Interview with Professor Peter Goodfellow, 17.07.2014

PG: Peter Goodfellow
PH: Peter Harper

PH: It's Thursday, July 17th 2014 and I'm talking with Peter Goodfellow at the Academy of Medical Sciences in London. Peter, can I just start by asking where were you born and when?

PG: I was born in 1951 in Londonderry, Northern Ireland because my father was employed as a sergeant in the British Army and he had been posted to Northern Ireland. He once boasted that although he'd been shot at by three different groups of people he never actually shot at anybody else, Northern Ireland and Palestine being two of them, I can't remember what the third one was. So from Northern Ireland he was then posted to Germany and I lived the first four years of my life in Germany. And it is reputed by my parents that I spoke German although the fantasy that I would one day go back to Germany and the German would come flooding back, failed to materialise in any form whatsoever.

So when I was four years old my parents moved back to the UK. My father had been given the choice, he either had to become an officer or he had to leave the army. There was no way he wanted to be an officer so my parents moved back to the village they both came from in the Fens, a little village called Littleport, about 16 miles away from Cambridge, north of Cambridge, but very much not part of Cambridge. So between the age of 4 and 14 I think I went to Cambridge maybe three or four times. Our big town, the one which was the Fen big town was Kings Lynn, which we used to call Lynn. So if you wanted a big town you went to Lynn, you didn't go to Cambridge which was a very foreign sort of place.

PH: It's a long way from anywhere isn't it, Kings Lynn?

PG: Littleport was a long way from anywhere, so I had a rather strange childhood in the sense that I started off in classes for the educationally subnormal and the village was a relatively large village but it also had a very large hinterland so the school actually, the primary school I was sent to was quite large and they had a class for the educationally subnormal which I was put in. And the school was a sort of school where there were two types of teachers, either the teachers had taught my mother or they had gone to school with my mother. And so one of those, a Miss Ducker, kept an eye out on me even though I was in this class. I'm not sure if this is a true memory as we were discussing earlier, this is the memory construct, I think there's an element of truth to it; I was sitting in the back of the class and because we were the thick kids, instead of giving us pencil and paper they used to give us little slates with chalk. And my mother worked as an unqualified accountant for a local firm, i.e. she did the books, and she taught me how to do all basic addition, multiplication, division, and so I was bored sitting in the back of the room divided 27 in 3042 to find out what the number was, and Miss Ducker caught me doing this.

And the long and short of that was she took me to the head mistress and I have this memory of feeling like I'd done something bad, I'd been caught doing magic I wasn't supposed to be able to do until I was much older and therefore I could be in serious trouble. And I almost mentally tossed a coin, you know, "Shall I fake it and pretend I can't do this stuff or should I

just do it?" And for some reason I just decided I would do it. And to give the school their credit they took me out, the maths I was doing was three or four years advanced for the age as taught, and they took me out of that class and put me in the top stream and got a peripatetic language teacher who came in and worked with my reading.

I didn't learn to read until I was late 9, early 10 and then it was like a switch had been thrown. I read voraciously, anything and everything. As long as it had words in it I would read it. I often think that if it hadn't been for Miss Ducker I'd be picking potatoes now like all of my school sibs were doing, are doing. This is how these things go. So I went from the primary school to a secondary, a grammar school, because I passed 11+ and again it was one of those things where it was a miracle, that the school all thought I wasn't going to be able to do it because of the language problems. Great rejoicing was found when I passed the 11+.

And that was a very dislocating experience. So the way it worked for that generation after the war was that effectively the UK needed more people in the middle classes so they opened a window with the grammar schools, especially in academia. I don't know about you, Peter, but many of my colleagues have been through the same sort of process of working class or peasant class into the middle classes because of the grammar school system. And that was sort of exemplified by the fact I had to wear a uniform whereas the kids who I grew up with didn't. So that put a big barrier between us. And I actually had to go 16 miles every day, I had to cycle a mile to catch a bus to go 16 miles to school there and back every day from the age of 11. So suddenly I was sort of taken out of the environment I grew up in and I was shoved into this new environment where I didn't know anybody; until I went to secondary school, I didn't know anybody whose parents owned their own house. I just didn't, that wasn't part of the world in which I lived. And apart from the vicar perhaps and the one doctor in the village, I don't think I knew anyone who had been to university. It wasn't a concept that was around.

PH: I was going to ask you about that: were you the first person in your family then to go to university?

PG: Oh yeah, absolutely. Well, I think this is just a quick point of oral history which is worth noting: my mother was the abandoned child of a prostitute so my social grandmother was the woman who was paid by my biological grandmother to look after her child so she could continue work. And then the biological grandmother disappeared leaving my social grandmother with my mother and although I use those words, I think I can say that nobody on this planet has ever loved me the way that my social grandmother loved me, and it's a complicated thing to do with a fact that social structures meant that my mother and my grandmother couldn't actually fully love each other because of this peculiar way that they became mother and daughter. So it all got transferred to me in a strange way. But I tell that story because my mother passed the equivalent of the 11+ when she was a child but the grammar school wouldn't take her because she was a bastard. And you know that's within living memory.

PH: That's amazing.

PG: And I find, so the answer is, no, none of my family had been to university and my mother and father both left school at 14. They became middle class aspirants because of the army. The army educated my father. He was a boy soldier, they turned him into a mechanical engineer. His hobby was electrical engineering and by the time he was a sergeant in the

occupation army in Germany he actually had a servant, you know, so the servant they got was a child-minder, a nanny for me, hence speaking German as a child.

PH: At the age of four.

PG: Yeah. But I think taking them out of the village, showing them the world and being exposed to stuff allowed them to imagine there was a world outside, so they became very focused without knowing how to be middle class, they were very open to being middle class. I think they followed myself and to a slightly lesser extent my brother in, you know whatever we got into like bird watching as a child, my parents became birdwatchers extraordinaire, you know. By the time I'd given up bird watching they were off spotting lesser spotted things in the Outer Hebrides [laughs]. And my brother was into plane spotting and I remember vividly sitting in a meal one day when I'd been back to visit my parents and this plane flew over. My mother said, "Ah, there goes a 773/87" which she'd picked up from the noise going over. So I guess it's a way of saying my parents were both very smart and had had a glimpse of the world but hadn't been able to explore the world. And as I said to you not only was I the first person to go to university from my family, I don't remember anybody from the village going to university before me. It is possible but it just wasn't part of our culture.

PH: So at what stage did you start getting an interest in science?

PG: There's two answers to that. One is that water flows downhill and I'll explain that in a moment. And the second is that I wanted to be good at something. Like all small boys I would have preferred to play football for England, that would have been a reasonable sort of thing to do with one's life but it was clear quite quickly I wasn't good enough to do that.

PH: You weren't tempted into the army by your father?

PG: No, well my father was grateful for what the army gave him but very resentful for the class structure within the army. And I remember once as a child, not knowing one thing, saying, "Oh, I think maybe I'll go to become an officer in the army" and he went ballistic. I mean he said, "If you do that I'll never talk to you again!" And it was so unlike my father but he had felt very looked down upon by the officers and didn't want to be like they were looking down on other people so there was a very, no, so the answer is no.

My father was actually a champion, he was the top rifleman in the army of the occupation in the Rhine and shot at Bisley and stuff like that. But I very quickly found that I had no interest in guns and things that went bang and stuff which never appealed to me. But I wanted to be good at something. I mean I think that may be a legacy of being sort of looked upon as being stupid. I wanted at some point to be really good at something and academically the stuff that I kind of found out I could do was physics, chemistry, biology, and I didn't come top but I came in the top two or three of the class in those areas. And so water runs downhill; because I could do that and found it much more difficult to do the other stuff I stuck with that. I'll tell you two school anecdotes: one is that teachers leave imprints and one I've written about actually previously was the chemistry teacher who when we went in for Sixth Form said to us, the old cliché, "50% of what I'm going to teach you is right and 50% is wrong, and I don't know which is which." And to me that was a real sort of glimpse of the future. It's that the stuff they teach you isn't absolute, it can be, it's okay for you to question things, you know, because there's the sort of learning by rote you go through, particularly in science in the early stages where "this is the truth" you know. DNA has four bases and the bases are… and so on and so forth.

PH: Did they teach you that at school?

PG: No, I'll tell you a true story which I have published on… okay, three stories from school. You asked for one. Second story about a teacher was, it taught me something about life. Because I was so poor at languages when I went to grammar school they had a remedial class English so right, I was straight into the remedial class for English. And the school took the attitude you know the poorer you were the worse teachers you got, so we got supply teachers and all the rest of it. And then there was a new head of the department of English who came in and said, "No, it's actually my job as head of department to actually take the weakest kids." And so that guy transformed something in me by saying, "There's a difference between creativity and knowing the rules like spelling." So up until that point everything I'd ever written in English always came back covered in red, you know, you couldn't see what I'd written because it was so red. And he said, "Go away and write an essay on anything you want, whatever interests you." Well, I was a 14 year old boy so I went away and wrote this essay about, you know I was madly in love with this girl and I wanted to sleep with her and she wouldn't sleep with me and ta dah, ta dah, this long story. Finally she said she'd sleep with me and as I ran across the road to meet her I got run over by a bus. And this guy [laughter] this guy did two things: the first thing he said to me was that, "Here's the key to the Sixth Form library, you'll find some very interesting books."

So the Sixth Form library is where all the dirty books were and the books which had sex in, because he kind of figured out I probably needed to know what happens instead of getting run over by a bus. And the second thing was he basically, he encouraged me in language and so one of the, I think the only prize I ever got at school was the English prize at O-Level and I'm the only boy who ever got the English prize from the remedial class so there you go. That, I think going back, that point he made about, it's your responsibility if you're good to actually work with those who are not so strong, is a sort of life lesson and somehow that influenced me in some way I can't explain. So then the third story, so I was 14 and my parents reached an aspiration, I always thought we were very poor because we didn't have the stuff other kids had, but we weren't poor, it's just my parents were always saving up to buy their own house because to buy their own house was an achievement. And my father worked in Cambridge so he used to commute every day and they bought the house in a village called Oakington which is just the other side of Girton and we moved there when I was 14. This almost completed my total social isolation because now we moved to another place, I'd already lost my friends once, you know, and again going through this sort of period. And I fell in love with the vicar's daughter, her name was Rowena. The only problem with this was Rowena loved her horse, so there was rather the strange ménage a trois as Rowena followed her horse around and I followed Rowena and the horse.

Now Rowena was at the Perse School for Girls and she got, I think, a little tired of me following her around so she asked me whether, you know, she could fix me up with a date with one of her friends. I think I kind of got the message that she really wasn't interested so I thought, "Okay." So I went on a blind date and it was to a coffee bar in Cambridge and I met this girl and the date didn't go well; so she came in and I can't remember how we recognised each other but she asked me what I did. Well, I thought this was a really stupid bloody question, right, "I'm a schoolboy, what do you think I do?" So I'm sort of thinking now, "What am I supposed to say?" So I said, "Oh, I do biology." She said, "Yeah, my dad does biology." I said, "Oh yeah?" She said, "Yeah, he discovered the structure of DNA." And she must have seen this blank look on my face because she said, "You know, the Golden Helix, the stuff of life?" So I go, "Oh, *that* DNA!" [laughs] I hadn't a clue what she was talking

about. So I often think if I had only made it with Gabrielle I could have been Crick's son in law. What a lost opportunity! [laughter]

Going back, so biology, chemistry, physics, and I actually was better at physics and enjoyed physics but the teaching in maths was so poor at the school I went to, no kid ever got higher than a D grade at A-Level and I just opportunistically figured out you know if I can't do maths, I can't do physics, chemistry smells, so I think I would rather do biology.

So, and it fitted in with the sort of natural history stuff, the bird-watching and I came from a peasant background so I knew about plants and food and stuff like that. So it all felt okay apart from the fact I was useless at what biology was in practical terms, dissections and neatness of drawings and all that sort of stuff. And classification of plants [laughs] was eyes glazing over. We had a biology teacher whose main claim to fame was his dyslexia was probably even greater than mine. He told us once in a moment of weakness that his girlfriend always used to send his letters back with the errors corrected [laughs]. He told me that it was no good in going to university which I absolutely wanted to. I wanted to go to university so I could be a school teacher. Why did I want to be a school teacher? Because that was the highest thing I'd been exposed to. And at that school, you know, I wasn't going to be a priest, and the school said, "You're not smart enough to be a doctor" so [laughs] "and we don't send people to Oxford or Cambridge so you know look for something." So this guy said, "Don't do biology or botany or zoology." He said, "You've got to specialise in life."

PH: This was at Cambridge now was it? Or still in Kings Lynn?

PG: No, well, I went to grammar school at Soham which was 16 miles away from Littleport and also 16 miles away from where we moved to so I was still commuting every day 16 miles. And so he said, "Do microbiology." So I sort of sat down to sort of figure out what microbiology was and got an interview in Bristol and I remember reading, God I've forgotten, Postgate? Postgate, I think, book on *Man and Microbes*, it's a classic text, my brain's going, I think it's Postgate. And in there he sort of described things like using bacteria in mining to extract gold and all sorts of weird and wonderful things. When I went to the interview in Bristol essentially the course in microbiology was what I call the Spit and Shit Brigade, it was medical microbiology basically. So when they asked me, "What do you think microbiology can be used for?" I gave them electron extracting gold from slag, from lead mines, that kind of thing. They kind of figured, "This guy's a bit different." So they offered me two E's which basically meant, there were only 16 kids on the course, they wanted me to go and as Bristol had been my top choice, off I went to Bristol.

PH: Yes, so Bristol must have been very unfamiliar ground for you?

PG: It was wonderful. Basically I knew that there had to be more in life than cabbages in the front garden. And also my way of rebelling from my parents was not to ride motorbikes and stay out all night, it was you know, much more subtle non-confrontational, but I was going to plot my way out of here. And so basically when I went off to university I left home, really that was it. I love my parents and became very close to them again later in life but you know there was a bit where I just wanted to be the person who made the decisions about my own life and not have to ask them for money and stuff. So essentially I went off to Bristol and worked in the summers. One year I worked as a technician for the National Institute of Agriculture, botany, where they taught me to drive.

PH: Where was that?

PG: In Cambridge. I worked on predictive harvest yields, you know basically setting the price for wheat you need to know how much wheat there is in the country. So this was trying to look for correlates between that you could measure which would predict accurately what the harvest would be. The second year I worked as a [unclear] which was a great career, I loved doing that. So essentially once I'd gone off to university I left home. I had met Julia and just sort of lived together from the age of 18 onwards, so that's how that works.

PH: May I ask, was she a student at Bristol?

PG: Yeah, I met her the first day of university and we were brought together by my needle phobia. So at Bristol, that year when I went in, I think that Epstein of Epstein Barr, Tony Epstein, must have persuaded the university to take a blood sample from every student who went in. So none of this stuff about informed consent, we were just told, "You're going to be bled." And the way they did it was when you registered for the course they gave you a piece of paper and on the paper was a number and you had to go and put your arm through a hole in the wall, carrying your number, so that the technician the other side you couldn't see, was bleeding you, took the piece of paper, stuck it on the test tube, bled you and put the blood in the test tube. Well you know, if you, like me, have a needle phobia for reasons I won't go into but to do with a botched operation as a child, I sort of peered into the window and said, "Excuse me, anyone in there? Excuse me!" [laughs] "I'm going to faint if you put a needle in my arm." And they were standing, right, so it wasn't you were laying down or anything, so the guy says, "Don't be stupid, just put your arm through the thing." So I put my hand through and of course next thing I know I'm laying on the floor, a whole lot of people looking over me. One of the people was a girl called Jackie Bean who actually lives in London, I'm still friends with her. And Jackie said to me, "Would you like to come, I saw you signing up for the same course I'm on, would you like to come back and have a cup of coffee?" And I was thinking, "Jesus, this is university life! This is why I came! A girl's asked me for a cup of coffee!" [laughs] So off I went with Jackie back to her room and it turned out she was sharing a room with another girl and it was Julia.

And I spent a couple of hours and at the end of the two hours I had switched allegiance from Jackie to Julia and Julia said, "Why don't you meet me after chemistry tomorrow morning and we'll go and have a cup of coffee?" I was getting used to the idea of coffee with girls, it seemed like a great idea. So I went trotting of the next morning, 11 o'clock, standing outside the chemistry building and had this thought, "Shit! I'm not sure I can remember what she looks like. What colour was her hair? Jesus, why would anybody, I think it was sort of dark, she wasn't blonde…" Anyway I was sort of doing this and then out runs this girl, throws herself into my arms sobbing. And I go, "There, there, there, it's okay." She says, "I don't want to do chemistry, it stinks! I hate chemistry, it smells so bad." And I went, "There, there, dear, you don't have to do chemistry. I'm sure we can find something else for you to do." So she'd signed up for physics and chemistry and she just switched into physics and maths or whatever, so that solved that problem. So that was how we met basically and lived together ever since then. So she did physics and then her PhD in low angle X-ray scattering and then went to Stanford; when we went to Stanford she worked on the synchrotron at Stanford doing the structure of nerve growth factor. So she moved into biophysics/biology from that side but always with an emphasis on the computational mathematics component of it.

But getting back to Bristol, yeah for me it was like heaven, you know, a big city, it's a wonderful place, oh my God, you know. And something happened which was slightly, two things happened at Bristol which were transformative. One was I found biochemistry easy. I had never found anything in my life easy before and it was sort of autocatalytic, the easier I found it the harder I worked. And Bristol had a system then that every kid had to do, who was doing biology, medicine, dentistry, anything with biology had to do the biochemistry key course in the first year. So there were 1,500 of us doing this course and I came joint top the first year with a guy called Peter Little, who you may have come across? So Peter and I came joint top the first year of all the students doing that course. It was like, "Shit! I've found something I can do!" That was really exciting for me and so that just made me, I was a pretty boring student, you know. I worked, I played soccer and I had sex with Julia and that's all I did for three years, it was great. I didn't go out and get drunk every night, I didn't do all that, I just worked and played the occasional game of football. And the second thing which happened was a guy called Mark Richmond, do you know Mark? Okay, so Mark had come from Cambridge to be the professor of microbiology so they'd hired in a molecular biologist to run a department which up until then had been a spit and shit department and essentially all the other kids doing the course. So at the end of the second year I basically had full credits for, I did extra biochemistry courses, I had all the credits I needed for a microbiology degree and a biochemistry degree. And in the third year of the course, you could pick and mix anyway, so I was fully qualified to do biochemistry and microbiology. But Mark was trying to sort of, he was into R factors, do you know? Do you remember the R factors?

PH: Vaguely.

PG: Okay, so these are plasmids which encode the resistance factors which had just been discovered, the reason why you got bacteria resistant to penicillin was because there were these R factors which could be transmitted between bacteria and this was clearly important and interesting, and of course was eventually the basis for recombinant DNA technology because the same elements were used for constructing plasmids, so essentially plasmids were derived for R factors. So Mark offered a course, which was a third of my final year course, which was molecular biology. And because he came from Cambridge and because I was the only one who elected to do this course, he taught it to me like you and I are talking. So he basically would say, "Go and write me an essay about carbohydrate as the structure of, as the hereditary material." And I'd go away and I'd think about carbohydrate as hereditary material or "could you, if you had the instructions for an organism, could you construct that organism?" You know it was designed to make me think and question and engage and so that and another teacher, a guy called Gilbert Howe, TGB Howe, who had worked, he had a first degree in classics and then done a PhD with a guy called Smith Kearney in Ireland, working on gene regulation, what nowadays we would call transposable elements. So there was the same phenomenon that McKlintock found had been found previously by this Irish school in bacteria. And there was a big debate beforeoperon about how you control gene expression. And Gilbert taught me, like Mark did, about it being an intellectual exercise, that you should think about things and that there wasn't necessarily *an* answer. And so they encouraged me continuously to build that side of me and in those days there was a sort of spotter system. I think it's much weaker now, but there was a sort of funnel that if you got a good one, you told your mates, and I was clearly spotted as a good one so I was sent off to see Sydney Brenner for doing a PhD at…

PH: What year have we got to by the way, Peter?

PG: I went to university in '69 – '72 so it would be '72-'75, so '72 I was looking for a PhD position. And you have to, my background was really molecular biology and if it was genetics it was haploid genetics or merodiploids, and it was not, I had no training at all in classical genetics. In fact the only training which was available to me was in fungology, a course we were taught in second year which I used to skip because Wednesday morning was a convenient time for Julia and I to spend in bed rather than me going off and doing fungi practicals. And so [unclear] analysis was I had no idea what it was about, it was incomprehensible gobbledygook as far as I was concerned. So anyway I got sent to Cambridge to see Brenner and he basically said, "Get a first and come back and chat about, we'll chat about your project." I thought, "Well bugger this, what happens if I don't get a first?" Went to see Pritchard in Leicester and he was doing microbial genetics, stop me if you don't know these people.

PH: No, I do know.

PG: So he was doing basically classical bacterial genetics and I got to, was sent to Oxford to meet this guy, Walter Bodmer, who was newly come back from the States and was doing human genetics. So I went trogging off to have an interview there and quite enjoyed myself and apparently sort of shocked them all by sort of pontificating and joining in as though I knew what I was talking about. But they only had two places and they'd already promised the two places so I got a telephone call saying, "We'd really love you to come but we don't actually have space for you." So I said, "Fine." I think I would have preferred to go to Oxford or Cambridge, mostly for the snob reason that I was going to show those bastards at school that I could go to Oxford or Cambridge, there was definitely an element of that. But going to Leicester wasn't the end of the world. I think it was Leicester. When Alec Jeffreys got given some prestigious college fellowship that freed up one of their MRC fellowships so Alec getting that meant that I then got the PhD position he would have got, and so off I went to Oxford. Now, I had no idea. I sort of read Cavalli-Sforza and Bodmer and thought, "Bloody hell, I don't know any of this stuff. It's maths. Julia, help! I need to learn some maths. I need to learn some computing." This lasted a week before we started pulling each other's hair out.

So I was really scared going because I figured I just didn't have the skill base to do this. So I turned up, basically pretty quickly I was working in Julia Bodmer's lab learning how to do HLA typing and I got given the project of providing the immunological assays to support a collaboration between Mike Crompton and Walter's lab on purification of HLA. So that was where I started. But in the lab they were doing this stuff, other people were working on somatic cell hybrids. Oh shit, this looks pretty interesting, and you know I've got plenty of time, my main project doesn't take all my time, so maybe I'll start doing some of this stuff? And to cut a long story short I basically figured out that we could probably use antibodies against cell surface antigens in just the same way as people are using isozyme analysis to do human-mouse differences. So without telling Walter I started trying to use antibodies for defining human antigens and by luck and by good fortune, one of the antibodies I found was an anti-beta-2 macroglobulin which was human specific, didn't react with the mouse, and that allowed me to map the gene for beta-2 macroglobulin onto chromosome 15 and of course, you know, we can say that it's not on chromosome 6, so that was the sort of tag-line, it's not in [unclear] or anything because it's on a different chromosome.

And that was published as an article in *Nature.* So that was my first publication. And to give Walter his absolute due, he never, he never beat me up for doing stuff, right? You know some supervisors would say, "You're supposed to be working on that project over there."

Although he had no feel for actually doing the experiments he was a wonderful supervisor in creating, and I learned from him, I didn't realise I'd learned from him, but the real skill of a supervisor is to create an environment where people working with you can be successful, what I call mutual exploitation. No, I am creating this environment so you do stuff which makes me famous but at the same time makes you famous, if you put it in very crude terms. And Walter had a wonderful lab and it was a wonderful time and so Alec Jeffreys and I were the same cohort going through. And most of the graduate students from my era just went off and became professors in their own careers, so there was Kay Davies, myself and Alec were all in the same cohort going through. Kay was in the biochemistry department whereas we were in the genetics subdivision of biochemistry.

PH: Was Veronica van Heyningen there too?

PG: Yeah, so Veronica, so that in the lineage of PhD students, someone called Bengt Bengtsson who used to be professor of genetics at Lund.

PH: I know him.

PG: You know Bengt?

PH: Because he's got a kind of interest in history.

PG: Bengt has a history, yeah, he's very interested in history. He's written a history of Lund University and is chairman of the Lund University Historical Society and all that sort of stuff. So Bengt was Walter's first graduate student and then Veronica was Walter's second. She basically was doing the somatic cell genetics stuff. And then I came in as the third in that lineage and so Veronica basically, I call her my mother, she sometimes gets slightly annoyed about this but she was, she sort of house-trained me, you know. I was a sort of happy, joyful puppy and she rubbed my nose in it when I did things which were inappropriate. So she taught me simple things like if you do an experiment on a bench and there's a drawer in the bench, close the drawer because if you spill something it will go into the drawer. Now that sounds obvious but you need your mummy to tell you [laughs]. So, yes, Veronica and I we've been close ever since…

PH: Can I ask: the cell hybrid techniques, had you imported them across from Henry Harris and John Watkins, or had it come around a different way?

PG: No, no, Walter had basically, did he actually do it? You'll have to ask Walter, I don't know. It didn't come from Henry Harris. We were definitely on a different lineage, we were much more sympatico to the Green lineage because of Ephrussi and Green. And so I think Walter got, we definitely came from that lineage, not from the Harris lineage. So Henry, Henry and Walter were very different styles. Henry liked people to call him Professor Harris and he wore a, he was a professor who wore a shirt and tie and suit and I remember the absolute horror and shock in a seminar he was giving when I asked, "Henry, could you explain X or Y?" like there was this intake of breath that anybody could be disrespectful as to call him Henry. And each year he used to give this, so funny, he used to give this lecture which was the cancer gene, so he'd give this lecture where he'd fuse together these tumorigenic cells and non-tumorigenic cells, and they looked at the chromosomes and the analysis was that cancer is caused by a gene on chromosome 6. And you'd come back next year and cancer is caused by a gene on chromosome 12. The last year I remember him giving it he said, "It's mitochondrial!" [laughter] So we had very little in common with him. The only thing that I

remember from that time, which became important, important, that's too strong a word, it came back, was the radiation hybrids. So he had been doing those, the original radiation hybrid experiments, and I knew about them at the time when he was doing them but we kind of felt they were rather uninteresting because you just fragmented the chromosomes and it didn't really tell you very much. And it was just the selection around the selectable locus. So that bit was the connection. It wasn't that Henry and Walter were enemies but they weren't particularly sympatico, perhaps is the way of putting it.

PH: So what happened then after you'd finished your PhD?

PG: So I was a superstar as a PhD student. I have to go back but I think I published 13 papers in 3 years and half of them were in *Nature* and *Science* and so on, and half of them I was first author, you know. I thought that it was like a continuation of being an undergraduate, you know? It was easy and I was really good at it and I didn't realise how much the contribution was to that environment that had come from Walter, you know? Yes, I think I was an enthusiastic, hardworking kid but he provided an environment where you couldn't fail to be successful. I guess you could but it was, all the wind was in your sails and it was a wonderful time. When I left the department I sat down and did a quick run through the known genes mapped in the human genome and I'd been involved in 10% of all the genes which had been mapped in the human genome. It was like, you know, you can do this stuff. While I was there Hugh McDevitt had been on sabbatical and Hugh basically said to me, "You should come to Stanford and do a post-doc with me." And so I agreed, Julia who was doing a PhD at Oxford at the same time, although with the Open University, she was the first woman ever to get a PhD from the Open University.

They had a research unit there but nevertheless she was the first woman ever to get a PhD from the Open University. And she got a post-doc in chemistry, as I said before and worked with [Slack ?] and I went over and worked with Hugh. Now it was a different world in Hugh's lab, completely different structure and everything I touched for 2½ years turned to shit, which was a really good sort of lesson. Now, having said that, I published eight papers in 3½ years but it was nothing like the quality and productivity I'd had and I made a really big error. I worked on, Hugh wanted me to go to his lab to work on a project in developmental biology and there was a dominant theory at the time which had come from Francois Jacob and Dorothea Bennett and a few others that there were genes in the T locus which code for antigens which are found on the surface of developing embryos and for some reason on sperm, which were controlling development, which was a reasonable sort of hypothesis , it's just that all the data was based on this crap. And I spent 2 years trying to reproduce this and it was, I won't go through it, it was serological nonsense. But every time I tried to publish stuff I had great difficulty because going against the current dogmas is a murderous thing for an individual to do. And when I proved it was wrong, everyone just said, "Well of course we all knew it was wrong."

You didn't get any points for turning over the dominant hypothesis and of course the people whose hypothesis you've turned over are out to kill you. So in particular, Dorothea Bennett, who was at Cornell, actually offered me a job and when I went, Walter went to ICRF he recruited me going back to Oxford, you know, there was a whole cohort of us, it wasn't just me doing it as you know. It was Veronica and Ian Craig and Ellen Solomon and Martin Bobrow, and all these people were my friends and colleagues, and to this day are my friends and colleagues. So we had our own secret handshake club or whatever, you know, or just people you grew up with and you knew very well and you trusted and so on. As I say, I'm still close friends with all of those individuals. So when Walter went to ICRF he recruited Ellen to

go with him and offered me a job back in the UK. And Julia and I had been struggling to find jobs in the same city. In fact I almost, Julia got offered a job at EMBL and when I went there and had an interview with Kendrew I remember him telling me, "As long as EMBL exists, we'll never give a job to somebody like you." I thought, "Well, that's great" because he basically thought all this genetic stuff was soft science, it wasn't serious stuff. So I'd like to say with great pleasure that I was invited at one time to be head of that institute. [laughs] So, but anyway, the point of that was that Julia was offered a job there and I was told I couldn't get a job there so I actually explored doing dog breeding for a while. But in the end Julia had a job offer, a post-doc offer back in London and Walter offered me the job at ICRF. So I came back.

But I learned some things from the post-doc which were important. The first was, you know, it's never just you, it's the environment as well as you. Hugh had been through a very difficult time. His wife was alcoholic and having a breakdown and life was very difficult for him so he wasn't around in the lab, and I kind of tried to take over the lab because no one was running it and he got a bit pissed off when he discovered I was running his lab, understandably but never the less. And I spent two years working on stuff which was fraudulent to the extent that I actually went and worked in the labs of the people doing these experiments and discovered that they were fraudulent in the sense that they were data selective. So an experiment which worked was one which gave you the result you wanted and anything which gave you a result you didn't want was a failed experiment. And actually that's a classic error in our science, I'm sure I'm guilty of it too. You have a view of what the answer should be and if you don't get the answer you want you look for all the possible reasons why that couldn't be true, but if you get the answer you want, "Oh, on to the next experiment!" Anyone listening to this would think that was awful but that's part of the reality of human beings.

PH: I've met this during my interviewing several times, and that was very much the case with the human chromosome number. Once it had got established as 48 about a dozen other people all got 48 because that was what they were expecting, until someone came in from outside and it found that it wasn't.

PG: Yeah, yeah, absolutely. We see what we expect to see. It's a real difficulty. And there's another combination of that where fields get stuck because all the people in the field are all thinking about it in the same way. Somebody else comes in, doesn't have our, what do you call this, creative ignorance, you know when you're not bogged down with what you think of the facts, you come up with different ways of doing it. A journalist once asked me when I went to industry what I missed about industry compared with academia and I said, "The creative ignorance of the young is the thing I miss the most." Students who would come in each year and say, "Why can't X be true?" Because they forced you to re-examine every year all of the stuff you just took for granted. So I learned about environment. Hugh taught me to write grants, he was very good at that. He made every post-doc in his lab basically write the grant for the next post-doc and that was invaluable training for going forward. And I learned that you should define your own agenda. It may be good science to attack other people but actually that's not a great career path and so set your own agenda. Don't actually spend your time trying, that's sad, but that was the truth; I spent two years, turned over a field, and that field probably had 50 papers in *Science and Cell* and it just died. I never got my stuff published in anything better than the *Journal of Reproductive Fertility*, you know, it's sort of just the way that the world actually works.

PH: How was ICRF staffed then and did you have tenured faculty people?

PG: Yeah, we were running the Protestant system. So I grew up in a part of the Fens where we didn't hate the Jews and we didn't hate the blacks because we didn't have any Jews and we didn't have any blacks. Until I went to Cambridge when I was 14 I can't remember seeing a single person who was not Caucasian, there was just no such thing. But we really hated the Catholics because they were a nice percentage, about 10% of the population were Catholic so that was a nice percentage to hate. And I remember my mother saying, you know, "The first boy I fell in love with I couldn't marry because he was a Catholic, and I don't believe in mixed marriages." [laughs] So we had, at ICRF, we had a very Protestant structure which was there was no one between you and God, so there was the director and then there were group leaders. So there were no departments or subdivisions. There was God and there was you. And that basically was great for a starting person because it meant that whatever you did was yours. And in fact ICRF worked very much on that principle. As a starting member of the faculty you were given a 5 year contract, it may have been 6, no it was 5 years, and an unlimited amount of money. The only thing you were limited by was space.

PH: I remember that!

PG: I had 400 square feet and in that 400 square feet at one time I had 14 people working and that included desk, tissue cultures, the whole thing. And yes, we did work shifts because basically it was very crowded. But all the time I was at ICRF I never had my own desk. We just had a space in the corner where whoever needed to do stuff, did stuff. And basically, when I look back on it, it was wonderful. The only thing they basically said was, "In 5 years' time we'll come and review you and if you've published lots of stuff in good journals and we think it's good science we'll give you tenure, and if you don't we won't." So after 3 years I' d just done the MIC2 stuff on the X chromosome and showed that there was something on the Y chromosome as well, so it was just about that time, I had plenty of publications and I got tenure.

PH: So, may I ask, was the whole of ICRF pretty well into major gene mapping?…

PG: No, no, it wasn't at all.

PH: Maybe the bit I'm kind of familiar with.

PG: The people you knew would be Denise Shear, Ellen Solomon, and me, and that was the sum of people who were doing anything to do with gene mapping. So I came back and was going to work on developmental biology and mouse genetics and discovered it was going to take me three years to get the strains into the country so I figured I wasn't going to do that, I needed to come up with something else. What I had done, I'd taken monoclonal antibody technology, because I knew how to make hybrids, I'd taken monoclonal antibody technology to the Bay area, so you know in those days when it was sort of being disseminated out, I was the person who in the Bay area sort of taught everybody how to make monoclonal antibodies, and actually fell out with Hugh because I tried to, he had a big contract from NIH to make mouse antibodies so there was the standard anti-H2, anti-H2 specific antibodies, and I said, "We can convert all these to monoclonal antibodies if we, all three, must spend 3 months in the lab, we can transform this whole area." And he didn't get it. He just could not see that that would have been a good use of the time. And I think also, I suspect in the back of his mind, there was this thought, "Well, if we do that then I lose the grants to keep the strains to produce the antibodies" or something. But it was interesting because he's a very smart guy but he just didn't get it. Anyway when I came back essentially I had to think about

what I would do and I started just to sort of think, well, be productive while I was thinking, was playing the same trick I'd played with Beta-2 macroglobulin, which was monoclonal antibodies made in mouse and invariably human specific, so we can use that to map genes which are related to these antigens. So I just did, started doing that, and that led me into the genetics of the sex chromosomes because of MIC2 and molecular biology came along and it was kind of obvious you needed to do molecular biology and I started putting those things together.

PH: Can I ask: MIC2, now what exactly is that?

PG: Okay, so MIC2 was a monoclonal antibody which was the first monoclonal antibody ever used, put into humans, for therapy. It was put in at Stanford by a guy called Ron Levy who stills works today using antibodies to treat patients. And he put it into patients to treat T-cell leukaemia, CLL, and maybe ALL, I can't remember. Anyway he treated two or three patients and they seemed to do okay but it didn't really go anyway, and he thought that antibody was T-cell specific, and Andrew McMichael had brought that back from Stanford in his lab, and I was just collecting, I was calling up my mates, I knew Andrew McMichael when I was at Stanford, and John Bell, calling my mates and sort of saying, "Have you got any monoclonal antibodies I could map? I've got this panel of hybrids and any monoclonal antibody we just put through it, you know? Easy way to publish a paper and who knows what you might find?" So he sent me this antibody and I discovered immediately it was actually expressed on every cell type so it wasn't you know, you had to have the most insensitive assay in the world to call it T-cell specific because it was expressed using my standard radioimmunoassays at high levels on everything basically. So we just quickly found it was on the X chromosome. But do you remember Ruthi Voss?

PH: No.

PG: Ruthi was a geneticist from Israel who came and did a sabbatical in Ellen Solomon's lab. Unfortunately she died in a car accident 20 years ago. I loved Ruthi, she was a wonderful woman, but she brought with her on sabbatical a strange hybrid which had three human Y chromosomes in it so I had this hybrid which had Y chromosomes in it, and we were vaguely thinking we might try and make monoclonal antibodies for things on the Y chromosome when we found MIC2, that was a gene on the Y chromosome as well as the X chromosome which was cloning for this antigen. So that was how we kind of got into the Y chromosome and we also found there was this polymorphism on red cells which got me working with Ruth Sanger and Patricia Tippett, on the genetics of Xg and so on. So we started to put different pieces together and the first, like everybody else we were vaguely dabbling and thinking about cloning Duchenne muscular dystrophy, or at least mapping genes on the X chromosome using cDNA. I had a post-doc who was doing those sorts of experiments and that started to introduce into the lab molecular techniques and so, as time went on, we shifted from being sort of antibody based to being DNA based, I guess, pretty quickly . It was obvious that was where the future was.

PH: So, coming onto SRY, before SRY there was all the confusion, well I was thinking there was David Page's, was it ZFY? I mean how did the story evolve with regards those genes and how did you get involved in that?

PG: It is relatively straightforward. When I told you a little bit about the cell surface antigens on sperm development control, one of those antigens was actually something called HY, which was being serologically defined by the same people that were doing this stuff . And so I

worked a bit on HY serology and realised it was complete garbage. So I knew that HY as defined serologically was a nonsense. It was clear that there was something which was HY, which was a minor transplantation antigen that you could define in the mouse, but practically that was the only species where you could do that because you needed to have inbred, something which was inbred before you could have the only differences, whether you had the right chromosome. And so I knew that HY, I'd sort of knocked around sex determination because I'd shown that HY serology was a nonsense and therefore a lot of the stuff being written about HY being the sex determinant gene couldn't be true. So when we knew that we had something on the X and the Y chromosome, and as our molecular biology tools got better, it became obvious that you should analyse chromosomes using molecular techniques and so we started to focus on sex chromosomes, and the stuff with the pseudo-autosomal region and the slippage of the pseudo-autosomal region into the Y chromosome being the cause of XX males, just meant that we were in the right place to start thinking about that problem and realise that we had tools that we could use to think about trying to clone the sex determining gene.

And essentially, this has been written about several times, but essentially there were three groups, myself, Jean Weissenbach and David Page, who were left with the tools and the inclination to try and clone the sex determining gene, and essentially we were all using the same approach, which was to construct a map across the Y chromosome using DNA from XX males and XY females to try and identify the minimal, classic positional cloning, the minimal region where the gene ought to be. And MIC2, which we had cloned and shown to be pseudo-autosomal and mapped it, and cloned the pseudo-autosomal boundary, we knew that it was the closest marker distally to the gene, and so we started walking. And we'd identified a CPG island by using pulsed-field gel electrophoresis which we thought must be the next gene down. And it was the next gene down and it was a gene called ZFY and basically we had just isolated it when we read David Page's paper saying that he had cloned this gene and he had been walking from below it towards it, and that he presented evidence that it was the sex determining gene. And I should say that by this time I was working closely with Robin Lovell-Badge and his colleagues at Mill Hill and we'd already sort of said, "Look, we can do a human mouse flip-flop here. What we learn in one we can do in the other and so on. Let's do it together." And we just basically said anything which either of us publishes in this area we'll jointly publish so that we don't end up with squabbles about whose work it is and whose work it isn't. And so we did that and David, you know, I was devastated that David scooped us, and I'd had a group of five people walking for two years in a chromosomal walk which was brutal, the Y chromosome is full of repeats. It was murderous, awful work, and we got scooped.

I remember one of the post-docs in the lab, a guy called Paul Goodfellow, no relation, as we were sitting down crying, Paul was saying to me, "You know there are lots of people who'd like to be failures like us." And that was such a wise thing. [laughs] You know it's easy to feel sorry for yourself but you know actually there are a lot of people who would like to have been in the position of failing that we had done, so it put it into some context. And so you know we sort of took a deep breath and started to think about what we would do and what experiments were worth doing when Paul said to me, "You know, are you absolutely sure it's right?" And I said, "It looks pretty good to me." And he said, "Well, you know, there's at least one hypothesis which you can always use to test this which is any XX male which has been created by transfer of Y material should have the pseudo-autosomal region. So if you could find pseudo-autosomal region positive X chromosomes, then you know, the other way around, then you know that's how that was created. So basically we had a whole load of DNA from a number of collaborators and we found some patients from Mark Fellous[?]

which we were able to show were definitely SRY positive, sorry, were Y chromosome, had all the elements they should have but didn't have ZFY. So that told us that essentially… so we, I didn't explain that very well. We took sequences that were just south of the pseudo-autosomal regions and they were Y positive. So we had Y positive XX males who didn't have ZFY. And as soon as we found two patients like that we knew that it was a mistake and there had been other indications. We'd done stuff which Jenny Graves. David Page, my lab and Jenny's lab had collaborated on looking for SRY in marsupials, sorry looking for ZFY in marsupials and it wasn't on the Y chromosome in metatherians, so either metatherians were using a different gene or it wasn't the sex determinant gene. So it was beginning to be a bit of a feel that maybe there was something more complicated but it was those patients from Mark Fellous that told us that the sex determinant gene hadn't been cloned. And we'd walked straight through it. Basically it was a very small gene which wasn't particularly well conserved and we had just walked through it, and we found it when we went back and looked more carefully which again, going back to what we were talking about before, we thought it was going to be where that CPG island was and therefore that's where we wanted to get to. We did look as we went but as I said, you know, actually it was a really horrible mess of repeats and we had had to break down everything we had again to get unique probes out to find something we could use in southern blots. So, as I say, the rest has been pretty well documented. We cloned the mouse gene and Robin showed [metatransgenic ?] animal that did the sex reversal. And we found de novo mutations in XY females, which proved that this was the gene.

PH: So the SRI gene…

PG: SRY!

PH: Why do I keep calling it SRI? The SRY gene then… had you actually come across it at the time David Page published?

PG: We'd walked through it.

PH: You'd gone through it.

PG: We'd walked through it. Look, the gene is 300 base pairs without any introns and is actually poorly conserved and so the whole of that region is stuffed full of ALUs and line repeats and all the rest of that shit; so essentially we had walked through it but our focus had been, we were looking for unique probes as we went, checking to see if there were any conserved sequences by doing zoo blots as we went but you know we actually thought we needed to get to that CPG island where ZFY was. And it wasn't until we were clear that wherever the sex determinant gene was it had to be north of ZFY and south of the pseudo-autosomal boundary, that we went back and looked very carefully through that again. As I said, it took us another six months or maybe even longer, sub cloning everything to get more probes out to try and find something. But once we had a probe everything then went very quickly and Robin did the transgenic stuff. We looked for the de novo mutants which is a formal proof that this is a sex determining gene and that led to the definition of the SOX genes and another flow of things happening. Yeah, so that's what…

PH: Just tell me about the SOX genes because I kind of know a bit about that from the clinical end and I know about sex reversal things but…

PG: Well, one of the hypotheses which I always used to justify looking at sex determination and it sort of was true and not true was that making the decision to be male or female is kind of an important biological decision and so the argument we made was that if you could understand this process you might be able to understand other processes where decisions are made. And it turned out in a certain sense that was true because there are a number of genes in the genome which are structurally related to, homologous to, SRY, which are used in making developmental decisions. And we got a glimpse of that by finding that there was a whole series of these genes that we started to map and started to investigate. You probably know, SOX 2 is important for pluripotency and SOX 7 for cartilage formation and it turns out that, sorry SOX 9. SOX 9 is probably the original sex determining gene, at least it is the sex determining gene in all vertebrates in the sense that its dosage controls sex determination in all vertebrates. So whereas SRY only controls sex determination, it's only found in mammals, eutherians and metatherians, it's [not even?] found in prototherians. So yeah, so we glimpsed that these genes might be important and we called them SOX genes because we were trying to say, "Well they might be a bit like HOX genes which were the famous genes at the time. So we thought, "If we call them SOX people will think they're sexy."

So that's how we got into that. And then, after we'd done this work on sex determination, I reached the point of having to decide what I was going to do with my career. ICRF was a wonderful place to do science but it's actually a really brutal place, it used to be a brutal place to grow old because tenure at RCIF only meant that they paid your salary and the amount of space that you got depended on your productivity. So you could be a fully tenured member of staff with no lab and that was how you were basically encouraged to be productive. And at some point you start thinking, "Do you know it might be tough to hang around here" because it's kind of obvious to your peers that what's happened to you when you've reached this stage. But I think also I felt that romantically I wanted to put something back into the academic world which I believe had given me so much. I thought that, you know, if it wasn't for universities I wouldn't be here, I would like to go give something back. A romantic view. So I let it be known that I would be prepared to listen to offers and I got a telephone call saying, "Peter, you've just been elected to the chair of genetics in Cambridge." And I said, "Well, that's very nice, I didn't know I'd applied." And they said, "Well you haven't but you've been elected." I said, "Well, that's very nice, what are you going to offer me?" And there was this silence. They sort of said, "We don't think you understand. We're offering you the chair in genetics."

And I said, "I don't think you understand. I'm not coming to do anything unless you offer me space, money, you know, I can't just take a group of people from here to there if I've got nothing to take them to." So there was um and ah and they said, "Right, okay, well I guess you're not coming?" And I said, "Yeah, I'm not coming." And in the way of the world my lab heard some rumour, nothing was ever put in the public domain, must have heard some rumour and came to me as a group and said, "You bastard! You're going to Cambridge and you never told any of us." I said, "Look guys, I'm not going to Cambridge. I'm not going anywhere without telling you but I'm not going to Cambridge University." They said, "Prove it." I said, "I tell you what, if I go to Cambridge University I'll put earrings in. I'll have an earring in each ear." They said, "Okay, fine." So a year later the same thing happened, I got a telephone call saying that "you've been elected." And I knew the person who had been previously elected and what he'd been offered in order to get him to go and then he turned them down in the last moment. So I said, "Well, I'll go if you give me exactly the same offer as you gave…" And they said, "Oh, how do you know about that?" I said, "I know exactly what you offered him. If you offer me the same I'll take the job." So um and ah and they got back to me the next day and said, "Deal." I said, "Okay, I'll come." So I called a lab meeting

and said, "Well, you know a year ago I told you we weren't going to Cambridge, well, um, we're going to Cambridge." Next morning I found this thing on my desk which was an appointment to go and have my earrings put in. So I went home and told Julia and Julia said, "No bloody way are you having earrings!" I said, "Well, you know, I promised." So she went into the lab and she held a lab meeting of my lab where they negotiated the forfeit. So the forfeit was a pony tail. [laughter] So I got converted from earrings to pony tail.

PH: You did have, I remember you had one earring, I'm sure.

PG: No, no, never, never!

PH: What year was it now that we've got to, that you went to Cambridge?

PG: Oh God, it would have been '84. I was at ICRF in '81, it's '84, '85 I guess, something like that. I was there 13 years and so came back in 1980/81 so yeah, '84, '85, something like that. So I went to Cambridge and I found it both easy and hard. The easy thing was I found that I could do administration and I could organise things. I just found I could do the managerial shit. I found that although I pissed off Cambridge I figured out how the system worked very quickly. You know the only place that any decision was made was the finance committee of the Council of the School of Biology. All the other committees were irrelevant, that was the only one which actually made any decisions, the rest was window dressing. So I pissed everybody by saying, "I'm only going to that committee. I'm not doing the Faculty A and I'm not doing the Council of the School, I'm going to that meeting there." But essentially I tripled the number of students that the department had doing genetics and I tripled the amount of money we got in research income in the department in the four years, five years, I was there. So I could do that sort of stuff. But when I went, we had sort of agreed that we'd move the family there and it just turned out to be practically impossible. Julia was going to commute and it was just too hard a commute for her so I did the commute because literally I used to cycle 5 miles to the station one end and 2 miles to the other end and so I was back to a significant commute, and when you get wet four times a day [laughs] there's a point where you go, "I'm not sure I really want to spend my life doing this."

PH: Can I ask, where were you living, in London?

PG: In North London. So we've always lived in Belsize Park / Hampstead area.

PH: And you had how many kids by that stage?

PG: Two children. And so I was cycling from there down to Kings Cross, catching the train and then cycling from the train up to, down the street. So it was just sort of hard and I was sort of thinking, "Do I want to do this?" And I'd been doing other stuff. So I'd started a company in California. When I went to Cambridge I actually took a 30% drop in salary. This was the days when, before the RAE, you know, you got paid peanuts for, it didn't matter who you were. Cambridge couldn't recruit people. I mean Jeremy [Jared?] Diamond wanted to come as head of the zoology department and they wouldn't pay him. So you know they expected him to take a two thirds drop in salary in his case. I took a third drop in salary and didn't care that much, but while I was in Cambridge I started a company in California and I was truthfully earning more working two days a month in California than I was earning as professor of genetics in Cambridge. One of my graduate students left the department and went to work for McKinsey and her sign on salary was higher than what I was being paid as head of department. [laughs] So that, it's not about money, but you know it sort of I think

one thing the RAE did, it at least created a market so that you got paid a little bit closer to the income that you were generating for the university in some ways. What did I learn from Cambridge? I thought that it would be like Mark Richmond with me. And I what I discovered was that most of the undergraduates only wanted to know the answer to one question: how do I get a 2:1 and I found that very disappointing.

That was the first. The second was that there was incredible financial pressure on me because I could raise money, to raise money. And the university was so incompetent. So the department of genetics employed five gardeners to do horticultural research when there wasn't a single person in the department doing that research but they wouldn't let us fire them because they had no way of getting rid of anybody. And I had several acres of land and greenhouses which were not used, which we weren't allowed to sublet or do anything with but were on my books, which you know, all sorts of stupidity within the university. But crudely put, I went from having one graduate student every 3 years to having three graduate students a year, which works out as a tenfold increase, nine fold increase, if you work it out, because I could. And that brought money into the department. And when you start doing that, you know, I ended up with a group of 30 people whereas I'd always worked previously with a group of 10-14 people. And when you have 30 people you end up having sub-labs, you know. You have post-docs who run bits for you because you don't really run it, and anyway I was also running the department. So I sort of found myself sort of doing, not doing what I'd done before in the same way, and not really finding the romantic solution that I was hoping to find.

PH: I guess also if you were commuting that distance you didn't really have much time to see much of Cambridge and the atmosphere, you know, outside work.

PG: I didn't do any of that stuff. I mean I hold the record for, it's another long story, I could spend all this time telling you anti-Cambridge stories but I won't. I hold the record for the highest number of colleges which refused to take a professor, which is 13, so… Colleges are like primary schools. As a professor you have to have a college but no particular college has to take you. So the way that they deal with this is they invite you to dinner and they have a look at you and decide are you one of them. And in the end I just got tired of it, I called up the vice-chancellor and said, "It's not my problem, it's your problem. I tell you what, you find a college which will take me and I promise I will go to dinner, behave myself and just get this over and done with." So in the end I joined Churchill. But I was no attraction because I was very upfront about it. I was not going to partake in college life because I lived in London and I was no adornment. And because I was chair of a small department I brought no political benefits to the college either. And in fact Cambridge should get rid of the department of genetics and just put it as part of biochemistry because it's so small that it has no political weight within the system so it can't get stuff done unless you've got a conniving bastard like me in charge. So you know…

PH: I guess that situation goes right back to R A Fisher, doesn't it?

PG: It was Fisher's department, yes.

PH: Yeah, not perhaps changed, or hadn't changed…

PG: So when I first went into the department I was given an office which was about half the size of this room, that was the office. And remarkably it had a cupboard on the wall down one side, which was exactly like that wall panel there. So the cupboard was this high. So I said,

"What on earth is that cupboard for?" And they said, "Well, it's where Fisher kept his bed." Fisher was such a tight-fisted bloke, in order to have his college room tax free, they had to sleep outside of his college room a certain number of nights a year, so he used to sleep in his office and then wheel the bed away to save himself a little bit of money. [laughs] So yes, Cambridge is a very strange place. So to get out of Cambridge, as it were, I wasn't looking to leave Cambridge but essentially I was open to the possibility and Dai Rees, who I have an enormous amount of respect for, came to me and said, "Peter, you know, we need a new head of the MRC. I'm not going to be around forever. If you got a whole lot of your friends together and formed a caucus you could probably influence who is going to be the next head of the MRC." And so I thought, "That's interesting, is that how the world works, Dai?" And he said, "Yeah, just get a few people together, your friends, people who you think are important and come up with a list of people you would like." So I did this and to cut a long story short, I found myself being on the shortlist for the job of the MRC, which I suspect was what Dai was doing [laughter]. He was a really devious, clever, wonderful guy.

So there were three of us on that shortlist and to cut a long story short the one member of the committee told me that they voted for me but the chairman was somebody was somebody who I'd crossed previously who was the chief government scientist who was chairing the committee and he said, "If you elect this guy, I'll resign." So I didn't get the job as head of MRC, which is probably a great relief to the MRC, but George Post was the industrial person on the committee. And George came and saw me afterwards and said, "Peter… You don't want to work for these guys, you want to come and work in industry." And by that time I'd started another company and I was more getting interested in how you convert academic knowledge, if you like, into things that actually help people. So for the commuting reasons, for the stupidity of how Cambridge was organised, I didn't see myself staying there forever. And so I think the emotional commitment to leave was actually when I agreed to go forward as a candidate for the MRC. So in a sense I'd sort of moved myself so I was open to George recruiting me to go off to industry so that's what I did. I went off to industry.

PH: And how did you find it? It must have been, I mean, it must have been a very big change?

PG: It was very different. I think I alluded to, I knew that I could manage things. I know it sounds arrogant to say that but you know, some people can manage things and some people don't. And I found I could do that stuff relatively easily. There were all sorts of cultural changes but actually I loved the opportunity to learn something new. In Academia actually you get put in a box so while I was in Cambridge was the time when, you know, I didn't talk about the radiation hybrids and the genome mapping and that stuff which we did at this same time. It gets overlooked now but if it hadn't been for the radiation hybrids the human genome project would have had real trouble because it was the only way that you could, because the YAKs were all rearranged it was the only way you could match together the physical map and the meiotic map. So the radiation hybrids actually formed the framework which enabled them to do the assembly of the human genome project. And all the radiation hybrids that were made in Cambridge I actually made with my own hands because I was the only one who knew how to make somatic cell hybrids. And we made radiation hybrid maps of chickens and sheep and pigs and horses and all sorts of weird and wonderful things, and we didn't talk about the SOX 9 cloning which Dave was involved with, which we did as well. I think emotionally cloning SOX 9 told me I could do it again. I know that sounds slightly silly. We cloned SRY and once I cloned SOX 9 I sort of felt, "You know, shit, I can do this. It's no longer really a big challenge." So I think there's another strand which is I was looking for a challenge.

But the reason I told you this diversion is another of the things we did in Cambridge was with Alistair Compston. We had a shared graduate student called Steve [Sorcer?] who's a really good guy, and I helped them, or we together did whole genome mapping and then association studies for multiple sclerosis. It took me forever to get the money to do that experiment because it kept getting turned down because "Goodfellow doesn't know anything about multiple sclerosis." It pissed me off no end, "What's this guy doing who does sex determination expecting to work on something like multiple sclerosis?" Instead of looking at the frigging project and figuring out what it is we were trying to do. So yeah, so we did the first whole genome analysis and whole genome association studies with multiple sclerosis, which was a long haul but eventually led to the recent stuff about T cell activation in multiple sclerosis.

PH: And you had a good clinician to collaborate with.

PG: Yeah, absolutely.

PH: You've got to be sure it wouldn't let you down on that side, which can easily happen.

PG: Nowadays it would be called the epitome of exactly what you're supposed to do but then I got that turned down by the Wellcome Trust and by the MRC and it wasn't until I basically went to the Wellcome Trust and said, "This is really stupid" that they did one of those behind-door stitch-ups where they agree between them that they would jointly fund it or some money would change hands. It was ridiculous, you know, it was an experiment. We had the patients, the technology was available, all we needed to do was put the two together. So anyway… in industry everything I did I didn't know. I loved it, you know. Every day I learned something new. I learned some chemistry, I learned some pharmacology, I learned some toxicology, I learned an enormous amount, I learnt an enormous amount of medicine because suddenly you know I was expected to be able to converse about you know, the molecular mechanisms underlying asthma or heart failure or all sorts of stuff. I actually really enjoyed the education.

PH: Was your remit right across the board? Were you head of research?

PG: I was head of research right across the board for SmithKlineBeecham, and then in GlaxoSmithKline I basically, it was organised in a slightly different way, so the pieces were, I was called Discovery Research which was sort of platform technologies but that included preclinical stuff as well, the job size in both cases I had a few thousand people reporting to me but with slightly different components. But within that I sat on all of the committees that made decisions about portfolio decisions, so you know I was involved in trial design and going to the FDA and all sorts of stuff which I'd never been exposed to before, which I really enjoyed. I think having the opportunity to do something completely new I found challenging and enjoyable. What wasn't enjoyable was for 10 years, every two and a half days I went on an aeroplane. So you know that's just…

PH: That's a lot of travel.

PG: Yeah, so I never had less than a million air miles in my account and that was, you know, flying family and friends around first class wherever they wanted to go.

PH: Was your work base still in London or was it scattered?

PG: I was only at home about, yeah, I always lived in the same place, which is Belsize Park, Hampstead.

PH: Did they have a sort of headquarters or labs or anything?

PG: I was peripatetic. No, no, so Stevenage and Harlow were two sites I had a lot of people on. So originally I had people in Philadelphia and Harlow and then I had five main sites, I had 300 people in Japan so you know, you become very peripatetic.

PH: Did you keep your own group at all, or wasn't that feasible?

PG: No. Some people did it but I feel it's, some people would be offended by this, it depends on how you do things but I think if you're running a large organisation, having your own lab is hobby science. For me, and it's sort of what happened in Cambridge, I no longer felt that it was really part of me. Yes, the radiation hybrids I did with my hands. Yes, I oversaw the use of the hybrids, the SOX 9 project, the multiple sclerosis stuff but I wasn't actually in the lab sort of smelling and touching in the way that I'd done at ICRF. I'm not saying it's right or wrong but the more responsibility you have, the more remote that stuff becomes. I think its analogous to clinicians who no longer go to clinics. You're doing an important job but it's not the same job as when you were really responsible for patients. Does that make any sense?

PH: It does, and one of the reasons I think clinicians are lucky is that you don't have to give clinics up when you get more senior, you can carry on doing it until you finish, and that's quite often what keeps one sane.

PG: Maybe, you know, as I said, for me it's not that one's better or the other's worse, it's just the way that I felt engaged. I'm very happy doing science the way I do at the moment which is I help start companies and work in venture capital, reviewing projects. I don't do creative science anymore and when I was at GSK and SB, I didn't attempt to do creative science, I attempted to create an environment, a very large environment which could be successful at making drugs, which is a different contribution perhaps is the way I would put that.

PH: Were there any things you really missed having gone into industry?

PG: I told you: the creative ignorance of the young, absolutely. I miss the, I was always an opportunist scientist. I could be interested in anything from plant biology to plankton. To me I just like the relationship between DNA and phenotype, if it comes down to it. I don't really care very much where that DNA is and what that phenotype is because that's sort of almost irrelevant. In, when you're making drugs, if you find something interesting and it's not, when you're doing applied science if you try to do something applied and you discover something which isn't related to what you're trying to do, you end up having to kill it. Whereas when I was doing academic science, I went where the science took me. I did an experiment and I found something interesting, "Okay, I'm working on sex determination." You better find out what that is but that's fine by me. And like the multiple sclerosis, it wasn't at the time I had a big interest in multiple sclerosis, it was this, I found a project where I could actually explore what whole genome analysis, what the problems were, what the association studies could do, and so I saw it as, you know, "We'll go over there." You don't do that in industry.

PH: Did you miss the kind of community at work?

PG: Yeah, exactly, that's the third thing I was going to say. The analogy I use is if you belonged to a medieval order of monks you could go anywhere in the world and essentially there was a floor to lie on. And in academia I could go anywhere in the world where there was a university and I could find someone who was a colleague or a student or had touched my academic existence. When you go off to industry you sort of almost instantly lose that, you know. It's not so bad now but we're talking almost 20 years ago so it was us and them, and I remember going home telling Julia I was going to go to SB and she said, "Oh great, do you think you guys could fund an area detector for the lab?" And go, yeah, that's actually how my friends now see me, a potential source of funding. So yes, I really did miss that community and I'm not part of that community, I'm only part of what I would call my own peer group, right, so people like Veronica and Martin and you, people who I have a shared history with. I'm part of that peer group but I'm not part of the group of the people who are 10 years and 20 years younger than me.

PH: I can certainly say we missed you too.

PG: [laughs]

PH: It rather seemed, at least from someone like myself, it seemed as if you just vanished off the face of the earth for a while in terms of going to meetings and things.

PG: Yeah, I was trying to do something different, you know. I didn't want to pretend, it was almost a deliberate decision. It was, you know, I'm not trying to pretend I'm a super academic or an academic with benefits, I'm actually trying to do a job which is to make drugs. And quite frankly, it beat me. It's the most difficult thing in the world to do and you learn very quickly how much we don't know, right? So we kid ourselves that we know things but actually when you scratch the surface of it we know almost nothing about human physiology and pathology and how it works. You and I come from a reductionist view of monogenic disease and it's been very useful but you know look how long it took us to find out how dystrophin works. I'm not sure we really are sure how dystrophin works at this moment and having worked with a company working on repairing dystrophin I can tell you, we have no idea what's going on.

PH: So what year was it you left industry and moved to Canterbury? Presumably that was Julia's job at Canterbury?

PG: Well, what happened was that there were, I didn't get a job which was, there were two of us who were candidates as head of R&D and the other guy got the job, which was probably the right decision. He was a lot younger than me and also, it's fine. You know, I was, obviously at the time I was disappointed and other companies offered me similar jobs afterwards but I took a deep breath and I said, "What is it that you really want to do? Do you really want to continue this sort of lifestyle?" which effectively meant I was paid vast amounts of money to spend all my time on aeroplanes. And I could see myself becoming so important that I can't actually be here talking to you because every time I'm talking to you I'm actually worried about the next person I'm going to see. So there's a car with its engine running outside, I'm going to get in that car and it's going to drive to my private plane which is going to take me to the next person who I'm too important to actually talk to. And it's actually, academia is relatively flat. It might not feel like it but it's relatively flat.

PH: Genetics especially, I think.

PG: Whereas in industry you know the power is concentrated in very few hands and very big decisions are made which, you have to go very high up in the organisation in order to find someone who can make a decision, which is really what it comes down to. Anyway I just decided I wanted the job of being R&D and if I'd got that job I would have wanted the job of being CEO. But not getting that job as head of R&D basically meant I decided, "What is it you really want to do?" It wasn't an instant sort of thing, I actually spent three months as a hermit building a garden. I've got a house on the Isle of Wight with an acre of land that goes down to the sea and I terraced the side of the hill with my own hands and did that for three months and figured out, "Well, what do I really want to do?" And that sounds a bit silly but I said to Julia, "Look, I think I've decided I want to live where you are, so why don't you decide where you want to go and I'll just follow wherever you go?" I also decided I didn't want to go back and be an executive anything. I didn't want to go back and run an institute. I was offered academic jobs as well as industry jobs but I just crudely felt I'd had my turn. I know that might sound very alien but I just sort of felt, "You know, I enjoyed it, I don't regret a moment of anything I've done but I don't want to go and run human genetics at the Sanger Centre," which they tried to get me to do, or other academic jobs.

So I decided I would do one day a week venture capital so I worked for a firm as a one day a week partner essentially, and I sit on, I do not seek it but if people ask me to sit on academic boards I sit on them. I sit on a couple of boards of charities and a couple of companies, probably fills another day. I used to do half a day a week teaching various places. A bit less because my parents have been ill and they live in Australia and that's another long story, and the rest of the time I garden, produce my own food and build bicycles and every so often I go and do a little bird watching or you know whatever, that's it. And I make it easier for Julia to continue doing those jobs. Now having made those choices, you give up things. I jokingly tell people that it's true, you give up power. I do not seek power or seek to do stuff which gives me power. So young women don't want to sleep with me anymore because I don't do that sort of power thing anymore, either academically or, you know, I don't play in the academies or… If they ask me to do stuff, I do it but I have no interest in taking a position which has social weight to it. Do you understand what I'm saying?

PH: I understand absolutely.

PG: And it's a personal choice. I'm not deriding anybody who makes a different choice. Julia does all that shit. Yeah. Good luck to her. I'm not against it, I just decided I wasn't going to do it anymore.

PH: How long is it since, she's vice-chancellor…?

PG: Yes, vice-chancellor.

PH: Of the university of…

PG: Of Kent.

PH: Kent. You live in Canterbury now, or near?

PG: Well we sort of live, we still have our house in North London and I guess we're in London three nights a week but not necessarily the same three nights. You know Julia does a lot of science and higher education politics in London. You know, she's on the Council of Science and Technology, she's on HEFCE this and HEFCE that, and UK Universities this and that and

so on. Yes, she does all that sort of stuff and that's in London so that brings her here. And the company I work for is in London so they usually bring me to London one day a week for that and other bits and pieces.

PH: Nice place, Canterbury, though?

PG: Yeah, it's a bit sort of… [laughter] smaller than London. And I also discovered it, well silly point but it's… it's very hard to make friends when your wife is the boss. You know, if I say to someone, "Oh, come and have dinner." I'll be cooking in my shorts and they'll turn up in a suit, you know…, I just discovered she's the boss, you know, so that makes people find it very difficult to be natural.

PH: Fair enough.
One area we didn't talk about, I'd be interested just to know how you feel: the gene mapping meetings, I always look back on those as being a rather special period, the gene mapping workshops.

PG: Yeah, they obviously, they were important because they created a community of people who were interested in similar things. And people outside the field or people today looking backwards perhaps don't quite understand how we were not regarded as real scientists, you know. It was like, "Why would anybody bother to do this stuff? It's a pointless exercise." And my own view, and I tried when I did have a little power, to promulgate this view: you know Victor [McKusick] was, for all his faults, I loved the guy. He was a visionary, you know? He kept plugging away doing this boring stuff with his little notebook, you know even I thought he was a bit bonkers but it actually was important. And without all of that stuff you know we wouldn't have got to the point where we have the human genome. And without the human genome stuff we wouldn't have all the other genomes because it became the driver of biomedical science. And so that I think was a privilege for us to work in that space. It was a privilege for us to be able to map monogenic diseases and clone the genes involved and begin to glimpse, notwithstanding we've got a long way to go, to glimpse what was going on. And journalists have asked me, "What do you feel about your academic career?" and I say, "I mapped and cloned the human sex determination gene. And for the history of time I will have done that. Robin and I will have our names on that cup." And to actually put your name onto a fact which is going into the textbooks, it doesn't matter that your name's not on it but you put your little brick in the wall, you know? I made my contribution, I'm proud of that contribution and it was a privilege to be present when molecular biology met human genetics. And if it hadn't been for us doing human genetics there would have been nothing for molecular biology to meet [laughs].

PH: That's true.

PG: So that fusion came from both sides and I think it was a wonderful opportunity, and yes of course there's still lots of wonderful opportunities today. But you know when I started doing this as that schoolboy I'd not heard of DNA. I didn't know that there was a code. Yeah, people were sort of thinking about it but you know it took a long time to figure out that sort of stuff and we were there!

PH: Yeah.

PG: That happened in our lifetimes. I think it was a wonderful privilege actually. It didn't feel like it at the time, it just felt like going to work but… It actually did feel like it at the time to some

degree. No, we were excited, we were excited. But I think that community, although regarded by some as second class citizens actually was, embraced technology pretty quickly, you know, it wasn't like, "We don't like DNA sequencing, we don't like this." Actually it was a community which was trying to grab every technology that came along.

PH: I've been asking everybody one thing, Peter, and that is whether you can identify one particular person who has been special in terms of how your career and things developed…?

PG: Walter, Walter obviously. No, he created a wonderful environment for me and he was a wonderful mentor. I think he went off and did administration too early. You know running ICRF, I think he did a great job at ICRF, but I think he could have done a greater job if he'd continued doing science. I know he would be furious with me for saying that but if you run a large organisation you're not putting the same amount of yourself into the science which is going on in your lab, we had that conversation. So yeah, Walter almost certainly had the biggest influence but you know you pick up pieces from lots of people along the way. Very few people who I've met who I felt were, this is arrogance again, who were intellectually superior, but at the end of the day I would bend the knee to Sydney. Sydney is a smart guy. He is just smarter than me, I had to admit it.

PH: [laughs]

PG: Fred Sanger was an amazing person. Alec Jeffreys has science hands. It must be some sort of something but his hands, his experimental abilities were just unbelievably good. Mine were okay but never exceptional. And Alec was absolutely that way. Who else?

PH: Well, those are some pretty key people.

PG: Rob Portland, who I loved, who was a wonderful guy. And again he was one of these scientists who did it with his own hands, you know. He took a sabbatical to learn how to do molecular biology so he could clone the genes he was interested in. And he went over to George Brownlee's lab and learnt how to make oligos. You know, he wasn't going to order them, he wanted to know how to do it. He was, when he died it was a real loss to British science.

PH: Well, Peter, it's just past 4 o'clock. Is there anything that you feel I haven't touched on that's really important? We can't go over everything but is there any gaping hole?

PG: Well, it depends on whether we're talking a view of science, so I would say I think you and I share a heritage and a love for that period of science we lived through. We come from slightly different backgrounds but actually it was a church which allowed many people to worship and we talked about Victor [McKusick] a little bit but there were some key individuals that I think never got all of the credit they were due. Perhaps Victor clinically because his clinical side, got credit there, but I tried very hard to get him elected as a Foreign Fellow of the Royal Society and everyone just turned their noses up. I couldn't get people to understand the contributions that he had made. So I think on that side, science side, I think we're probably...

On a personal level, a lot of my motivation in life has involved Julia. We've never worked together and couldn't but it's almost like the best of academia, our competition itself was a very creative thing, you know. In a certain sense we were competing against each other, not

in a negative sense, but there was always an element of competition in our relationship. I also think that my view of the world changed completely with having children so if you were to stand back and say, "What is the most important thing to you?" Well, none of this stuff actually. My children have been the most important thing, and continue, my family continues to be the most important thing. And sometimes that gets lost in these sorts of histories.

PH: It's true.

PG: You know success, and all the rest of it, but actually when it comes down to it most people would trade all of that shit to make sure that their families were okay.

PH: Well, Peter, I'm going to turn the machine off but thank you very much indeed.

[END OF TRANSCRIPT]