Jean Frézal



Personal Details

Name Jean Frézal

Dates 1922 - 2007

Place of Birth France
Main work places Paris

Principal field of work Medical Genetics

Short biography See below

Interview

Recorded interview made Yes

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Personal Scientific Records

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Summary of archive

Biography

Jean Frézal was brought up in Bourges, France, and studied medicine in Paris during World War 2. He began genetics research with Maurice Lamy, first Professor of Medical Genetics in France, at Hôpital Necker, Paris, and in 1953 spent a year at the Galton Laboratory London, with Lionel Penrose. On return to Paris he worked in the fields of inherited metabolic disease and human gene mapping, creating the gene mapping database 'Genatlas'. As successor to Maurice Lamy he built up a comprehensive Medical Genetics research institute and service at Hôpital Necker.

Interview with Professor Jean Frézal, 22nd April, 2005

Part 1

PSH. It's 22 April 2005 and I am speaking with Professor Jean Frézal at his apartment in La Baule, Brittany. Jean, in this part of the discussion I would like to ask you a little about yourself and how you became interested in the field of medical genetics. So may I ask first of all, did you come from a family with a special medical or scientific interest?

JF. Absolutely no. I was the first MD in my family and the reason is futile. My father was a journalist, thought he had a medical capacity and he thought I was made for surgery, because I had very thin hands and I must be very adroit. As I was a good son I decided to become a medical student. I became a medical student in 1939 just at the beginning of the war. I lived in the centre of France in the city of Bourges. I don't know if you know Bourges. It is a very nice city.

PSH. I have been there once.

JF. With a wonderful casino. And so I got to Paris and I spent all the, with exception, the main part of the war in Paris and I was lucky enough to continue without interruption to my medical studies.

PSH. That must have been a very difficult period for everyone.

JF. It was a very difficult period but fortunately enough I was living with a family and I had no big problems. So, in France the curriculum for medical students is to prepare competitive examination, the main is internat. Internat des hôpitaux de Paris. After the war I was nominated at the competitive Concourse and I chose several classes. Among these places there was one with Professor Maurice Lamy.

PSH. Yes.

JF. I had no idea who Professor Maurice Lamy was. The only thing I knew about him, he was one of my examiners. His father in law was a friend of an uncle of my wife. That is the reason why he accepted me to give a place in his department and I was in function in his department just at the time he became the first professor in the world of medical genetics.

PSH. I see. I didn't know that. I thought he was Professor of Paediatrics.

JF. He was Professor of Paediatrics, but as a matter of fact, the chair of medical genetics and it was in 1951. If you are interested I can give you a copy of the inaugural lecture.

PSH. I would be very interested.

JF. Because you know it's a reflection of what highly educated people, very liberal like Mr Lamy, very tolerant, thought about the main problems at the

time. So I was there and Professor Maurice Lamy became professor of genetics.

PSH. But at the time you started he would have been, or was he already, Professor of Paediatrics?

JF. He was becoming, and I went to the Sorbonne and I take instruction and I had essentially three professors. One was Ephrussi.

PSH. Yes. This was Boris Ephrussi.

JF. Boris Ephrussi was an extraordinary man. Speaking wonderful French. His discourse was inspirational, extraordinary man. Boris Ephrussi, Georges Teyssier. Georges was entirely different. Georges Teyssier was a very typical type of French university member. He was a communist. But as a matter of fact he was a tyrant.

PSH. There is often a difference between people's personal and political aspects.

JF. Like Haldane

PSH. Yes. Now how do you spell his name. I haven't

JF. I think it is Teyssier.

PSH. Right

JF. And the third one was L'Héritier. L'Héritier was a typical product of normal superieur. École Normale Superieur. He had a puerile streak but he was very intelligent, very clever. He was a good synthesis between the biological and theoretical mathematical aspect of genetics. So that was the first team and I passed the examination without problems and I told Professor Lamy I was ready.

PSH. Did your courses include practical studies as well as theoretical?

JF. Yes. Practical study, for instance mating of Drosophila and counting Drosophila.

Fortunately enough I knew Mendel's views.

It was a very nice time. At that time at the Sorbonne for genetical study, we were 30 in a class.

PSH. Really? So many.

JF. So many.

PSH. Were these all people who had had medical training or were they biologists?

JF. Mainly biologists. I was the unique medical student among them. Among the biologists there was a student in psychology who had the obligation to have a biological certificate which was very good. As it was very good it was suppressed.

PSH. And I think several people followed you with this pattern. I think some years after, Pierre Maroteaux also did training . . .

JF. Pierre Maroteaux and some of them, yes some of them. But I was very close to the professor and to the people. I must say one of them a fourth man, younger, who at the time was Chef de travaux. Georges [Visey] who has just died this month. He wanted to create a laboratory in Toulouse and he asked me if I wanted to go with him to do genetics, not medical genetics but fundamental genetics, but I was already engaged in medical genetics

PSH. What was his name again?

JF. Georges Visey. He was a specialist of Ascomycetes.

PSH. Oh yes, fungal genetics. So while you were doing these courses were you also at the same time working with Lamy?

JF. First I had to finish the internat for four years and after that I went to Professor Lamy and he found a post for me, a very modest post. It was the first level of CNRS. At that time a first level of CNRS was not very much money you know.

PSH. But it was something.

JF. Yes absolutely.

PSH. And did this involve also doing clinical work at this time?

JF. Yes with Professor Maurice Lamy. Certainly. Professor Maurice Lamy was a very good clinician. He did his thesis on streptococcus and scarlatina. He had some view of the biology but he was fundamentally a clinician.

PSH. And am I right that also he continued practicing and writing papers on general paediatrics as well as genetic disorders for many years?

JF. Yes yes.

PSH. So can I ask Jean, what was the first project or topic of work that you became involved with?

JF. With Professor Lamy?

PSH. Yes.

JF. Professor Lamy. It is very curious because Professor Lamy thought it could be important to make a linkage study

PSH. Already at that stage?

JF. Yes yes yes. In the original lecture he said that if we had a map of the gene of man we could make prediction etc. He lectured us and he thought I should engage in this work and for that I go for a term at the Galton Laboratory.

PSH. Ah yes. So may I ask, had Professor Lamy already developed links with people at the Galton?

JF. Not really links. Professor Lamy was a good friend with Professor Penrose.

PSH. Yes. So what year was it you spent at the Galton?

JF. It was in '53.

PSH. '53. Yes because at this time there were many very brilliant people at the Galton laboratory I think.

JF. First of all there was James Renwick.

PSH. Ah yes. He is someone, to lose him, it makes me very sad.

JF. Yes me too. James Renwick.

PSH. George Fraser was there?

JF. Not at that time. He was later on, but people involved in gene linkage, Bette Robson.

PSH. Bette Robson. Cedric Smith?

JF. Cedric Smith yes. But Cedric was a theoretical aspect.

PSH. So coming to the Galton, so many people have spent time at the Galton and they have very different stories to tell. It must have been a very unusual experience for you?

JF. It was. For instance, I arrived one day in the Galton and I talked with Professor Penrose – very kind, very kind. And Jim, it was Friday I think and James Renwick offered for me to go with him to collect blood samples in the country. So we took a very small car and go to Poole and visit a family and I was absolutely very surprised because it was so unusual. In France to go to a family, ring the bell, enter and such with people and finally get the sample of blood, it was marvellous. So I spent three days with James and we went back to London via Salisbury

- PSH. Yes, the cathedral?
- JF. I was there also at the same time as Marco Fraccaro but Marco Fraccaro stayed a longer time than me.
- PSH. I think so, yes.
- JF. Two years I think. Some times we saw Marcello Siniscalco. Marcello very 'le cheri de ses dames'. It was a very very nice time and Professor Penrose was always very kind. Bienveillant with me and always he tried to help me. And when I came back to France I was alone, because I could not speak to anybody. You know when I decided to engage in medical genetics, I told people, two kind of people, my colleagues and my bosses. My colleagues thought I chose this way because I had the opportunity to make a career. It was not wrong. But why not. And one of my bosses had absolutely no idea about genetics. He said to me "Oh genetics. It was a monster of the Fly"
- PSH. The Fly?
- JF. The monster and Drosophila.
- PSH. Ah yes. And would it be true to say that in these years, quite soon after the end of the war, people were very affected by the misuse of eugenics by the Nazis.
- JF. Not really. When I was with Professor Penrose, I learned to be not eugenist minded and I remember in '57 I was invited to give a lecture in the Netherlands and in the Netherlands the geneticists were still strongly. . .
- PSH. Really.
- JF. Ah yes strongly. . . It was not the terrible side of eugenics but anyway it was the sterilisation of etc etc and in my conference I told, I tried to develop Penrose's ideas, but it was not really appreciated by many of my audience.
- PSH. That's interesting because as you say, Penrose had very strong views on this and he had I think, especially for us in Britain, a very good influence on how medical genetics . . .
- JF. Totally different views, and that's of eugenics and that's of human genetics.
- PSH. Indeed. Yes. When you came back to France were you able to develop linkage studies at once or did you return to more clinical genetic studies?
- JF. No. We really do at that time kind of epidemiological genetics. That is to say study of some pair of families with malformation, diseases, and at that time I was especially interested in diabetes.

- PSH. Yes, I saw that you had written at this time in the 1950s several papers on genetics and diabetes.
- JF. Yes. One of them in the Annals of Human Genetics which was quoted by Falconer, because I thought I was one of the first to develop the idea that diabetes could be multifactorial, or if not multifactorial with a major gene and modificator. Something like that.
- PSH. And it's still proved very difficult to, even now.
- JF. Yes it was. As a matter of fact it is not that
- PSH. One of the papers I saw around this time which perhaps relates to your work on diabetes was your study on haemochromatosis.
- JF. Yes it was a book about the same time but I was less clairvoyant. I think I said haemochromatosis was a recessive disorder, I think. I don't remember.
- PSH. I think you may have said, that it was dominant, but only partly penetrant. Because then I talked with Josué Feingold, because he came later to study didn't he?
- JF. Yes.
- PSH. I noticed, Jean, that at this time you began many studies of gastro-intestinal and other enzymes.
- JF. Yes in co-operation with Jean Rey and as a matter of fact, coming back from London I had some ideas, and during my stay in London I visit everywhere as a ward of Professor Charles Dent, who was a marvellous man and he introduced me to the concept of inborn errors of metabolism which at that time was completely unknown in France. So I think I was one of those who introduced the concept in France. In '58 in my first book on inborn errors of metabolism, and made with Jean Rey. So among our patients there were many patients with defect of intestinal absorption. So it was an occasion to study the malabsorption of sugar, some form of coeliac disease, of lipid malabsorption etc.
- PSH. Can I ask did you have a laboratory yourself, or were you using the facilities in somebody else's laboratory? How did that work?
- JF. We had a laboratory at Professor Lamy's department and [unclear] was a friend of the professor but really [unclear].
- PSH Was Jean Rey primarily a laboratory worker or was he also a clinician?

JF. Clinical but he was more gifted than me as a laboratory worker. With Jean Rey, we had this part of the work and the second part was amino acid disorders.

PSH. And I suppose that perhaps led later to some of the screening?

JF. We began screening in France in '66.

PSH. For phenylketonuria?

JF. For phenylketonuria.

PSH. That's very early.

JF. Very early.

PSH. Very early.

JF. In France at that time there were ourselves, Jean Pierre [Farieux?] in Lille and the laboratory of Evian company, who made quite a lot of tests and after that I was an organiser of the screening programme in France and I made everybody in harmony of working together.

PSH. Did the Evian company make the dietary products?

JF. No no. It was absolutely 'désinteressé'. They never made any products for PKU except for mineral water!

PSH. So they expected you to . . . One other thing on these metabolic disorders or the enzymes. Had you interacted much with Bette Robson on enzyme studies while you were at the Galton, or not?

JF. We had not interacted. We know we followed the rest of the world. Wilkinson? The specialist at the Galton?

PSH. Oh .

JF. Hopkinson yes. I knew Hopkinson.

PSH. Can I then ask you, at what point did you start to come back to studies of linkage?

JF. Early. It was in the '70s, perhaps a little before '70, because we presented our first result of linkage, not linkage, of mapping at the Paris Congress in '71 by hybridisation. I think it came from the relationship I could have with people like Ephrussi. Ephrussi was a precursor for the study of hybridisation and at that time I had a younger colleague who worked with me, Nguyen Van Cong. And so we began and were at the Congress of '71. Our group was one of the very few who presented the result of mapping and we were right against Frank Ruddle.

PSH. And so did you and Van Cong then develop the hybrid cell techniques with Ephrussi or . . .?

JF. No by ourselves.

PSH. By yourselves. That's interesting. Also at this time I was reading, you were doing some work also on the X chromosome and the early mapping of this with

JF. Yes it was a compilation of [unclear] mainly.

PSH. I saw some papers. I think it was on patients with intersex and sex chromosome and

JF. Thank you for reminding me. At the time I worked with Natalie Jussieu and Natalie was a very good specialist, fantastic. And so the paper you mention was written essentially by Natalie under my

PSH. And were you using, may I ask, the chromosome studies with Jean de Grouchy also?

JF. Yes of course, but you know, I had a special relationship with Jean de Grouchy. Sometimes very good, sometimes no and he was very, Monsieur Lamy say Jean de Grouchy he is 'enfermé dans la mauvaise humeur'. But I am grateful for the work of Jean De Grouchy.

PSH. At which year did Professor Lamy retire?

JF. In '67.

PSH. And am I right that you were appointed as director to follow him?

JF. It was more difficult than that because I succeeded to him as Director of the Research Unit of clinical genetics, unit from Inserm. But for the Chair, the Chair was given to Professor Royer, who knew nothing about genetics. He was an excellent paediatrician, but it was the order of succession of, you know, like in the sovereign's family. It was not my turn.

PSH. So it went to the person whose turn it was, not to the person who necessarily knew about . . .

JF. Absolutely.

PSH. This was I think very common in the past.

JF. It was.

PSH. Can I ask, was this before the reforms of Debré in medical education?

JF. The reform was already in application. You know the application of the reforms Debré began in 1962. I was very involved in that. I was a close collaborator of Professor Debré for the reform.

PSH. Can you clarify for me, I get confused. Am I right that the father was Robert Debré who was originally the professor, head of Paediatrics, and that his son was Michel Debré who was minister of health.

JF. Exactly. No Michel Debré was never Minister of Health, he was Prime Minister.

PSH. He was Prime Minister right. Under de Gaulle?

JF. Under de Gaulle. Yes. So it was a good configuration for the success of the reforms.

PSH. I see, so I gather he had appreciated the ideas from his father about medicine and was then able to push them through.

JF. Absolutely.

PSH. It must have been very difficult.

JF. The link was very strong between the father and the son. I remember at the time of the war, of the Algerian war, I had very frequent meetings with Professor Debré for the reform, sometimes we were in a meeting I have a letter to depose to Matignon for the first minister and often during our meetings, Madam Debré asked Professor Debré to, [unclear] it was very strong, a very strong link.

PSH. Can I ask, you chaired the Human Gene Mapping meeting in Paris but at what point did you first start becoming involved with the Human Gene Mapping meetings?

This must have been close to the beginning.

JF. The first one.

PSH. The first one?

JF. The first one.

PSH. Was that New Haven?

JF. Yes. I was at New Haven and I was with Frank Ruddle. The first one, because it was not very long after the Paris Congress. But I missed some of it, because that time I was President of the University, so I had many things to do.

- PSH. Yes indeed. I remember myself that the two of us were responsible for the clinical disorders committee. Those meetings were a very great experience I think. I enjoyed them. Especially the early ones.
- JF. Me too. I enjoyed very much. So I was, in '85, the Human Gene Mapping Conference was in Helsinki.

PSH. With Albert de la Chapelle.

JF. With Albert, and I put my candidature for organising the next one and I was chosen by the jury. It was very interesting because one of the conditions they put to me was to develop a database and, what I never said until now, but I think I have to tell somewhere, to make my own database and not to use the American one which was not good. So I accepted and I was very . .

At that time I had absolutely no experience of databases. It was the beginning of another time for me. But also in '70s I thought that somatic cell hybridisation became tedious and less fruitful than at the beginning. So as soon as we had polymorphic sondes [probes], we switched to linkage. At that time I was also counsellor at the French Muscular Dystrophy, AFM.

PSH. AFM.

JF. I was on the scientific council and I proposed to map the gene of spinal muscular atrophy and I spoke to Nguyen Van Cong, after that I spoke to Arnold and Arnold said you are right to try, but if you keep Nguyen you never will succeed. Nguyen was a man of hybridisation, not of familial studies.

PSH. No, the two are very different.

- JF. Two are very different. So I asked Arnold "who?" and he said Judith Melki. And it was at that moment when we switched with Judith, after that with Joceline Kaplan. Did you meet Joceline Kaplan?
- PSH. No. Just a minute, we have two Kaplans because Jean-Claude Kaplan and Joceline Kaplan. No not yet. I have in the past but this time no. This is someone else who I must put on my list to see I think.
- JF. But you know at the time she was just at the big Congress of Genetics and Ophthalmology in Paris and she is a very important physician. But Joceline Kaplan was one of my pupils you know. Since the beginning she wanted to work on eyes and genetics. So when we have the linkage study she was very successful. She was a leader in this field.
- PSH. Can I ask you Jean, when did you develop the idea of Genatlas. Was this after the Helsinki meeting when they asked you to make a database?

JF. Yes. If you are in Paris I shall show you a photograph. It was a meeting in Bethesda when I was mandated to organise HGM9. One day I got a call from George Cahill. You know George?

PSH. I do.

JF. He is a wonderful man. A great scientist. But he was [unclear] and he told me there was a meeting near Miami, Coconut Grove. I don't know if you have been to Coconut Grove

PSH. What was the place Jean?

JF. Coconut Grove.

PSH. Coconut Grove. No I have never been.

JF. Wonderful place.

PSH. Very opulent I expect.

JF. He paid for a voyage on Concorde.

PSH. On Concorde. Good Heavens!

JF. We spoke and I was thinking about the problem of the database because Albert and other people told me I have to make a database and my first idea was to ask Marc Lathrop to help. But he was not very helpful, although he was very expert. And one day, at that time we had a biophysician in the medical faculty who was interested in bioinformatics, and one day Martine come and speak about our project and I say I have a name for our dataabase. It would be 'Genatlas'.

PSH. Very good name too.

JF. I thought it was good.

PSH. Excellent name and excellent Atlas.

JF. And so I went to this meeting in Bethesda and the American people, not only American but also Albert, British, Peter Pearson and many others. Bodmer, Walter Bodmer. I have a database. Genatlas had something like a [unclear] you know and with say 30 genes. It was large. It was the beginning of Genatlas. It was meant for HGM9 and there were many problems but

PSH. Was this around the same time that you made links with CEPH and Jean Dausset?

JF. The links with CEPH and Jean Dausset were later. We were not exactly in the same way but we were very close together. Very friendly.

PSH. Yes. Now I think soon Jean, we should pause and before we pause, there are two questions I have asked everybody I have seen. The first of these questions is which person in your career has had the biggest influence on the development of your work? Can you identify one person, especially?

JF. Penrose.

PSH. That's very interesting.

JF. Penrose. I was very influenced by Penrose's spirit you know.

PSH. So many people who I have talked with have named Penrose in this way. He was a very inspirational person.

JF. Absolutely.

PSH. The other question I have asked to everybody is, if you had to choose one piece of work that, is there one particular area or piece of work you feel a special affection for or value for, that you feel has been your biggest contribution? At least, the one that makes you most happy.

JF. Difficult to say because it's changed, but now if I did it again my choice would be cellular biology.

PSH. Yes, but among the work that you have done in the past, would you be able to name a particular thing which you did that you can look at and say

JF. Metabolic, metabolic disorders, and mapping.

PSH. Yes well these are two very satisfying areas. Jean thank you very much indeed. I think we should give you some rest now because I have exhausted you. So now I will turn off the machine.

End of tape.

Jean Frézal Part 2

PSH. This is the second recording of my conversation with Professor Jean Frézal and this part is mainly concerned with the more general development of medical genetics

In France. So Jean, from talking with both you and other people I have the feeling that medical genetics began with very close association to paediatrics.

JF. That's right. That's exactly and two pioneers were Professor Turpin, who was a paediatrician and Professor Lamy was a paediatrician and until very recently, paediatrics were strongly linked with genetics. Now paediatrics may be strongly linked to genetics, but other disciplines appear to have strong links also with, like neurology etc.

PSH. Yes, it is the same with us. Can I ask, the centres involved, am I right that Professor Lamy was always based at Hôpital Necker?

JF. Not always, but for the main part of his career.

PSH. So the part of his career when he was developing genetics

JF. He was at the Hôpital Necker.

PSH. Whereas I was told that Professor Turpin was first at Trousseau and then at the end of his career moved to Necker.

JF. It's true.

PSH. At Necker, was Professor Lamy in overall charge of the paediatric service or was that Professor Robert Debré?

JF. There were several service clinics for child diseases and disorders, which was held first by Professor Robert Debré, after Professor Robert Debré by others and after by Turpin.

PSH. I see.

JF. And Professor Maurice Lamy was never the head of the clinic for child disorders. He was specifically professor of medical genetics.

PSH. I see, yes. Was the change from Hôpital Trousseau to Hôpital Necker, was this part of a more general rearrangement, or was it just that Professor Turpin moved?

- JF. It was not a general rearrangement. A chair was free after Professor, I think it was Professor Catalat. After Robert Debré, Professor Catalat. Professor Catalat retired and the chair was free and Professor Turpin postulated; he was elected by his colleagues.
- PSH. So would Jerome Lejeune then have moved with Professor Turpin because he was part of the same service?
- JF. Yes, but he has also a laboratory at the building of the old faculty of medicine, Rue l'école de médicine, 6th arondissement.
- PSH. That's very interesting to know. One of the things which is quite difficult to understand coming from outside France, is the relation between the hospital services and the CRNS and research and university units and
- JF . It's not very simple. Before Debré's reform there were two bodies. The University one side and the hospital the other side, and some of the services in the hospital were directed by a member of the university and they were called clinics. This is why Professor Robert Debré was titular head of the clinic for sick children, but the majority of the services of the hospital were not services of the university. After the reform by Debré all the services had occasion to become both part of the university and part of the hospital administration. It is the reason why they were called . . . After the reform Debré, the union, so it is the reason why the organisation of university and hospital were called sordes hopitaux universitaires, university hospital.

PSH. I see.

- JF. To define the union of the two parts and when you were in one body you were automatically in the other, in the other side. So I was Professor of medical genetics and I was physician of the hospital. I beg your pardon but you mentioned CNRS. CNRS and Inserm are entirely separate. They are linked by association contract but they are independent bodies. CNRS is dependent from the minister of research, INSERM dependent of Minister of Health.
- PSH. And those would be mainly to do with fundamental research.
- JF. Mainly, but some were but INSERM was partly clinical, partly fundamental, and CRNS is mainly fundamental.
- PSH. And would it happen quite often that within say a hospital and combined medical service, there might be also located a INSERM or CRNS unit?
- JF. It's very frequent.
- PSH. In our country this happens also and when this is the case, when the director of the research unit retires, the unit does not necessarily continue. They may close it or transfer it.

- JF. It's the same in France.
- PSH. So then for instance, at Necker during your time, would there have been the hospital, the combined hospital and university appointments and also an INSERM unit or CNRS?
- JF. They were not combined. The hospital and university units could be associated with INSERM or the CNRS but it was not compulsory. The association between the university and hospital were compulsory.
- PSH. But for medical genetics at Necker am I right that you were also director of the research unit as well?
- JF. Yes of the research unit, INSERM. And Professor Turpin was also head of a research unit with Lejeune.
- PSH. And am I right that Professor Turpin had many very long interests with Down's syndrome as a genetic disease, going back many years?
- JF. It was true, but as a matter of fact, for instance he published works on
- PSH. Dermatoglyphics
- JF. Dermatoglyphics but nothing really very significant.
- PSH. I have managed to obtain the book which he edited, La Progenèse, I found a copy and it was interesting to see the contributors at this time.
- JF. It was more or less his preoccupation. The book has an aspect of public health, even a small perfume of eugenics.
- PSH. Yes, although I notice that there was also a chapter by Penrose. Before Professor Turpin and Jerome Lejeune moved to Necker was there much contact between the two units or not so much?
- JF. You mean with Turpin and ourselves?

PSH. Yes

- JF. Very few. I think Professor Turpin and Professor Lamy were not close friends and I was not a close friend to Lejeune.
- PSH. Yes. One of the things which interests me is that after Lejeune moved to Necker, I imagine that this must not have been the most easy situation for everybody to be in the same hospital, or was it no problem?
- JF. There was no problem. No. There were some cytogeneticists making an arrangement between them. For instance Grouchy was a cytogeneticist of some of the clinical wards and Lejeune of others, and they were a good

entente between Lejeune and Grouchy. So there was no problem, really no problem. And I have no problem really with Lejeune you know. It was a question of 'epiderme'.

PSH. Yes and also am I right really that your own interests have never directly been in clinical cytogenetics?

JF. No no, never.

PSH. Can I ask, am I right that the three main workers with Maurice Lamy who developed medical genetics were yourself, Pierre Maroteaux and de Grouchy during those years?

JF. Yes entirely true. Maroteaux was very important you know.

PSH. Very.

JF. Fantastic contribution. You have seen Pierre Maroteaux?

PSH. Yes. Wonderful.

JF. Small man, nothing at all!

PSH. Yes. Was there any plan, in terms of the evolution of your interests, that Pierre Maroteaux especially developed the bone disorders and Grouchy cytogenetics and yourself the more metabolic area. Was this some conscious development or was it just something which happened?

JF. I think at the beginning it was something that happened, but we took account of the fact that it was admitted that Maroteaux was specialising in bone disorder etc etc.

PSH. How did this affect the teaching of genetics in the medical school? Were the three of you and Professor Lamy, were you responsible for the teaching of medical students?

JF. No. At that time there was no official teaching of medical genetics in the faculty for normal students in the curriculum, but I created in the 60s the teaching of genetics for graduate students and I continued this into teaching for years and years, until I retired and some time after.

PSH. Before you began that, were the medical students taught any genetics at all? Did they have some basic genetics from people like Ephrussi?

JF. They had basic genetics in their first years of their curriculum

PSH. And would that have been taught by the people at Pasteur Institute or some other?

- JF. It depended. Some times from medical faculty, science faculty, research organisation.
- PSH. Thinking more widely across Paris, were there any other hospitals in these earlier years who had a particular interest in what one might call either medical genetics or genetic disorders, or really was it mainly Necker and Trousseau?
- JF. You know, the answer is yes and no. Because there was interest in all those things, metabolic disorder or other disorder of course, because sometimes at Pitié Salpétrière there was permanent interest in neurology and myology but the focus was not on genetics. There was very few focus on genetics until recently, until the last 10 years perhaps.
- PSH. Yes, others were telling me that. I was surprised because I had thought that with the great experience of many neurological genetic diseases there might have been some more general interest in genetics, but it seems that this, as you say, only came recently. For instance Michel Fardeaux was .
- JF. Michel Fardeaux was interested in myology for years and years. Excellent pathologist but he had really no contact with genetics until the founding of the research council of AFM. At that time it was the beginning of genetics and he took an interest in genetics, but it was a late interest in genetics.
- PSH. And the other person who I have spoken with about this was Jean-Claude Kaplan and he told me that, although he was working very much on biochemical and other disorders, again he only became really involved in genetics when molecular techniques became possible.
- JF. Exactly.
- PSH. If we move outside Paris, how did genetics, medical genetics develop in the cities other than Paris. Was there any other strong development at the time when you were starting, or was it all much later.
- JF. At the time when I was starting there was a centre in Lyon with Jean Robert, Professor Robert.
- PSH. Yes I remember him well and I didn't realise he had started so early.
- JF. He was four years younger than me. He began rather young. He certainly wanted to study genetics. He had a real interest in genetics and that was genetics in neurological disorders.
- PSH. Was he a neurologist by his training?
- JF. He was. He was a neurologist. He was a very good clinician but he was very partial to measuring genetics. He published a book in human genetics

and in this book on human genetics he didn't use the term segregation, which is quite a

PSH. I remember him. I also remember he had a colleague with worked with him who had some profound deafness. I think he was working in the laboratory. I remember speaking with

JF. Boscitti?

PSH. It's possible, I don't remember the name but he had really very profound hearing problem.

JF. I don't know. I don't remember who.

PSH. Apart then from Lyon, what other cities developed at an early stage?

JF. Marseilles. Marseilles with Professor Francis Girot, also a paediatrician, also a clinical geneticist. Professor Girot was a very clever man and he built clinics with association of cytogeneticists and clinical genetics. Biologically they were not so developed in the centre of Francis Girot.

PSH. Did he train or did he learn genetics from some other place, I mean in the same way as you had a link with the Galton? Did he have a link with somewhere else or did he just develop it himself?

JF. Himself.

PSH. And then am I right that Jean François Mattei, he succeeded Girot.?

JF. Yes. But now Jean François Mattei is no longer in Marseille.

PSH. He is in the Ministry?

JF. He was in politics yes but he is no longer there. He is the president of the Red Cross.

PSH. I see.

JF. It is mad because Jean François Mattei is very gifted. He was very gifted. But his wife is still working, Marie-Jeanne Mattei.

PSH. This brings me to one of the points to ask you and this is the development of the 'Troisième Jeudi', because people have told me this was a very good way in which people were brought together from across France. I wonder, how did this begin?

JF. Which one?

PSH. The meeting, the Troisième Jeudi.

- JF. It was you know 'suite' of my teaching of genetics. The first and second generation of the students decided that after their teaching, to meet regularly together under our tutorship in Paris and it was the beginning of the third Thursday, and it began when I was President of the University, but early in the 70s and it has always continued, and every month we have a meeting and there was approximately more than a hundred people every month, which is a permanent success.
- PSH. It's very good, yes. When I was here last year, the conference that I gave was one of the Troisième Jeudi occasions. So do you know, has somebody kept all the records or the programmes of these meetings? Are they kept together somewhere, because it is an interesting history?
- JF. Perhaps. I can ask if they have a list of the programmes.
- PSH. They may have. Did many of the people who trained with you go out to start medical genetics in other cities across France?
- JF. Yes of course. I must say at the time most of the people who specialised in medical genetics were formed by myself.
- PSH. Yes and I am trying to think of the different cities.
- JF. You can say in Lille, Nancy, even Strasbourg, Lyon, (not very much, the Lyonnais) Bordeaux, Toulouse, Montpellier, Rennes, Caen.
- PSH. And one of the other organisations, perhaps a little similar, the Club de Conseil Génétique.
- JF. It is very closely linked but entirely different. The Club de Conseil Génétique was formed by Robert and Robert didn't much like the Parisiens, so he thought he must have an organisation which can be a little against the Parisiens. He came I think from Paris so he founded the Club de Conseil Génétique. But who was in some ways a success, rather different from Troisième Jeudi but it was not a school of teaching.
- PSH. I understand.
- JF. But now they have so many meetings that you know Club of Conseil Génétique has not the same success.
- PSH. The other activity that I want to ask about Journal de Génétique Humaine. Am I right that this was started by Franchescetti?
- JF. Yes. Franchescetti.. And Robert was for a time editor and it was not a good journal.
- PSH. I seem to remember that it was not edited very carefully. I remember one could read an article and it was clear that there had not been very much correction or refereeing.

- JF. No, it was never well corrected, many mistakes, and now it is in English.
- PSH. And what is its name in English then? Is it still . . . It's not the same as Archives de Génétique Medical?
- JF. I don't think so. It's edited by the same editor of Geneva, it is the same editor as Journal de Génétique Humaine.
- PSH. I will have to find that.
- JF. Journal of Human Genetics perhaps.
- PSH. It's possible. Quite possible.
- JF. Journal of Human Genetics.
- PSH. You have seen the field evolve over 50 years and how do you feel yourself about the way the subject has developed during this time? Do you feel on the whole it has done well or have there been problems? Obviously there are problems, but what is your overall feeling?
- JF. I think the evolution is very interesting, the big expansion of medical genetics; I am very happy to see that medical genetics is now in all parts of medical discipline. In cardiology, neurology, gastroenterology etc etc. Everybody speaks of genetics, of medical genetics. The path of genetics is more or less extended, but it is. The problem now is not the Mendelian disorders, it's the rest and the problem of susceptibility and multifactorial which remains in a very . . .
- PSH. Fluid state
- JF. Fluid yes. Absolutely.
- PSH. Yes, it is interesting to me that some people expected that it would be very easy to solve these problems with molecular techniques but I never thought that it would be, and indeed it has proved really very complex indeed.
- JF. Very complex of course.
- PSH. If I can just finally come back to Paris and the one group I have not asked at all about so far, is the group of the Boués for prenatal diagnosis. How did it happen that prenatal diagnosis in those first years was part of a separate unit? Was it just expertise?
- JF. It happens. But the Boués were very crucial at the beginning of the organisation, when it was developing and you know, obviously they have some relationship with people, with cytogeneticists who have been formed by

Lejeune necessarily, but most of the cytogeneticists have not the prejudice of Lejeune.

PSH. No. I think those are the main questions I was wanting to ask you but are there things which I have not mentioned at all Jean that you feel are important for me to be told? Things which I have omitted to ask about?

JF. You have been very very exhaustive.

PSH. I hope it is exhaustive, not exhausting!

JF. Of course you probably omitted some points. You know, to summarise if I look at medical genetics in France, we are now have strong, good organisation which is not under the French principle of Jacobin principle, is very free by spontaneous association of people who want to work together. And I am very happy to see that the young generation, the first generation were not extremely well informed, but people of very good quality you know.

PSH. Excellent.

JF And work very well. Look at Rennes, a lady like [unclear] very good and in Toulouse a man who worked on eye disorders was first class you know, other examples of very very good people. And I think there is a good consensus about the problem of ethical mentability in a group. That is to say some openness of mind but really we are very cautious. The point is that the genome was a revolution from a biological point of view, but until now not for medical genetics, so we have to go ahead on our way.

PSH. But France is really a very strong contributor to the whole international scene of medical genetics, and I am so pleased to have been able to speak with you Jean because you have been the main founder and developer over this time.

JF. I have made a good contribution. I have been the respect in France of two men, Professor Robert Debré. It was Professor Robert Debré who inspired Professor Lamy and he said to Professor Lamy, Debré said, you make so and so you are the cardiologist. He said to Professor Lamy you are to do genetics. Genetics? Said Professor Lamy. Yes Monsieur. And Professor Lamy was for me very important you know because he was by his spirit. He was a humanist. Real humanist in the French sense of the term. He was a man of the lumière. The light. And he has been very, he was very useful for my career so I have a profound respect for this man and I have respect also for men who are contributors. Jean Dausset was an exceptional man. You know we don't speak of men for instance the transfusion centre. There was a man for instance Cartron. I don't know if you know Cartron?

PSH. I don't no.

JF. Cartron is a man who found there was not one, not three genes gene but two.

- PSH. I should have known that.
- JF. Not one, not three, but two. [unclear] And there was a very good group.
- PSH. Well thank you Jean, it has been a most fascinating time talking to you and I am very grateful indeed.

(End of interview)