Felix Mitelman

Personal Details

Name	Felix Mitelman
Dates	Born 1940
Place of Birth	Poland
Main work places	Lund, Sweden
Principal field of work	Cancer cytogenetics

Interview

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INTERVIEW WITH FELIX MITELMAN

9 June 2013

PH Peter Harper

FM Felix Mitelman

It's Sunday, June 9th 2013 and I'm talking with Professor Felix Mitelman from Lund, at the European Society of Human Genetics meeting in Paris. Felix can I start at the beginning and ask when were you born and where?

R: I was born in 1940 in Poland but when I was six years old I moved with my parents to Sweden.

I: Can you tell me a little bit about your family background? Was there a medical or scientific background in any way?

R: Yes, there was. My grandfather was a Feldscher, you know what that is? It's a profession which existed in Europe, mostly in Eastern Europe, they were army field surgeons during wartimes but otherwise they provided some health care services, especially in the countryside. They were not doctors but they had some, I don't know really what kind of training…

I: A sort of field worker? Medical field worker?

R: Yes, my impression is that they served as the local doctor in small towns and villages in Poland even though they did not have the full professional qualifications as physicians. In the 20s or so they actually became licensed to practice medicine in rural areas. Well, grandfather wanted my father to become a "real" doctor and so to please his father he studied medicine and graduated from medical school but he never practiced as a doctor. After he had finished medicine he studied economics, and later worked as a bank director in the small town where I was born. After the war he became the financial director of the newly formed Film Polski, the start of Polish film, in Warsaw. His medical degree, however, turned out to be very important in Sweden. So, his father's wish that he study medicine turned out to be a blessing and this was important in my decision to study medicine or rather my parent's decision that I should do that. As long as I remember the idea was that I would study medicine, a profession that could be practised all over the world. So, in a way I had no choice, I was destined to study medicine.

I: Your parents left Poland in 1946. This was under the Communist regime?

R: It wasn't really clear in '45-'46 what would happen. A provisional communist-dominated government had been installed, but there was also a government in exile in London which was recognised by several countries. Free elections had been promised but were postponed and so as I understand it

the situation was very uncertain but clearly the Soviet Union increasingly took over power. But this was not the only reason for them to leave. Practically all relatives had been killed during the war and they were afraid to remain in a country where all the terrible events that they had experienced had taken place, and possibly could happen again. My parent's decision to leave the country was very much encouraged by a cousin of my mother who had emigrated to the United States with his brothers and their father at the beginning of the century. He, uncle Charles, was poor but his two brothers were very well off. Charles bombarded my parents with telegrams warning them about the future in Poland. "Leave that country as soon as possible. Come to the United States, to New York, my brothers will take care of the economy" My mother was a dentist and they would arrange a dentist office for her and my father could work in the brothers' business. How that would have worked out I don't know, but anyway they decided to leave Poland.

I: So, why did they decide to go to Sweden?

R: Well, they didn't. It was just by chance that they ended up in Sweden. They were going to the US but in those days there were no direct flights from Warsaw to New York so you had to stop either in Berlin or in Stockholm. Naturally, just after the war they didn't want to go to Berlin so they chose Stockholm. When they arrived in Stockholm it turned out that they had no visa to the US which they thought Charles had arranged. Obviously this was a misunderstanding. So there they were on transit in Stockholm waiting for the visa and they had no money. You were allowed to bring then I think $2 each. Charles sent some money so they would survive but time went by and after a few months they realised that they had to find some work.

My mother being a dentist was very welcome in those days in Sweden. This was at a time when dentistry was developed as a nation-wide, paid by the state, service and so dentists were needed, particularly in northern Sweden. Few Swedes would go to the extreme north, at the polar circle, where we ended up. My parents didn't know anything about the place where my mother had got the job. They had found out that some 70,000 people lived there. It was like a small town in Poland. It turned out that it was the entire northern county that had 70,000 inhabitants. Where they arrived then in October or November was a very small village of maybe 600 people, snow, dark and cold. They were sure that they had been deported to Siberia, that this was a trick by the Swedish government. But anyway my mother began to work and I started at school and we were awaiting the visa. The visa finally arrived but it took a year or so. In the meantime, two of my father's brothers had emigrated to Australia and they wrote letters saying "Why are you going to New York? Come to Australia, Melbourne; this is paradise" "Here you have two brothers, and we'll arrange everything for you." And by a strange coincidence a sister of my mother had also ended up in Melbourne. So, the obvious question was "Why don't we go there?" My childhood has revolved around this question, "Shall we go to New York or to Melbourne?" And well, to make a long story short, we stayed in Sweden. My parents found that this was a good and decent society and they decided to stay. The problem was what would my father do? The medicine he had studied in the 20's in Poland was of no use and he couldn't possibly start to work as a doctor and the economics was of no use either. Then he found out that in Austria you can become a dentist with a medical degree, in Austria dentistry is a medical speciality; it was at least then, I don't know if it still is. So he actually went, 50 years old, to Austria and studied dentistry for three years, became a dentist, and then they both worked as dentists in Sweden.

I: And what was the name of this small town or village that you were living in?

R: Överkalix. It's a very small place. At the polar circle.

I: Really far north?

R: Yes.

I: And you went to school there throughout your…

R: I went to primary school there, and when I was 16 I went to high school in Luleå, which is a town some 120 km away, and after three years I graduated and it was time to study medicine, which had been decided for me.

I: So where did you go then to study medicine?

R: Well, the problem was that I didn't have sufficiently good marks to enter medical school. It was not as difficult in those days as it is now but still it was quite difficult to be admitted to study medicine. But there was in those days the possibility that if you study other subjects at university, and almost anything was okay, that would increase your points. This was I think a very good system because many students learned various subjects outside their future professions. The easiest subjects, according to the students, were sociology, ethnography, statistics and genetics. And so I studied these four. [laughs] And that was my contact with genetics.

I: Where was it?

R: This was in Uppsala.

I: Uppsala.

R: Yes, because that was the closest university. The university in Umeå didn't exist then and so in '59 I came to Uppsala and I was there for 3 semesters and made the exams in these four subjects, which was enough to enter medical school. Then my parents had moved to southern Sweden, to Småland, which is quite close to Lund and so it was reasonable that I would study in Lund. So I started medicine in Lund in January '61.

I: And when was the first time that you had any contact with genetics in Lund?

R: It was just by chance two years later during my medical studies. A friend of mine, we were on the same course, had also studied some other subjects including genetics before medicine. Many of the medical students, in those days, had studied genetics in order to enter medical school. And so we were discussing one evening that if we undertook an additional advanced course in genetics, then we would get a bachelor's degree, and to have an academic degree as medical students sounded nice. And so we did this, and it was interesting but I can't honestly say that it fascinated me. It was just a way to get the extra points for the bachelor's degree, but it became the starting point because I had at least come in contact with the subject.

I: And who was head of department then?

R: It was Müntzing. About two years later, during the pathology semester one did a small scientific project and since I had some knowledge about genetics I thought that I might try to do this on something in genetics. Then I was brave and I went to Albert Levan and knocked on his door, which I don't understand how I dared, because I didn't know that he was such a kind person, I mean a professor in those days was such an important person but I did and he accepted me as a student. And so I did a small work which led to a publication, my first publication, it was on a Rous rat sarcoma cell line that I inoculated into the cheek pouches of Chinese hamsters and I looked at the

chromosomes of the sarcomas that grew in the cheek pouches. I have forgotten the results. Anyway it became my first publication.

I: I see, I have it from *PubMed* 1965 in Hereditas and you were the only author on that paper.

R: Yes. In those days, at least in that institute, if you had done the work you were the only author even though Professor Levan had rewritten almost everything. He came with his bicycle to the student house where I stayed and left the manuscript in my mail box with a letter saying that ”did I mind that he had made some small changes….”; it was in fact totally rewritten, but he wouldn’t be an author.

I: That’s nice and indeed I think that was the custom in most places.

R: Yes, if I look back at my earliest publications I was the only author on several which today would be impossible.

I: So what, what age would Professor Albert Levan have been at that time roughly?

R: He was born in 05 so he was 60.

I: And am I right that he was not head of the institute but head of group?

R: He was head of a group which was called the Cancer Chromosome Laboratory which was within the Department of Genetics, but he was not a head of the department. Müntzing was the head of the department at the time. Levan had a quite small permanent group. He had guest visitors from abroad who came for shorter or longer periods but it was a quite small laboratory.

I: So at what point did you become part of that in a more full-time way rather than just doing it as a side project?

R: I finished medicine in ’69 and in the meantime I had worked for some time, almost a year altogether, as an orthopaedic surgeon which I liked very much. Probably whatever you start with you find interesting, and I think I was reasonably good at it also, and I think I would have become an orthopaedic surgeon. By chance one day I met my professor of pathology, his name was C.G. Ahlström who was a very nice person and a good scientist. He had introduced the Schmidt-Rupin strain of the Rous sarcoma virus which could induce tumours not only in chickens but also in rodents. Anyway as I recall it I met him on a Saturday morning in the book shop where one usually ended up on Saturdays and he asked me what I was going to do. I told him about my surgery plans and he said, “Why, I think you should do something…” to the effect, “why don’t you do something scientific? At least come on Monday and we can discuss it.” And so I saw him on Monday and that was the start of my scientific work at the Department of Pathology in Lund. Ahlström and Albert Levan had initiated a project where they studied the chromosomes of sarcomas induced by RSV in different animal species and I was assigned to rat tumours which became my PhD thesis. A few years earlier Joakim Mark had finished his PhD on studies of mouse sarcomas induced by this virus and he became my supervisor. I worked on this project for 3 years.

I: And then at what point did you graduate to human genetics?

R: I finished my PhD in 72 and then I began to doubt if I really wished to continue with pathology for the rest of my life. The experimental work was fun but I never liked to do autopsies. The prospects were very good, there were few pathologists so the future was bright but I wanted to work with patients. After all, that was the reason I had studied medicine. So, I moved to the Department of Internal

Medicine and I was assigned to one of the wards where leukaemia patients were treated. There was no department of haematology then. And so I started to study leukaemia chromosomes. I had to learn human chromosomes and to make bone marrow preparations and of course banding which had been developed at that time. In order to learn how to obtain good quality banded bone marrow preparations from leukaemias I visited some of the few persons who had experience in this field namely Peter Nowell and David Hungerford in Philadelphia, Janet Rowley in Chicago, Avery Sandberg who was then in Buffalo and Jim German in New York. By then I had received a small grant from the Swedish Cancer Society which covered the cost of a technician and the two of us started to do some clinical cytogenetic work at the Department of Medicine, mostly research but some of the results were also used as a diagnostic help.

I: Was there any clinical cytogenetics already in Lund?

R: Yes, there was. Nothing official, no department, but there was a paediatrician whose name was Bertil Hall who did studies on constitutional chromosome aberrations. He had written a thesis on Downs syndrome in 1963. He was of the same age I think as Karl Henrik Gustafsson, you know, in Uppsala, who also wrote a thesis at the same time on Down's syndrome. Hall had a small lab with one or two technicians at the Department of Genetics where Albert Levan was and he did chromosome studies on blood samples from patients in the southern part of Sweden. Hall also provided some genetic counselling at the Department of Paediatrics at the hospital.

In '72 or '73 I met Jan Lindsten in Stockholm at the annual meeting of the Swedish Medical Association and Jan told me that there were plans by the local government in Southern Sweden to create a clinical genetics service in Lund. Of course this had been initiated by Bertil Hall. Jan Lindsten had been asked by the local government about his opinion and his advice was to establish an independent department of clinical genetics at the hospital, just as the one in Stockholm where he was the head. And then he said, "Wouldn't that be something for you?" And I said, "I've never thought about it." And really I hadn't because I didn't know anything about constitutional chromosome abnormalities or genetic disorders. I had so far only worked with rat sarcomas and leukaemias. Also, in my mind Bertil Hall was the only candidate for such a position. What I didn't know was that Hall apparently was a problematic person and had several enemies, including the director of the hospital. I later learned that the director had said once, "Only over my dead body!" would he become head of any department at the hospital in Lund. And so, since Hall was the only clinical geneticist at hand, the decision to establish the new department was postponed. In the meantime I worked happily with my leukaemia research combined with clinical work at the Department of Medicine. Then Bertil Hall suddenly died in '74 and after that things got started. It was quickly decided to establish a department of clinical genetics at the hospital and so suddenly there was a position available as the head of a department but nothing else. [laughter] There were no labs, no offices, there was nothing.

I: I'm familiar with that situation.

R: The position was announced in early 1975. I still wasn't sure that this was really something for me, but I applied and so did Maj Hultén and Jon Jonasson and someone whose name I have forgotten.

I: Were the others at that time working in England or was it before they went?

R: No, it must have been before.

I: So they were from Stockholm?

R: Yes they were. Well Jon Jonasson had worked with Harris in, is it Oxford or Cambridge?

I: In Oxford.

R: Oxford. And he'd done some good experimental work that indicated that the tumor phenotype may be a recessive trait. He was probably back in Stockholm, and Maj Hultén was certainly in Stockholm at that time. The reviewers found all three of us to be incompetent, because we had no formal training in clinical genetics, which was correct. I certainly knew nothing of human or clinical genetics. But anyway I was appointed [laughs] as the head of the new department. This was a pure hospital position. So in '75 I became the head of the Department of Clinical Genetics with no positions and no space, well I had a technician and some research money from the Swedish Cancer Society and also actually there was an agreement that the hospital would take over the two part-time technicians that Hall had had at the Department of Genetics.

I: Yes.

R: Then the professor of clinical chemistry generously offered some space in his department at the hospital. We got a small office, a room for karyotyping, part of a small lab, and were able to share a tissue culture hood with the chemists. That was all. [laughs] And I didn't know anything about medical genetics. I left the Department of Medicine in early June, and we went to Greece for vacation as we usually did in those days and I bought Stern's book *Medical Genetics* or maybe *Human Genetics* and I read it carefully during this vacation time. That was my only education when we started.

I: It's quite a large book.

R: It's quite a large book. [laughs] It wasn't that clinical.

I: Not at all. But a very good book.

R: And so we started. One important reason why the hospital started this service was the need for prenatal diagnosis. The diagnostic service previously provided by Bertil Hall on constitutional chromosome aberrations was of course also requested by the paediatricians in the region, but the main reason for establishing the department was the requirements from pregnant women for a prenatal diagnostic service. It was of course a very modest start. I remember well that we had 5 prenatal diagnoses from July '75 until the end of the year. And we treated them like babies. Once we had planned to go on a one day visit to Margareta Mikkelsen in Copenhagen to learn some tissue culturing modification but one of the technicians refused to leave our prenatal cultures; she didn't dare to leave it for a day. [laughs]

I: So thinking in terms of the overall development of medical genetics in Lund, when did you begin to do any clinical genetics or genetic counselling work, or did you recruit some other people to help you?

R: That began immediately in July '75. I did the counselling but there weren't that many, mostly discussions around prenatal diagnosis. Then each pregnant woman should meet a geneticist before deciding on prenatal diagnosis, and I was the only one. I was alone for several years until Ulf Kristoffersson came around 1980 or so, I think. So for 5 years I was the only doctor but early on we got a secretary and some technicians, the number of technicians increased to 5 or 6 after 5 years. But then I also had another 2 or 3 research technician and research grants and I put all this together, I didn't distinguish between research and what was clinical work. We had a budget in the hospital and I mixed this with the research money, I'd share the costs for the clinical samples with research and…

I: In those days it was possible to…

R: Yes, no one cared. And I started to get people from abroad because we did some good leukaemia work, later also solid tumors, and young people from abroad came to learn. They had their own money from their home institutes. Some, but not all, were PhD students, and so the group increased and in 1979 we moved to a new place, actually back to the Department of Pathology. We got some additional space within the department, but it's always been an independent department of clinical genetics. Then, in 1985 we moved into a new building at the hospital where the department still is today.

I: Thinking of your research during this time and looking at your very extensive publication list, how easy was it to maintain your research while you had these clinical genetics responsibilities?

R: Well the clinical genetics responsibilities weren't that heavy. The laboratory work was done by the technicians and they were very good and I only had to supervise them, and initially the counselling wasn't too demanding, maybe half a day twice a week. When the work load increased the staff increased and I got some young doctors who took over the genetic counselling. And, there was no or very little bureaucracy, very few meetings, so I could spend most of my time on research. I regarded myself as a researcher rather than a clinical geneticist; the clinical work was a means to be able to do research, but I didn't put my heart into it, let's put it that way. And to be honest I think I worked a lot also [laughs]. The clinical leukaemia material was of course the basis for my research and led to international collaborations, the most important was the international workshops in chromosomes in leukaemia, where I met all those scientists who were known in the field at the time. This was a unique, nice and fruitful collaboration among cytogeneticists, pathologists and haematologists in order to obtain a well characterized large patient material that none of us had individually. In 76, I had published one of the first series of banded leukaemia chromosomes, I think there were 30 cases altogether. This was at that time one of the biggest series in the world but obviously too small to be able to draw any conclusions. By combining such data from different centers we could establish several clinical-cytogenetic associations. This collaboration continued for many, many years and became very important in that the results of the workshops helped to introduce cytogenetics as a diagnostic procedure in haematology. The workshops never found any new abnormalities; that wasn't really the idea, but they were able to establish important clinical-cytogenetic associations, in particular when we could show that the cytogenetic abnormalities had prognostic implications. And it all started actually with me and Janet Rowley on a bench at the International Human Genetics Congress in Mexico in '76 I think it was.

I: I remember it. I was there, yes.

R: As I told you, I had met Janet before in 74 in Chicago and we had corresponded since then. And then we met at this conference and we sat down on a bench outside one of the lecture halls and the idea came up that why don't we try to combine the leukemia materials from those centers that had published a reasonable number of cases. At this moment Albert de la Chapelle walked by and we told him what we had in mind and he thought that this was a good idea and suggested that we might have such a workshop in Helsinki next year because he was going to organise the 1977 Chromosome Conference in Helsinki and many of us would be there anyway. So we decided to have the first meeting a few days before the Chromosome Conference in Helsinki and this became the starting point of the international workshops on chromosomes in leukemia. The original study group was very small; the cytogeneticists were Janet Rowley from Chicago, Sylvia Lawler from London, Herman van den Berghe from Leuven, Avery Sandberg from Buffalo, Dieter Hossfeld from Hamburg and Albert de la Chapelle from Helsinki, and we were so formal in those days that we also invited Jan Lindsten, who

was the chairman of the ISCN, so he would oversee that we followed the correct nomenclature. In addition there was one clinical haematologist from each centre. This was in '77 and then we had new workshops on different topics every second year and the number of participants increased and we became life-long collaborators and friends. This collaboration was indeed unique at the time and led to many clinically important findings, and all this started with a conversation on a bench in Mexico City [laughs].

I: At what point did you start thinking about and creating your catalogue of chromosomes and cancer?

R: Well it started actually as a scientific project in the mid 70s. I had published together with, well, we haven't mentioned Albert Levan's son, Göran.

I: Yes, I was going to ask about him.

R: We collaborated quite a lot in the 70s and early 80s before he moved to Gothenburg. Göran and I knew each other from the time I did my first experimental work at the Department of Genetics. He was then regarded as quite lazy by his father; in those days he was more interested in playing the clarinet, gambling on horses, and he was a very good golf and bridge player. So he wasn't that focussed, to put it mildly, as his father would have wished. But when we started to work together he went through a metamorphosis and became a devoted and hardworking researcher and we published a lot together, especially on experimental tumors, but also on human tumors. One of these studies, which was published in 1975, was called 'Clustering of aberrations to specific chromosomes in human neoplasms'. It was essentially a compilation of our own data and what had been published by others. This was the first of a series of such "clustering papers" where we put together our unpublished data with data from the literature. What we found was that certain chromosomes were more often involved than others in rearrangements and we also included the genes that at that time had been localised to specific chromosomes, very few at the time of course. I remember we had a sentence in the first clustering paper saying something like 'hopefully when more genes are being localised perhaps an explanation may be found why some chromosomes are specifically involved in neoplasia." So there were reasons to continue to collect literature data. I also started to add something which I was interested in, namely the geographic location of the patients. That goes back to the rat work we had done before. My thesis was on Rous-induced sarcomas, then Göran and I studied sarcomas in rats induced by DMBA and Göran studied carcinomas induced by DMBA and together with work by Japanese workers on DMBA-induced leukaemias we concluded that it seemed as if there was a pattern in that the inducing agent was important in determining the chromosomal aberrations. Leukaemias, sarcomas and carcinomas induced by DMBA seemed to give rise to a similar pattern of non-random chromosome aberrations, whereas the RSV-induced tumours had another pattern. How could one test this hypothesis in humans? One idea I had was that if an inducing agent in the environment in some way influences the pattern of chromosome change in human tumours then this might be seen when comparing the chromosome aberrations in cancers of professionally exposed individuals, and so we did a study on leukaemias, where we looked at the professions of the patients. This was published in 78 and there was clearly a pattern in that some aberrations were more common in those that we regarded as exposed to potentially carcinogenic agents; I think an expert in occupational medicine might not agree to our classifications but anyway there seemed to be a pattern and interestingly a similar pattern was found also by Janet Rowley in patients with secondary leukaemias, patients who had been treated for cancer by cytostatic drugs and later developed leukaemia. I then thought that geography might be another way to indirectly study the effects of different exposures which might be different in different parts of the world. And indeed we found some striking geographic differences. Some translocations were more common, much more common, in Japan for example, than they were in Europe and so on. I was of course

encouraged by these findings to continue to collect information on the geographic origin of cancer patients with characteristic chromosome aberrations. But as the number of cases increased this became quite difficult. This was before we had computers and so I collected information on cases from different countries in different boxes but to extract data on combinations of specific karyotypic changes in different tumor entities in relation to individual countries was not easy. For several years I used cards in which one could manually represent the presence or absence of specific changes by holes in predefined positions. Do you remember them?

I: Punch cards?

R: Yes. You put a…

I: Rod through them.

R: Yes, there were holes at different positions for particular abnormalities and when you entered the rod at any position all cards which didn't have this abnormality would fall out, wasn't that so? For example, if one wanted to see cases with trisomy 8 you put the rod through the hole in that position and the +8 cases would remain on the rod whereas all the other cards would fall to the floor.

I: [laughs]

R: And this is how I worked with this material until the late 70s when computers became available. I then had to make a choice: should I stop this project because it was too much work; or make the effort to computerise the data? I decided to go on, primarily in order to continue the research on geographic heterogeneity of various aberrations. So one could say that the Catalog was in a way a by-product of this geography project because in order to be able to continue I had to collect data on everything that had been published on chromosome changes in cancer. At the same time, cancer cytogeneticists found the clustering data of interest and useful. Around 1980 I discussed this with Janet Rowley and her colleagues in Chicago and they urged me to regularly publish the total updated material on which the clustering papers were based. I remember I said, "Well I'm not sure I want to be the clerk for the cytogeneticists." I mean it's not fun to do this, [laughs] to collect all these data, but since so many had told me that the material was of general interest for the cytogenetics community, I decided to continue and I approached publishers and asked if they would publish the data as a book but no one was interested. Finally, Harold Klinger who was then the editor of *Cytogenetics and Cell Genetics* said that he would talk with Karger and they decided that they would print the Catalogue as a supplement to *Cytogenetics and Cell Genetics*. And so the first catalogue was published in 1983 as a supplement to this journal. It contained some 3,000 cases. Two years later again people asked me to publish an updated version but as before the problem was to find a publisher. Karger didn't want to publish it any more for economical reasons but then Avery Sandberg, who was a cancer cytogeneticist and the editor of a book series called *Progress and Topics in Cytogenetics* offered to publish a second edition of the catalogue in this series. The number of cases had now increased to 5,000.

I: And who was the publisher? Was it Wiley?

R: No, it was Alan R. Liss who had a quite small publishing house in New York. I met him for the first time in 1985 when I brought the material for the Catalogue to New York. In those days it was printed out in my place and then I carried the prints to the publishers and they photocopied the material and made a book out of it. I then got to know Alan Liss who was a very nice person and this led to three publishing projects which are still ongoing: the *Catalogue*, now in the form of a database, the journal *Genes, Chromosomes & Cancer* and the textbook *Cancer Cytogenetic*. Sverre Heim and I are just now working on the 4th edition of this book. Alan Liss later published the third edition of the Catalogue

but then Liss sold the company to Wiley and so it became Wiley-Liss and later Wiley bought Blackwell and it became Wiley-Blackwell.

I: Yes the world of publishing has changed totally.

R: So I continued with the catalogue. You can ask why. It was a lot of work but people found it useful both in the clinic and scientifically and that was an important argument. But a problem was that the book became bigger and bigger and by 1994 the 5th edition consisted of 2 large volumes with more than 4,000 pages which wasn't very user-friendly, and so in 1998 the 6th edition containing 30,000 cases was published as a CD. At that time the internet became an option and I thought that it would be a great idea to have the information freely available and searchable on the internet. There was no reason why people should buy this information because the work we did was paid by grants from the Swedish Cancer Society. But Wiley of course didn't like the idea, they wanted to introduce some system where you would pay for the service. I didn't like that and so in 2000 I organised a meeting at the NCI in Bethesda with representatives of Wiley, scientists involved in cancer cytogenetics, including Janet Rowley, Cynthia Morton and Jeff Trent, who was very active in those days with Francis Collins at the NIH, and the director of NCI who then was Richard Klausner. The topic of the meeting was to discuss how can we make this information available to the scientific community? NCI offered to have the Catalog on their web site but Wiley disagreed and claimed that because they had published the Catalogs in the past they had a copyright on the material which I actually still doubt. I mean, these are published data which I have extracted; the authors or the publishers of those publications may have a copyright but not the publisher of the Catalogs. It was a long discussion until Wiley finally realised that they had lost the battle. The decisive argument was offered by Jeff Trent. I knew Jeff quite well, he said "We want this information and if Wiley refuses we're going to do it ourselves in-house at the NCI. It's a pity that Felix has spent 25 years of his life on this, but we have the resources to repeat the work, and so we will have it anyway" and when Klausner said that he would support such a project, Wiley realised that they had to agree to allow the NCI to put the database on the NCI website. So in 2000 the Catalog became freely available to the community. During this meeting the question came up how the new internet-based database should be called in order to distinguish it from Wiley's product *Catalog of Chromosome Aberrations in Cancer*. A simple solution would be to call it *Database of Chromosome Aberrations in Cancer* but then people might not understand that this was actually a continuation of my Catalog. Someone then suggested that why not simply call it the *Mitelman Database of Chromosome Aberrations in Cancer* because then it would be apparent what it was. I thought that it was embarrassing to have my name on it but everyone agreed that this was the best solution and so that became the name.

I: It's been a fantastic achievement actually that, and may I ask do you still maintain it or have you handed it on largely to other people now?

R: Well, I actually do increasingly more myself now [laughter] again. Since the late 80' or so I shared the work with two very nice and hardworking collaborators, Bertil Johansson and Fredrik Mertens; they started as PhD students in my lab and when they finished their PhD they became increasingly involved and we divided the work between us; we did more or less a third each. This was of course a great help for me. In fact, I am not sure that I would have been able to continue without their help. They have done a fantastic job. But until then I had done it all myself and it became a real burden. I travelled everywhere with this work. I brought forms where I wrote down the karyotypes and I sent them to a secretary who entered the data into the computer.

I: I remember seeing you at meetings with these…

R: And now that I have more spare time I do most of the work myself, but Fredrik and Bertil systematically check what I've done and correct any mistakes I've made. During recent years the workload has increased because we started to include gene fusions. At the beginning this was not so much extra work because there were so few fusions known but with the increasing use of next generation sequencing several hundred new gene fusions are reported every year. On the other hand, the cytogenetic data don't increase as much as it did in the past and the work has in general become easier nowadays because one can copy/paste karyotypes and gene fusions from the publications. We have to adjust and correct for accuracy so that they follow the ISCN and gene nomenclature rules and so on but still it's much less work than it used to be.

I: What you have said reminds me of Victor McKusick with OMIM and there , I went to some meeting because they were worried what would happen to OMIM after Victor and he was meant to retire from it so they divided the work for 6 other people to do and then 5 years later…

R: [laughs] They complained?

I: No, they looked at who did the work and still Victor was doing three quarters or more of the work and these others were doing the rest!

R: [laughs] And his work was really something fantastic.

I: Can I ask: from the catalogue have you been able to use it a base for synthesizing and making general conclusions on cancer and chromosomes? Do you think it's been helpful with that?

R: Yes it certainly has. For example, we have been able to describe different patterns of non-random chromosome variations and karyotypic pathways, including imbalance maps, in a number of different tumour entities. All these studies would have been impossible without the database. The breakpoint map of recurrent chromosomal rearrangements in human neoplasia, which was published as a special issue of *Nature Genetics* in 1997, was based entirely on the database. Another example of data synthesis was the demonstration that chromosome aberrations in cancer follow a power law distribution and also in another study that the genes involved in gene fusions form interconnected networks. More recently, in 2004, we suggested, again based entirely on data in the database, that fusion genes may play the same important pathogenetic role in malignant epithelial tumours as in leukaemias and sarcomas. Until then the general consensus was that fusion genes were not important in epithelial carcinogenesis, because so few fusion genes had been detected in carcinomas. We calculated the number of cases with abnormal karyotypes in different tumour entities, including epithelial tumours, as well as the numbers of fusion genes which had been reported in all tumour types and found that the association followed a very nice straight line. So it means that the more cases you study the more fusion genes you find, which is perhaps reasonable [laughs] but this was anyway not appreciated until then. And now it has turned out that epithelial cancers have so many fusions found with next generation sequencing. You know that last year 600 new fusion genes were published in cancer, only in 2012. During the 3 decades from the first fusion genes were reported in the early 80s, when the findings were guided by cytogenetics, there were also 600. So for 30 years 600 were found based on cytogenetics and cloning the breakpoints. And now in one year you have 600 [laughs]…

I: It's amazing.

R: It's amazing.

I: Can I ask you: when did you start to have contacts with the constitutional gene mapping community and the human gene mapping workshops?

R: Well, I was not active but I participated in the first workshop, was it New Haven?

I: It was New Haven.

R: It was decided then to have a committee on neoplasia, like the committees on different chromosomes. So neoplasia was treated as a chromosome; I think the first chair persons of the neoplasia committee were Albert de la Chapelle and Roland Berger. The committee regularly summarised all characteristic abnormalities in neoplasia. Later, after a few years, I became involved and I was on this committee for many years with Jeff Trent, Roland Berger and Yasu Kaneko, I was the chairman of the committee between 1988 and 1996. We didn't really have much contact with the other committees because they worked on their genes on specific chromosomes; we mostly summerized chromosome changes and the cancer genes and they weren't that many, after all, perhaps 20 fusion genes were known in 1990, probably less than 100 at the end of the 90s; something like that. And then the committee disappeared whenever it was, around 2000 maybe.

I: Yes, it was I think after the 2000 London meeting they disbanded this in the favour of separate chromosome meetings.

R: Yes.

I: Which I think was a disappointment for many of us.

R: You mean it was that late, 2000?

I: I think that's right.

R: Because I think, I wonder if the cancer committee…

I: Maybe cancer had left.

R: Yes, I think that cancer had left before; had been omitted; they weren't interested and also there was something with the organisation of these meetings which was problematic. Someone took over this and there were some conflicts there which I don't remember.

I: I don't remember either.

R: No.

I: I was going to ask just a couple of things before we finish: one thing as an outsider to the field is: you have really spent your whole career in Lund, was that just because it proved a good place to work and a nice place to work or was there any special reason?

R: Well the reason was that I was so young when I started the department. The usual way in those days was that after you finished your PhD you would go for a year or so to the States as a post doc. But that was at the time when I moved to the department of medicine and had to learn a new profession. I mean I was going to become an internist and so I couldn't really go. And then I became the head of this new small department, and so I couldn't leave for several years. And then the department grew and we became one of the leading centers and so people instead came to us from abroad to learn.

We had a very large number of foreign students in the lab when cancer cytogenetics had its high peak and we had started working on solid tumours in the '80s when almost nothing was known about chromosomes in solid tumours. We had PhD students on every possible organ. So one PhD student worked on prostate cancer, one on lung cancer, one on breast cancer, and so on, one student on practically every organ. And this was so exciting that there was no reason for me to move. Then the chair of clinical genetics was established in 1980. So I had to stay to fulfil my duties as a professor. There was a very good system in those days that as a professor you could have a sabbatical every 5 years and my plan was to collect the sabbaticals and then I could go somewhere for maybe for 2 years or so; but then they changed the system [laughter] and so I lost all my sabbaticals. So one thing led to another, but no, there was no reason really to go anywhere, which would have been nice probably, but then I travelled a lot anyway and met people.… And Lund is as you know a nice, small town.

I: Yes, very nice.

R: And it's easy to reach places, I mean if you look at Paris where we are now it would take so much of your time just to go to work. So I've been happy in Lund.

I: I've been asking every person I've interviewed two questions and the first is: which particular people do you think have had a special influence on your own career and professional life?

R: Certainly two people: Albert Levan was of course the most important one because he introduced me to this field and he opened so many doors and was so kind to me. The other one who has meant a lot is Janet Rowley. We have collaborated for many years, we haven't published very much together but we have always been in touch and shared ideas and questions, and we started the journal *Genes, Chromosomes and Cancer* together in '89 and worked with the journal since then. I would say that scientifically these are the two people, but then there are a number of others of course, I mean collaborators who have been very nice and good and helped me in many ways. I should add my professor in pathology where I started my career, Professor C-G Ahlström, who was very generous and helped me a lot at the beginning.

I: The other thing I've been asking everyone is: if you had to just choose one part or area of your work, which do you feel you would choose as your favourite contribution, not necessarily perhaps the most important scientifically, but what you feel is maybe your particular one?

R: Well in terms of pleasure it was a paper I published in *Nature* in 1984 because I did all calculations by myself at the kitchen table at home late at nights. I identified the breakpoints in all known chromosome aberrations seen as the sole abnormality in human cancer and leukaemia, and found that they affected a surprisingly limited number of chromosomal regions. It was such a fun to see this pattern in the kitchen at home. Otherwise I think the best science was the early Rous virus work, the rat experiments. That could have been developed much more, the role played by the inducing agent in determining chromosome and genome rearrangements is still an open question. The most important work is probably the specific chromosome aberrations and the gene rearrangements we have found in different cancers which are used as diagnostic and prognostic parameters. As a doctor I think that is the most important work because it's used today in the clinic for patients.

I: There are lots more things Felix we could talk about, but I think it's time to draw things to a close. But is there anything important that we have not mentioned at all that you feel ought to be on the record?

R: I don't think so. Nothing I can come up with; no, not really. I think I've said more than I thought I would say. [laughter]

I: Well thank you very much. I'll turn off the machine now but very many thanks.

[END OF TRANSCRIPT]