Marco Fraccaro

Personal Details

Name	Marco Fraccaro
Dates	1926 - 2008
Place of Birth	Pavia
Main work places	Pavia, Uppsala
Principal field of work	Human cytogenetics
Short biography	See below

Interview

Recorded interview made	Yes
Interviewer	Peter Harper
Date of Interview	21/04/2004
Edited transcript available	See below

Personal Scientific Records

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

Biography

Marco Fraccaro was born and educated in Pavia, where his father was Rector of the University. After qualifying in medicine in 1951 he specialised in Pathology, becoming interested in genetics, and in 1954 spent a year with Lionel Penrose at the Galton Laboratory, London. In 1956 he accepted a post with Jan Böök in Uppsala, developing human cytogenetics and being involved with a number of initial human chromosome abnormalities. In 1961-1962 he worked in Oxford at Alan Stevenson's MRC unit before returning to Pavia to establish a human genetics department, with a focus on human cytogenetics.

INTERVIEW WITH PROFESSOR MARCO FRACCARO, 21st MAY, 2004

PSH. I'm talking with Professor Marco Fraccaro in Collegio Cairoli, Pavia, in his office there on 21 May 2004.

Marco to begin with, may I ask you about your early years. Am I right that you come from an academic background?

MF. Yes, well if I was to start from scratch, I studied medicine in Pavia and my father was a Roman historian and for many years was Rector of the University. Incidentally he was nominated Rector of the University by the Allied Forces in April '45 when Italy was liberated by the English and the Americans and my father was practically the only member of the University who was not a fascist, he didn't belong to the party so he was nominated the Rector. But as I say I studied medicine even though I never practiced it. And after taking the degree my interest in genetics came out because I was at the Institute of Pathology, what we call in Italy anatomia pathologica, pathological anatomy, pathology, and Professor Giordano who was Professor of Pathology was a very intelligent, even though a rather strange man, he was very interested in congenital malformation, the pathology of congenital malformation. He published papers especially on anencephaly, the pathology of anencephaly and similar syndromes. Actually he was a genial man because in '56, '57 he published a book called – very few people know about this - La Pathologia Chromosomica. This was before the chromosome story but his point was that he chose to call it Pathologia Chromosomica, chromosomic pathology, because he was seeing the chromosome as a pathology, he preferred the term chromosome to the term genes. And so this book in Italian with its title, which looked very strange at the time. He never said in the book that this and that condition must be due to a chromosome abnormality but he said that genetic pathology was a pathology which affected the chromosome because the chromosome was .....

Anyway, incidentally from that short period as pathologist, I can claim my only medical genetic success which was the condition called achondrogenesis which was called Parenti Fraccaro syndrome, now its called I think achondrogenesis type 2 or 3, there are so many. And because we came across this condition and we did, I did a very careful histological, and there Giordano directed me, then I realised that the condition was affecting the development of cartilage so we called it achondrogenesis. But then I soon realised when I started to read and look around, I realised that there was not much possibility of doing human genetics in Italy. I wish to stress the point that in Pavia there was what was the best school of genetics in the science faculty in Italy. Probably you have heard the name Adriano Buzatti-Traverso and Cavalli Sforza took his medical degree in Pavia.

PSH. May I ask what year would this have been that you took your medical degree?

MF. I took it in '51. '51. So I started to look around and I think, I don't remember how it came to my mind to try to go to the Galton, probably because, oh yes, I came across a copy of the Journal called then, Annals of Eugenics, but was already edited by Penrose I think, in those years. So I applied for a British Council scholarship, I got it and then off I went to the Galton.

PSH. Which year would that have been?

MF. That was, I arrived in London I think in November '54. '54/'55 was the academic year and that, probably you are not interested about the Galton because that is another side of the story.

PS. I am always interested in anybody's ideas about the Galton.

MF. The Galton, as a matter of fact, was in those years, at University College, it was an extraordinary environment as I told you because J B S Haldane. I attended J B S Haldane's lectures and I took a practical class in genetics with Helen Spurway, Haldane's woman, whose English for me was very difficult because I didn't know English very well and one thing that I remember that she told the class not to throw away the few Drosophila left in the bottle we were handling and I understood the opposite. I threw all of them away, just to give you an idea. And of course I was there as a postgraduate, so I had access also to the senior common room and then the environment for a young man like I was, that was very stimulating because you could drink coffee with, Haldane, Medawar was around there and a lot of people were coming actually both to University College, Young was there. University College and a lot of people were coming to the Galton of course. Jim Renwick was there as a young man and Bette Robson, Ursula Mittwoch, Kalmus, Sheila Maynard-Smith. Maynard-Smith if I remember was in the Zoology Department which was very good. There was a very good anthrolopologist, you might have read the name, he published papers in the Annals of Eugenics, Barnicoat he did some pioneering work I think. And the great friends of the Galton were Bob Race and Ruth Sanger who were not at the Galton but they would pop in quite frequently. And Harry Harris was then the London hospital and precisely in those years, Harris was starting his work on diabetes, if I remember correctly, in '54 and there were in the academic year I stayed there, was a constant coming and going of foreign, American, mainly American, Boyer I remember and then, now I forget but it is not difficult to find. You have seen this book about Penrose they published so there is a lot of information about the Galton.

But it was through the Galton, one day, I came to know this later, but Jan Böök who was nominated Director of what was called in English, Institute of Human Genetics, but the official name in Uppsala was Statins Ras Biologica Institute, Institute for Race Biology, and Statins meant that it was not a

University, it was depending directly from the Government was paying. And I came to know after that that Böök had come to ask if Penrose could suggest somebody could take the place of Vice Director of this relatively small institute and with a view to start to put up a lab and to start some kind of experimental work in genetics, and as a matter of fact, if I remember correctly, the first idea of Jan Böök was to look at chromosomes in anencephaly. So I came back to Italy but I got in a few days after the visit of Jan Böök, to Penrose at the Galton I got the offer of this post in Sweden, which I took up on 8 January 1956. When I arrived in Uppsala, the Institute was actually the old University Chemistry Institute. It was a building from the 18th century, I think, Berzeluis had been active there and I started to set up a lab with the idea, of course Böök knew about Tjio and Levan's discovery of chromosomes and he knew also what kind of materials Tjio and Levan had used – human fetuses - so immediately we got contact with the obstetric clinic and got this fetal material and we started. The first thing I did was to set up the tissue culture.

PSH. Had you had any previous experience?

MF. No I didn't have any previous experience in tissue culture and a matter of fact I must say that I wasted some time, because by a series of arrangements I finally ended up to go to the Institute of Histology at Leiden University in Holland where there was apparently they were all devoted to tissue culture, but I soon discovered that was the old fashioned tissue culture, either organ culture, I think these people were trying to cultivate pieces of thyroid implants surgically and things like that, but they had no modern techniques at all. Because as you probably know, I mean the development of tissue culture had been when it was realised the cells could be dispersed and cultured as a single structure and not coming out from the explant as was the classic Carrel's tissue culture.

But at the same time, there were the first attempts to culture blood cells. There was a man called Osgood in the United States. I read this paper and I tried to apply the method but I never succeeded. As a matter of fact it was in '58, Kurt Hirschhorn and Rochelle Hirschhorn, while Kurt was a young man and he was working in, I think a New York hospital with a man called Wilkinson who wanted to start some kind of human genetics. You should realise that formally in those times, there was, the Galton Laboratory was officially labelled now for the study of human genetics and the Institute Uppsala was called the Institute for Human Genetics. There was no other Department or Insitute of Human Genetics anywhere in the world so probably they read this and Kurt came and stayed some months in Uppsala.

PSH. Was this 1957 or thereabout?

MF. I think it was '58 we really started to work in tissue culture, but at the beginning we got immediately good chromosome preparations using Tjio and Levan's methods. I think there had been several claims of people saying that after all they did, but in my memory I always acknowledge the fact that it was Tjio and Levan's paper more than T. C. Hsu's paper to influence, and we started to think to look at the pathology, the chromosomal pathology after

Lejeune's published the discovery of Trisomy 21. Actually I knew Lejeune. I met him in Copenhagen and we sympathised. He was a very intelligent man. Later on he had this limitation with his catholic extremism which really pervaded him, even diverted him by objectivity I think. Even though I always respected his opinion. And there was a meeting, there were two meetings in '58 and I met Lejeune at both. One was a meeting on radiation, radio-biology organised by Buzatti-Traverso in Venice and I was invited from Uppsala because of the experimental work I started off, with the cell suspension, taking advantage of having got the technique to visualise chromosomes and to handle cells in culture and dispersed system in Petri dishes practically. We started to irradiate cells Actually I remember we were going up to Svedberg Institute. Svedberg won the Nobel Prize for the ultracentrifuge. He was an old man I think. He was more than 75 but I met him and he was very active and we irradiated the cells in his department facilities and I got results. And I think that, incidentally we didn't publish these results, I don't know why. Probably because I was not considering them complete enough but they were among the first data about the irradiation of human cells. There was a lot of work had been done with animal cells, ascites cells in suspension, but it was Chu in the United States was then.

PSH. That was Ernest Chu.

MF Ernest Chu. C.H.U. He was at Denver too. But at this meeting Buzatti knew about this work. He was invited and was very lavishly supported, there was plenty of money at that time for radiation biology . Hollander, the great chief already of radio- biology in the United States officially, was there. And I met Lejeune, who was at this meeting and he told me you know now I can tell you and I will publish it soon, don't rush home and do it yourself, I am now sure that the Mongols have 47 chromosomes.

PSH. And was this in the summer of 1958?

MF. '58 yes. And actually then we met again in August of '58 at the International Congress of Genetics.

PSH. Was that the one in Montreal?

MF. In Montreal , where both Tjio had a paper and then was known, not to the public because at that time, you see even a great breaking-through news like that would not get into the newspaper. Took some time before. But then came after the publication.

PSH. He was quite lucky in a way that nobody else did go straight home and publish first.

MF. Well you see, there is a point that where now, many years later would have happened surely. But at those times there were relatively few people. But then you should realise there were very few people who were in the conditon to, because the situation was like this, everything was easy, that is why it was easy for me to make the experiments of X-ray radiation of human

cells in vitro, because we had these fetal cells growing very rapidly and very well, but to look at chromosomes then you had to make skin biopsies or, the method was already set up by Charles Ford in Harwell, bone marrow, and so it was not so easy. The thing we did of course in Uppsala was to start to culture skin biopsy, with the idea of looking at chromosomes, and we discovered that chromosomes of the anencephalic were normal.

Anyway Lejeune, I think that his communication to the Academy in Paris was in March '59. He had two papers, one after the other. One for a few cases. And so we immediately confirmed the thing because we went home. We got hold of a couple or three Mongols. I call them Mongols because at that time . . .

PSH. Everybody called them Mongols.

MF. Everybody called them Mongols and I think, I don't remember, whether it was Ernie Chu who told me that he, as a Chinese, of Chinese origin was not feeling at all offended by the term Mongolism, for a Chinese 'Mongol' is meant an inhabitant of Mongolia, not as the Western people would say, would refer to all Asians, but apart from this, as a matter of fact we published a paper which I think was a very good paper which escaped attention. We published in Acta Paediatrica Scandinavica, I think was '59, the end of '59 and if you re-read that paper, first of all you immediately detect an attitude which was very common at the beginning of the human cytogenetics business. There was a sort of inferiority complex towards classical genetics, classical cytogenetics, which was mainly plant genetics. There was no inferiority complex with mammalian chromosomes because the only text available to summarise and show all known chromosome number and appearance of chromosome of mammalian including man was published in Switzerland by Matthey.

PSH. I have a copy.

MF. You have a copy. So have I.

PSH. I managed to find a copy and the drawings are beautiful.

MF. The drawings are beautiful, but I mean of no use.

PSH. Very difficult to count.

MF. Of no use. But there was this, if you read the paper, incidentally that paper contained a very beautiful, two very beautiful photographs of satellites, on acrocentric chromosomes and of satellite association.

And so we started our activity and we immediately confirmed because if I remember correctly, I am not sure actually, I have to check, but the first paper by Charles and co-workers, Charles Ford and co-workers, on Turner, were made on bone marrow preparations.

PSH. I think that is correct, yes.

MF. So we wrote a very short letter, immediately to the Lancet, it looks very naïve, to say that we have studied fibroblast culture of Turner patients and found them also XO, because in our paper on Mongolism in '59 we insist very much that if you weren't sure you should wait for other tissue to be examined, to be sure that the trisomy was not confined to one mosaic in the system. This was done on fibroblast. But also, well of course it now looks naïve, but it was the pre-occupation even at the beginning that there may be mosaics.

PSH. May I ask, in your work on Turner's had you had contacts with Paul Polani, because he was collaborating with Charles Ford.

MF. I had contact, yes nearly immediately with Polani, not when I was in Sweden but because I met all of the English people I think when I went in '59, was it '59 or beginning of '60? I don't remember. I was invited to give a seminar at Harwell and there was Charles Ford. Because I met Polani and John Hamerton at a meeting that was a very curious meeting. It was in '58 I think - there is a small book – organised by Davidson at King's College, have you seen that? That was on sex chromatin.

PSH. I don't think I have seen it.

MF. It was a very curious meeting because, it was in '59 I think. Was on sex chromatin, you know Davidson had found the drumsticks and Barr was there of course, well Barr and Davidson were the two sex chromatin men who organised that, but that coincided with the beginning of the chromosome era. At this meeting I met a lot of the people. I met Polani only once while I was at the Galton, and this is to give you an idea of Lionel Penrose's wit. He said "He is a countryman of yours, Paul Polani. He is a very good paediatrician." He said "the only thing is I can't persuade on him not to call me 'sir' all the time". Because when I talk to him he say "yes sir, no sir" and I met at the Galton. Just going back, the Galton was really an excellent place at the centre of the world to meet people from everywhere. I remember when all people were coming there from everywhere, and then this meeting at King's College about sex chromatin of course. I remember we had, when I say we, I mean I forgot, I mean I and Jan Lindsten. Jan Lindsten when

PSH. How did you meet him? Was he then in Uppsala or was he

MF. He was then a medical student in Uppsala and he came in '57, late at the end of '56 as a medical student asking to make an internate at the Institute. And we went on very well. We worked very hard day and night, because those were really . . .
We were very proud, I have a photograph of that standing near, because we got that wonderful, we were among the first in the world to get that wonderful machine, it was the Zeiss ultramicroscope. Was not in any 'ultra' but it was all automatic you know. First of all was drawing of chromosome and then you have to photograph either you screw a camera, a Leica, on the microscope and then you have to find out the right exposure. Try this; with the ultramicroscope everything was automatic. You would put the cell on focus on the screen, push a button and it was still a slide. The first slide gave wonderful photographs and everything was automatic. It was a great improvement for people who had to spend hours at the microscope.

PSH. Can I just ask on that, I get the impression that one of the reasons why so many of these cytogenetic advances occurred in Sweden, was the very high standard of microscopy and the equipment. Is that true do you think?

MF. Well with the Swedes machines were always very popular. I mean we didn't have any contact with Caspersson. Caspersson, he had started. He had all this measure with these machines and I think, I don't remember correctly but I think, I don't know whether Tjio and Levan had the ultra microscope Zeiss but equipment, there were no financial difficulties in those times and . . .

PSH. Because that must have been a big contrast with the French group, where I heard that the microscopy was very primitive.

MF. Very primitive, but this is my point, I always call machines a painful necessity. I never liked. I was never very good even microscopy and things, but I mean for practical work it was an advance. But the fact that Lejeune was primitive, but Lejeune likes to be primitive you know. But that demonstrated the machine was not really essential. Because he did excellent work. Then of course from that period on, I mean the history comes out from the publications. It is very easy I think to reconcile. But I was telling you this meeting on sex chromatin, if you have not seen it I think you should try to have a look there, and I think it was the second or third Turner we looked at. She was a Turner clinically, because, this is a good example of another of my Swedish experiences. Our first patients, and we examined in Uppsala, were coming from Eskilstuna which is a town North of Uppsala, from a paediatrician called Kaiser, in fact he holds a paper Fraccaro, Kaiser & Lindsten and Böök, Fraccaro, Kaiser, Lindsten. Because I was not having the contact but Jan Arvid Böök must have had the contact. I mean the local paediatricians were reluctant. Paediatricians and clinicians they didn't understand the importance you see. This paediatrician in the hospital in Eskilstuna understood immediately. He gave us the first patient.

PSH. Was this skin biopsies?

MF. They were skin biopsies.

PSH. Not bone marrow?

MF. And bone marrow also. Both were possible. The third Turner we did had 46 chromosomes, 46 chromosomes and had an extra isochromosome. And I must say, it was Charles Ford who immediately, it was the only example where both botanic cytogenetics helped, because Charles Ford and I was there with these chromosomes to show them to Charles at this meeting at King's and he said well this could be an example of isochromosome for the long arm of X. I think he said it should be that. We published it, very few lines in Lancet, to say there was also this possibility that some of the Turner, and that was important because it was pointing out even now indirectly, that the information lacking to give Turner's syndrome was on the short arm, that having three long arms of the X and only one short arm gave you the Turner phenotype. That was rather important for the time.

PSH. Was that the first example of an isochromosome to be recognised?

MF. Yes.

PSH. So was it at that point, Marco, that you became especially interested in the sex chromosome abnormalities as opposed to the autosomal re-arrangements?

MF. Well as a matter of fact we were interested in sex chromosomes but later we did also, when I arrived in Oxford we published a paper that nobody quote and nobody noticed. With John Edwards we published the first case of autosomal translocation.

PSH. Right. I'll come to Oxford in a little while if I may. But while we are in Sweden, can you tell me a little bit more about Jan Böök.

MF. Well Jan Böök. It's a very sad story because he was an intelligent man. He realised immediately that he had to change this race biology business. He put up the Institute. He was not working himself in the lab.

PSH. Was he an epidemiologist more?

MF. Well I don't know what he was originally, but as everybody else, his type of clinic, was later called clinical genetics. I think he published his scientific thesis of this monography on mental retardation in a Swedish district I think. And he was a physician, medical. And he had a very good way of utilising data because it is very careful. He described also some new syndromes. I don't remember what he had and he published them in this Journal Dahlberg was editing. It was called Acta Genetica Scandinavica, something like that. But then you see of course, he was very enthusiastic because he didn't take part in anything. He was not working at the lab and of course both I and Jan Lindsten realised that for our career that was a unique occasion and we agreed that the first paper would carry Böök's name but after that we thought, I thought, and Jan was younger but he also had this idea of making a career, because to work, Jan then stopped his medical study.

You see in Sweden there is a system where you can study medicine giving your examination, and then you can stop and write a scientific thesis and get the title of 'medical doctor' because you wrote this scientific thesis, but not the authority to practice medicine and you can write your scientific thesis before even taking the examination of internal medicine as such. As a matter of fact Jan finished his medical licentiate, it is called in Sweden, many years after when he was already well-known for his scientific work. So we started to say, I mean to say to Böök, that we would prefer he wouldn't put his name first because we were all in favour of alphabetical. At this time you see alphabetical order was the rule. Nobody would, if they were in alphabetical order you say this more important because this is the first, that is the last. This is the whole thing that came out later. So I thought well, all the work we do, you put your name first people might think that you . . . you see this happened quite often. So we had some discussion, but then he started to, it was a very sad story because I think he started to take some drug. But then

actually that is the reason why at this time, this is a good example of John Edwards' activities, John started to persuade me to move to Oxford, to come because he was, well you know John is a very intelligent man. Not very good in practical work in the lab, but you come to Oxford to this unit and he talked me over. So since I couldn't see very much future for me actually in Uppsala because I mean to become a professor in Sweden in those times, it was very difficult there were so few . . .

PSH. Which year are we in now. Are we around 1962 or something like that?

MF. No we are at the end of '59 at the very beginning because I went to Oxford in '60, stayed there two years, '60/'61.

PSH. So did you go to the Denver meeting from Oxford or from Uppsala?

MF. No I went from Uppsala. So Oxford was '61/'62.

PSH. Before we come to Oxford then can you tell me a little bit about your impression of the Denver meeting.

MF. Well I wanted to finish the Böök story. As a matter of fact, then we maintained good relations with Böök. As a matter of fact I went back many years later to Uppsala to write the paper on radiation, which actually became a bulky paper, I don't know why, it was a mistake, but we published it in Gedda's journal the Genetica Gemmelogica. So John started to talk me over, so I had a double problem now. I mean the idea of moving to Oxford was very appealing, not because I knew indirectly that, I mean Stevenson was not a man really interested in this. I think he was a strange man too, but the amusing thing was when finally John persuaded me to move to Oxford, when I arrived in Oxford he had left and went to Birmingham. So I found myself . Oxford was appealing to me, the idea of moving to Oxford because actually my father had got an honorary degree from Oxford in '55 so the idea of going to Oxford. . . There I continued to work and then I had the problem to place, I felt responsible for Jan Lindsten, because Jan wouldn't stay in Uppsala because of this difficulty with Böök but there was a very good endocrinologist in Karolinska. Luft. Luft was the Secretary of Nobel Prize Committee of Karolinska at that time. He took up Jan and there he wrote this scientific thesis on Turner syndrome. So off I went to Oxford and now I come to recent history and . . .

PSH So how many years were you then in Oxford?

MF. Two years.

PSH. Two years.

MF. See there is one thing about Oxford that I still now don't know how it happened. You know now in the 60s was an Oxford that was still Oxford, with the classic idea that people had of how Oxford should be, especially outside Oxford. Now it is an Oxford which does not exist any more. But Balsdon was a Roman Historian, a Senior Fellow of Exeter College. My father got his honorary degree in Oxford because of his relationship with the Oxford Roman

Historians especially with human arts and was a Professor of Roman History, Sir Ronald Syme and his people and after a few months I was in Oxford I got a note from Balsdon asking to go to Exeter and see him and meet him. I didn't know him personally and he had me elected a Member of Senior Common Room of Exeter College which I still am, I think, formally.

MF. And because as you know, people like Stevenson for example were never really. . . Those who were in Oxford and not attached or having access to any college, they felt

PSH. Excluded.

MF. Excluded you know. Now this is very much diminished because they increased the number of colleges. At those times, I had then, Oxford was very good because you could have easy contact with Charles Ford group at Harwell, with Searle and with Mary Lyon. You know Harwell was really a concentration. Genetics in Oxford was non-existent then. Actually when I arrived at Exeter, Allison was there and one of the first things which amused me very much. He had just, I remember it was Balsdon and another fellow; I said I was a geneticist I hope you don't plan to experiment on us as Allison did, because he had divided you know, there is probably a genetic condition. I don't know whether that was published, when you eat asparagus, your urine has a special smell and

PSH. And there's a polymorphism.

MF and there's a polymorphism. He said, he forced us to eat asparagus. More than we could stand it and then smell our urine.

PSH. Oh dear.

PSH. So did you have also contacts again with the Galton during your time in Oxford?

MF. Yes I went occasionally. As I say Penrose was very very shocked by, not having been.

PSH. Not being involved with the Down's chromosome discovery?

MF. Then when I was in Oxford and Darlington was Professor of Botany you know he was at Magdalen and there I was talking with Charles and with other people and so we decided to make this Oxford chromosome conference. But then I had an important collaboration with John Hamerton who had quarrelled with Charles and moved to Polani at Guys, because at the beginning of nineteen hundred and sixty, the W.H.O. asked me to run a course to teach people to prepare human chromosomes. So indeed that was in Basel because Klinger was in Basel then at the Anatomy Department and he had done quite early work on sex chromatin, Klinger, and then on chromosomes. Then we started the Basel colloquia. I don't know whether you have heard about that?

PSH. I haven't.

MF. This was really a series of extraordinary events We had this Basel colloquia. A small group of people were invited to the Anatomy Department in Basel at the beginning. They discussed general problems, not much about chromosomal abnormalities but what could be inferred from the study of human chromosomes and I think we started in '61. I have all the documentation there. And so there was free discussion with no real presentation of paper. Of course there was a lot to discuss because we knew nothing.

PSH. Can I bring you back again now to the Denver 1960 meeting, because I have talked to several people about this and it does seem to have been a very critical point in the field developing.

MF. Well, critical in which way?

PSH. I suppose in bringing together the concepts in the field and perhaps bringing it across the Atlantic to America.

MF. Yes that is true. Because in United States there were then Puck and Robinson who also had done early work but the other Americans were Ernie Chu, was Michael Bender there? I don't remember. But not many Americans. Hungerford was there and there was nobody else from the United States.

PSH. I think not.

MF. There was Hungerford and Ernie Chu I think, were the only ones who published normal karyotypes, because what was strange, looking back at them now was if you read the report it looks quite naïve and as a matter of fact Patau criticised it immediately. Well it was an easy critique to make because all this thought to measure a chromosome without realising there was a way. But I think that Denver, the idea was still going around in the minds of many people including myself, that we would find a lot of trisomies. You know. Lots of trisomy and so this concentration on measuring chromosomes because if you ask now, now we know that the only trisomies are 21, 18 and what is the other one?

PSH. 13.

MF. 13. and that is all. I mean the idea of having a standard nomenclature not to create confusion now looks useless. The bands alright, but still I think the idea was that we needed a standard. Then you know everybody, it was a matter of discussion whether a number or letter of chromosome which looks ridiculous now. But you see the psychology. I was studying very carefully Kurt Stern and Muller, they were really impressed by, it came as a shock to everybody, to all general geneticists the human chromosome story because it was unexpected I think to them. So my recollection of Denver was very useful discussion but most of it quarrelling about, call acrocentric then it was finally agreed numbers but groups and letters, which sounds ridiculous now really but as a matter of fact it was this European prevalence. Makino was there, Makino the Japanese was there, he was completely deaf poor Makino was, he

say yes, yes, because he had also published what had been a pioneer chromosomal . . .

PSH. Can I ask now what year was it that you came back to work in Italy.?

MC. Now what happened was this, I was in Oxford and, well actually as I told you an important event happened in Oxford. Should correct a full statement that you find on top of the cover of what I call Cytogenetics, now it's called again Cytogenetics, founded by Harold Klinger.

PSH. Yes. Cytogenetics and Cell Genetics.

MF. No. Now it has changed again. Stupid. Really is stupid. Klinger was a great friend of mine. It is called now a molecular something. But anyway, we decided, we were talking about having a Journal, call it, I would call it Human Cytogenetics was the obvious title to call it. And to do that we had a meeting in Oxford at my place. There came Charles Ford, Polani, John Hamerton and I think even Darlington, probably say no no no no, I am happy with plants. Do the journal but leave me out. And we decided, in a way it was fun with Klinger because Klinger was a friend of Karger the printer in Basel. It was a collective effort made by this and we met in Oxford. I don't remember why it was there but surely Polani and Hamerton were there. Because with John, I invited, the W.H.O. course in Basel was completely useless because the selection of the participants made by the central office of the W.H.O. we got 12 people from 12 different countries. I think if one or two men intend to do some work it was more than the other people. But anyway on that occasion we did the chromosomes of the Gorilla, the first, which was quite important because you know the first, everybody asked, we said well we have 46 not 48. What about our cousins and in Basel was a very good zoo director, was very friendly with a couple of Gorilla they had then and he told me it was possible to draw some blood and the skin biopsy from the female. The skin biopsy from the female, not from the male and we published in Nature the first chromosome number for whatever reason was 46. Michael Bender was working with primates at the same time in the United States and they did the chimpanzee and the Orang Utang but the Gorilla was quite . . . I remember there was a huge article in the Oxford Mail with my photo. So we founded Cytogenetics, the Journal.

Now in '62 there was the radiobiological unit of Euratom, the atomic energy agency of the European Community, directed by Appleyard. He was a Canadian actually and they started a very good policy. They decided to support promising young researchers who were working from the Community but working outside the Community to recuperate, to combat the brain drain. He contacted me and we went down to Brussels. He said here there is money to put up a unit, you must find a place. They give you space and not support, because to be effective, they think you must present yourself. Bring in money and not ask for money. The only thing you have to ask for is space. He said we prefer that you find a place, which is not your place of origin. So I started to look around but you see people in Italy wouldn't understand much of that because the condition was not to go to an institute of genetics where they were already doing genetics but to do a thing by yourself. So I tried in Padua but they didn't even understand. It was very difficult. So finally I said well

look, the only place I found. I went back to the pathology department where I started from and then was director another man called Caballero who was a very intelligent man. They were very short of money and he understood immediately and made a bargain.

He said well look, your young people have only 3 pipettes. I can give you as many pipettes as you need. So he gave me space and we started and called it the EURATOM unit for human radiation in cytogenetics and I started at the end of '62 and then I started also part-time to teach biology to the first year medical students. Then in '68 I got a chair.

PSH. And did you then develop the unit gradually to be more than cytogenetics? Did clinical and other types of genetics come in?

MF. That was much later of course. We didn't at the beginning, we did very few chromosomal analysis. Remember there were only very few in '62 in Italy, there were very few people doing chromosomes. One of them was Decali here in Pavia, at the Genetics Institute. Buzatti Institute.

PSH. What was his name?

MF. Decali.

PSH. Decali

MF. Yes he was a student here.

PSH. And he was a biologist?

MF. Yes he was a biologist not a medical man.

PSH. So nobody in the medical school was doing this. And elsewhere in Italy by this stage?

MF. Then they were starting. I mean after all '62, things had already started but very few people were making a routine examination. Then when I got the chair in '68 then I became Professor and then we started to do routine work on chromosomes to make money for the Institute.

PSH. Yes. Can I then ask, at the time you came back to Italy which were the other main centres in Italy?

MF. In Italy there was a very good centre in Turin which Cepellini - you probably heard his name. He was a man, mad but a great and very brilliant man.

PSH. And that was I suppose concentrated on blood group and immunological genetics.

MF. Blood groups; he was a very good immunologist. They started association of blood group and diseases, things like that. Very brilliant man. Then there was the only one called the Human or Medical Genetics, and then

there was the science faculty in Naples, Siniscalco was there . Both Cepellini and Siniscalco came to the Galton since Siniscalco was at the Galton I think for a time. Even Cepellini was there. I think Cepellini had the merit to force poor Cedric Smith, because I think, I don't remember whether the shoes or not, the belt, but Cepellini called to Cedric, you have met Cedric Smith, you remember?

PSH. Yes but I didn't know him well.

MF. He was a vegetarian and had nothing of leather but he forgot about the belt, which Cepellini pointed out. He was very proud. It was one of my memories of the time. Cedric Smith, you see he was a key figure at the Galton. He was a mathematician and since most of the work there was based on statistical medicine, even some problem of gene frequency, so everybody was asking Cedric Smith's advice of course.

PSH Then apart from Naples and Torino, what was the situation in Rome?

MF. Well in Rome, I don't remember when Gedda came out. Now Gedda you have to realise one thing. Gedda was for many years, he was a man who answered directly to Pius XII th, the Pope. He was president of the what is called Actiona Catholica, Catholic Action, which was not a party but the association of Catholic and depending directly on the Vatican. He was a Vatican man. I never understood what was his origin, he was a physician and he found that he got money, I don't know from where, probably from the Vatican and directly funded this Mendel Institute in Rome and he organised actually, the International Congress, was it the 2nd, I don't know.

PSH. I think so.

MF. It was the 2nd in Rome. It was '60 I think or '62.

PSH. Would I be right that he was never formally trained in genetics.

MF. No no. He was very active in the Actionia Catholica in the famous election in 1948 when there was the risk that the Communist party would win the election, he founded this Committati Civici, a Catholic thing against communism. He was very active. But I don't think he knew any genetics actually, but he did manage to find good co-workers, but you know he had the money, he was a very good organiser and I mean the Congress in Rome was . . .

PSH. I was not there.

MF. You were not there. You were too young of course.

PSH. Yes. So is it fair to say that really the . . .

MF. But mind you he became very soon Professor of Human Genetics. In Italy the system was then to have 3 men concorsa national. There is a chair, you apply and they make attend 3 men and they make only 2, Cepellini and Gedda. Then what happened, this is typical of the average Italian character.

Italians we are always more keen in avoiding that something else gets things, more than getting for yourself. So for a long time Cepellini and Gedda were the only Professors of human genetics in Italy.

PSH. And that was before you were given your chair?:

MF. That was before. But mind you I got my chair in '68 but not in human genetics. I got my chair in general biology for medical students.

PSH. Ah.

MF. So I found myself with a certain claim to fame for my work on human chromosomes at the end of '62 but I moved from general biology to medical genetics then, many years later, after I got into the 70s. For a long time Siniscalco become professor and Siniscalco was never where he was supposed to be. You see I applied for the chair of human genetics in Leiden. Siniscalco got it. But he was never in Leiden. When he was in Naples he was in Leiden. When he was in Leiden he was in the United States. Then he went to the United States. So Naples, Siniscalco also developed quite good work with human genetics. While in Milan, it wasn't in a University, was an old woman called Joan Ferrari. I must say that Gedda after a while, then he retired because he was quite old. Cavalli-Sforza when he become professor, became Professor of Genetics in the Science Faculty.

PSH. In which city?

MF. In Parma.

PSH. In Parma. Right.

MF. First. Then came to Pavia and then went to Stanford, Cavalli is a Pavia man, a friend, a pupil, a friend of Buzatti. So that was the situation. Now there are several chairs everywhere.

PSH. Can I ask you two things to bring this to a close. Marco, who do you feel has been the person who has had most influence on your scientific development and thought?

MF. Well they were Buzatti Traverso, the few times I met him here in Pavia before leaving, because he was a man, you realise, was different from the other professors, indirectly because I had nothing to do. But intellectually what changed my life was the Galton atmosphere. Penrose, mind you Penrose would never tell you anything directly but he really. . . I mean my experience at University College, I would never, I couldn't possibly have come back to Italy to find the same situation I left, with no hope of ever doing anything after having had this experience at the Galton which was a difference of attitude and mentality more than of experimental work, because there was no experimental work practically. Actually at the Galton I knew, I read Bette Robson's work on birth weight, so before going there I collected from the local obstetric clinic a huge body of data of some years of birth weight of Italian children, and I went there and I published then two papers in the Annals of Eugenics, of Human Genetics, on birth weight of an Italian sample. That was

my work at the Galton but was not that even then, for me was very fundamental to say, by a crude data like birth weight you can by way of approaching it in a way to try to solve a general biological problem, because at those times, I mean now every stupid really, can make some kind of good work, although you have probably noticed this. Even at the beginning of the chromosomal era, there were a lot of people who didn't know really what to do, but when molecular biology became widespread now everybody . . .

PSH. I am always amazed in talking to so many people how they say without hesitation that Penrose and the atmosphere of the Galton at that time were the key factors.

MF. Very difficult to define really but that is my feeling.

PSH. My last question is, of the work that you have done, which piece of work, or area of work do you feel most proud of.

MF. Well, I don't feel proud of anything really.

PSH. No but if you had to choose one contribution that you feel that you have made.

MF. Well I did nothing really extraordinary, but I think the sequence, we did a lot of work with autoradiography. I started it in Oxford and then continued here in Pavia. We published the first with autoradiograph for XXXXY Janet Rowley when she was in Oxford. I think that really, talking seriously, I don't have anything outstanding, I didn't discover anything but I think I did reasonably good at the beginning. Then we had some experimental work here in Pavia, published a paper here. I always had good ideas but I got bored and jumped from one subject to the other and we published a short paper in experimental research. We tried to study with autoradiography the first stages of embryonic development in blastocysts to see if the nuclei were synchronised in DNA replication and things like that. But I can't say I consider that . . .

PSH. No but do you feel that

MF. After all if you think carefully the most original thing I did was my first paper, in Italian, on achondrogenesis.

PSH. Well that indeed is an important contribution.

MF. Which is also a demonstration that you can write in any language but if the thing is worth, sooner or later it becomes known.

PSH. Marco we have talked for quite a long time and I think I should give you now some rest.

End of recording.