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Professor Kay Davies CBE in interview with Dr Max Blythe
Oxford, 12 November 1996

MB Professor Kay Davies you were an April Fools Day baby in 1951.

KD Absolutely, yes.

MB Stourbridge.

KD Thank you, yes.

MB Right in the Midlands there. So we have placed you. We have placed your origins pretty securely. Tell me about that early life in Stourbridge your parents and your family.

KD We were right on the edge of the country. So it was a lovely place to live because we used to go away every weekend, sort of somewhere into Wales. Because in those days there was no traffic, and with two brothers, the best thing to do with three kids is just to get out of the house, basically.

MB You had two brothers.

KD Yes.

MB One older and one younger.

KD One older, one younger, two years either side, and I was the piggy in the middle.

MB But you were saying you got out a lot. You were kind of outdoors people.

KD Yes. Well both my parents loved the country and so that's what we were out doing; picking the bilberries, swimming in the rivers, that sort of thing.

MB So it was a great natural history component in the background.

KD I think that is where the love of biology and various things really started.

MB Especially on those kind of Welsh borders.

KD Snowdonia. Yes the Berwyn Mountains etc.

MB You got right out into Wales.

KD Yes.

MB What about parents, apart from taking you out and taking you about. What did they do? Tell me about your father.

KD My father was a toolmaker at British Leyland. Initially he worked shifts, so we didn't see that much of him, but then he went onto day work. He was a craftsman and, actually in his later years he actually then bought himself a lathe and used to make things. So in fact for my child, now, I have got these wonderful things.

MB He still uses his skills.

KD Yes I still use his skills, you are telling me!

MB And anything that needs fixing.

KD Yes anything that needs fixing.

MB You just call him up.

KD Yes absolutely. Dad comes down and does it, anything from the garden gate to something more intricate like a little wheel on somebody's trolley.

MB You had better put him on the record. Your family name was Partridge and he was called...?

KD Harry Partridge.

MB And your mother was more of a driving force. Was that right?

KD Yes she doesn't like sitting still. Well that is where I get it from really.

MB In my notes I describe it from what you said, as someone with a metronome ticking inside.

KD Yes she drives you nuts. She never sits down for a minute. She is always onto the next job.

MB But very efficient.

KD Yes.

MB And a bit of that might have rubbed off?

KD No, she was extremely organised, that is exactly right, because she had this part-time job working in the glass factory, and she used to make sure she was home for us for when we came home from school. So it was ideal really.

MB And she was a great gardener?

KD And she was a great gardener, yes. I mean that is the love of her life, that and reading books.

MB So father is a very practical person, helping in the garden a bit and she...

KD He does a lot now, but he didn't used to do as much. But she will tell you the Latin name of every flower in your garden, whereas he will tell you how to dig it out and where to move it.

MB It still looks pretty good that garden does it?

KD Oh yes. It looks fantastic, actually.

MB Stourbridge. You have said that it was in an excellent kind of setting in those days because it really was countryside.

KD Well, yes because it was right on the edge of the Black Country and....

MB As a girl just around there, what was it like growing up in Stourbridge, does it have a village feel to it?

KD A little bit, and particularly since my parents moved into the house that they were in and still are in, when just after I was born, in fact, and there were several houses around, so it is an immense community now, that still exists, where we all grew up together. So most people had two or three kids and they were all more or less the same age and we always used to go to the end of the garden out into the fields.

MB So you were part of a big jamboree really.

KD Oh yes.

MB Lots of friends very early.

KD Of course we still keep in contact. I mean, I go home and those friends are visiting.

MB You go home a lot.
KD Oh yes, very much so.

MB You, I think used to go down to the canal and ...

KD Oh well, that was a cycle ride, of course, as well, because we used to go out on our bikes and out towards Kimber, over Kimber Edge, and that meant going over the canal on the way.

KD How did those brothers figure in your life? Were they close?

KD We weren't as close then as we are now. I think if there are three of you, you quarrel a lot actually. Which ever way it goes, it is two against one.

MB Yes. And did you get the worst of it sometimes?

KD Not always.

MB But they were there. You go to school in a local primary school eventually.

KD Yes, which was a mile and half away, half way.

MB Has it got a name or is it just a local .....

KD No. Gigmill Junior School and it is still there.

MB And that had impact because I think a headmaster there was quite insightful and quite helpful.

KD Yes. He was very keen on maths. So he used to come into the classes and ask particular maths questions, and really inspire people to sort of think about it, and tell you jokes, mathematical jokes or little puzzles which you could take home. I mean he was really in love with the subject and that really did inspire me a lot.

MB Was that the first time when you really felt that you stacked up in a special way because I think you got out some of the conundrums that he set in quite a quick way and they became an important part of your life?

KD Absolutely. I used to look forward to those a lot.

MB And as I say you came out on top quite often.

KD Yes, and it became a great challenge for me, and of course he nurtured that. So that made a big difference and also it gave me confidence because I was quite a quiet mouse, and sometimes still am.

MB I don't believe it, but that really was important. And he was called?

KD Mr Powell. In fact, he still follows me because, occasionally in fact, just recently when I got the CBE last year, he wrote a letter to my parents because he doesn't know where I live of course, and that was rather special.

MB That was good of him to write.

KD Yes.

MB That must be very satisfying for him.

KD Yes.

MB What of that school otherwise; were there important relationships, important things that happened there, apart from Mr Powell?

KD Not really. I guess there is one school friend that I still have, who actually lives locally here in Oxfordshire.

MB That is a friendship that has carried over many years.

KD Yes.

MB Going from there, you got a place at the Stourbridge Girls High School.

KD Yes, the High School which no longer exists.

MB Was that a kind of scholarship examination?

KD No, it was the eleven plus, the classic eleven plus. Yes.

MB And you went across there. Was that a very important move?

KD It was a big move for me because I found going to a bigger school quite an intimidating process, I guess. And I can see that in my son now. You forget these things until it happens to the next generation, but going from just a few hundred to several hundred is a lot at that age.

MB You clicked into gear and started to work, because you had strong points, like mathematics, and so you found your feet quite quickly and make your mark.

KD Absolutely.

MB So you did settle in.

KD And again I had some very good teachers. And it wasn't until later in the third or fourth year that I started to do chemistry, and I had a brilliant teacher then who was really concentrated. I mean school was her life, and bringing girls on, in particular.

MB Although that school was really geared to classics and more traditional grammar school education, and science was like a wing that some people got involved in, but not the main stream. Is that right?

KD That is exactly right and in fact I had to make the choice between Latin or biology, and had to do Latin just in case I decided later on to do languages instead of science. I mean there was an enormous push against doing science for a woman at that stage.

MB So at school you were actually saying you lost out on the biological sciences.

KD Yes I did.

MB But the chemistry was not going to be denied once you had got into the science in the third year.

KD No, because I think once you had done 'O' levels, as it was then, you had to do physics, chemistry and maths and, you know, I think if they hadn't tried to push me towards languages, I would have done physics, chemistry and biology as those 'O' levels, but as it happened, I don't regret doing Latin because I think it was a good exercise.

MB Coming back to the teacher who was good on the chemistry side. Who was that?

KD Miss Presley. She was a great golfer.

MB She came into your life in the third year?

KD No, no. In the sixth form.

MB Oh in the sixth form. Science was turned on, you were suggesting, when you were a bit younger than that, and you did want to do significantly well.

KD Yes that's right, but that was much more maths bias. It was just that I had a certain aptitude to do maths things very quickly.

MB Were you hard working?

KD Yes, but I think I always have been.

MB Very conforming, working to get everything done.

KD Yes, terribly boring in that respect. But, you know, I think young girls tend to be like that. They tend to be much more focused and motivated.

MB Just staying with that.....

KD I didn't feel any different than anyone else. I think all my colleagues tended to be fairly hard working. I don't think I was particularly intense, but I certainly was motivated to get the homework done.

MB You were studious and taking it all very seriously. Those early years, you also did other things apart from just going to school though. I think you played a musical instrument?

KD Yes, I played the piano and I enjoyed that. I only took it up to Grade V or VI. But music is very relaxing and that has always been with me and I always work with music at home.

MB And you are into sport.

KD Yes, I play tennis quite a lot and I certainly played tennis quite a lot then, because I used to play for the school occasionally and I used to play for the school hockey team.

MB So there is a balance there, and you also had a range of family interests. Because it wasn't just family at home; your mother had a sister who was younger who you helped on occasions, so you did a lot of baby-sitting.

KD Yes that's right, because there was a decade difference between my mother and her sister so, in fact, I was coming up to ten or eleven and she had her children and so I was just coming up to the right baby-sitting age. And actually they live just north of London, so I used to, in the holidays, go off and do some baby-sitting for them. And that was a great experience for me because it was away from home long before, on a regular basis, before I went off to university.

MB I think it was a contact with Oxbridge because your aunt's husband was an Oxbridge figure.

KD Yes my Uncle Paul went to St Peters.

MB Who is your aunt.

KD Olga. Yes.

MB Right. So Paul and Olga made an impression.

KD Oh they certainly did.

MB You were a people watcher in a way and you found him interesting and he was somebody you admired quite early.

KD Oh absolutely.

MB Like Mr Powell and Miss Presley.

KD Yes, because he always aspired to doing things well. He had enjoyed his Oxford days so much that he was always talking about it and how well he fitted into the system, and what an experience it was and how it helped him in business later on.

MB So as a young teenager...

KD He was also a great doer. I always remember him riding up and down the road on his red motorbike. You know, if someone was going to do something mad, Paul would always do it. And I always remember that and I sort of admired that freedom of spirit really.

MB Relationships with the girls at that school, they were quite good. You had some further good relationships that carried you on.

KD Yes I did. I mean that was a pretty close knit community in the sixth form and again with only three of us doing chemistry 'A' level, that sort of pulled us together.

MB Now let us take that sixth form story in now, and Miss Presley, let us bring that on stream; she really did make a massive impact.

KD Yes she did. She was very practically biased. She used to be there with hands on and with three of you, of course, she could give a lot of individual tuition.

MB Just the three of you. And she used to leave you and ...

KD And go off and play golf. She was a spinster and she loved golf and she loved teaching chemistry. She really sort of ...

MB Was it like Mr Powell, did she leave you kind of things to work through?

KD Absolutely. She couldn't leave us doing practical work, even in those days that was considered a little unsafe.

MB But you did do that kind of risky practical open flame stuff in those days that would never be allowed now.

KD Oh yes indeed. Making hydrogen cyanide and that sort of thing and just smelling it. Yes, those sort of practicals would be banned these days.

MB What a start.

KD Yes.

MB What was so good about her teaching? I am trying to put her on the map so to speak.

KD Because she was so inspiring. I mean she could see it from all angles. It wasn't just a case of coming in and learning and doing the next chapter. I mean she would make a story about it, you know, what relevance organic chemistry had to drugs or plants or whatever.

MB So all that teaching kind of pointed to new insights.

KD Yes it did.

MB So very quickly you decided chemistry was probably going to be about it.

KD Yes, and she was a pusher too. I mean I never dreamt of going to Oxbridge and naturally neither had my parents. It was Miss Presley who first suggested that we might think about that. So she was definitely making, forcing all three of us and actually the other two went on and did well too.

MB So you worked for Oxford entrance.

KD Yes that's right.

MB From that first year in the sixth, I guess, because you came up to Oxford after just two years in the sixth form.

KD Yes. In fact that was just going through my mind as you asked the question because I was definitely coming up for interview - in fact I was going through some old photographs - in a stiff suit as we used to do in those days. I had never worn a suit in my life before, it was terrible.

MB You felt out of your depth.

KD I certainly did.

MB So you came up for interview. Did you do examinations in the colleges at that time or were they kind of ?

KD No. They gave you little tests to do, but it was quite a friendly experience. It was mostly across the table type of chat.

MB And you were offered a place.

KD Yes and I was offered a place. I was very fortunate actually.

MB Somerville, a pretty class college.

KB Yes, and then again they were very welcoming and supportive.

MB This was quite a thing for somebody coming from Stourbridge, from a High School, quite a success story.

KB Yes. But I also found it very difficult. I found it hostile at first because everybody then had seven 'O' levels, four 'A' levels, three 'S' levels, and you see my school never did more than seven 'O' levels and would never do more than three 'A' levels, and I did two 'S' levels.

MB Most of these students had spent an extra year preparing.

KD That's exactly right.

MB So you came up as a baby in the Oxbridge family.

KD Yes, and everyone is very insecure when they come up at eighteen, so there is a tremendous amount of competitiveness, in everything from the very material all the way through to the academic side. So it was tough.

MB And you came across, at that time, a lot of people, I should think, from the public school sector.

KD Yes, most of them, in fact. But not everyone in my year, which was fortunate. So there were two other people in that year, in that chemistry, who were in the same similar background to me, and so in the end it didn't really matter.

MB No, but at the beginning it was quite hard settling in.

KD Yes it was.

MB I mean you were a home loving person. You had left home, that was a big shock to the system and then all of a sudden you are in with a lot of people who haven't quite had similar backgrounds, and you are pushed into quite a big pond.

KD That is exactly right. But on the other hand Oxford is very competitive, but on the tutorial basis you at least have the opportunity of shining at your own level, and I

think that is it's real strength because it builds you up in confidence in a gradual manner.

MB So the tutorials in Somerville really helped.

KD Yes.

MB Do you want to talk about the tutors in Somerville?

KD Well Eva Richards was a good one actually, and whom you may know. She was very inspiring. And, of course, Jo Peach, who is still at Somerville now, did a lot and again getting the biological slant because that is what I really wanted. And she was the organic chemist who was for ever saying, 'Oh this is applicable to that? And eventually I went on to do my final year in chemistry, in biochemistry and again it was Jo Peach that suggested who I might go and see for that.

MB I am trying to trace that feel for the biological that came in quite early in that course. Was that really Jo Peach that began to develop that, or was that there a bit?

KD No, it was there a bit even coming from the 'A' level, but she picked it out and defined it as we went through the tutorial schemes.

MB So that was a big support to that interest, that she gave. In the actual lecture rooms though, it must have been rather unsympathetic, initially, because you move around quite fast. It's not quite like the quiet family atmosphere of Stourbridge High. That must have been quite a thing to accommodate to.

KD Actually it was the men that I found particularly difficult. You were six women in a class of a hundred and eighty, and we always used to sit on the front row. It was amazing. So you were never short of boyfriends because there weren't enough women to go round in that particular subject. So you met a lot of people very quickly. But on the other hand there was quite a lot of pressure because of that.

MB You haven't talked about growing up in the sense of boyfriends. Was that part of life by then? I mean you have had school boyfriends, you've not missed out on that.

KD I've not missed out.

MB But nobody of any significance.

KD I had a boyfriend for about two years before I came up to university, a steady boyfriend as they used to say in those days. Very old fashioned

MB But that didn't last into the Oxford years.

KD No it didn't.

MB But there were boyfriends in the Oxford years.

KD Yes there certainly were. That is how you saw all the other Oxford colleges. No I mean Oxford did offer a lot because there were so many different things to do.

MB Was the chemistry as exciting as you had anticipated?

KD No. I mean I think I found it hard at the start. The organic side was fine, and I know I found some of the physical chemistry just less interesting, and the inorganic positively boring, from my point of view

MB So that reinforced the move towards the biological and the organic.

KD Yes.

MB When did it start to take shape, and to move towards ideas of projects and the fourth year kind of honours project and things like that? When did that start to arrive?

KD Well, I think for the first year probably it never even occurred to me. And in the second year, well, I had people like Tom Blundell, who is a structural biologist, who tutored me for part of the time. And again that gave more emphasis about what biological molecules are all about, and proteins and enzymes and all the rest of it. The second year in chemistry you don't have exams at the end, which gives you an enormous freedom to sort of read round the subject and think about what you really want to do. That was really valuable for me. I mean I think if I had done biochemistry and just been thrown in at it, I am not sure I would have had the room to breathe that I had in chemistry. It has been a very good training in the end.

MB Were there any other lecturers in those early years who fed the appetite?

KD I don't think so. I can remember one who just drew lots and lots of benzene rings on the board. There was a competition about Tomlinson, how many benzene rings she could draw on the board in an hour. I mean she was truly inspiring too, but I don't know I don't think there is anyone in particular really.

MB But by the time you came towards that fourth year you had come to really focus in on a possible project.

KD Yes and that depended much more on the tutorial system within Somerville College rather than anything else I think.

MB What did you decide to do?

KD I decided to look at the structure of DNA and the proteins around it. So I was looking at chrometid structure before it was finally solved actually. Looking back on

it now I can't believe, I mean when you see the answer you can't believe that you didn't know that histones as they are called, these proteins wrapped round the DNA, instead of the DNA wrapped round the histones. And so I worked with Ian Walker doing NMR. So it was a sort of physical chemistry study of a biological macromolecule structure.

MB How did you come to work with Ian?

KD Well again it was Jo Peach that recommended me. And he also had a chemistry background so he realised the need. Because there are only certain people that you could do a chemistry Part II with. There was George Radda who is very much enzyme based, and other people doing NMR or something physical as I did with Ian Walker. Because it was always considered a slight risk, you know, if you changed subject slightly, you might be less likely to get a First. Well, I never thought I was going to get a First anyway. I really wanted to do well, but I also wanted to do something that I was really interested in. I suppose everyone wants to do that and I decided to do ...

MB Did you feel that a First was on stream?

KD No I didn't.

MB You were just going for…

KD I just didn't feel chemistry inspired me enough to even push that far. I think, you know, you have really got to have a flair and I didn't have a real flair for chemistry.

MB But you were moving in the right direction.

KD But I was certainly beginning to get excited now.

MB In the territory you were going towards.

KD There was enough there to keep me going but I felt that I hadn't quite made what I was looking for.

MB That relationship with Ian Walker was going to prosper.

KD Yes it was. Yes, in fact he was the person who encouraged me to do a research degree, because I was unsure of myself then. As I say, I was interested in the science but it wasn't something that was totally all consuming as indeed it is now.

MB You thought you might teach or something and go away and not do research.

KD Yes. Well I hate to admit it but because of Steve who was then my boyfriend and later to become my husband, I thought the best thing to do was teaching because I could then be mobile. I shudder to think that I thought like that in those days, but I did.

MB But you did, yes.

KD And I went for the interview for the Dip Ed which is the year that you do for teacher training, as it was then.

KD You have overtaken me, you have got to Steve before I was going to put the question. Lets put Steve in now. He came into your life very early on in the chemistry course.

KD That's right.

MB Second year.

KD The second year, yes.

MB He was the guy who finished everything and who got top class results to preparations, is that right? He could always give you odd crystals that you hadn't made.

KD So you didn't have to do the synthetic organic chemistry bit because he could give you a bit. You had to go through the practical, but if mine didn't work Steve always had some spare compound to get a good spectrum of.

MB He is the classical Raymond Blanc of the chemistry lot.

KD Yes.

MB And that relationship just started in a quiet way.

KD Yes.

MB Facilitating your success.

KD That's right. He was very popular with women for that exact reason, so you could always go and get the stuff.

MB So you had a gallery of people who liked his results.

KD Absolutely.

MB When did that precipitate into a decision that this was a steady relationship? By the third year?

KD No, no the second year when we went on our tour of Europe together, in fact.

MB Right. So that was a very serious development, and life has never been the same since.

KD I mean he is in love with science too, but in chemistry rather than synthetic.

MB But you are both in love with each other.

KD Or something like that yes.

MB It happened. I want to go back to Ian Walker now that we have Steve in your life. He persuades you to do a DPhil. Did you decide to get married at that stage, before you take that on?

KD Yes, but that was a simple practical thing, because my father would have had to pay for my grant if I would have stayed unmarried, in fact, at that stage.

MB Skulduggery.

MD That is exactly right. So that was sorted out in the interest of economy. In fact, they changed the law after that, so it wouldn't have mattered. I don't regret getting married that young, it hasn't made any difference.

MB And you got great support while you were doing that DPhil. Steve was already one year into a DPhil.

KD Well, in fact the chemistry is ...he was in the same year in chemistry but chemists do it in two years because of this extra year, and because I changed the same subject, I needed to do it in three. So he was always a year ahead of me. So he did his right up at the end of two years, so I could support him. I don't know how two people survive writing up theses at the same time. It must be hell that's all I can say.

Mb But you had that kind of mutual support. You supported him through the dark ages and then it was support for you.

KD Yes and that was really reading through lots and lots of scripts because those were the days when you didn't have word processors of course.

MB It's hard to think back that far isn't it. Kay, just checking that DPhil in. It was an important project, it was exciting and it did capture you. I mean you were confirmed in the research kind of line then. Was it a slime mould?

KD Yes. In fact Ian Walker had just done a sabbatical to try and change tacks a little bit, and introduced this slime mould called *Physarum polycephalum* which is this wonderful yellow slime.

MB Crawls over filter papers.

KD Yes that's right in nice little circles and you can make it divide synchronously

MB It is a great tool.

KD It was.

MB And what did you do with it?

KD Well, we looked at nuclear transcription. So we looked at the chromatin structure as it went through the cell cycle.

MB Right. You were still deep into chromatids.

KD Yes.

MB And describing that cycle?

KD In what sense of.

MB What happened to the chromatids in the cell cycle.

KD Well, what we had to do was to look at it either in metaphase, when the chromatin is really condensed, to see where your RNA polymerase was and why it was inactive. And so what we were looking at was digesting the histones off to see how compact that particular structure was versus sort of S-phase when it is very active indeed in DNA synthesis, when the structure is much looser, and so on through the cell cycle.

MB So you are really kind of charting important associations between DNA and RNA transcription.

KD Yes and sort of disassociating those proteins away from the DNA and looking at the phosphorylation, acetylation of the histones.

MB What was the final title of it?

KD My thesis, you know, I can't remember.

MB I know you can't. Sorry about that.

KD I think it must be something like 'Chromatin structure of *Physarum polycephalumi*'. All I can remember is that it is red and it is on my top-shelf, but I actually ....because we never used to write the title on the binding as we do now. I shall have to go back and look at that.

MB Anyway. We get that through. Ian Walker is no longer alive.

KD No, unfortunately he died at the age of forty nine.

MB Do you want to say a little bit about his support and the kind of person he was because he was a major assister of your progress?

KD Yes again he was very much in love with the science and he was also in love with teaching both at the undergraduate and graduate level. And so, you know, he was always in there on Saturday mornings with his young son between his legs. Ian was very into flamboyant shirts and check trousers and this little Julian was quite an amusing little kid. He used to bring him in on Saturday mornings and just talk to people about science. So in that sense he was very inspiring. And I used to go back and visit on Saturday mornings, you see, because we were always in Oxford, even when I was working in London.

MB So that was a close association. I think on one occasion you said he wasn't kind of probably a high flyer as a scientist, he was a very sincere supporter.

KD Yes.

MB That is a terrific tribute to him.

KD Yes. Well he loved to paint and do lots of other things as well, and his family were a very strong and large part of his life, so he divided himself like that.

MB You got that research degree in hand, and then all kinds of possibilities arise. I think Steve went through off on to the Continent to work in Paris.

KD Yes.

MB Was that before you had finished the DPhil?

KD No. Steve went to the inorganic chemistry lab to work for Malcolm Green on an ICI Fellowship and then he got the opportunity to go to France with Sir Derek Barton, one of the top guys in organic chemistry and I was at that time applying for a fellowship at Wolfson College, a JRF.

MB Which you took.

KD Which I took, yes.

MB And you were going to stay working in the laboratory on...?

KD On the extension of the *Physarum* work because as Ian had introduced it into the lab, it was pioneering in a sense that no-one had really done an awful lot of work on that organism.

MB It must have been a very impressive beastie. It must have raised a lot of interest internationally.

KD Yes it did, but I think the real problem was that it didn't have good genetics. So we knew eventually we would have to change the system in order to do proper genetics.

MB But it gave you that key start. It showed you quite a lot about chromosomal RNA activity.

KD That is exactly right. And so I really needed a JRF to consolidate and build on everything I had learnt during my DPhil and so I applied for this two year fellowship and, in fact, in the end, I just did it for a year. And the reason for that was I then had the opportunity to go to France as well. And not only that Steve was clearly going to stay and not come back, so I thought I had better go and join him.

MB He had got hooked on the place.

KD Yes.

MB You said that in that first year at Wolfson you went backwards and forwards across the channel.

KD Yes. I used to do the route by car and by train. Whatever was cheap, whatever happened to be on special offer.

MB You were sent Valentine cards with special week-end offers.

KD They used to have special channel runs around February 24th, they called them Valentine runs. So I was there.

MB And did that link with Paris also take you over, because you were surely going to go there.

KD That's right. It was a question of which lab I would go to. And I really wanted to learn a lot more about proteins because if I was going to have a career in biology I needed to do more than just physical biochemistry and that's why I decided to do go Saclay and learn about purifying RNA polymerase from yeast, in fact.

MB Right. What date was that?

KD 1978.

MB So you go off to Paris and do protein work. Did that prove as satisfying as you thought it would?

KD Yes because again Andre Sentenac who was head of that lab was again one of those scientists who was absolutely fascinated by science and he too had just come back from sabbatical. It is a good time to catch people because they are really ready to go when they come back. He had been to John Carbon lab in the States to learn about cloning and so he wanted to come back and clone the polymerase genes, and of course cloning was just beginning. These were the days when you had to prepare your own enzymes, your own ligase, your own restriction enzymes. And so there was a lot of contact between the Pasteur, in the centre of Paris with Francois Rougeon and Andre's group just trying to get cloning going. So I really learnt a lot and, in fact, a lot of my initial cloning was all learnt in French – 'le cloning' to me, not cloning.

MB And you cloned a gene while you were there.

KD No we got as far a purifying all the sub units, so we could do it in fact.

MB Right. So it was on stream.

KD That's right. But they went on and cloned it after I left. I didn't stay on long enough to see that through, but I certainly learnt about cloning because you have prepared all the vectors and plasmids at ridiculously low copy number, which we would never dream of using now. I mean it is amazing how fast the field has changed.

MB Pioneering. And looking back, as you say, many of the operations now can be done so swiftly that took weeks.

KD And we used to have six restriction enzymes instead of several hundred to choose from in order to do the experiments, so it's quite a revolution.

MB Was Paris a revolution?

KD To me, yes. One thing about the French, it is every man for himself to a certain extent, and enjoy yourself. And because you don't have the Channel, you know, you could get to the weekend and decide to go for a weekend to the Loire valley, a weekend to Strasbourg or even drive to the south of France and that was very nice. And Paris itself is such a wonderful city. It is very good for cinema, it is very good for museums, and you could just go into Paris and park your car on the pavement and go out. You can't do that nowadays in Paris, that freedom of being able to just go out and enjoy yourself after work with friends.

MB And the French have that particular joy of life. They can shove everything away and go to the country, and that you hadn't had over here.

KD And not only that, you know, the CNRS where Steve worked had this system where you could get on a bus on a Friday night and go to sleep in these bunks and wake up on the ski slopes on a Saturday morning, ski all day Saturday, go to bed Saturday night, get up Sunday and do the same thing, and then come back over Sunday night and go back into lab on Monday morning. I mean nobody in the UK would dream of doing that. So I used to do that a lot and so did a lot of skiing then.

MB I was going to ask if you became a proficient skier?

KD A proficient skier. I did become a skier I am not sure if I became a proficient skier.

MB Kay, just before we wind down from this half of this mornings recording. I would just like to talk about the woman that had grown up since the Stourbridge High School days. And I think it was rather snappy young woman that crossed the channel on this regular basis who made her own clothes. Was this still happening?

KD Oh yes, I was much more independent though. It did me good for Steve to go away. I think it was hell for us both for the year but then I had to do much more on my own and drive the car. And, actually, I learnt to drive a car on the left hand side of the road. I have to be careful because I never really drove a car in the UK. These are the little things. So the Paris experience did a lot for me.

MB You have really moved sideways from this idea of dressmaking that I was trying to focus on, but you did do a lot of dressmaking.

KD Yes that is another thing that my mother always used to like to do. So she used to make all my clothes.

MB She was a maker of all your clothes when you were a girl.

KD So I got taught all of that and when I went to college I did...

MB She liked you going out looking very smart.

KD That's exactly right.

MB And that's not stopped. You have kept that.

KD No I have kept that.

MB That is a bequest that you have not...

KD I don't have time to make my own clothes now, but I used to enjoy it.

MB In the mini-skirt period of the sixties you made lots of mini-skirts you were saying.

KD Yes and it didn't cost very much, it didn't take very long to make either. Looking at some of those photographs I don't know how I had the nerve.

MB There is a sense of fashion there.

KD Oh yes and the maxi coats. I used to have a lovely coat. In my first year in Somerville I had a maxi coat with a fur trim that went all the way down to my ankles. So you can imagine this very short purple it was, purple skirt up to here and a maxi coat down to there. Yes fashion was something else. Trying to be Mary Quant, but not quite getting there.

MB So that was all happening. In Paris this sense of growing up and developing cultural interests also took you to buy paintings and objects of art. I think you had a very fine time in Paris that had all kinds of bonuses that you brought home, and I think quite a lot of those gains of Paris years are still in your home.

KD Well that is right. Well, I mean most of the pictures come from Paris. It is very nice to look back on that period.

MB Well we have got you to Paris and at that stage we'll wind down before bringing you back to another culture shock.

KD Back to London, yes

MB Kay you have come back from Paris. You probably could tell me about how that return to England was precipitated, because at one time it looked as though Steve might stay there for quite a long time.

KD Well, yes and we were enjoying it. It was just that a job came up in the chemistry department in Oxford and he really felt that that would be worth going for and so he applied for that job and got it. And I really didn't want to come back to Oxford at that stage. Mainly because I had become interested in cloning and genetics and that hadn't really started in Oxford, it was very much a Cambridge thing with Fred Sanger in DNA sequencing and so on, and I was given the opportunity to go to London instead because Bob Williamson was just thinking about, he was also on sabbatical in Paris at the time that we were in Paris for that final year, and he was going to go back and start on this linkage project with cystic fibrosis.

MB He was at St Mary's?

KD He was at St Mary's. Yes he was the Professor of Biochemistry at St Mary's, so I met him in Paris and we discussed the papers that were coming out, the work of Y W Kan in particular.

MB That was a big time in that particular field.

KD Yes it was extremely exciting because it was the first time DNA diagnosis had been used for prenatal diagnosis in beta-thalassaemia. Beta-thalassaemia was something that Bob had been working on for years, but just looking at the protein level and a little bit of cloning, but not really thinking about the linkage approach. And he could see the impact of that on cystic fibrosis, as many of us did at that time. And there was the classic paper of Ray White and Dave Botstein in the American Journal[1]. And I remember reading that and thinking, yes, we really could. I could just see how this was going to revolutionise the field, but I wondered if it would really work. And so you know I came back to London to set up that group with Bob.

MB Where did the money come from for that.

KD Some of it from the Cystic Fibrosis Research Trust, but actually, we decided to set it up on a model system which is not CF but in fact Duchenne muscular dystrophy and the advantage there was that we knew it was on the X chromosome and that it affected only boys, and therefore it gave us a start. And we had a clue that it might be on the short arm in a particular place because females that had breaks in that particularly area were also affected by the disease. And so if you knew what chromosome it was on we could at least go and try and purify that chromosome, which had never been done before. Try and make a library of that particular chromosome and then start making restriction fragment length polymorphisms, RFLPs as they are called.

MB Before we get into that deep story which is a massive one, your first great development of perspectives internationally, because you linked in with lots of other research and got into clinical fields.

KD That's right.

MB I want to just tease out a couple of things about life as a woman in science because I had a feel when you said, 'I didn't want to come back to Oxford and just follow in Steve's footsteps' that there was a little bit of wanting to have an independence in science and to prove, as a woman, that independence. Is that right?

KD I am not sure if it was as a woman, it was much more as a scientist. I mean I had definitely been bitten by then. I mean I knew that this was something I wanted to do and I knew that this was a field that I really wanted to explore more fully and I couldn't have done that in Oxford. I just couldn't have done that in Oxford at that time.

[1] The American Journal of Human Genetics

MB Right so it was genuinely the 'bug' had bitten and you came back to Mary's to work with Bob Williamson, who is a fascinating character.

KD Yes. A highly motivated energetic individual.

MB Not creating comfortable environments sometimes.

KD Well not with other people but I never had any problem.

MB But a great reputation for being a man of energies and not always subtle.

KD Not always subtle but he was always pushing ahead, so from that point of view he is a man of great resource man you know. You could say 'I need so and so for my next experiment', and Bob would try and find someone who did it. And the good thing about Bob is that very early on he set up this collaboration with Peter Harper on which our whole research programme depended. It was very much a partnership between that clinical side with Peter and the patients, because I didn't really know what Duchenne muscular dystrophy looked like at that stage, and the molecular biology in London.

MB So you came back and formed this association, Bob Williamson, Peter Harper, Kay Davies.

KD Yes.

MB What kind of a team did you build at Mary's. How did you start off?

KD We started off with a couple of graduate students, Marion Hill and Jo Murray.

MB Quite a small team.

KD Yes.

MB What were the first steps? Can you take me through the foothills of that research?

KD Well, the first thing was to purify the chromosomes and this is where a great friend of Bob's from the Glasgow days came in, Bryan Young. I mean he was a fantastic guy and, in fact we are still in regular contact because he has now moved to London. But he was sorting chromosomes at that stage and he produced some of the first and finest papers in that field. But that meant, you know sitting in front of his machine all the way through the night trying to get the chromosomes.

MB What were you sorting it by laser?

KD By laser. So you shone a laser beam through these stained chromosomes. The chromosomes were stained with just ethidium bromide at that stage.

MB And you could just manipulate them into groups.

KD Yes into groups and of course with the X chromosome because of its size, we could just about get it pure just on the shoulder of chromosome 7.

MB And where did the chromosomes come from?

KD Well, we actually cheated with that, we used a 4X cell line rather than 2X cell line.

MB So you are just using a standard X chromosome. You just wanted a standard chromosome, nothing from families or any genetic background that had problems. You just wanted a standard line.

KD Yes. In fact, we chose one with 4X chromosomes, so that is slightly abnormal because we were just interested in the X and for the same amount of effort we could get double the amount of chromosomes.

MB But that must have been hours of separating.

KD Yes it was.

MB Looking at the screen. I mean it was a great manual involvement

KD Yes, like sitting through the night watching and continually adjusting this machine. So we used to go to Glasgow and do that in shifts, and then of course you would come back to the London lab and you had a hundred and fifty nanogrammes of DNA, which was a very small amount in those days of cloning. And you knew that was enough to do one experiment. And the question was, could you set up enough controls so that the one experiment worked. And, in fact, it didn't for the first couple of times.

MB More Glasgow, more sorting.

KD Oh yes.

MB So that was several months of really hard labour.

KD Yes. In fact, we were in direct competition with the group in Boston. So there was a tremendous amount of pressure, but on the other hand we all got on so well that it was tremendous fun to see whether we could really do this.

MB This was Kunkel's group.

KD This was Kunkel's group in Boston with Sam Latt then.

MB There were several teams interested in that chromosome at that time.

KD Yes, but it was mainly Sam and Lou Kunkel that were competing directly with us against this...

MB Did you feel there was a race?

KD I felt the beginnings of real competition. I suppose I had only just joined Bob's lab and I hadn't really been exposed to the international scene at that level in human genetics, so it didn't bother me too much. It is the next phase when it really got very competitive indeed.

MB But initially you are looking to find the gene of muscular dystrophy.

KD Yes it was. So the next stage, once we had got all those chromosome fragments in a test tube, was to just pick them out at random and try and find any that co-segregated with the disease. And fortunately, the first one we picked out turned out to be on the short arm, and ten per cent of the time it actually segregated with the DMD. And of course those studies we did with Peter Harper, through the families.

MB So these are Cardiff, families from that Welsh area that Peter was actually garnering in for you, and he stayed involved in this project for a long, long time.

KD Oh yes and is still involved.

MB What was the impact when you first started to meet patients, Kay I know that didn't happen in the first year?

KD Well, we didn't meet patients directly, necessarily, it was Peter that did it. We used to go to the annual conferences and just the spirit of those families was just marvellous.

MB So you became bounded in an emotional way as well as scientifically.

KD Yes because these families are so motivated to help not only their own children, and sometimes they realise that their own children can't be helped, but they are so motivated to push the research forward. And I always remember the executive director of the Cystic Fibrosis Research Trust, Ron Tucker, used to come and visit us regularly to make sure we were 'doing all right' to quote him exactly. And he was also very much on board and pushing, and he realised the full potential because it was he that persuaded Bob to keep going on this linkage approach for cystic fibrosis. And Paul Walker, who was then the Executive Director of the Muscular Dystrophy Group, I mean those two were great friends, was also very encouraging and would visit the

lab constantly to find out what was going on and try and relate it to the families and the people who raised the money for the research.

MB I am trying to pinpoint the actual time for this so that anybody following our conversation will know that this was the beginning of the eighties.

KD Yes.

MB You came back in 1980.

KD That's right. In fact, the Botstein and White Paper came out in 1980 and in fact we published our **Nature** paper with the first chromosome sorting in 1981, and then that first marker from muscular dystrophy, which you know was really amazing, was in 1982.

MB Can you tell me about that first marker? Can you go through a bit of that story with me, because it was amazing?

KD Well first of all, at that stage we didn't know even how often we could find polymorphisms with which we could follow disease, because we had Y W Kan's data on beta-thalassaemia which was spectacular in itself because it was DNA diagnosis. And then Ray White's group had actually published in PNAS a restriction fragment on polymorphism on chromosome 14, but we didn't know whether those were going to be spread all over the genome or not at all in those days. So you know to see…in fact we isolated several and we produced the first linkage map of the chromosome in collaboration with Ray White's group in the end with Dennis Draner. So yes, and then we realised, of course that they really were going to be all over the place and that you could map almost any genetic disease with it, providing you had the right families.

MB And the actual gene that you were involved with, the muscular dystrophy gene, that was colossal.

KD Yes, but that really was a race because the Muscular Dystrophy Group in the States identified three groups that they were going to fund for this race, this gene hunt. And that was: Ron Wharton's group in Toronto, and Lou Kunkel's group in Boston, and my own. And, in fact, it was very friendly competitive because we used to have regular meetings and the Muscular Dystrophy Group would host one meeting and the Muscular Dystrophy Association in the States would host the other. So one would be in Cambridge by the MDG and that is when Lord Walton, you know John Walton, was chairman. But every year there was always something new because of the you know…

MB It's a great race to the summit.

KD Exactly right, but it wasn't until 1986 that Lou Kunkel cloned the gene first and that actually was announced…

MB And you were close to doing it by then…

KD Yes we were.

MB You were very close.

KD Oh yes, but we didn't win, but never mind.

MB How did that feel because you did feel close?

KD Yes we did. We were disappointed because we didn't get there first, but it didn't stop us because we managed to...I mean it was such an incredible gene, something that we had never imagined, and it still is the biggest gene known in man, and that explains why there's such a high new mutation rate…

MB Thinking on how many kind of triplets, how many base pairs, what are we thinking about here Kay?

KD Well two thousand, 2.7 megabases which is 2.7 million base pairs. So I mean that is huge.

MB And this is not all coding.

KD No. Only a very small proportion of that is coding. Fourteen thousand base pairs coding...

MB ...for a very critical protein - muscle protein.

KD Absolutely, and a large one as well. I mean, in many ways that was unfortunate because if you want to cure this disease then you are going to have to target every muscle with a large structural protein, and that is going to be difficult. But that is what we are trying to do now.

MB So at that stage you were getting the idea of a vast gene that was producing a vast protein.

KD Yes.

MB Not an easy story but one that is just compelling.

KD Yes. It made it easier to find, not wishing any disrespect to Kunkel, but it may be easier to find than any other disease gene because most of the patients just have

holes in their genes. So it was easy to recognise, and that made it easy to diagnose, so instantly that revolutionised diagnosis because you could do a very quick diagnosis.

MB Kay I am just going to recap to make sure that I have got the story if I may. What you started to do was to identify the fragments of that gene very early on and to characterise it.

KD Yes.

MB To look at the nature and character of it, and then grow it up and produce a library of fragments that were characteristic of that gene working normally, and then to match against that fragments from people who seem to be in families carrying disability and to look where the difference were,

KD Yes. In fact, you could see therefore they had gaps. But the gaps…

MB But you then have a diagnostic tool.

KD That's right.

MB You develop the first diagnostic screening for this disease.

KD That's right. So the first prenatal diagnosis was using in markers that we had done. It was done in collaboration with the people in Holland, which again emphasises the international and the spirit of collaboration in spite of the intense competitiveness.

MB Was Martin Bobrow involved in this.

KD Yes Martin Bobrow was involved in that stage.

MB On the Dutch side.

KD Not directly, no he wasn't, but he was later on in many of the diagnostics because quite a lot of the diagnosis was done at Guy's Hospital.

MB That bringing in the patients though you are working with something as elegant and incredibly time consuming, at that time, as chromosome fragment sorting, but in Cardiff you are garnering whole people with stories of family history and bringing these two stories together, the mega-story and the micro-story.

KD That's right. And the other thing I always remember, and this was with Martin in Guy's because there was this one woman that had several abortions of just males because she had a DMD brother. And then this test came along and of course we could do it directly, and she conceived twins and the twins looked the same but, fortunately, we could then tell the sex by looking at the Y chromosome, and she had

one boy and one girl. There is a lovely picture actually they took of Martin and I holding one baby each when these kids were born, both normal. That was a fantastic moment and a fantastic moment for that particular family.

MB Did you bring it?

KD I didn't bring it. Actually, I couldn't find it.

MB That was a great emotional moment.

KD Yes. So I think, you know, that really did make a significant difference, and it made a significant difference to the field, I think, because everybody knew then that you could go and do this with any genetic disease. Well in fact, they realised that from Y W Kahn's result, but really it is the first time a random marker had been used to diagnose disease.

MB And that was about 1982-83. I must have been quite a long process in those days.

KD Yes, in fact, the first prenatal diagnosis was probably done in '83.

MB I am trying to work out the time it took to diagnose. It must have been quite a long process in those days.

KD It used to take three weeks to do a single test.

MB Different now.

KD It certainly is, you can do it in a few hours.

MB But that was a real labour process. So you get there. How does it follow up once you have got that satisfaction you have created the first prenatal diagnostic process for muscular dystrophy? Where did you go to from there?

KD Then you have to, particularly for a devastating disease like Duchenne, you have got to think of treatment. And this is just simply one step on the way to working out what the gene does, and then going on to develop a treatment. And now it's a long haul.

MB So you started thinking about treatment way back in 82-'83.

KD As soon as the gene was cloned, actually. Well actually, before then, but I think our thoughts were concentrated the day in 1986 that the gene was cloned. Then the next stage was, really, what do you do next with this information.

MB How far had you got at this stage, towards the story of the other end of the business of the disease, which is dystrophin, the absence of dystrophin from a critical microskeletal role in the muscle cell, kind of binding the machinery to the outside membranes of the muscle? How far had people actually tied dystrophin into the story?

KD They hadn't, in fact, because the first few papers about what dystrophin was doing and what it was attached, to were not strictly correct.

MB They got it wrong.

KD They got it wrong, well, in detail, they didn't get it wrong in principle. So there was quite a lot of ….then it was time for the muscle physiologist to come in and help us out because we were really genomic DNA people.

MB So you started to network a bit.

KD Yes.

MB '86 '87? And were the results on stream quite quickly about dystrophin?

KD It took a bit of time to find out, and I am not sure even now we know exactly what it does, but it took quite sometime before we knew what complex of proteins it associated with and how it was anchored in the internal part of the cell and what role it was really playing.

MB But we are now clear it links the internal machinery to the...

KD Cytoskeleton. Yes that is right, the structure to the extracellular matrix, so it really is stabilising the membrane.

MB But no one has an idea of the structure because it is so vast you can't crystallise and get it into x-ray crystallography and...

KD No, last year it was a dime, this year it is monomer. So I think you know, you are having to crystallise domains of this protein as you have to do with all these macromolecules to start to understand them.

MB But that is *en route* now, and people are beginning to get a feel and put it together, but it will be good when you actually see the final shape.

KD Yes.

MB Just coming back to your view that once the gene was there and cloned one began very quickly to think what could be done to correct the defects that result at the

dystrophin end, what were they early thoughts you would put in reverse transcriptase mechanisms, rebuild the gene in the cell?

KD No, no. Even in the those days you are thinking of viruses and gene delivery. But because our strengths lay in the DNA recombinant field we also wanted to know about whether there were other things like dystrophin in the cell and that's why we were very fortunate in trying to look for this other protein, and actually so was Lou Kunkel at the time. So we were screening libraries at very low stringencies so that we might catch related proteins to dystrophin, because if there was something else like dystrophin there may be by comparative analysis we might understand what dystrophin did, or we might be able to get the other protein to replace dystrophin.

MB Kay what I can't work out is why you felt there might be something like this amazing protein, another protein like it?

KD Well, it was just at that stage that, I had moved from London to Oxford. That was the difference. I was then immersed very fortunately in David Weatherall's department, the Nuffield Department of Medicine, and that was 1984. So you couldn't talk about anything except globin, and of course globin has the foetal globin genes and the adult globin genes and of course, if you get persistence of foetal haemoglobin then you still get an anaemia, but in part it can compensate for the adult globin gene. So following along on those lines…

MB So you found a way of thinking that led you...

KD Yes to think about, well may be there might be relatives of dystrophin. Yes.

MB Where did that story go next? Did you actually get something to flag label and say good thinking?

KD No, no. In fact it came slowly because there was such a race to get the whole gene. Because what Lou Kunkel had done was to identify the gene, but he hadn't cloned the whole 14 kilobases. And it was quite difficult in those days to even see a 14 kilobase messenger RNA on a northern blot. So we could certainly do that, but we hadn't got the whole gene in the test tube. And so we felt we really ought to clone the whole lot so we could express it, produce antibodies and look at the protein. So it was through those studies we picked out something that didn't quite fit and fortunately we didn't throw it away, and that was what Don Love picked out one day. And we purified that, localised it to somewhere other than the X-chromosome. We could see it was closely related to dystrophin but it wasn't anything to do with dystrophin and at that moment Diane Hill from New Zealand, a DNA sequencer who used to work in Fred Sanger's lab for a time, passed through. And she is DNA sequence mad and still is. I had recently done a visiting professorship with Diane and she said 'Well have you got anything that will be useful to sequence'. And sequencing 2.3 Kb, which is what this clone was, was a lot for us in those days. And so I said, 'Yes, Diane, if you have any spare time, you can sequence this clone'. And, in fact it was Boxing Day of

that year, she sent me a fax, and said, 'You can't believe the result of this clone, Kay, because you're right, it is very closely related to dystrophin. It is extremely closely related to dystrophin, in fact? And that was the beginning of the utrophin story.

MB You say that it was Boxing Day of that year. What year would that be, Kay? Where had we got to by then?

KD 1989.

MB And so I'm taking it that you've got a fragment, a chromosomal fragment, a gene fragment that actually doesn't belong, that's a little bit out of touch with some of the material you are screening.

KD So it's eighty per cent similar, but not exactly right.

MB So it's not quite matching but got into your tube somehow.

KD No, no, we managed to pick it out of a library because it was cross-hybridising. Because we were screening to get to the end of dystrophin, so what we would do is pick out ten things that were definitely dystrophin and **this**. And just one of these.

MB And that came out.

KD Yes, in fact, it was like this one (photograph is displayed on the tape). This is his filter which is mainly blank, and those are his orientation marks and there is this one black spot and so he just took that. It is a nice clean screen. And he's put here, 'From these small beginnings', because I got him to sign it before he left. Actually Don (Love) is a New Zealander too.

MB So that was a great moment, a bit of celebration.

KD Yes, it certainly was. And particularly when we realised how closely related to dystrophin it was. And then John Tinsley went on, the post-doc who followed on from Don, and sequenced the whole lot, he cloned the rest of the gene, which turned out to be quite difficult. But when you could see the other end of the molecule coming out just as similar as the carboxy terminal, then it was very exciting indeed because that really gave a hint that utrophin might be able to be used to replace dystrophin.

MB An unbelievable thought, but all of sudden it's there.

KD We're not there yet but, yes.

MB I'm not going to let you get that far yet because I want to keep us down in the foothills of this work. But we couldn't hold back on that, I think, we'd got to get

through, we'd got to get there. I just want to take you back because we mentioned coming to Oxford, and David Weatherall's department and the influence of the globin work.

KD It was the influence of the clinicians too because I was in the heart of clinicians at St Mary's, which was certainly helpful. But we were very much interacting with Peter Harper, but they were further away from us, in Cardiff.

MB And then you came to the John Radcliffe in Oxford.

KD Exactly. In fact, we were sandwiched in labs between wards seven and eight.

MB So you really were immersed in a clinical environment. I just wanted to ask about that departure from Williamson's unit at St Mary's. How did that come about because you were going so well? It was a great team. What exactly happened to break that up? What were the factors there?

KD There was nothing intentional, but eventually I would probably have come back to Oxford if Steve was staying, only because it was more convenient, but I wasn't going to do it until the scientific opportunity arose. And I applied for an MRC senior fellowship encouraged by Bob to be an independent investigator.

MB So it was a natural step.

KD Exactly. And not only that, he was basically motivated by cystic fibrosis. Cystic fibrosis was his mission. And I was really hooked on muscular dystrophy.

MB You were on a side-track from that.

KD And so we agreed, and he was very generous in letting me go. I had worked so hard in developing the Duchenne story that I would take that with me to Oxford, and he would continue using the same technology which we'd set up together, and he would apply that to cystic fibrosis. So I went to the MRC interview and, actually, it was Sidney Brenner who was on that interview committee. A pretty intimidating experience, who said, 'Well wouldn't you one day like to move back to Oxford, as an independent scientist', and I said 'Yes, if the opportunity arose'. And he then put me in contact with David Weatherall, who of course I knew because he was already eminent in the haemoglobin field. And he generously gave me a lab in the NDM (Nuffield Department of Medicine) at that stage. And that was just when David was making plans about the Institute of Molecular Medicine and the new building. He said it was going to be there in two years, and it was there in four, I think, so that's not bad. So that gave me a real opportunity. And of course, he then left me alone because he was working on the thalassaemias but he had some very bright, good people working in his labs and we interacted a lot.

MB So it was a good (?) in there, very early on, and you were allowed to bring some colleagues down as part of your team.

KD Yes, yes so in fact I brought two, Susie May and somebody else. I have forgotten his name now, it will come back to us.

MB Bob Williamson he didn't stay at Mary's, he eventually went to Australia and I am trying to pick up his part in all this.

KD Last year he went to Australia.

MB So he continued the…

KD So he continued the cystic fribrosis story, yes.

MB And that went quite well at Mary's, and you continued to feel strongly associated with Mary's.

KD Oh yes. There were a lot colleagues still there and we used to swap techniques. And you know St Mary's is at Paddington and so if there was half an hour before the train left, I used to drop in for a cup of coffee or even you know before MRC meetings I would drop in at eight o'clock in the morning and talk to Charles Coutelle or Steve Brown, because Bob wasn't always there and Pete Scambler, all of whom have gone and made their own careers now.

MB And I think you make a good link with Stan Peart in that period.

KD I had met Stan Peart at that stage…

MB He was still around and making a lively contribution to research.

KD Indeed he was.

MB Are there any other people from that? I am thinking of Bryan Young who eventually came to London.

KD Bryan moved down to London to work for the ICRF, again on chromosome sorting and cytogenetic technology.

MB And you have continued to collaborate with him.

KD Yes, yes and I go and give a lecture in his department on an annual basis, so we catch up and we see each other at meetings.

MB Oxford. Was that a good return to Oxford? I mean you said it was nice going into the Weatherall department.

KD That's right because in fact George Brownlee had come into the University at South Parks Road and set up cloning. So it was very much more genetic, but nevertheless the right choice was to get the clinical interface within David's department.

MB And that new institute when it came I mean you felt that was a good unit.

KD Oh, it was fantastic.

MB Good collaboration.

KD Yes it was.

MB Thinking again on the family scene, Steve's there enjoying his Oxford lectureship which has now turned into one of these new professorships.

KD Yes.

MB Congratulations to him. Thoughts of a family in the mid eighties?

KD No, wait a minute, lets see. We moved into the house, I have to work backwards nine years ago. Where are we now '96. Yes, about 1987 I guess.

MB So by '87 you were beginning to think of…

KD I think when I was thirty six I decided. I had always wanted to have children and I think he didn't know whether he did or he didn't, and we had to make a decision because I would be too old for it if I didn't, and so I made the decision.

MB Do you usually make the decisions?

KD No…

MB You share them.

KD To tell you the truth I think we thought, OK, maybe we should have a family, but I think we both thought it would never happen, and it kind of did rather instantly.

MB At an embarrassing time?

KD Yes because I had just got my MRC tenure, my permanent position. I was coming up to the year of my five year fellowship and I had to be renewed. And in those days you couldn't renew senior fellowships so I had to go up for a tenure interview then. And it was just after the tenure interview. So I was extremely conscious of the fact that this might look extremely bad you know, woman gets tenure

then gives up to have children, and people used to say that sort of thing in those days too. But certainly not David Weatherall. I must say….I was incredibly nervous when I went into his office to tell him, and then he came round from behind his desk and kissed me and congratulated me, and I was a bit overwhelmed, I have to say. I mean you know that is indicative of the support I have had, really.

MB Yes so that was an important step on the home front rather than on the research front, and you went through that pregnancy and Nicholas was born in '87.

KD Early '88.

MB Not the best experience of childbirth.

KD No I had a bit of a difficult time with him coming into the world. Now he is fine.

MB And you have since that time combined still as much research.

KD Yes. One thing that commuting to London on a daily basis to Bob's lab taught me is that if you are sufficiently well organised you can get it in between eight and six. And, you know, you just have to organise other people to go back and do one or two things for you, but generally you can get it done if you need to get it done.

MB Kay, we ought to look at the eighties because you produced quite a few books and quite a lot of writing in those years. Was that all packed in between eight and six pm?

KD No, no that was done in the evenings.

MB So there was quite a bit of midnight oil.

KD Yes. But I enjoyed that because it introduced me to other people in the field, because I edited a lot of things and I learnt a lot about the science, if you do that sort of thing.

MB And what of the teaching?

KD You mean of the undergraduates.

MB Right.

KD I didn't do any at that stage. I did the occasional lecture to clinical students. I was never called upon to do any teaching.

MB What I need to talk about now is the way in which you got involved with a department in London in a senior post at the Hammersmith by about 1990.

KD Yes.

MB Just let's mark this up. You have got a child who is two, you have a fairly busy family life, you are now into the utrophin work at Oxford that's consuming a lot of your time, but don't know where the fragile X story actually fits chronologically?

KD That started because again we were sort of fiddling around with that, and fiddling around doing the odd experiment on linkage with Marcus Pembrey at Great Ormond Street, that's Bob and I did that. And again it was another…

MB It just trickled along for a number of years.

KD Yes.

MB Since the Mary's days, but so eventually it was going to come good.

KD And since we actually had the resources, the X-chromosomes and so on, when I moved to Oxford I set up a small nuclear group to run along side the Duchenne stuff to clone the fragile X gene. So that was developing.

MB Kay, take me to the Hammersmith story. How did that come about, that appointment?

KD Well, I think, you know I had my tenure and people were thinking about personal chairs, and I had been discussing the future career opportunities with David. So I either stayed on in the IMM on external staff, and the question was how would the Institute itself evolve over the next fifteen years. And I didn't have an independent position because I raised all my own salary and group resources which didn't matter, so I was in no rush to do anything. So I wrote a letter to Dai Rees who was then head of the MRC.

MB Right.

KD And asked him if I could meet him and talk to him about what my prospects career wise were for someone in my position, employed by the MRC. And it just so happened that at that moment they were looking for a new director of the Clinical Sciences Centre, which is this new venture in London. So he talked to me about that mostly, actually.

MB And so you became director of an MRC unit.

KD Yes.

MB Was the Hammersmith a happy time?

KD Yes, it was. I mean because I learnt a lot from the experience. Everyone was unbelievably supportive and I was then again in an environment of clinicians that really wanted this to work. So there was a tremendous spirit.

MB I got a feeling of an overlap with Oxford that continued all the time.

KD Yes because my groups, the vast majority of my groups, stayed in Oxford and my new people I recruited a corps within the neuromuscular unit that Victor Dubowitz set up at the Hammersmith. With Victor we started the spinal muscular atrophy work. That was always described as the impossible genetic problem because you know there were just these sporadic cases. Well, first of all Victor single-handedly collected all these families that had two affecteds and then we doubled the frequency of the disease in the British population by writing round to all the paediatric neurologists. So then we really believed it was a solvable problem. And then again there were international teams who where competing with us to try to find out where that gene was and that included Lou Kunkel again, actually.

MB Well how did you go with that?

KD Well the French won but that was all right because we got a magnum of champagne for that. Again it was a huge spirit of collaboration.

MB But again you ran them close.

KD Yes.

MB That must have been a terrific feeling.

KD And it still is. It is a fascinating disease because it is such an unstable part of chromosome 5, so we are uncovering, you know, novel genetic mechanisms of genome variation.

MB Are you still involved with that then?

KD Oh yes. I still have three people working on that and I still go to the annual meeting of the Jennifer Macaulay Trust which is the spinal muscular atrophy parents association, and give them an up date, you know where we are internationally on that scene.

MB Hammersmith administration, was that a lot more administration than you had been used to?

KD Well yes it was, than I had been used to certainly. But if you are going to be a director of anything you have got to expect extra administration, but I also had a deputy director Jane Cope who was scientist, but an administrator from MRC, so she was very supportive. But obviously I had to do some administration.

MB I was just thinking of the kind of budget you had for that.

KD Yes millions, but that was OK because it was all divided into fairly responsible units. You just gave each group unit their particular budget, but I had to write an overall strategy document about where the whole thing was going to go. But it was such an exciting time because you had all these molecular biologists wanting to interact with the clinicians - these clinicians that didn't have the molecular biology. And then the potential of gene therapy, of being able to deliver genes and diagnose disease. I mean it is a wonderful opportunity just right now in science.

MB Fifteen or sixteen years in which the whole of that molecular area of medicine has been transformed.

KD Absolutely and so that was a fantastic opportunity.

MB Any other people you want to mention from Hammersmith who really made a contribution to the success that you had there.

KD I think there were. Well, Colin Dollery, as dean then, also had that vision and was extremely supportive. And of course there was everybody from Robert Winston, who was doing the IVF who wanted the diagnosis and wanted to learn about the developing embryo so that he could do everything for women at that end, all the way through to Karol Sikora who was highly motivated by what was happening to his breast cancer patients. So I learnt a lot and I learnt a lot about management of people, I learnt a lot about science and I learnt a lot about administration, I really enjoyed it.

MB Kay, at that point we are getting towards lunch time and we will wind down for some lunch and then I want to come back and go into the development of the dystrophin story further after lunch.

Part II

MB Kay I want to come back in this afternoons session and talk a bit about utrophin because that is really where the story has been moving forward quite fast in the last five or six years.

KD It certainly has.

MB I think there was some animal work, is that recent work?

KD No, no it has been known for some time but since the early nineteen eighties there was this mouse that had a mutated dystrophin gene and yet is very mildly affected. So one way of treating muscular dystrophy is to discover why the mouse is so mildly affected whereas in human, obviously, it is a devastating disease without dystrophin.

MB How did that mouse work take place? Did you carry it out or was that done in another laboratory?

KD It was actually discovered by Graham Bulfield in Edinburgh, looking for another completely different enzyme. And he noticed that this particular enzyme was elevated in this batch of mice and it didn't turn out to be a mutation in the enzyme he was looking at but a mutation in dystrophin. It's known as the mdx mouse, muscular dystrophy X- linked mouse.

MB So this mouse complements for dystrophin with utrophin.

KD Well, there must be some sort of compensatory mechanism, either that or there are large differences.

MB And that happens in other mammals does it? I have got a feeling there is an upgrading of utrophin in certain damaged muscle.

KD Well one of the theories is, for example the cardiac muscle isn't very badly affected in the mouse, and in that particular tissue utrophin is over expressed. There are about four times the normal levels. So one theory is that the mdx is very mildly affected because it has utrophin to compensate for the lack of dystrophin. But there is no formal of proof or that at least there wasn't until recently.

MB So where ever utrophin is upgraded, then the disease is downgraded.

KD That's right.

MB But what efforts are being made to actually introduce utrophin into muscular dystrophy patients muscle.

KD Nobody is doing it at the moment because nobody actually really believed it would work. So one of the experiments we are trying to do, and even to get funded, is to take utrophin and then reintroduce that into the mdx and see whether we can cure it. Because what people have done is to use retroviruses and adenoviruses to introduce dystrophin into the dystrophic mouse and cure it that way. And the question is if you do the same experiments with utrophin will you produce a cured mouse. And certainly the experiments we have just done recently, show exactly that, and we could just not believe it. I mean that was another landmark result really.

MB That's like almost now.

KD Yes.

MB You are sitting on this great story.

KD In fact I presented it in a meeting in France at the Association Française contre les Myopathies in Versailles and a few people came up to me afterwards and said, they congratulated me, and said they didn't think it would ever work and its worked spectacularly. I mean the muscles of these mice look completely normal if you put utrophin back in. So the question is can we get it back in nature and if we can then we have a real opportunity to treat the disease. So we are on a crest of a wave and are really excited about this now.

MB This work is being published quite soon.

KD Yes published in a few weeks time. That's right.

MB In **Nature**. So watch this space.

KD Indeed.

MB Bearing in mind the time of this particular interview. Taking that question up though, if you can put utrophin into mouse muscle easily.

KD No you can't put it in easily. The challenge is still that we have got to put it back in but what we can demonstrate is that if you do put it back in you can get a dramatic reversal.

MB And you are using virus methods.

KD No. We simply introduced it into the very early embryo in the mouse and then demonstrated that if you had utrophin all the time instead of dystrophin you could cure the mouse. So that means that if we could find a way of upregulating it pharmacologically, if you could give someone a small compound, small drug for example, which upregulated utrophin you might be able to cure the disease without thinking about viruses or anything to deliver the gene. That is one aspect of it, that opens a whole new approach to therapy which may or may not work, but at least it is a new avenue. And secondly because these patients, well everybody has seen utrophin before, if you reintroduce utrophin to replace dystrophin you won't get an immune response by the patient, and one of the major problems of the gene therapy, of course, is that most of these patients have not seen dystrophin because they don't produce dystrophin normally, so there is a response. So even for the conventional therapies utrophin may be the way to go. So we are getting a lot of requests now for our utrophin gene, and of course we will make it available so that as much progress can be made, really.

MB Kay, did this initiative start with a conversation with Jim Watson?

KD Well, yes, it did because when we had done…

MB That is in 1992 we are playing with.

KD That's right because in 1989 when Don Love and Diane Hill and I sequenced the gene we new that we could probably compensate, but again nobody really thought that would be possible and, in fact Jim Watson has a friend at Cold Spring Harbor who has a son who has quite severe Becker muscular dystrophy and clearly Jim had been chatting to John Cleary, whom I have now met, actually. I meet him every time I go to Cold Spring Harbor. And Jim, as we were going up the steps after a drink in the bar asked me, 'Tell me something exciting about muscular dystrophy, isn't there a new novel way of approaching the disease'? So I said, 'Well it is a long shot but the long shot is utrophin could technically replace dystrophin. ' And he said, 'Well you know I've got a friend who works for a company in New York who might be able to think of ways in which you could upregulate utrophin if you could prove that that is true'. And so a lot of exchange, Jim and John Cleary paid for one of my students then to go and work in Oncogene Science. And essentially the charities quite rightly, because they have got patients to think of here and a lot of other priorities, did not want to put money into this project until they were absolutely certain that utrophin really could replace dystrophin. And in July, you know I was able to ring them up in confidence and say, 'This experiment not only works slightly, it works spectacularly well'. And so they now are and we are setting up a collaboration to get that really to work.

MB So you see massive funding being kind of lavished on finding a way of upgrading this particular gene on chromosome 6.

KD On chromosome 6, yes.

MB And utrophin being a massive answer to the debility of muscular dystrophy.

KD I mean my dream would be that upregulation of utrophin would cure muscular dystrophy. I mean that would be the end of a major chapter in my life because having dedicated the last fifteen to curing muscular dystrophy, you know, at the very beginning, then it would mean a lot. I don't know whether we will do it but I think we can probably get the answer in two or three years because now we have to set up an accurate assay and then, with Oncogene Science and Jim Watson in New York, we can actually set up ....You know we can now screen now with modern day technologies and robots, we can screen a quarter of a million products very easily. And so if there is a product out there that will upregulate utrophin we will find it.

MB Kay you have just had one terrific experience finding that utrophin does so much to compensate. It is like a new beginning now in prospect. The whole future possibility for curing muscular dystrophy lies ahead and is in the hands now of pharmacological work on this upgrading. Who is doing that?

KD Well I think a lot of people will join us in competition and so they should. I mean now it's a whole new ball-game we need to get in different types of scientists who understand about regulation of genes. I mean it is interesting because going back

to David Weatherall and the globinopathies again, the one clinical trial for the haemoglobinopathies is the upregulation of the foetal gene to cure thalassaemia, and of course it works in a minority of patients. And the question is can we get it to work in a minority of DMD. And once you have got it to work in one then of course you begin to understand the system.

MB So this could be a meeting ground of many interests.

KD Oh yes, and that is going to be fun science again because I am going to learn a whole new set of experiments from other people. I mean I will be able to contribute my expertise so it is going to be great and I am really looking forward to that.

MB How does it feel to be on the start of something like that?

KD Well, I don't have any trouble getting up in the morning. Mind you, I never did that anyway, but I mean.

MB But it's one of the great times of life.

KD Yes it is. So we are very really excited about this.

MB But not many people know about it.

KD Well they will do in a couple of weeks' time when the *Nature* paper comes out.

MB So we are in a privileged position of discussing something that is not kind of public knowledge really.

KD It is embargoed as *Nature* would say. Yes.

MB Kay, just now looking to the wider commitments to that muscular dystrophy field, the international responsibilities. You have already said you have developed lots of relationships that were meaningful, but you have had a kind of representative role internationally you have been on international committees. Perhaps we could talk about becoming a committee person and promoting things at that level. Was that something that had to happen?

KD Not necessarily. I think I am fairly motivated towards international, well not fairly, I am very motivated to both sharing data and collaborating internationally. I think it is very important to me that, you know genetics is very much shared to every corner of the world. So it has just been a natural step together with other colleagues, to actually you know become a member of the Human Genome Organisation, drive those committees through there formation stages, writing the report in the UK on the promise and progress in the Human Genome Project, and so on. I don't want to be on too many committees because I prefer to do my science, obviously. But I still think a

major part of my role is serving on committees, and actually, slightly immodest I suppose, I think I am rather good at it, so I don't mind doing it.

MB How much does it take you away from the bench? In fact, I will put the question another way. How much do you manage to be at the bench now?

KD I do not do an experiment, but I am never away from the raw data. So I think once I stop having contact with the data as it comes off, on almost a daily basis, then I stop being a scientist. And that was the transition from going to the Hammersmith where that was becoming increasingly difficult, and then coming back to the science, and for me that was chalk and cheese. It is just bliss to be back, immersed in science again, coming in, in the morning, and the graduate students and the postdocs coming in and saying, 'Have you seen this have you seen that'? And then that is what science is about.

MB A voyage of discovery.

KD Yes that is the best part.

MB Do you tick at an even rate or do you have great patches of emotional involvement and then take a bit of a break? How does it actually pace through your life? I mean, is it consistent?

KD I think it is probably. Yes it is consistent and the reason for that is I don't just work on muscular dystrophy: there is always the spinal muscular atrophy and the fragile X stuff as well. And there are some things up here and some things down there, and science is like that and it is a challenge.

MB It is a balancing act.

KD It is indeed and you have got to keep the morale of the whole group up. So I mean, sometimes I will go home emotionally exhausted simply because just holding everybody up when it doesn't work, is much more difficult.

MB And what do you do when those days of emotional exhaustion hit the deck, as it were? What do you do?

KD Go home and play some loud music.

MB Loud music.

KD Well, anything I mean, that is where music plays its part, and playing the piano is a way to recovery.

MB Do you still play.

KD Oh yes, but not very well.

MB And there is guitar in the story somewhere.

KD Yes, but I haven't played that for a long time. When I first came to Oxford I played in the folk club then, but I haven't touched that for a long time.

MB But that is relaxation.

KD Yes it is.

MB And time with family. Do you ever go back to those kind of early days, recapitulating some of that venturing out into the country with present son and husband? Does that family life take place.

KD Yes, it does but not at the scale it used to when I was young, simply because I won't sit in a traffic jam. You know, if you go to Manchester for the weekend, you spend eight hours, four hours getting there and four hours getting back.

MB But the wish is there.

KD Oh yes, but you can do it, that is the great joy. I mean, Oxford is a nice place to live; you don't have to move very far before you can get on your feet and see some decent country and walk by the river.

MB You get to 1995, and we have talked of a CBE. That must have been for international work, was that what it was for? I want to put that on the map. I know it is embarrassing you.

KD Yes. It was for contributions to genetics in the international scene, really.

MB That was a proud day.

KD Yes. It was a bit of a shock.

MB A bit of a celebration for the Stourbridge folk as well, was it?

KD Yes it was.

MB Kay, just looking back over the years of that career and digesting what we have covered now, and thinking of the prospects for the future. Perhaps, we could talk of what it was like being a women growing in science, because we haven't talked about whether that was easy or whether in the days you became a research scientist that was tough, and what the reflections are at this stage, whether there is any bitterness or whether you feel you have had a particularly good hand of cards.

KD I have been lucky and I have been at the right place at the right time. But, on the other hand it has been a struggle at certain periods, and I can see it is getting easier but I don't think it is ever easy. I think the higher you get up, the tougher it gets, whether you are a man or woman, but I still think it's tough for women at the top, just getting into those positions at the top. And I guess looking back...yes, I got squashed a few times, but you have to bounce back. And the most important thing is don't do it if you are going to be bitter because inevitably there are going to be set-backs that will make you feel bitter and that just sours you. So I have never been an ardent feminist, I don't believe in discrimination pro-women so that women get the post ahead of a man without it being really deserved. It is going to take several generations and as long as you are patient, you know, women will get there. But I certainly feel now there is less discrimination than there was. Ten years ago it was pretty bad.

MB No actual example of feeling left behind by things or hard done to.

KD Or even prejudiced against; oh absolutely, simply because Steve was in Oxford then they assumed I would stay in Oxford, oh yes. I mean that certainly has played its role. Some of the people that would have stood against me then are my greatest friends now, and I don't feel any bitterness, that is part of time and they now appreciate me as a scientist. You know, I have no regrets, prejudices or bitterness for that at all.

MB Using the intellect of that scientist you have just summarised, the background of, looking to the future, you say you are on the beginning of a whole new genetic front.

KD I mean that is where I have been luckiest of all, to enter genetics in 1980 when you have got your sort of ten years formative science behind you and then you have got all that knowledge. We are going to have all these genome projects so we are going to have all the tools to answer all the biological questions. I think it is the most exciting time that we have ever had in biology, whatever field you are in, whether it's chemistry or biology. So I am looking forward to the next twenty years, if not thirty years. There will be a lot. There will be disease; there will be new drugs to combat disease. I think it is going to be fantastic.

MB You are seeing the genetic disease in a big way, single gene diseases, will really be pushed off the map widely.

KD Probably, yes, because we are talking about diabetes, infectious diseases. I mean, you know, I went to a talk on Thursday where Craig Venter talked about how many bacterial genomes he had sequenced in the last six months. You know, next week it will be TB, new strains of TB. And these are things that he couldn't have even done three years ago. It is that fascinating combination of the very fast robotics and abilities that industry can do, combined with the innovative science and the real problem solving that academics can do, together with industry. All the boring stuff has gone. I don't have to spend two years trying to clone the X chromosomes and I

don't have to spend another four years looking for the DMD gene. It will already be there on my chromosome and I can now clone a new gene, dial it up on the computer, spend three days designing an experiment just by sitting in front of the computer. But the cleverness of it course is to design the right experiment now and the tools will all be there. I think that we have amazing opportunities.

MB In looking at that robotics, isn't that kind of taking it away from the academic arena though, and sticking it into firms all over the world?

KD Yes, it means that we have to collaborate with industry, otherwise we are not going to have access to this information.

MB What about things like copyrighting because that is becoming a big, a big issue now, people grabbing a bit of gene and saying that belongs to me. Is that going to be a major problem to that progress you see?

KD No. It will pass because there is simply going to be so much new information out there. The Patent Offices are not going to be able cope.

MB What a thought.

KD And people will fast realise that the real inventive stage is what do these genes do and how do we find things that interact with these genes as targets for drugs and combating disease. So you know it is going to completely change it. So I think the patent issue has been a major problem but I think it is something that is going to pass now. I mean people are just going to become more inventive and less paranoid about that phase.

MB Kay we are at the end of our a very exciting life story for me. I don't know whether I have missed anything or feelings inside that you want to convey to me because I already have got a passion springing at me from the discussion of your research that I think actually measures what you are about. Did I miss anything?

KD I don't think so. I think it is just exciting to be a scientist because there is absolute motivation every day to go in there and do something. I have no difficulty in keeping on going and actually you know, if you have a problem in one, you know, you are worn out, or you are fed up, you can go and do your science, and if you are fed up with your science you can come back and come and read 'The Hobbit' to your son. From that point of view life is perfect.

MB And is Steve there still kind of sorting you out and keeping you moving when the days aren't as good?

KD Oh yes. So if I get down he throws me back in, and I couldn't have done without him, actually, because of that. You just need someone strong enough to say,

‘Go back and fight’, because they will let you sink if you want to let yourself sink and that is true.

MB Thank you for taking me down that journey of your life. Thank you very much.

KD Thank you