Jean-Pierre Fryns

Personal Details

Name	Jean-Pierre Fryns
Dates	Born 11/01/46
Place of Birth	Belgium (Waasmont)
Main work places	Leuven
Principal field of work	Clinical Genetics
Short biography	See below

Interview

Recorded interview made	Yes
Interviewer	Peter Harper
Date of Interview	01/06/2007
Edited transcript available	See below

Personal Scientific Records

Significant Record sets exists
Records catalogued
Permanent place of archive
Summary of archive

BIOGRAPHY

Jean Pierre Fryns was born in the Flemish part of Belgium and studied medicine at Leuven University, qualifying in 1970. As an undergraduate he undertook genetic research with Professor Herman vanden Berghe, focusing from the beginning on clinical genetics, malformations and the genetic basis of mental handicap. He is now head of the Leuven Medical Genetics Institute and is involved especially in the phenotypic delineation and molecular basis of X-linked mental handicap.

INTERVIEW WITH PROFESSOR JEAN PIERRE FRYNS, 1st JUNE, 2007

PSH. It's 1 June 2007 and I am talking to Professor Jean Pierre Fryns at the Centre for Human Genetics Leuven. Just to start things off Jean Pierre, were you born in Leuven?

JPF. No, no, my father is from the south of the Netherlands very close to Maastricht and then the family moved to Belgium in the early 20th century, about 1910, and they became farmers. But my mother was born in the east part of the Flemish French border so at home we spoke both languages from the beginning. That was fairly useful and so I came to Leuven in '64. I graduated medical school '70 and Herman, he called for students to do sex chromatin studies in psychiatric patients in '66.

PSH. He was telling me that.

JPF We were about I think 15, with Jean Jacques [Cassiman] and myself and so two of these young guys stayed here and we learnt to cut chromosomes and do everything during these studies.

PSH. Was that before you actually qualified in medicine? Was that during your student training?

JPF. It was student interest yes. We spent vacation periods here. So it was a very small group. You had Van den Berghe, his co-worker was Verresen who became a Professor of Anatomy in West Flanders in Kortryk, a small satellite university from Leuven. Herman, he went to Seattle I think in '69 and so I was even not graduated. I had to start to do consultations and to see people and then I spent four years in paediatrics and yes, I was mainly interested at that time already in malformations and in cytogenetics. From that time the first papers came out, the first one was on cat eye syndrome if I remember well. It was clinically diagnosed and confirmed by chromosomes. To identify the small extra chromosomes as from chromosome 22 origin took us 20 more years. Then I was in military service in Germany for six months but I was lucky. I had to work there one week and I could work one week here. So that was '75 and then things started to grow. Herman was much more interested in onco-haematology. So that was '76/'77 and so my first job, my first duty was to organise something which had quite high quality, so I was forced to try to be a good clinician. Then one of the good things from the beginning, I talked to psychologists and social workers and so on and then things grew over the years and I finished my PhD in '86 because I didn't have time. I was so busy to see patients and so on. And then progressively I have been very lucky to have very good, young, collaborators. Very good young people here. Young! The oldest one will be 50 now next year, Eric Legius and I try to give everybody a quite specific topic but they have to know everything and to be able to see all types of patients.

PSH. Can you tell me, when did Herman begin clinical genetics here, as opposed to his chromosome lab?

JPF. Well I think the first patients were from the official start in '66 and I think that at that time, some two or three patients came every week.

PSH. Was that mainly for chromosome problems?

JPF. Yes, mainly for Down's. And then Herman became interested in Turner's syndrome but I remember, to find 50 Turner patients, we had to look at all Flanders, to part of Wallonia here and we had a collaboration with Joy Bylsma in Amsterdam, Delleman and we had meetings together and some of these people who came to the Turner's sessions were not Turner and some of them I saw ten years later they had Prader Willi or whatever, because we didn't know so much you know.

PSH. So was it really when Herman was away in Seattle in 1969 that you started seeing patients for your own dysmorphology interest?

JPF. Yes. It was a time that things. Here is a PhD of Herman, 1966 about Turner's syndrome. It was a clinical description of so-called Turner's syndrome.

PSH. It's interesting because several people, I think, did not Jan Lindsten also write his thesis on Turner's syndrome?

JPF. Johannes Nielsen I think, there was not so much choice at that time.

PSH. I suppose so. That's interesting.

JPF. And then going to the institutions for psychiatric and mentally retarded, we were amazed to see many more males than females. So we came into X-linked mental retardation, which is still gong on.

PSH. One thing that Herman mentioned that because he had changed the culture medium, it was some time before Fragile X was detected. He sounded as if he should have somehow found that.

JPF. Most people did at that time. So that was the reason why the marker chromosome from labs, nobody could find it any more, because all people had used enriched culture mediums. I remember there was a very nice cytogeneticist in Lyon, Madame Colette Laurent. If you need it I will find the name and she had a male boy and a mother with the Fragile site X and she prepared a paper and she sent it to Jean de Grouchy and he sent it back saying it was bullshit. It was '67 or so. So two years before the paper by Herbert Lubs. And then it took six or seven years to find out that all these males with the big testes had almost all fragile X.

PSH. Did you find many families in your own survey of mental handicap and did you at that time on clinical grounds feel this was something unique or was that only with hindsight later?

JPF. Well, my experience, we visited many of the schools and when we went to the schools for boys older than twelve or thirteen, I could make the diagnosis like that. Because they had the long face and macroorchidism and then the director of the school, he was a very nice psychologist, and I still have contact with him, took me to the garden school, three, four or five years and he said 'this boy, and this boy I tell, you are the ones, fragile X they will be positive also' and I didn't see anything. And he said "well they have the same behaviour now as the others had 15 years before". So I think one of the first papers on the psychological profile of Fragile X was with Jos Jacobs and myself in clinical genetics, a long time ago you know, and that was the reason also why we became much more interested in behaviour because behaviour teaches you a lot about diagnosis. So dysmorphology is much broader than just a clinical examination. It is looking at people and therefore I have a consultation room which is a large one and they can move like they want. The same for Smith-Magenis syndrome. If you don't know the behavioural phenotype, you will never do the test to confirm

PSH. This must have been one of the first recognitions of behavioural phenotype as opposed to a structural one?

JPF. Yes. So at that time we started to have educational psychologists and one was at the PhD on Fragile X later on. We had one, Ann Suillen, who had PhD on 22 q11 on behaviour phenotype. And so on. It was fairly early quite recognisable but what you have never seen you don't recognise.

PSH. And the change with time is really important.

JPF. Oh yes. I don't know whether you know this green book on Fragile X written by, I think the editor was the lady with the nice blonde hair from

PSH. Clare Davison?

JPF. Mmmm?

PSH. Are you thinking of the Kay Davies book?

JP. Davies yes. So the first chapter was mine on the phenotype and it's still very valid if you read it.

PSH. Yes I think I have that book. It's in the March of Dimes series.

JPF. It's a green book but I've got to look at . . . [goes to get something]. I think this is it. So we have many, many families which came from Belgium you know. One of the most interesting things at the time was that we had 83 families in '84.

PSH. That's very many.

JPF. Yes because we screened the whole male population in institutes and then we had a discussion about the normal male transmitter and I had to

convince Vogel by adding a photo post–mortem on the grave of this male. He was the grandfather, but he was normal so we did not understand anything about at that time, but ..... It's 84, psychological profile of the Fragile X and this is the first study on behaviour – yes.

PSH. That's very valuable.

JPF. And still now we find interesting things. We look now at autistic children with quite good mental performance and the number of premutations is much higher than expected.

PSH. Yes.

JPF. The second part of the X-linked mental retardation was studied at the beginning of the [?] So I think we worked with about 50% of the X linked families without fragile X and at that time Jamel Chelly, it was'95 I think, he worked with Tony Monaco on Menkes.

PSH. Menkes

JPF. Then he came back to Cochin in Paris and he phoned me to discuss further work on XLMR. Then we decided to make a consortium of unknown families and we started to do linkage and this was with Ben Hamel. Nijmegen also had a very long tradition of interest in mental retardation and then Ropers, he moved from Nijmegen back to Berlin, to the Max Planck but he was still in the consortium.

And Claude Morraine had collected and he was all his life interested in the X-chromosome and mental retardardation and so we put all these families together and everybody had access to the DNA and the oligophrenin gene was found so on. So it was a very, it's still a very exciting period.

PSH. Absolutely.

JPF. And now in the consortium we have broadened the interest to autosomal genes in mental retardation and in autism and it's a growing experience.

PSH. How many different X-linked loci are there now?

JPF. Oh!

PSH. I lost count some time ago.

JPF. I don't know exactly, but I think there's at least 35 genes now which lead to quite non specific mental retardation.

PSH. Coming across, Jean Pierre, to dysmorphology in general, apart from your own interest, were there any particular people who influenced you in becoming involved in dysmorphology, either in this country or elsewhere?

JPF. Well I have very good contact with Jan Bylsma. He was a very nice man. He was a very good clinical geneticist so in the Dutch part it was Jan and then you had the man from Nijmegen who died, Ter Haar, so we were 3 or 4 with the same interest. And then on the French side you had some young guys at that time, [?] who was a little bit younger than me. So finally I decided to start the European Dysmorphology Meeting. We meet every year in Strasbourg and a lot of young people attend and I think the most important thing is that they learn to look at things. The only way to learn the job.

PSH. What about links with the people in UK and America? When did they begin?

JPF. I had very good contacts with Marcus Pembrey and with Dian Donnai and then Helen Hughes. So it were all the same people and in the States, I attended quite a lot of the David Smith meetings and then I started Maastricht from zero in '88/'89 and they were a very nice group. Clinical genetics with Connie [?] do you know her?

PSH. I do yes. Because Maastricht, Geraedts has been there a long time.

JPF. He is still there.

PSH. But he is not really clinical.

JPF. Joep is a biologist.

PSH. Yes that's what I thought

JPF. When I had to start clinical genetics he called me whether I would like to come for, he would have liked to have me there but I said I cannot leave what I have built up for 15 years and so I tried to go then once a week and then we had Connie and Christine de Die, and many young people working very well still. Joep is a very nice man.

PSH. Did you have contact with Chris Höweler.

JPF. Yes, I had a lot of contacts with him and I still remember, well John Edwards he organised these Monday morning meetings in January. I think it was the third Monday of January and always he had from, well Herman was with me and I remember that we discussed about imprinting, but there was no conclusion at that time because everyone was very sceptical about the idea of Chris at that time.

PSH. Yes, because although I have never been involved directly with Fragile X, all the time one was looking across from myotonic dystrophy and seeing that some mechanism of this type must be involved, but it is amazing really that for so many years there was no mechanism which really satisfactorily explained things.

JPF. And then in France I had Maroteaux. When I had problems I took them to France and I went to see him, and also with Jean de Grouchy I had very good contacts already very early on.

PSH. How do you see the way in which things have built up in Belgium? I heard the early years from Herman, but I still find it quite difficult to see how the transition happened from essentially a unit that he had developed to something rather more multifocal? Did it happen, gradually or . . .

JPF. Yes it was unplanned and dependant on the people coming in and being interested, and so Herman, he was mainly interested in onco-haematology as you know, to find chromosome changes. You have the 5q minus from Leuven here and so on and so on, and then he was interested in cell biology so he developed a large group on cell biology but they missed the molecular biology. So all these people, who are now in the Flemish Institute of Biotechnology, it is a separate huge group but they are interested in Alzheimer and I don't know what else, but they have never been looking at genes. They look for mechanisms and it was a choice at the time. So when we started here with molecular biology to do some research, it was not before the early nineties, we started quite late.

PSH. No, I understand. Now, the main groups, are they still your own area of dysmorphology and Jean Jacques [Cassiman] and Gerry [Evers-Kiebooms] on the psychosocial? Which other groups are there which have evolved in more recent times?

JPF. So, I am director of the whole clinical thing, including chromosomes, everything. Oncology is in my group who . . .

PSH. That's a lot.

JPF. Yes I have about 150 people now in that group. And the second big group is the VIP group and they get a lot of funding . . . this is called the mental support by the Flemish government. We have finances from Government funding, the people and then health insurance of course.

PSH. Do you mean you get it directly from health insurance or does it just come indirectly by the insurers providing things?

JPF. Insurers.

PSH. Because it is a little different from the UK system where it is all funded from taxes rather than by insurance companies.

JPF. Different. So we are paid when we do chromosome testing costs, I think it is about 300 Euros now, so if we do a thousand, we get a thousand, three thousand euro. If we only do ten we only get ten.

PSH. How do you see, looking ahead, the changes with so many other medical specialties wanting to do their own genetics and become involved?

Do you see that being quite an easy transition, or do you think it causes some problems?

JPF. I think up to ten years ago, nobody was interested in genetics. Now everybody is Interested,. So my advice to the hospital and to the university was to build a central core facility, but it costs money and so we will invest and I hope the university will do and the hospital a little bit so that everybody can have access for DNA extraction to that unit and you have to store material. For example I know we have a huge psychiatric clinic here outside Leuven which is attached to the University. I know from the Head of Department there that they have stored themselves, DNA, from 300 schizophrenia people, which we doubt informed consent from, . . . You see it's stored away in the deep freeze and I think we have to change and to create a central facility.

[Break for telephone calls]

JPF. We had a prenatal diagnosis this week for a positive triple test of 1 in 60, normal echo, and direct FISH only one each chromosome centromere. So I discussed with this lady for one hour and I said I need at least to know at 18/19 weeks whether the heart and everything is normal and I explained then that most of these girls do very well and then people go to shop, and then she went to Brussels and she saw a very young clinical geneticist who wrote a letter for her that there is an indication for pregnancy interruption. But the problem is we only know about the centromere. If for example it is a variant centromere, maybe the child has two normal X chromosomes. So this makes things quite difficult you know. So the gynaecologist who phoned me, I said you should not be under pressure from people. You cannot prevent them doing things but its not our medical job to say to the people stop all Turner pregnancies.

PSH. Absolutely.

JPF. It's getting a big problem you know, for example up to some years ago we had a clinic with orthopaedic people and Prof Luc De Smet is a hand surgeon so we saw a lot of Turner, was the most frequent one, with transverse limb defects. What amazed me for the last 4 or 5 years the number of kids born with that are decreasing. Because they stop the pregnancy. They see an echography at 15 weeks a small cleft hand and this and they stop the pregnancy.

PSH. And who is giving advice, just the obstetrician?

JPF. No they go to private clinics in the Netherlands mostly and in France there is a legal convention that you can interrupt the pregnancy after 14 weeks. Therapeutic indication . . . So it's very difficult you know.

PSH. I don't think we have such . . . We have the same problem but people don't go around different centres in the same way, at least very few people.

JPF. But everything is very close together here.

PSH. Yes that's true.

JPF. It is 15 kilometres, 10 miles between Brussels and here and you can have three genetic centres in there.

PSH. And if people go to three genetic centres, does the cost of all 3 consultations, is it covered without problems by insurance?

JPF. Well the policy to charge people is also different from centres. Our counselling sessions are free because we get a grant from the Ministry of Health, the Flemish one, and also all counselling for Huntington's are without change. We don't charge people anything and you know, all the centres, how they manage it I don't know but their health insurance doesn't pay for consultations here. But to come back to your question about how to organise genetics in the future. Well I think what we try to do is to have good contacts with the big peripheral hospitals. A big peripheral hospital in this country is 800 beds. It's nothing. So we have consultations in ten of the bigger hospitals in the Flemish part and one in the French part. For the adult ones we have a multidisciplinary fetal cardiac genetic centre, so called, in which we have patients with the cardiologists, see patients together. But the molecular things are done here. So we try to make - ophthalmic genetics also which has been growing very, so Thomy de Ravel is taking care of that. In the house we have also

PSH. Is that Thomy de Ravel who was in Johannesburg.

JP. Yes.

PSH. I had forgotten he had come back.

JP. He spent a sabbatical here for 6 months and he was not married at that time and was travelling to Johannesburg; he was very lucky that he met a girl from Brussels working as a chef de cabin on a Sabena flight and they married and he was in South Africa and finally he decided to come here and I think he is very happy here and he will finish his PhD.

PSH. How about screening, Jean Pierre? Is there some definite policy in terms of population screening and what you do about this both in terms of regulating things like newborn screening or cystic fibrosis?

JP. Well the metabolic screening and the CF screening at birth is done, well newborn screening we have official newborn screening centres. They screen now for PKU, galactosaemia but the genetic centres are not involved in that.

PSH. Is that done through biochemistry?

JP. Yes.

PSH. And what about, I'm thinking in UK, the cystic fibrosis screening involves a lot of molecular work as backup and the same with haemoglobin screening. Would that involve here, or is it rather separate from medical genetics?

JP. It is quite separate, but I think all the molecular work is done in genetic centres but there is no screening programme except if you have a pregnancy with indications, it could be CF, screening and examine the parents. But it is on clinical grounds, not just blank screening.

PSH. And for antenatal screening, say for Down's, would that also primarily be done by biochemistry?

JP. And if positive they get amniocentesis or CVS and that comes to the genetics centre.

PSH. And do you think this is likely to change with all the use of fetal blood DNA, or not yet?

JP. Well we have a programme now, a research group, working on fetal DNA. If the regulation stands as it is now in Belgium, private companies will not yet reimburse them for the tests, so it is not very attractive, but I don't know whether we will be able to, well I think the force of the centres is that we have coupled technology with counselling.

PSH. Absolutely.

JP. And I hope the politicians and other people will understand that this is also the lowest cost price.

PSH. Do you feel the politicians are now listening and interested or do they tend just to follow their business instincts?

JP. I think that at least in the Flemish part, politicians are quite well informed. They come to visit as they are interested in a small country and you also have many politicians who have a child or a family member with a genetic problem and it makes them very sensitive of course.

PSH. Indeed.

JP. Flanders has only six million people, six and half. The same as Manchester.

PSH. Jean Pierre thanks very much. I think I should let you get on with your work now.. Thank you very much for sparing a bit of time.

End of recording.