

INTERVIEW WITH PROFESSOR CATHERINE TURLEAU. 20.04. 2005

CT Catherine Turleau

PH Peter Harper

PH It's 20<sup>th</sup> April 2005 and I am speaking with Professor Catherine Turleau at Hôpital Necker, Paris.

Are you happy if I call you Catherine?

CT Yes, no problem.

PH May I ask first: how did you become interested in genetics, cytogenetics, yourself?

CT It was completely by chance. At the end of my professional studies I was looking for a job. I ended up in the laboratory of Jean de Grouchy.

PH So you were a paediatrician ?

CT I was in the process of specialising in paediatrics. By chance I stayed in this laboratory because there was a grant available from the National League against Cancer.

PH In which year was this that you started with Jean de Grouchy?

CT 1968.

PH 68, yes. And this was here, in Necker?

CT Yes, but in another ...

PH Another part. And may I ask: the first piece of research which you did – what was the subject?

CT The first subject was acute crisis in chronic myeloid leukaemia and clonal evolution in chronic

myeloid leukaemia. And so this was the subject of my professional thesis. And at that particular time there was a Mexican researcher, Cristina de Navarre , who was working with Jean de Grouchy on this subject. This was the first description of clonal evolution in chronic myeloid leukaemia.

PH So that was your medical thesis. Am I right that after this you started work on primate cytogenetics?

CT Yes

PH So when did you begin work on that?

CT I don't remember exactly but in 1970, something like that. I think that the first publications must have been in 1970, 1971. But in fact the two things were somewhat together.

PH So, may I ask, was the primate and comparative cytogenetics, was this already an interest of Jean de Grouchy, or was this something quite new? CT Oh, I think it was an ancient interest.

PH I have a list of publications and this comparative cytogenetics developed very strongly over the years up to 1970. Can I ask, at the time you began this work, did you already have banding techniques?

CT Yes

PH Because these must have been very new at this time.

CT Once the banding techniques were available, we used them for this work very quickly.

PH Was it yourself who first introduced the banding into the de Grouchy laboratory, or were there other people also using it at this time?

CT There were quite a few of us. Given this new development everyone contributed equally.

PH How many people at this time were working in this group with de Grouchy, approximately?

CT Less than 10 persons. Maybe 3 research workers and then some technicians. It was a very small team.

PH I am interested how the laboratory of de Grouchy related to the work of Jérôme Lejeune. Am I right that Lejeune's laboratory had already moved to Necker when you started?

CT Yes. The two buildings were quite close together.

PH So for me it seems curious that in one single hospital you have two distinct cytogenetic groups. I can understand that Lejeune had moved from Trousseau and was already well established, but were there good links between the two labs?

CT Yes, because de Grouchy and Lejeune were friends. And they had lunch together every

week. Each week, each Saturday, they traditionally had lunch together and they exchanged ideas. So that is the reason why there were a lot of shared ideas between the two laboratories : as much on the evolution of species as on other subjects. But more between de Grouchy and Lejeune than between the other laboratory staff.

PH But in terms of sharing techniques and new adaptations, you would link closely.

CT No.

PH That's interesting because so often I think across the world one sees that groups working on similar areas can still remain very separate. Can I ask you at this point a little bit about Jean de Grouchy as a scientist and as somebody to work in the laboratory of. Was he a very inspirational person in terms of giving ideas? What did you feel at the time?

CT I think that it was he who initiated ideas in the laboratory. He was the one who took the initiative to develop this thing or that.

PH So among the areas of work at this time, there was the comparative cytogenetics. And am I right that already at this time he was starting to look for more detailed chromosome abnormalities, or did this come later?

CT No, no. From the beginning the main activity of the laboratory was medical cytogenetics. And we see patients.

PH Right, so was the laboratory mostly funded through medical channels?

CT Medical, yes.

PH And would this have been different perhaps from the Lejeune laboratory which had fundamental genetics finance?

CT No. Both laboratories, in fact, had clinical genetics as their main activity. Seeing patients, doing genetic counselling, etc. It was above all medical. It was just that one of the laboratories was a hospital laboratory and the other laboratory belonged to CNRS, a research organisation. But the activities were identical.

PH Right, so the Lejeune laboratory had CNRS funding but you had mainly hospital funding, is that correct?

CT No, the opposite. In fact, Jean de Grouchy was Research Director at CNRS and he had a research role, was really a research worker. While M. Lejeune had established a hospital laboratory and he had an annexe with Bernard Dutrillaux.

PH This wasn't at Necker then, was it at Trousseau?

CT I don't remember exactly, but it was outside the hospital.

PH Now I understand. May I ask, were you yourself involved also in genetic counselling along with your cytogenetic studies?

CT Yes

PH And did Jean de Grouchy also see patients?

CT Yes

PH How close were the links at this time between the group of de Grouchy and people like Jean Frézal and others in Necker?

CT Umm ...

PH I don't wish to raise any problems, but it's interesting to know if they were close or distant or separate, or how you saw it.

CT It was a bit, that was always a little bit complicated because there has always been a rivalry at Necker between the cytogeneticists and medical genetics, because cytogenetics had existed first, had put in place many things, and medical genetics had arrived a little bit later; there had been a time lag, so that inevitably a rivalry developed between the two groups. But in reality the laboratory of Jean de Grouchy was integrated into the laboratory directed by Jean Frézal.

PH Am I right that Jean Frézal's laboratory was more like biochemical, metabolic genetics or not, because people have told me that Jean Frézal for many years did not really believe in cytogenetics. Is it fair to say that, or is that not so?

CT Cytogenetics has always been considered a bit minor as a discipline, but at the same time this was rather unfair because cytogenetics contributed a lot. But really everything was very complicated, very mixed up, since the Director of the unit from the beginning was Jean Frézal. Jean de Grouchy was one of the research staff in the unit of Jean Frézal.

PH So this was the CNRS research unit. You must excuse me because, especially these more political things, I am ignorant of. So Jean Frézal was Director of the research unit and then within this unit were different groups, including de Grouchy's group and then Frézal's own group, and perhaps others?

CT Natalie Jussieu, who worked on sexual differentiation. And also Pierre Maroteaux.

PH Pierre Maroteaux. Yes, I have seen him. And Josué Feingold also?

CT Josué Feingold at the beginning. And Marie-Louise.

PH Yes.

CT So this was a very historic unit, Unité U12. And it was a unit that brought together most of the groups that afterwards became dispersed or separated, a little bit everywhere. Then everyone was in this building which was located at the end of the hospital, which was called 'Clinique Maurice Lamy', and everyone found themselves there, all the groups.

PH Before that they were in different parts.

CT There was Pierre Maroteaux, Natalie Jussieu, Feingold, Jean de Grouchy.

PH And Lejeune?

CT No, Lejeune was completely separate.

PH And this building, then, was this opened after Maurice Lamy had died, or maybe after he had retired?

CT I think that it was after he died. I don't know exactly.

PH That is very interesting. Can you give me an idea as to how the work of your group with your work and de Grouchy's work, how it evolved over these years? What were the main themes that developed? I mean the comparative side and the clinical side, but when did the gene mapping come to be part of the research? I don't need to know exactly when, but how did this happen?

CT Gene mapping was the main subject of Frézal's group. In our group we worked especially on comparative gene mapping, because human gene mapping was a reserved area for Jean Frézal.

PH Ah. But you were allowed the primates ....

CT It was the same techniques, the same premises, the same equipment, the same everything, but simply that the one studied man and the other the primates, so that comparative gene mapping was a little bit of a reserved area.

PH So the use of hybrid cell lines – was this something which you had the main responsibility?

CT No, initially it was the Frézal group.

PH I see, yes.

CT (Indistinct name).

PH Oh yes, the name I remember. And then, returning to the more clinical work, looking at the papers I see there are many papers on identification of small microdeletions. This must have been one of your areas also. Were there particular techniques that allowed that to advance, because this is well before FISH and such techniques. For instance, did you use particularly

the techniques of extended chromosomes and other things to identify these?

CT It was mainly high resolution banding.

PH Yes. The patients, would they have been patients from here at Necker or other parts of Paris they would send to you?

CT Yes.

PH I should know this already but the first edition of your book, the Atlas, when did that appear? The trouble is these computer printouts only give papers, they don't give books, so it's a great pity. That's a very famous book.

CT Yes. I don't remember the year of publishing.

PH But you were part of the project from the beginning.

CT Yes, yes, yes. It took a very long time, because we had talked about it for years and years before really launching into this adventure.

PH Yes, I am interested because producing a book like that it is very much work and would I be right that most of the photomicrographs and the preparations, this was your responsibility, maybe that de Grouchy suggested that something was there and it was for you to do?

CT Non, non. No, no. We truly worked together, the two of us. Very, very closely. We stayed on in the evenings, the two of us, in his office.

PH Because very often when senior researchers become old they don't stay in the lab, but some people very much like to remain closely connected to the lab and perhaps de Grouchy was someone like this. Because I was told that in later years Lejeune for instance was not so much in the lab but giving lectures and travelling.

CT It was different.

PH Different, yes. One question which I was asking the others, and you may be able to help, was

how cytogenetics developed outside Paris in other centres in France and people told me that for a number of years people would come from other centres to learn new techniques and so would they have come both to your lab and the Lejeune lab, or was it mainly to one or the other?

CT It was a bit of both. But in fact the first training course to be put in place was set up by M. Lejeune. And so the first people to be trained in cytogenetics in France were trained within that framework. Thus it was a University training scheme, because M. Lejeune was in charge

of University teaching.

PH I see. So would these meetings at first perhaps not have been at Necker but at the other lab, or did people always come to the Necker lab?

CT All the people coming, at least for the theoretical course, all came through Necker. And then afterwards training courses were set up at Marseille and in other places, but at the beginning it was Necker. And at the start it was essentially paediatricians.

PH I see. So these would be medically trained paediatricians wishing to set up cytogenetics in other cities?

CT Yes. And later there was a conflict between these paediatricians and the biologists, histologists, who said 'no, cytogenetics is a biological science and we are going to recover it..... And so there was a kind of minor conflict.

PH Is this still a difficult issue? Because I think in many countries the relationship between medical specialists and laboratory specialists causes some difficulty. Is it still a bit of a problem here also?

CT Yes.

PH Because I have gained the feeling that the development of medical genetics, including cytogenetics, in the first years in France, was very strongly paediatric and people have told me that some of the paediatricians did not wish to see it go outside, that it was just part of paediatrics, and that must have caused some difficulties I can imagine.

CT Yes, but it is more complicated than that. I think that the people, the paediatricians trained at the beginning, were more competent than the people who came after...

PH Yes, it's perhaps natural, because with the increased specialisation it becomes very difficult to be both a clinical paediatrician and a laboratory person, and probably now impossible. You have to choose. Whereas at the beginning it was possible to do both.

One subject which was told to me, which seems to have been a difficulty, was the time when prenatal diagnosis began. I was told Lejeune wished everybody to sign some paper to say that they refused to do this, and this caused divisions within the cytogenetic community. From your perspective, working in the de Grouchy laboratory, did this affect you directly or was it only really the people with Lejeune who were involved with this problem?

CT That wasn't a problem because there was never any question of us carrying out prenatal diagnosis.

PH It was completely separate?

CT Yes. I think that the people who really found it difficult were the ones in the provinces who were obliged to respond to demand, whereas we in Paris had the team of Jöelle Boué. It wasn't a problem at all. Each time there was a prenatal diagnosis we sent it to Jöelle Boué and it was done with no difficulty at all. As far as the de Grouchy laboratory was concerned, there was never any opposition to prenatal diagnosis. Simply we sent it to Jöelle Boué. So we did not have any open conflict with the laboratory of M. Lejeune. It has been dramatic for cytogenetics generally.

PH It's of interest to me also because I have the feeling that for their philosophy Lejeune and de Grouchy were quite close, but perhaps de Grouchy was less dogmatic than Lejeune.

CT He was not dogmatic at all.

PH That's interesting because it does seem to have been quite an important factor in how French cytogenetics evolved, the difficulties arising from Lejeune's rather fixed views.

CT I think that it was dramatic because in the normal course of events, cytogenetics would have come into the hands of people like Bernard Dutrillaux, Alain Aurias, Pierre-Marie Sinet, who were all students of Lejeune, because M. Lejeune after all had a team of very competent people. And that problem has rather rebounded on this group and they have not taken the place that they should have occupied in France. And this has held back the development of cytogenetics in France. Because the pupils of Lejeune, as a result of this restriction, have not been able to find their place.

PH Yes. I spoke with Roland Berger but I have not spoken with Dutrillaux because, am I right, Dutrillaux would have followed Berger in the laboratory of Lejeune, or was he also in the de Grouchy laboratory? You must put me right.

CT No, no, they were always together in the laboratory of M Lejeune. But quite simply Berger was somewhat against leaving the laboratory of M Lejeune much earlier.

PH I see. But they were there together?

CT Yes, for a year, two years together.

PH Can you tell me, after Lejeune had died, how did the different groups, did they join together at some point or have they still remained separate in terms of the clinical cytogenetics? Is there now one cytogenetics service or does there still remain something separate as a result of the two original groups of Lejeune and de Grouchy?

CT Well....

PH It's complicated, I think.

CT So, M Lejeune had retired some time before he died, and when he had retired it was necessary to find someone as successor for either the hospital or the university post that he occupied. And Michel Vekemans was appointed to take charge of M Lejeune's laboratory. So he came, it is a bit complicated, he incorporated the team who did prenatal diagnosis, because that had not been possible with M Lejeune, and he took in all the post-natal group who had been with M Lejeune. He reorganised the laboratory so that there was a prenatal, a post-natal and a haematological section. And during that time Jean de Grouchy was still active. So that continued in the same way for some time. Eventually Jean de Grouchy retired and I took over as Director of the research unit for four years or so. But after four years we had to propose a new research programme and our unit was too small. So I merged with the unit of Claudine Junien, who had been with the Boués, and who also needed to re-establish a unit.

PH Is it true that Claudine had begun as a cytogeneticist and not as a molecular biologist ?

CT No, no, she had started by doing biochemistry.

PH With Jean-Claude Kaplan perhaps?

CT That's right; she was in the laboratory of Jean-Claude Kaplan, she did biochemistry, she had worked a lot with us on the dosage of enzymes in small animals with growth retardation to do gene mapping. We worked together a lot at that stage, to do gene mapping by automated dosage ; so she was a biochemist. And then she was one of the first to develop molecular biology, but in the laboratory of M Kaplan.

PH Is there a CNRS cytogenetics unit existing now or is all the cytogenetics now mainly hospital funded?

CT It's essentially hospital based. I did not get on well with Claudine, and so I left her unit. I am now with Michel Vekemans, but I don't have my own group; that's how it's turned out!

PH And can I ask, in terms of prenatal diagnosis, after the Boués retired, then, has this stayed as a separate unit or has it joined the rest of cytogenetics? Is there now prenatal cytogenetics for instance in this laboratory here, or is it still separate?

CT In each cytogenetics laboratory there is a prenatal diagnosis section. There are very few laboratories that are purely post-natal.

PH So that's very different from the early years where all the prenatal work was concentrated in one centre. Can I ask, de Grouchy, did he remain working in the lab, in contact, after he retired?

CT No

PH Because in his last years he was living in the South of France, is that right?

CT Yes

PH So was it at once that he stopped, did he stop completely after his retirement or was it just gradually?

CT I think he was a little.... well, at the end of his career he was very.... in fact he was angry about everything, I don't know why – about having to leave I think. He left being very angry with everyone, especially with me.

PH That's a pity. It often happens that, well I know it's not easy when you have been responsible for something for many years, to make some break, and some people do this better than others.

CT I think that he had been rather depressed after he retired, he had been very bad in his last years because he was no longer Director of the unit; in the end it's like that....for 12 years in the unit.... he was there, but I was Director of the unit, even though I did everything I could to avoid it! It was very difficult for him.

PH It is I think psychologically difficult for an older person, especially perhaps an older man, to accept that someone who has worked beneath them for many years now is ..... It happens very much.

CT And it's a great pity, because he could have done so much....I truly believe that in the end he was really not well.

PH One of the things I especially asked when I was talking with Simone Gilgenkrantz, and I asked Marthe Gautier, the difficulties especially in the early years for women to achieve a senior position in science and medicine. Is this something which you yourself found as giving problems, or do you think it was more in the early years, or perhaps still now problems?

CT That's difficult, because I have never been very ambitious, and things just happened like that.

I didn't have any particular difficulties in asserting myself.

PH That's good, so you yourself didn't feel that there was a block on your progress and career simply because you are a woman?

CT No, not as a member of CNRS, no, but perhaps if I had really wished to have a very high position I would have had difficulties, but since I never looked to have more than....

PH Because I sense that, again perhaps for someone like Jérôme Lejeune, he was not so happy about the independence of women in some ways and this must have given some difficulties in these first years especially. But anyway it is good to know this. It is something which I think in the whole world has changed, fortunately.

I'm just looking to see if there is anything I have not asked you that I have written down. I have been asking everybody I see two questions, and the first question is: which person in your career in science and medicine has been the greatest influence for you? Is there one particular person you could say yes, this person is the biggest influence on your work and career?

CT Probably Jean de Grouchy.

PH Yes, it's very understandable. And the second question I have been asking everyone is: is there one particular piece of work that you have done and been involved in that gives you the greatest pleasure to think about and where you feel well, if I had to keep just one of these pieces of work, this is the one that makes me most happy. What would you say?

CT It is the Atlas, of course.

PH Yes, I can understand, because it is very beautiful and it is both useful and beautiful, and it is something which is concrète, you can look at it.

Are there any other things you would like to say to me, because I am coming from the outside and there are many things which I am very ignorant about and also I'm not a cytogeneticist, so it's possible there are important things which I have just not talked about at all or asked you. Can you think if there is anything you feel should be said?

CT I think that you have a very good idea of the way things have happened.

PH Well in that case, thank you very much.