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Sir Walter Bodmer FRS in interview with Dr Max Blythe
Oxford, 4 December 1987
Interview 1

MB Sir Walter, I would like to turn your thoughts to your early days and to ask you to tell me something about your mother and father and the main influences of your schooling.

WB I was born in Germany, in Frankfurt am Main. My father was Jewish, my mother was not - she had a mixed English/Swiss background. And, because of Hitler, we had to leave Germany, but that was in 1938 and I was only two and a half then, so I don't remember anything of that time at all. My father was a doctor but he had to retake his medical exams because of the English regulations, so at the age of forty-six, or something like that, not knowing any English, it was quite hard. So we settled in Manchester then ...

MB A big change?

WB Well, it was! Although the only thing that I remember at the time, which was interesting because I had just learnt to talk, and I had learnt to talk German, and what I do remember of that time is first, not wanting to talk English and then not wanting to talk German afterwards. So although I later learnt German at school, and I still understand it reasonably well, and my parents used to speak quite a bit to each other in German and would speak to us - I was the youngest of three brothers - in German, we would always reply in English. Interesting asymmetry.

MB So you go to school in Manchester?

WB Yes, I went to school in Manchester and my first school, actually, was the preparatory department of the Manchester High School for Girls, which is interesting because my wife was the head girl of the Manchester High School for Girls! And how these things happen - we were in Japan, I think it was, and we were having lunch with the Japanese ambassador and it turned out that his wife had also been to the Manchester High School for Girls. I think that I was the only man who had been to the same school that she had been to! Anyway, that was just down the road from where we lived and then I went to Manchester Grammar School. I started in the preparatory department there, and it is interesting to look back on it because I was two and a half when we came, my oldest brother was six years older, the other was four years older, and they both went to Manchester Grammar School, and from knowing practically no English and then just at the beginning of the war being sent to Wales, my oldest brother had to learn a bit of Welsh. So I went to Manchester Grammar School.

MB A phenomenal school.

WB It's an amazing school. A large school, more than a thousand boys, all boys of course, still all boys, tremendous educational standard. Perhaps a little too narrow in some ways but, for me, it was a great time. I went, eventually, into the modern side because you had the modern side and the classical side, and that influenced things a bit because I did languages, I did maths, but I never did much science. The only science I ever took at school, apart from maths and physics, was a little chemistry. I never learnt any biology at school which, actually, isn't a terribly good thing when I think about it.

MB What horizons were forming at that stage?

WB Well, I wasn't very clear about what I was going to do and I, eventually, did maths. The reason I did maths, I think it is again interesting how chance influences what happens in your life, during the war they had women teachers who helped, because so many people in the war, and one of them happened to be a friend of the family and she said to my parents, 'If he is any good at maths and sums, you know, he ought to go into the maths six, they all get scholarships to Oxford and Cambridge from there.' And I had enjoyed doing the maths and seemed to be doing all right at it, so I said 'OK.' I didn't have any other ideas particularly, which in retrospect is odd, because my father was a doctor and I learnt a lot from him, I used to go round Manchester when he was doing his visits, house calls, which isn't so often done by GPs nowadays. And he had a very academic background and interests originally, and had done a certain amount of research but had been frustrated in getting a University appointment because he was Jewish. And he had wanted one of his sons to be a doctor, at least one of them, and I was the last hope, and I never quite understand why I didn't study medicine in fact. It was, I think, because the circumstances weren't quite right - there wasn't much science done, I didn't do much in that way, I drifted into the maths and by that time it was too late.

MB But though you have given me the impression that this was a great hope for your father, I get a feeling also that he put no undue pressure on you to go otherwise.

WB I suppose that was true, yes. I think that he would have liked it, but he saw that I was going in and he was very keen on us being successful at school and, I suppose, he felt 'Well, if that is what you are doing, and you are successful, then fine.' But he must have been rather disappointed.

MB What of your mother?

WB My mother was born in Germany, her father was English of Swiss origin, died at a young age, and then she settled in Switzerland after her father died, because her mother decided to move to Switzerland, and was brought up there. In fact, her two older sisters stayed there much of their lives. Her eldest sister is over ninety now, my aunt, and is totally Swiss, lives in St Gallen, speaks English quite well. She became interested in dance and she was a student of a very famous proponent of modern dance, called Rudolph Laban, which I got involved with a little bit because I used to act when I was at school quite a lot. I enjoyed acting and being on the stage and doing things, and I used to help with some of the performances they did. Very crude lighting…

MB There was never a thought that you might go that way?

WB Not into acting, no. I enjoyed it a lot, I used to have all the women's parts at school, I was Mrs. Malaprop and I was Maria in Twelfth Night, and even in the sixth form at school I played Lady Isabella in (?). I thought that I could never get away! Nowadays that wouldn't happen, you would have the girls' school across the road, the high school, doing things with the boys.

MB A nice balance in a home that has got modern dance interests and drama interests and medicine...

WB It was an interesting mixture because my father was quite musical, so we were all automatically taught the piano, that was important.

MB And you are an enthusiastic pianist now.

WB Not as much now as I would like to, but I played a lot when I was younger and still enjoy it. It is very good relaxation. So, at Manchester Grammar School I did a lot of different things and, from that point of view, if you wanted to do things other than the academic, it was a tremendous opportunity. I always feel that everything you do is important later in life. One of the most difficult things I've ever done, I think, is have to give the prizes at my boys' school, the Magdalen College School in Oxford. You wonder what on earth to say, and one of the things I thought you could say is, 'whatever you do, you can make use of later.' So acting at school, learning to play the piano, the maths and all these things which were not obviously relevant to what I did later, in fact are useful. And every time you give a lecture it is a bit of an act, so the acting is useful for that. So I did that, I swam at school, but the maths I did and that took me eventually to getting a maths scholarship to Cambridge, because that was the way things ought to go. The maths teaching at school was tremendous, there were things that I learnt at school that I never learnt better in maths, even as an undergraduate at Cambridge, which, in a way, is crazy because I ended up having done an undergraduate degree in maths from the ages of fourteen to twenty, doing virtually nothing but maths and a bit of physics, in terms of academic training, which I now think is appallingly narrow, and shouldn't be allowed to happen. I suppose it didn't terribly harm me in the future.

MB So, you go to Cambridge, college?

WB I went to Clare College and, again, there is an interesting story there. I was destined to go to Trinity - all the best mathematicians go to Trinity College, Cambridge - and the teacher at the school, they had it all mapped out, how you did those things. And I was one of the two who put Trinity as first choice, he went down the list for the major scholarships as one did then, then the minor. I didn't know where Clare was, I didn't have a clue about it. But I didn't make it to Trinity, but they had a very good maths director of studies, a man called Richard Eden, who used to take all the pickings that had been dropped out by the other colleges and picked me out for Clare. I had not a clue about it. But it was actually important for me, because in those days, still about half the people did their military service first, and half not.

The one who got the scholarship to Trinity had to do his military service first and was told that that had been made clear in the interview, and I escaped that. I suppose that things would have been all right otherwise, but it was actually important. It meant that I went straight up to University and didn't have that, sort of, break which could have had quite an influence. And Clare College was a very important influence on my life, it was a very friendly college, and later, when I became a fellow there, that was because I had gone there as an undergraduate. So, these little chance things that you have no control over can have a major influence.

MB Yes. I am trying to put that in a historical context - we are into the '50s now?

WB Yes, I went to University in 1953. I went up as an undergraduate - I was seventeen, which was on the young side, at Clare I was probably the youngest in my year. Mathematicians could do that. And, as an undergraduate, you have lots of spare time, you couldn't do maths all day.

MB So you had a very fun time at Cambridge, a terrific place to be.

WB Yes I enjoyed it. Everything is done at such a high standard - you try and get involved in a bit of the music and the technically professional pianist doing the accompanying. And trying to do a bit of acting, I used to act a bit but, you know, all the people - I think that Jonathan Miller was one of my contemporaries - there were people like that. Either you took that as your professional interest, or you did the academic things.

MB What were the great academic influences of those undergraduate years?

WB Well, I took that maths course, and in those days you could do the main maths tripos, as it's called, in two years. You could omit the first year if you had got a scholarship. And I chose to do that. I enjoyed it, but somehow I had the feeling that it was all things that had been done a long time ago, there was nothing, really, at the forefront. And I had not a clue as to what I wanted to do. I used to frighten my father by saying, maybe I would become an actuary, because he really wanted an academic training. He really wanted his sons to be something in the academic world, one way or another, that was his whole aim. But what happened is, in my second year as an undergraduate, we had a survey course in statistics by David Cox, now Sir David Cox. He was then in his last year, teaching statistics in Cambridge. It was a very good course, it was an inspiring course and it turned my interests to statistics.

MB Lucky that you just coincided with Cox in that way.

WB It was, in a way, because it is little things like that, again, that influence you. It struck me very much and then I decided, 'all right, I'm going to do statistics.' And in your third year there, you could do what we would now call probably a graduate course, part three of the tripos, which was a mixture of different lecture courses and you could chose to do them in statistics, in numerical analysis and in genetics, because of the mathematical side of genetics and statistics. And here is another accident, in a way, I had gone to see a man called [John] Wishart, who was the reader in statistics there and said, 'Look, I want to do statistics, would you take me on eventually, and what do you recommend me to do?' He said, 'Oh yes, I'll take you on. You do the part three in statistics and then you can come and do a PhD.' Well, it turned out, sadly, that the summer before I started doing statistics, he died of a drowning accident. The people in the statistics laboratory later said, 'Oh no, you have got to do the diploma in statistics in your fourth year after you have finished your third year.' And I said, 'No thank you, I am going to get married, and I have other things to do. I'm not going to wait around.' So that again was an influence, in a strange way. But what then really caught my mind, and my major interest, was because of the genetics lectures, because R.A. Fisher, the great Sir Ronald Fisher, was the Professor of Genetics there.[1] So he, with his mathematical and statistical interests, gave courses that went for the mathematicians which you wouldn't actually take as part of statistics. I had heard of Fisher, in David Cox's lectures, so I was told to learn a little genetics. I was given, as I call, three or four books I was told to read by a man called Owen, A.R.G. Owen, who was a lecturer under Fisher and a mathematician. One of them was a textbook on genetics and then the other, either two or three, were Fisher's books, *The Genetical Theory of Natural Selection*, a book on the design of experiments and possibly, also, I don't remember, *Statistical Methods for Research Workers*.

MB Terrific volumes there.

WB Yes, I mean, four books just for the summer, just to learn a little bit of what you are doing! But, what I did do, and what really caught my fancy initially, was the genetics. It was a totally new world to me, in those days it was still quite formal, but here I felt, was something that was not a hundred years old - although it was getting on to be a hundred - but was living now, with new things happening. And I suppose always, with that influence and my father in the biological side, I very quickly decided that that was going to be my real interest. I used to keep a diary at that time, and I still have a record of it - in my first term of the third year, within weeks of starting the courses there, I had determined that I wanted to work with Fisher, and do my PhD with him in genetics. It was a major switch, because until that time I really hadn't a clue what to do, which is another thing I feel is important to tell the young, not everybody knows - maybe you do if you study medicine, or if you go for the professions - but not everybody really knows what they are going to do in the future.

MB I've got that message of Fisher's influence, obviously in Cambridge in the mid-'50s at that time, things were happening in genetics. Was there any influence from that side coming at you? I mean, the DNA story, was that also poignant?

WB Well, that happened eventually, yes. Not so eventually, I suppose. You remember that I started doing these courses in '55/'56, and Watson and Crick - Watson, incidentally, was at Clare College, he is an honorary fellow of Clare College - that was '53. So it was fairly early days after the discovery of DNA. Now Fisher was a close friend of Francis Crick's, because they were both at Caius College, I mean the colleges have an influence. My first hearing of the structure of DNA was when Fisher, in one of his very mathematical lectures either in '55/'56 or the following year,

[1] Sir Ronald Aylmer Fisher (1890-1962) Balfour Professor of Genetics University of Cambridge, 1943-57.

took out of his pocket - and I still remember it - a crumpled copy of a paper that Watson and Crick had written for the Cold Spring Harbor symposium on the structure of DNA. He gave a beautiful description of the structure of DNA, very simple, I have still got my notes on it, then proceeded to go on with a very abstruse lecture on the mathematical theory of genetic recombination, or something like that. So that was I first heard about it, but because of that inter-relationship, Francis Crick was quite friendly with the people in the genetics department and in my early days as a graduate student there, starting to do my PhD, we had contact with him and that was an important influence. It was, sort of, casual. I mean, we didn't go regularly to the famous laboratory which, at that time, was in the Nissan huts at the Cavendish. But it did influence what I did, and it did influence the fact that, eventually, I decided I had to learn molecular biology, which was where things were at. But, you see that the course I did, first and foremost, were very mathematical initially, but then I realised that I knew no biology, I had not taken a formal exam in biology, nothing. I had learnt my genetics through going to the courses in the genetics department, I went to lecture courses in biochemistry and then to courses that Sydney Brenner gave, because Sydney was there at that time, and, of course, has been a very important influence in molecular biology and its research. A very lively person, he used to come in with a cigarette hanging out of the side of his mouth, with not a note at all, and he gave brilliant lectures.

MB So that was the third great influence at that time?

WB That was very important, to learn genetics then, because what I was doing was statistical and mathematical and I enjoyed it. And Fisher had said 'You must be practical.' And I remember when I went for my interview with the Agricultural Research Council, which gave me my studentship, and I got the message that I had got to be practical, and they said 'What do you mean practical? Do you mean working on a calculator, or something like that?' And I said, 'No, I was thinking of a garden or something!' I hadn't a clue what practical meant. But that was a very important influence of Fishers, he himself, many people don't realise, was a great naturalist and knew the materials, and although in the sense in which we talk about experiments now with test tubes, he didn't do that. He had a sense of the need to collect your own materials, to work with them, to know the problems of natural material, its variation, its incompleteness and the nature of experimentation. And that was a very important influence on me. Fisher was a very great man, I think, in many ways, one of the greatest scientists of this century. We owe a lot to him, more than people realise, apart from the development of statistics, the words, variance was a work that he introduced in one of the early papers on genetics.

MB And a good communicator, and a nice man.

WB Well, that's not so easy! He was not a terribly good communicator. We all had to go to his elementary genetics lectures every year, but in return he took you out to the Bun Shop, the pub next to the Cavendish afterwards. And they had tremendous insight, but, in formal terms, they were not terribly good lectures. And, as a person, he could be quite irascible, could be quite difficult, but he could be quite charming if you kept on the right side of him. I was fortunate, I did. He was quite charming, always charming to my wife as well, we married at a young age.

MB I suppose I should ask about your wife, Sir Walter, I was just coming back to that, because you mentioned that marriage was in prospect.

WB Well we met when we were both at school, we used to control our unruly charges from the High School across the road, where she was, and the Grammar School meeting at the bus stop on the way home.

MB And both went to Cambridge together?

WB No, she went to Oxford, I went to Cambridge. And I used to, illegally of course in those days, go across most weekends and if I had had any trouble there, they would have sent me down, I suppose. Anyway, she read PPE - politics, philosophy and economics - but we kept closely together, and married virtually the day after we got our degrees.

MB I want to take you through the final days at Cambridge, because eventually you make a big transition, you go to Stanford. What happened in the interim, the kind of Fisher years, and going to Stanford?

WB Well, in my time with Fisher, I did statistical and mathematical work, models of the evolutionary process and had a tremendous training in the quantitative side and a very rigorous training, in many ways, in statistics and its experimental ideas. All of which have ended up being very important for me, although you don't think of it at the time. Fisher retired during my time working with him, and my formal supervisor was this man, A.R.G. Owen, who was an interesting man but a little bit to one side, in some ways, in what he did. But when Fisher retired, they didn't appoint a successor for a few years and so Owen, myself and a colleague who were fellows, were left to teach all the genetics in Cambridge, which was a tremendous experience. So, I don't know, it must have been '58/'59 by that time, I got a research fellowship at Clare College after two years doing my PhD which was a great help and another important influence. I had to teach microbial genetics, well, there's no better way to learn than to teach, so I had to learn all this which was tremendous for me. And it made me realise that, really, the way that you had to go was in the modern way, the microbial genetics and the molecular biology, and eventually, I had to do the grand tour of going to the States and finding somewhere to go to.

MB Finding somewhere like Stanford and [Joshua] Lederberg?

WB Yes. There were one or two things that happened on the way though, that again were interesting influences later on my life. I had started doing some work with *Aspergillus* and with *Neurospora*, particularly with *Neurospora* which, in those days, were among the chosen organisms of genetics. And, as a result, I had spent a couple of months with [Guido] Pontecorvo[2] in Glasgow, who was the pioneer of *Aspergillus* work and that was important for me because he was a pioneer of what's called somatic cell genetics, using *Aspergillus*. The fact that you can get somatic diploid cells to segregate and I think that it is something you have been involved in yourself?

[2] Guido Pontecorvo (1907-99) First Professor of Genetics at the University of Glasgow, 1955-68.

MB	That's right.

WB	And he had thought, at that time already, that that could be applied to mammalian cells and had people trying to do mammalian, human, somatic cell genetics. That was an important influence on me too, because that was something I later ...

MB	That was way ahead of its time.

WB	Oh yes, he was an absolute pioneer in those ideas. It didn't work out for him, but I later became very much involved, and that became one of my major areas. So that had an important influence on me. And there was another influence in Cambridge that was important later, because Fisher - although he didn't work with test tubes - had tremendous insight, and in the days very shortly after the discovery of sex in bacteria by [Joshua] Lederberg and [Edward] Tatum, Lederberg with whom I later went to work, had become very interested in that. He had taken on a young Italian, Luca Cavalli-Sforza as a research worker in his department, because of his interest in bacterial genetics - he thought that that was where the future lay. He was always very bitter later that the University wouldn't allow him to give Cavalli, now a very distinguished human geneticist and bacterial geneticist, wouldn't allow him to give him an appointment, so Cavalli went back to Italy. He left behind, in a refrigerator, some glassware and I was the next person to use that glassware in Cambridge, in the genetics department, when I started to play around with *Neurospora*. Anyway, it was obvious that you couldn't play at these things, you had to learn properly, and by that time [John Thoday] had succeeded Fisher as Professor of Genetics. To his great credit, I must say, it was he more than anyone who said, 'Look here, Bodmer,' no first names in those days, except Fisher would call you by your first name if you could give him a ride in your car, you would never call him anything other than Professor or Sir Ronald or something! Actually, another thing about Thoday, because I had started doing a bit of work with *Neurospora* and enjoyed it, and when he came around the department looking to see what it was he was going to be taking over, and he new I was mathematical, saw me at a microscope, he said to me, 'What are you looking at, Bodmer, mathematical formulae?' Because he never quite thought, at that time, that a mathematician would become a little more practical. But he did encourage me to apply to go to the States, and my first thought, at his suggestion, was to go to CalTech which was a great home of genetics and of *Neurospora* work. I applied, and the great Max Delbrück was there, and I had met Max Delbrück through Francis Crick and actually talked to him, and as a mathematician had thought, well, perhaps he would be someone good to work with and he would have been prepared to take me. But I applied for a Harkness fellowship, which is the only thing I have ever applied for, I think, and actually totally failed. I think I failed, again how things matter, they wanted young people to go and be ambassadors for their country, you know, and not just do a bit of science. And when I said, 'Look, I've got a wife and two kids, and I am not going to go without her,' they said, basically, no thank you. That's what Eric Ashby later told me, now Lord Ashby was master of Clare College. So, again, that was an interesting influence.

MB	Perhaps a lucky break, in a way?

WB Yes, I mean CalTech was a marvellous place, but it meant after that, that I took things into my own hands and I had, of course, got to know about Lederberg. And I had the feeling, which turned out to be right, that he was a man of tremendous breadth who would tolerate a mathematician who wanted to go into the lab. So, on my own back, I wrote to him and I said, 'Look here, are you prepared to take me on?' He wrote back, and ummed and ahhed and said, 'I really can't take you on, why don't you try and go to CalTech?' So I wrote back to him, and I had heard that Stanford was quite a nice place too, and I said, I really want to come and work with you, I don't want to go anywhere else. I still have the letter he sent back, which is another lesson, he started off, 'Dear Bodmer, your persistence is very flattering.' Here was a man who was a Nobel Prize winner ...[3]

MB '58, I think.

WB Yes, and it was an interesting lesson which I had learnt earlier with Pontecorvo, because when I had wanted to go and work with him and do quantitative genetics with *Aspergillus*. He wrote back through my formal supervisor, and said 'That's a dreadful idea, how stupid, you've got to do biochemical genetics and, anyway, you can't just come for a few days and learn anything.' I was a young graduate student, and thought 'What on earth do you do about that?' So, I ignored it because he had said 'Well, maybe, if he wants to come anyway,' I wrote back and I said, 'Oh well, I am so glad that you would be prepared to have me visit for a few days.' In fact, I went for a few days and then went for a couple of months. It is a lesson, persistence, and it is a lesson I have learnt later with people who have wanted to come and work with me. So, Lederberg said, 'Oh, all right I will take you, but I can't take you next year,' so we decided to have our third child for the summer, so it would be a year old when we went to Stanford. Then a month or two later, he wrote back and said, 'After all, I can have next year.' That's why, when we went to Stanford, our youngest child was six weeks old.

MB What year is this?

WB That was in 1961. Now, by that time, I'd had my PhD a couple of years, I was a demonstrator in the department of genetics and I had been a fellow of Clare College - it looked as though I was established in a reasonable academic direction in Cambridge. We loved Cambridge, we had bought a house there, we thought it was a marvellous place, and here we were, off to Stanford for a year or two and then back to this marvellous academic setting. But, of course, it wasn't to be like that. Now Lederberg, knowing I didn't know much about molecular biology had suggested that, on the way, I did a course in molecular biology. Cold Spring Harbor was one of the great meccas for molecular biologists and Max Delbrück had started a course, the famous phage course, at Cold Spring Harbor which was really just for the likes of me - it was for people who had come in from a totally different area, like he had done as a physicist going into the quantitative side of biology, which is how molecular biology developed.

[3] Joshua Lederberg was awarded the Nobel Prize in 1958, at the age of 33, for his discoveries concerning genetic recombination and the organization of the genetic material in bacteria.

MB That was terrific provision, then.

WB And so people like me, and I, went there for a month and take the phage course. And, again, that was a tremendous influence because you could get immersed in a totally new world - I had heard all about it, phage and bacteria and making phage crosses - from Sydney Brenner and his lectures and the lectures I had had to give. But really to do it there was tremendous fun and a marvellous experience, and people I met there I still have contact with, throughout my life. And the people that you had seminars from there - you know, when we talk now about concentration of excellence, and centres of excellence, bringing people together, the intellectual stimulus of bringing people together is so important. I can't understand why people don't accept that now, university as a gathering of scholars, how they started. And those were the influences on one's life, that was a tremendous influence. Incidentally, I never know why Lederberg decided to take me and change his mind, I've never really found out, I didn't find out from him. I have a suspicion it was because Luca Cavelli was a pal of his, and had somehow heard about me, and maybe he had that intuitive feeling in him that here was this funny mathematician who wants to do molecular biology. Perhaps that's all ...

MB You never felt in a position to ask him?

WB I haven't done. It's funny because I know him very well personally and one of these days I'll go back and ask him, 'Why on earth did you take me?'! He probably wouldn't remember himself. So, I went to do that on my own for a month, and that was tremendous, and then went to Stanford and my wife followed. She said that she nearly turned back in New York, because there she was, with three young kids - our oldest was four, the next was two and the next was virtually nothing - and it was a tough thing, never gone abroad like that, never gone to the States before. It was quite hard actually.

MB That's coming up against it, isn't it?

MB Yes, and then she turned up and we had a little house. I know you've interviewed Gus [Gustav] Nossal, well I more or less succeeded Gus, I had sort of stepped into his shoes. And, indeed, people say that I look a bit like him and for a while I thought, 'Who's this guy, whose shoes I'm stepping into, following around?' And it was even more than that, because Esther Lederberg, Josh Lederberg's then wife was a very friendly and very thoughtful person. She had written and said can we provide you with any help and with this young couple with kids, what on earth are they going to do? She had arranged that we took over Gus' house, the house that they had rented and his car, not a terribly good car! So we got there and a bit of the clothing was in the drier and the most important thing, we have always told Gus and Lynn this, was the babysitter list on the wall - that was our saving grace, our lifeline that started us off so that we could have, eventually, a tremendous time in Stanford. It was a marvellous environment for a young person developing their career in a different way.

MB Was your wife a scientist also?

WB Well, she is now. She wasn't really at that time, she did - here in Oxford - politics, philosophy and economics and concentrated on the economics and the statistics. She always says that I put her off the philosophy of economics, you know. She worked for a while, there, as an assistant for a very well known economist, [W] Brian Reddaway, and really was starting on an academic career, if you will, in economic statistics in Cambridge, in the department of applied economics. But then the children came, and it was a bit hard to keep going. And after we got to Stanford when our youngest was about 18 months old and was, sort of, driving her mad, the delightful little fellow Ewan was and big fellow he now is, she decided she just had to go and do something else. At that time - and that's part of the story, of course, of what I did at Stanford - there was an opportunity for her to get involved in some of the work that I had just got involved in that had a statistical element. That was in early '63. So we have worked together, now, for 25 years and she has developed her own scientific career as one of the senior scientists at the ICRF [Imperial Cancer Research Fund]. So she became a scientist from that. But to go back to Stanford, I had gone there to learn molecular biology having got this initial spurt from Cold Spring Harbor and Lederberg, who is another remarkable man, again one of the great scientists of this century, a very remarkable man, having laid many of the foundations for molecular biology through his tremendous work on the genetics of bacteria. And a lot of ideas that are still so important nowadays of the way that viruses, phages, devices that attack bacteria, integrate into the chromosome - which is now fundamental to many of the things I am involved with in the cancer field, because oncogenic viruses, the cancer viruses integrate into the chromosome - all those ideas came from bacterial genetics. And, of course, now with the recombinant DNA revolution, that's all from the bacterial genetics, the groundwork that was laid by Lederberg and other people. He had, in contrast to what many people say, realised the importance of DNA at a very early time. The real definition of DNA as the genetic material had been the great work of [Colin] McCloud and [Maclyn] McCarty's, published in '44 and showing that DNA, a chemical extract a bacteria, could transform their genetic properties. Many people say that it wasn't appreciated by geneticists at the time, and Lederberg looked at it in a very interesting way and they said that it was clear that he did, and he tried to do transformation in *Neurospora*. And then, with the development of genetics of *E. coli*, the organism it developed in, they tried to do transformations with that particular bacteria and it didn't work. Of course, they wanted to do that because, as eventually happened, you wanted to put together the chemistry of the genetic material with what you could do with it as an organism.

MB Right.

WB So, he had tried to get DNA transformation going in *E. coli*, and it didn't jolly well work and it was frustrating, which is remarkable when you think about it nowadays, since the whole of the recombinant DNA revolution depends on doing transformation in *E. coli*. But, in those days, it wasn't possible so there was another system, with another organism, *Bacillus subtilis*, which was developing there, so I got involved in that. And I was involved in some of the earliest work on understanding the mechanism of how DNA gets into bacteria, that it actually gets in physically, and it was a tremendous training because another influence was [Arthur] Kornberg,[4] the Nobel prize winner, the discoverer of DNA polymerase and another major influence on modern molecular biology, was just next door at Stanford. And they had come together, brought there by Henry Kaplan, a very distinguished oncologist and scientist, who had the foresight to bring these great scientists into the medical school. The idea was that they would work together, the geneticists and the biochemists so I was assigned to work with Kornberg's group on how to make biologically active DNA with the polymerases. Again, that was an enormous influence, very exciting, and Kornberg was a great scientist and a total contrast from Lederberg and I always think that there are these two sorts of scientist like Fred Sanger on the one hand, who is the epitome of that - a brilliant experimentalist who, in some ways, they don't have flights of fancy, but they lay the groundwork of many of the technical advances - and then the people with enormous imagination in science, which are people like Fisher and Lederberg. So I was assigned to be the genetic assistant, I made all the DNA for the initial experiments on the interpretation of the way that the DNA polymerase worked that the Kornberg group used. That was a tremendous training for me, and one tends to forget the resources one had, in those days. Phosphorus-32 was just about, of course, used; tritiated thymidine was hardly there, I was one of the first people to use a scintillation counter in Kornberg's department. People, a fellow called Karl Schulkar, came - he had got the experience and I was learning - we were the first to use a preparative ultracentrifuge in Kornberg's department. You don't remember these things nowadays, and that was the tremendous training from the ground upwards. As I would say in those days, there were two DNases, enzymes that cut DNA; there was DNase I, the classical one known for many years which you could buy, and there was DNase II and you jolly well had to make it if you wanted it. That was another useful thing, it was the only enzyme I ever did purify, but I did once purify one. I went to the slaughterhouse to collect a spleen, it was calf spleen, to make DNase II. So that was very important training. I had thought, incidentally, when I went to Stanford that that was my future, no more population genetics, statistics, you know, I was really going to turn on in molecular biology. But, Lederberg's foresight was to allow people, in a way, to do what they want and to give them what they need, which again is an important lesson. I mean, here we are talking about the problem of science nowadays in this country, what do young people want? The last thing that young people want when they are starting in a new direction is to be told to apply for a research grant in order to support themselves. What you want is to go into an intellectually stimulating environment and have the resources to do what the environment makes you do, without having to get that support, and that's what Stanford did for me, it was fantastic. Only four or five years after I went there did I apply for my first grant, and that's the way it ought to be. Then you can justify your independence with your own financial resources.

MB By any standards, that's a period of great privilege.

WB Yes. And it was a time in the early Sixties, it was really a golden age from that point of view. It was an expanding time in terms of support, I never worried whether I

[4] Arthur Kornberg shared the Nobel Prize in 1959 with Severo Ochoa for the discovery of the mechanisms in the biological synthesis of DNA and RNA.

was going to get tenure or not, or what was going to happen. You didn't worry you know.

MB You were building as you went.

WB Yes, he had a grant, I didn't really think much about where the money came from, anything like that. You just did things, you signed requisitions and chits. Esther Lederberg watched over his shoulder, that was an interesting relationship too, she was a delightful person and we are still great friends with her, although she and Josh later divorced. But she was a terror in the lab, she would interfere all the time, and you had to divide your life into two and tell her, 'Get off my back' in the lab, but when it came outside the lab, there was no-one who could be more friendly and helpful. Well, there were other things and Lederberg, because of the breadth of his interests kept stimulating me on the quantitative side too. I had learnt, incidentally, at a very early stage, about computers as a vacation job before I went to University. I had been looking for something to do, and here's a bit of chance as well, because I was a statistician I thought that I would get a statistical job, and I applied first, I think, to ICI, they had a good statistics division - they haven't changed much, actually, in spite of all that people say about them. They said, 'Oh no, my young man, we can't take you on to do statistics until you've had a year's graduate experience in statistics.' This was for a vacation job, you might have thought that they would want some mathematician from Cambridge, ostensibly, about. So, after I had done my year's graduate work in statistics, I came back, you know and said 'Will you take me on now? I've done a graduate year...' 'Oh yes, we'll take you on, we'll give you a couple of quid a week and your lunch.' So I said, 'No, thank you,' and I managed to get a job doing computing, which paid me, maybe, six or eight pounds a week, but that was a big difference. I was about to get married and I needed the money! So I learnt computing that way, and that was very important to me because I was, actually I think, the first in this country with a man called Crosby, who is in Durham, to use computers to model genetic systems. It was the early days, I used to stand in the queue to use the computer in Cambridge, with the people who were doing the structure of proteins, the x-ray crystallography. So, I had become well aware of computing, and in those days you remember that there was no such thing, even, as assembly language, it was right down to the basics.

MB Yes, I do remember that.

WB It's amazing when you think of the change now, you even had to program floating point multiplications, people probably don't know what floating point multiplication is! Program that in decimals from a binary system, which was quite good experience. If you went back to that now, you couldn't do anything. So, I realised that computing could be used to do analysis and things like that and started, fairly early on, to use the computer to analyse our data and, you know, plot graphs from density gradients and things like that. Lederberg was just beginning to take an interest in computing, and he was a major influence, in fact then, has been on the development of artificial intelligence and expert systems. He was just starting then and my wife always says that one of the most important things that she did, that's not being quite fair on him, is to teach Lederberg how to use a card punch - starting him off in his computing! He encouraged that sort of development, and in fact, was very interested in the use of census data, and the one paper we ever wrote together was on how you could use census data for genetics. So I kept up with the quantitative interests in a variety of ways, one way was he introduced me to a mathematician there, Sam Carling, we had a programme in population genetics together for many years, we still continue to have contact which got me into other things. Also got some independent support and he introduced me to Rose Payne[5] at Stanford. Now, Rose Payne, soft money as one says in those days, was a pioneer of the tissue-typing field and that became an important part of my life and my wife's life in our scientific careers. She had started looking at blood groups on white cells, as opposed to red cell blood groups, which was a stimulus, incidentally, from the great and late Sir Peter Medawar,[6] because he had said if you are going to match people for transplantation, then the genetic differences you should match for, you should look for on the white cells and not the red cells, because his work had shown that you could get graft rejection stimulated by sensitizing someone with white cells but not with red cells. Now, Rose had started work with sera from blood transfused patients and those were complicated, and she had realized that rather like the way you can be stimulated in the rhesus system, that you might find the agents for doing the blood typing from women who had had children. So she had shown, along with another pioneer of the field I knew, that you could get useful reagents by going to multiparous women. She had got a crude agglutination technique and had all this data, and frankly didn't know what to do with it. I knew she didn't and Josh said to me, 'Why don't you go and talk to her, you know, maybe there's something interesting there.' And I did, I got her to teach in the genetics course which Josh had landed me with the students, and looked at this data and was fascinated because here was a whole new world of something you could do that somehow struck me that it ought to be important. The reason was, going back to Fisher and his teaching, he had taught about the blood groups - he was a major influence, of course, on the development of blood group research in this country, being the stimulus for the work that Grace and Sanger did - and his insightful analysis of the human blood groups had somehow left its mark on me that I thought, 'Ah! Here's another bloke who likes this thing, how fascinating.' But it had different problems and I was given some work by [Jon] van Rood, who was the other pioneer in this field, to look at and immediately there were some statistical approaches that were suggested as to how one could sort out these patterns of reactions. It was tremendously exciting that there was this possibility and that's how I got into the work on the HLA [human leukocyte antigen] field, as we now call it. And that's how my wife got involved because I was doing other things and I realised what needed to be done and the types of analyses, and Rose Payne needed a bit of help and I got a bit of support with Sam Carling in this grant. So we put Julia on Sam Carling's grant - it's an interesting thing that, not everybody would allow that sort of thing nowadays - and she worked in Rose's lab and we started working on the analysis together. We got a little program on the computer and the first program brought up four antigens; two of the first antigens, one of which had sort of been seen by Jean Dausset - for which he later got a Nobel prize[7] - and the second, and they defined the first locus of the HLA

[5] Rose Payne (1909-99) Pioneer and expert in tissue typing.
[6] Sir Peter Medawar (1915-87) Awarded the Nobel Prize in 1960 for the discovery of acquired immunological tolerance.
[7] Jean Dausset shared the Nobel Prize in 1980 with Baruj Benacerraf and George D Snell. It was awarded for the discoveries of genetically determined structures on the cell surface that regulate immunological reactions.

system and the other two which van Rood had seen. It was very exciting, a little simple statistics on very crude laboratory data were the initial definitions of the HLA system together with the work of van Rood.

MB Beginning to pick up a very important area of the human genome and the charting of it.

WB Yes, and that was very important. And, of course, we went on from that and eventually I took that work into my own lab a few years later and it became one of my major research interests and it became the research career that my wife pursued from those beginnings. So that was still quantitative, I never really left the statistics and the quantitative side behind but combined them with the laboratory side.

MB And this remained the main province of your interest, throughout the rest of the Stanford days?

WB Not quite, because there were two other things: first of all, I had established a reasonable career in molecular biology and had done some interesting work on the mechanisms by which DNA gets into bacteria and that was actually my main, initial, experimental work using some of the techniques that had recently been developed. I continued that until about '66 or '67, about five or six years, and then had made the very definite decision that I wanted to get into human genetics at the experimental level and saw two approaches to that, one was to take into my own lab the work on the HLA system, to do the typing and to use some of the new techniques that were just starting, so Julia moved upstairs into my lab from Rose Payne's lab and we set it up in my lab. The other was stimulated by the interest I'd had through Pontecorvo, reinforced by the contacts of Stanford to take up somatic cell genetics, to take up the genetics of humans working with cells in culture. Because Pontecorvo had laid the groundwork for the idea that that could be possible and other people, of course tissue culture had developed, and one of my colleagues in the genetic department there had been involved in early attempts to do somatic cell genetics, working with cell cultures, getting mutations in them. And just a few years before had come out the first work, and I had heard about it interestingly in a symposium at Cold Spring Harbor in 1964, the first symposium they ever had on human genetics - the second was just a couple of years ago, I was at that too - there I first heard, really, about somatic cell genetics from John Littlefield, because I had given our first substantial paper on the HLA system. So I thought, this is tremendous because now, apart from anything, we can put together the work on the surface antigens, these important things, with trying to do the genetics of cells in culture. And, again, that was an exciting time.

MB Phenomenal.

WB Yes, and it was at about that time, of course, that Henry Harris, working here in Oxford with John Watkins, had shown that the viruses which it had been known could lead to cell fusion had shown that you could actually use a virus, Sendai virus, if it was inactivated, to fuse cells of any origin.

MB I must say that he has just talked to us in this very studio, not very long ago, about that very thing.

WB Well, that was an important technical development and it made people realise, all though I must say at the time that it hadn't worried me at all, I had never questioned the fact that one would be able to do fusion between cells of different species and we had thought that we ought to be doing that. I think we had that idea that we wanted to cross human and mouse cells before the pioneering paper of Mary Weiss and Howard Green came out. Now they followed on the work in somatic cell genetics whose groundwork had come from Littlefield and then from the great Boris Ephrussi, who was one of the great pioneers of genetics with whom Mary Weiss had worked and done the early, actually making hybrids that grow out. And so Weiss and Green made the first human-mouse somatic cell hybrids that grew. Henry Harris made fusions, he didn't really grow cells out and do the genetic development, he was interested in other things, and it was Weiss and Green that did that. That paper came out just as we were setting up to do our own work in somatic cell genetics and, of course, was an important stimulus in at least the sense that it made us realise that we were on the right track. And so, without any experience of my own in cell culture, and with a young graduate student who had come as a population geneticist, Marcus Nabholtz and someone from the tissue typing field, an Italian visitor, we set up our lab there in somatic cell genetics in '66/'67. Pretty crude, but again it was very exciting...

MB Very early days.

WB Right at the beginning, because we thought well, here's a whole new world of things that you could do. So it was those two things, the somatic cell genetics and the HLA work that, of course, then became my major interests. And while we were at Stanford, we did the first hybrids with human lymphocytes across to mouse cells, which was important because we thought that you had got to be able to cross anybody, you or me, we can't always depend on growing cell lines out. In those days, it was much more difficult to grow a cell line out. We thought, how smashing if you could just take a blood sample, take the white cells from that and cross those. That was possible, because you could rescue the resting, non-dividing lymphocyte into a growing cell. And, of course, that was later the basis for making monoclonal antibodies, fusing lymphocytes and it lead to us doing some of the earliest, after Weiss and Green, the next real genetics was what we did. It was showing how you could assign a gene to a chromosome, in that case the X chromosome by manipulating things on the hybrid, because there were drug resistant markers that had been developed by John Littlefield and others, and we could show that you could select so that the marker had to be there, and that was on the X chromosome and then select against it so it wasn't there, and along with that went another marker, the G6PD [glucose-6-phosphate dehydrogenase] enzyme, which was know to be on the X chromosome. So, in some ways, that was the next real step in genetics and then, following that, and this was still at Stanford, we realised that if the chromosomes segregate like that then any pair of human markers should go together - either they should both be there, or they should both not be there. So we realised that that was a way of putting genes onto chromosomes. From Stanford at that time, in 1970 after the first paper in '69, we and alongside Frank Ruddle at the same time doing similar work, and the first two papers were published together in the same issue of *Nature*, on assigning genes to chromosomes using them.[8] So that's what I took with me to Oxford, when I came to Oxford in the, sort of, scientific work I wanted to do.

MB How did the change to Oxford come about?

WB Well, we had a marvellous time in Stanford. It was a tremendous environment.

MB This was four or five years, more?

WB Nine years. It was a tremendous time, a stimulus that was without parallel, but we had always thought that, other things being equal, it would be nice to be back in the old country. There had been various occasions, once even in Oxford earlier, Hans Krebs had quite surreptitiously invited me to the biochemistry department, which I later got to know very well, and said would I be interested in coming? He realised that what he had on offer wouldn't attract me. So when they advertised a new chair in genetics in Oxford, we thought it's either that, or we'll never go back, something like that anyway. Actually I had written off for application forms, because I thought that I would apply for that job, but I never did apply formally because I was written to, by Joel Mandelstam, who has just retired as the Professor of Microbiology, and who was one of the electors, and asked whether I would be interested. It came out of the blue, I was amazed, I didn't even know they knew I existed! So I said yes, I felt I couldn't say no, and sent a C.V. and letter saying the sorts of things I was doing and they invited me over, to my amazement, to say 'Would you like the job?' This was in 1969 and I went over - they were very good, I went over in May, it was a beautiful spring, and all the blossom was out and people were very nice, because Rod Porter, the late Rodney Porter,[9] the Professor of Biochemistry here had recently become the Professor of Biochemistry and I was given the choice - would I have my genetics sub-department in Biochemistry, Botany or Zoology? Because I was effectively E.B. Ford's successor, who was a well known ecological geneticist but had a personal chair. It was obvious that, as a molecular biologist, that it ought to go with biochemistry, and I had, in a way, the best of both worlds for them, because I could say that I would deal with the population genetics and all that, if you want me to, but I'm jolly well going to have a molecular biology and biochemistry and all of that. And so there, poor old Rod, and I always think about this, had to take this, sort of, blind date with this young kid from California! But we got on tremendously, he was fantastic and an enormous help.

MB A remarkable man.

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[8] Santachiara A S, Nabholtz M, Miggiano V, Darlington AJ, Bodmer W, 1970. Genetic analysis with man-mouse somatic cell hybrids. Linkage between human lactate dehydrogenase B and peptidase B genes. *Nature* **227:255**, 248-251.
Ruddle F H, Champon V M, Chen T R, Klebe R J, 1970. Genetic analysis with man-mouse somatic cells. Linkage between human lactate dehydrogenase A and B and peptidase B. *Nature* **227:255**, 251-257.

[9] Rodney Robert Porter (1917-1985) Whitley Professor of Biochemistry, 1967-85, University of Oxford. Awarded Nobel Prize in 1972 for Physiology or Medicine. He shared the Nobel Prize with Gerald M Edelman in 1972 for their discoveries concerning the chemical structure of antibodies.

WB Yes, a tremendous man. Also an important influence on me in a different way. I don't think that I was ever introduced, I later discovered how these things work. I suppose the electors had said, 'All right, we will offer it to Bodmer, if his face looks all right, and he doesn't look like a dropout or something'! Because they then did offer me the job, more or less on the spot. Peter Medawar, incidentally, was one of the electors to the chair. And I said, 'I've got to come back again, with my wife.' At least they paid my way back, I don't think that they paid for her. But they did pay for me to come back again and we came back, had a look at it and, actually, we went to have lunch with Peter Medawar, just months sadly before he had his stroke, at the National Institute for Medical Research. And he was very positive, and everybody was so positive that we thought, all right, this is the right thing to come back to. It was a major decision because we had had a marvellous life, I mean it really was a golden era in California.

MB I'm sure that part of you remains in Stanford.

WB It does, and part of our kids. By the time we came back, they were 13, 11 and 9 and they were Americanised. Mark, our eldest, went to Magdalen College School and they kept saying 'You American, when are you going back home'! But home for him was here in Oxford. So we have never had any regrets, we are quite sure that we made the right decision. That is not a negative comment on the time we spent at Stanford, it is just that you have to go to your cultural origins in the end. So we came to Oxford in 1970.

MB And that's where, at the end of this first interview, I am going to close down for this moment because we have to go to the Oxford story, and the later story, on another tape.

WB OK. Thank you.