great Britain too.

PH I think generally, whereas, maybe, this is not from my knowledge but maybe people generally found Lejeune difficult because of his rather rigid attitudes.

RB Yes it's true. And it was mainly true, I have something to tell you after the events of 1968. Because in 1968 he was very very unquiet because he was a young officer at the time and he believed that he could lose his professorship because of the events.

PH With student unrest?

RB Yes. For me it was not a factor, but it changed after that, completely, and when I decided to leave the clinical ward and go into research he explained to me very sympathetically. Be careful. You will be
married, you will have children. The salary is not important in research and if you keep your position as an MD in clinical work you will be paid better. You will have a better salary. Be cautious. Discuss with your wife. No it is to explain. At that time he paid attention to welfare of the only one collaborator he had. But after 1968 it was complicated.

PH Do you think at the regular lunches between Lejeune and de Grouchy, was this mostly scientific discussion or philosophical, or is that just speculation.

RB Ah, I was not under the table!

PH No.

RB But I think it was mostly scientific and technical, because de Grouchy was a little embarrassed by the attitude of Lejeune against the Pill and abortion. He didn't dare contradict Lejeune, but he was not entirely following his opinion and probably was not OK completely, but I don't know.

PH One person who I shall be seeing later this week is Catherine Turleau and am I right that she was principally working with de Grouchy?

RB Yes mainly.

PH So in the evolution of these groups, maybe that is something I should ask her. Did a point come after Lejeune had died and when de Grouchy was more old that cytogenetics all came together, or did it still stay separate?

RB No, I think that de Grouchy lab's old function had disappeared and Catherine Turleau was, I don't know, she came here probably for the first time and after she was as you know in the cytogenetics lab, but the lab disappeared.

PH So now really there is one cytogenetics lab at Necker.

RB Yes, but it is a good thing

PH Diagnostic

RB Nothing for research and now I came with my old pupils so to speak. The one is the chief of the lab now and it is a structure of research, an INSERM unit. And in the INSERM unit we welcomed one of our pupils of course, Olivier Bernard, who is a chief in my sense, who was trained of course by both of us and he is working in the protein lab and it is included in the unit lab.

PH Right.

RB So there is some research in cytogenetics, with molecular cytogenetics and so on.

PH I've been asking everybody who I have seen, Roland, two questions, and one of them is to ask which person in your career and work had had the most influence on its development. Is that easy for you to answer?

RB Very difficult, because it is a matter of personal feeling, and I would say, I know in clinical work. I know perfectly well it was a Professor of general medicine, I admired him very much because he was human with the patients, with everybody. Curiously it seems to me rare in the profession.

PH Sad.

RB OK, and after, probably Lejeune was important for me because I started with him and I learned directly or indirectly my cytogenetics at least, and after I know.

PH And the other question I have been asking everybody is, can you identify one particular piece of work which you have done which makes you most happy, or which you feel has been a contribution that you value.

RB You are trying to make people unmodest!

PH No, but I think most of us, whatever we have done and it may be more good or less good, but usually you can think of something that gives one pleasure. It may not necessarily be for good reason, but from your perspective.

RB OK. I think that it was in what I did on leukaemia because one, I think perhaps that the most important thing I did was description of one of the translocations in Burkitt's lymphoma leukaemia because we found the correlation between expression of haemoglobin light chain and the type of variant translocation and this paper was important for molecular biology.

PH Absolutely.

RB Because it began to believe in cytogenetics. It is my opinion, perhaps I am wrong.

PH No but it is important that it's yours.

RB Yes. Perhaps . . .

PH Are there any other things which you would like to say to me that I have not asked about, because you must remember I am very ignorant about the situation in France, even now, and I probably left out really important areas that you would like to identify.

RB You mean in cytogenetics?

PH Yes especially.

RB I don't know exactly. We had some people interested in meiosis but not so brilliantly you had in your country, and in tumours yes, you know that Gilles Thomas.

PH I don't. Not properly, no.

RB is not a cytogeneticist but he was working with Dutrillaux in Institut Curie and he described the first gene isolated in a solid tumour translocation for the Ewing sarcoma translocation, so it has some importance at the time but now he is not interested in this support. So what else I don't know. FISH is performed by everybody. Microarrays also, not everybody but many people.

PH But these early years were very special and it's these first years that I am trying to record for posterity.

Well thank you very much Roland for sparing the time and it is very good to hear your story.

RB It's one story. You know I am accustomed to say I have three versions of the discovery of Mongolism, Trisomy 21. Turpin, Gautier, Lejeune, and they are different.

PH I'm sure

RB And every little thing, I think the most honest is the story of Marthe Gautier, because she has no intention to present herself as an important person, a good scientist, etc, but the two others were . . .

PH This is why I am trying to talk with as many as people as possible because it is only by hearing something from different directions that you get an idea of what happened, so it is very valuable. So thank you and I will turn this off.