Sue Povey

Personal Details

Name	Sue Povey
Dates	Born 1942
Place of Birth	UK (Leeds)
Main work places	Galton Laboratory London
Principal field of work	Human gene mapping
Short biography	See below

Interview

Recorded interview made	Yes
Interviewer	Peter Harper
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Personal Scientific Records

Significant Record set exists
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Summary of archive

Biography

Professor Sue Povey (b. 1942) graduated in natural sciences (genetics) at Cambridge in 1964 and qualified in medicine in 1967. After brief clinical experience at University College Hospital, London, Huddersfield and working for Save the Children Fund in Algeria, she returned to UCL to join the MRC human biochemical genetics unit under Harry Harris in 1970. Having obtained an MD in 1977, she was deputy director of the unit (1989 – 2000) and was appointed Haldane professor of human genetics at UCL and editor of the *Annals of Human Genetics* until her retirement in 2007. Her interest in tuberous sclerosis continues in the curation of the *TSC1* and *TSC2* locus-specific mutation databases and she has chaired a working group drafting ethical guidelines for such databases.

INTERVIEW WITH PROFESSOR SUE POVEY, 28th JANUARY, 2008

PSH. It's Monday 28 January 2008 and I'm talking with Professor Sue Povey at the Galton Laboratory in London. Sue can I start at the beginning and ask where were you born?

SP. I was born in Leeds and my mother was a doctor and her father was a doctor. He trained in Aberdeen. She was trained in Leeds and he had some interest in genetics, a professional interest really, he was a GP but I found genetics books of his.

PSH. Being a GP in some ways exposes you to a lot of genetic conditions. Were there any particular things do you think that he was interested in?

SP. We are talking about someone who was qualified in 1899. He died in 1937 or something.

PSH. That's quite a long time ago.

SP. That's quite a long time ago so I thought it was quite far sighted that he had a Bates book on genetics and he also had an' Origin of Species'.

PSH. Yes indeed.

SP. But I think it was just for general interest really. I doubt if it was really applicable to anything in general practice in those days.

PSH. From those dates, did you come from a big family? Were you the last to be born in the family?

SP. No, my mother actually was 38 when she married and my father who was in the air force was billeted on their country cottage. I rather think that she was probably not expecting to marry; however she was married in '41 and I came along in '42 and my brother in '43. So there are just two of us. She was nearly 40 when she had children.

PSH. Apart from your parents being medical was there . . .

SP. My father wasn't medical. My father was a physics teacher after the war but when he was in the air force.

PSH. Was there anybody who was at all involved in biology or science generally, biological sciences or natural history? Was there any element of that that you came in contact with early on?

SP. As a child? Not in my family, no. But my mother was very interested in wild flowers and birds and she taught me quite a lot about that when we went in the country.

PSH. What about school? Was there any particular influence there that encouraged you to do either medicine or science?

SP. Well there was an excellent geography teacher so I might well have done geography. I was at a convent school. My father was teaching physics in the local Jesuit boys school and of course he was undoubtedly responsible for my interest in physics and I nearly did physics but I really wanted to be a doctor.

PSH. Am I right then, you went to Cambridge for your primary degree.

SP. Yes and that was partly because of my father because I was so sure I wanted to be a doctor and practice clinically, but he was less sure that I would enjoy that and it was really because he said you need to leave your options open. It would be better if you went to Cambridge that I did that.

PSH. It's interesting actually, my father gave me exactly the same advice except I went to Oxford. But keeping your options open is quite a valuable thing.

SP. Yes and indeed it turned out that he was right.

PSH. What did you actually do in terms of subjects at Cambridge?

SP. I did the standard medical course and part II genetics. Thoday was Head of Department at that time.

PSH. So you missed Fisher by a few years.

SP. Yes I missed Fisher, yes. I was one year behind Peter Cook. I didn't meet him of course until coming to the Galton lab but he also did a part II genetics. I also came very much under the influence of somebody who unfortunately died, Dr Stuart [Goronwy] Spickett, who was at the Department of Genetics and was interested in the genetics of susceptibility to leprosy and it was because of him really that we planned to go to India to look at a leprosy hospital and this was our main activity of a group of us in the third year of our degree really, to plan this trip in the summer between pre-clinical and clinical, to go to India in a Land Rover, two Land Rovers actually, of which we spent about eleven weeks getting there and back and three weeks actually looking at the genetics of leprosy.

PSH. But it was productive because you actually produced two papers. I checked in PubMed and at first I wondered is this the same Povey S.

SP. Yes it is.

PSH. And one of those was on familial factors in Leprosy.

SP. Yes, it was, yes.

PSH. So did you get any advice from the Cambridge geneticists on what sort of data to collect and how to analyse it?

SP. We had some advice from Dr Spickett before we went. He was going to come with us, at least he was going to fly out to join us but he told us during the year that he had a secondary cancer and would not be able to come, and shortly after that he became ill. He died in 1966. So we didn't really get much advice afterwards but John Horton was one of the people there, one of the students who went and he was very active. He and I were the main people who wrote the paper. I think we were the authors of the paper, but he was very proactive and he had a successful career as a scientist..

PSH. That was quite a complex thing to take on in family terms. Did you ...

SP. I don't feel it was a great contribution to science but it was very interesting educationally for us.

PSH. Would you say that kind of reinforced your interest?

SP. Oh yes, very much, yes.

PSH. Then you went on to your clinicals. Where did you do your clinicals?

SP. UCH.

PSH. At UCH. So did you make contact with the Galton once you had arrived at UCH for your clinical work or did that come later?

SP. I did actually but it wasn't a great initiative on my part, it was because in one of my firms I had some wild idea about Huntington's disease and I talked to the Registrar about it and he said "Oh I don't know anything about that. You had better go to see my friend Martin Crawfurd in the Galton laboratory". So being quite unnecessarily confident about my idea, I went to find Martin Crawfurd who was here in the Galton lab and he saw that I was interested and introduced me to Harry Harris. And I then did an elective period here for three months. Other people were going off to different parts of the world but I came to do genetics here with David Hopkinson and Harry and enjoyed it very much.

PSH. So what year was that you came up to UCH?

SP. It must have been late '65 or early '66 I think. I qualified in '67.

PSH. Would I be right then, you have never really, hardly left UCH and the Galton since?

SP. Well not for very long. I qualified in '67. I did the paediatric house job pre-registration and then a job in Huddersfield, for surgery, and then I did a diploma in tropical medicine and worked for the Save the Children Fund for a year and while I was doing that I remembered that Harry Harris had said I think you might enjoy research. If you decide this at some point you can write to me. And when I was out in the desert with 200 people outside and I didn't know what was the matter with any of them I thought, I think I would be better in research. I wrote to Harry and I'm afraid I came back and have never

moved since. I finished my contract but. . . I realised clinical medicine was not for me. I was too worried by it.

PSH. Being all this time at the Galton has given you a pretty unique overview of the place and before we kind of go on to what you did specifically, what was the Galton like when you first had contacts with it? I mean who was there to start with?

SP. Well the people who influenced me most were certainly Hoppy, as we called him, David Hopkinson and Harry Harris but Bette Robson was of course there and Peter Cook was there and they were all very central features of the establishment. Dallas Swallow was there as a student. So she has been there as long as I have, in fact a little longer. She was a graduate student and Yvonne Edwards was there. And then there was some people who were not in the unit. There were people in the Galton laboratory because we were in fact part of an MRC unit, MRC Human Biochemical Genetics which was built around the work of Harry Harris and biochemical individuality. But there were also of course Ursula Mittwoch and CAB [Cedric] Smith. I can't think of other people who influenced me.

PSH. Was Jim Renwick there?

SP. No. Jim Renwick came to seminars but he wasn't actually still working here. We saw Sylvia Lawler from time to time and she wasn't working here either but both of them were people very much in evidence and there were quite a number of international visitors. There were always international visitors here come to see Harry and Bette. The Hirschhorns, for example, were here on sabbatical in my early time here.

PSH. I'm trying to think when Harry Harris took over as head at the Galton.

SP. I think it was about '65.

PSH. So not long really before you made contact.

SP. Yes, because I would have made contact in my second year as a clinical student. He had come from Kings with Bette Robson and Hoppy had been with him at Kings. So he hadn't been there very long. When I first came I came to the main campus. The Galton lab was still on the main campus but by the time I returned to actually work here in 1970, this building we are in now, Wolfson House, had been built.

PSH. Where exactly was the Galton because I've only known it since it's been here, and not being from London the main campus for me is always a bit nebulous, so where exactly was it?

SP. As far as I remember, if you go in the main gate, which now has quite beautiful flanking buildings but that was only completed quite recently, but it was the old statistics building which was to the left as you go in from the main gate, from Gower Street. It was on the Gower Street site, quite near the entrance.

PSH. And is that where it always had been?

SP. I think so.

PSH. You know, since Karl Pearson's time

SP. I'm not sure. I think so yes.

PSH. When you came to the Galton, was there at that time much in the way of clinical studies going on or was it mainly fairly basic?

SP. Yes of course. I now remember two other important people who were there, one was Gerald Corney who was a member of the unit who ran a genetic clinic and did a great deal of the family liaison work and he had also some independent research interests but he joined in many projects and he was very very successful in pursuing families and getting them to agree to give blood and he travelled up and down the country doing that. This is the blood taking for the unit. It was nearly all done in people's homes but there was a genetic clinic, which was interesting in that people could write in themselves. They didn't have to be referred by their GP although Gerald always kept in touch with the GP. I never had any direct role in the clinic except on one fateful day when some patients appeared because of some cock-up in the system and Gerald was away and that was a memorable experience in several ways because we hadn't got a referral letter and they told me the problem was rheumatic heart disease, which didn't seem very likely. So as they had obviously worried all week about this appointment, I thought that I would take some blood for chromosomes and tell them to come back and one of them had a fit while on the end of my needle. And of course it transpired the question was Marfan's which I don't know if they were Marfan's but I hadn't recognised it. You can see why I was not really cut out for clinical medicine.

PSH. I guess the chromosomes were normal after all that?

SP. They were yes and I thought they would be. I do realise that, but I couldn't think of anything I could do which would at least seem like we had thought about them. It wasn't that we didn't care at all.

PSH. I always associate Gerald Corney with the running of the clinic here and being the main clinically orientated person, but did other people join in the clinic. Presumably originally Penrose must have taken part in it?

SP. Oh yes, I didn't overlap with Penrose at all, although when I was a student he was around and I did once go with him to see some identical, supposedly identical twins, one of which had Down's syndrome. I'm sure he had a clinic here. He was always very interested in Down's syndrome, but then he went to Harperbury. He never really overlapped with my time here so the only clinical person I really knew was Gerald.

PSH. Did he visit or keep in touch much or did he kind of keep very isolated?

SP. I think he visited very little.

PSH. And Harry Harris I don't associate with being clinically orientated after his very first very few years.

SP. No, I don't think so, no.

PSH. So he didn't take part in clinics?
SP. He didn't take part in clinics no. Really Gerald was the only practicing clinician. He had assistance from Debbie and occasionally Peter Cook who was medically qualified and was very proactive in collecting samples. He would also occasionally see people but I think the vast majority was Gerald.

PSH. I would like to come back a bit to Peter Cook and one or two other people, but when you got here what was your first project?

SP. Ah well, in those days what happened to everybody who first came was that they were given some enzyme to work on and told to see if it was polymorphic so the one I was given was peptidase S and Peptidase S is something you get in tissues. You don't get it in red cells and had to get the electrophoresis of the native enzyme working properly and indeed I didn't have to do very much about detecting the peptidase because there were other peptidases that people had detected. So there was nothing very clever about what I did at all, but what I very strongly remember was that you could not say it was not polymorphic until you had looked at five hundred samples. I can assure you peptidase S by the methods we had in those days is not polymorphic in humans. Although I did subsequently discover by chance when testing dipeptidase in mice for somebody that it was polymorphic within an inbred strain of mice. So then after that I was allowed to go and do something else after I'd realised that peptidase S was not polymorphic by our criteria. Then worked on peptidase C which was much more interesting because that had variation.

PSH. Was there already work going on on the peptidase family of enzymes?

SP. Yes, there was. They'd really devised that, Pete Lewis and Hoppy between them had devised ways of looking at these particular dipeptidases and tripeptidases using amino acid oxidase which was venom from Crotalus adamanteus, the eastern diamond backed rattlesnake which we used to mouth pipette of course, and then stain with dianisidine. Those were the days.

PSH. So presumably Hoppy and others were wanting to assess the variations.

SP. Yes the purpose of this was to do a sort of unbiased survey of how much individual genetically determined variation is there in soluble enzymes and the idea behind that was that we could see any change which altered the charge of an amino acid would be very likely to show on the starch gel, so you could work out what proportion of changes you would be picking up and indeed from what was found you could predict how many, in today's terms you can predict how frequent a SNP (single nucleotide polymorphism) will be and it comes out to be very close to what was found from the starch gels.

PSH. That's interesting. Was there any way at that point of mapping these genes and enzymes or was it looking for variation in a kind of undefined or unmapped way.

SP. It's interesting that at that time when I first got there my impression was that both Harry and Hoppy were not particularly interested in mapping. They didn't see this as very fundamental, but Peter Cook was very interested in mapping and Bette Robson was very interested in mapping. I have to say I don't think any of us really saw the tremendous clinical value it would have, or at least we could see the theoretically argument of course and CAB Smith had pointed out in a paper in1945 that it would be of clinical value but we thought it was such a long way off that really the appeal of mapping . . . Peter Cook once said to me the appeal of mapping is that it's like a great big crossword and there's only one solution. And it's either right or wrong and that was the challenge really.

PSH. Because for quite a while previously, I mean going back with Penrose himself, he was interested in mapping and then Jim Renwick and Sylvia Lawler must have done their original mapping studies.

SP. The great history of the Galton Laboratory was in preparing the ground for mapping, developing the theoretical basis then just because the markers of course were so few. So there was some successful mapping on the X chromosome and indeed there had been before I came quite a few autosomal linkages found but it was a fantastic amount of work for every positive lod score found, a fantastic amount for years, person and years worth.

PSH. So I'm really getting the picture then that the enzyme variation was being looked at in its own right initially rather than as a tool for mapping.

SP. In it's own right, not as a tool for mapping no. It was partly being looked at to determine the sub-unit structure of the enzymes, and that was very valuable in that respect, and to determine the amount of variation that is tolerated in human and from an evolutionary point of view as well. And there was an interest in whether there were functional differences between these variants because you could often demonstrate that there was a quantitative variation in the enzyme, acid phosphatase for example. There were only three alleles but you can generate a continuous curve of activity in which you can see the components of the different alleles in there. But the mapping was an interest of Bette and Peter.

PSH. That is interesting.

SP. And that was something that I became very interested in.

PSH. Well yes. Just before we go on a bit, I picked up one study that you did on phosphohexoseisomerase, which I have to confess I'd never actually ever heard of.

SP. It is now called glucose phosphate isomerase. It is the same enzyme and of course we had no idea then that it was a neurotransmitter. We looked

at it as an enzyme in red cells and it was the one I did when I was a student so it was the one that got me, really got me into genetics.

PSH. Because that I picked up as your sort of first biochemical. . .

SP. It was very kind of them to put me on the paper because my contribution was really entirely technical but in those days technicians didn't always get on any papers by any means.

PSH. That's true.

SP. But of course it was a good investment in a way, of theirs, because it encouraged me to continue in genetics I suppose.

PSH. After peptidase C what came next in your major line of interests, chronologically.

SP. The peptidase C was quite interesting because I remember the day on which it dawned on me that the reason we couldn't repeat a finding in somebody was one time we'd used white cells and one time we'd used red cells and the protein product was unstable and so it disappeared from the red cell. I think probably I then got interested in mapping and somatic cell hybrids which were just coming along and started a collaboration with Walter Bodmer's lab and Ellen Solomon and Peter Goodfellow on trying to find, because of course the wonderful thing about the isozymes was that although they were not on the whole, very good genetic markers because by today's standards they are not very polymorphic, in somatic cell hybrids you just need to be able to demonstrate the difference between the human and the mouse and then you can just see whether in a set of twenty hybrids which ones have the human enzyme and that chromosome must be there, so you don't need the intra-individual variations. So that was very interesting to do that and to map the enzymes that we had looked at the variation and we had struggled with linkage analysis with sort of, adenylate kinase had been mapped to be close to the ABO blood group, not by me, by Sandra Rapley a PhD student and that was one of the few successes of actually finding a positive lod score with an isozyme, whereas the somatic cell hybrid is so much quicker.

PSH. Was *Henry* Harris linked in with this kind of work or was he very much restricted to the application of hybrids in cancer?

SP. He was very much restricted to the application of hybrids in cancer. But in fact I did collaborate with him a little bit because I went to a seminar in Oxford. I can't remember how I came to be in Oxford, where he talked about some hybrids he had made and how they were not malignant but they segregated and became malignant again and that they were obviously losing a chromosome 7 but nobody could tell which 7 it was. I was too frightened to say anything at the time but then I wrote to him and said we probably could tell that by isozymes and he rang up and was very very enthusiastic and then that led to a collaboration and a paper indeed with Jamieson, and myself and Henry Harris. The isozymes helped to identify the fact that when you lost the normal copy of the chromosome the malignancy returned. But apart from

that though, he really was very focused on cancer and we were not really doing cancer.

PSH. Now where was Walter Bodmer then at this point? Was he at Oxford or had he already moved?

SP. When I first knew him he was in Oxford, yes and then he moved to become head of ICRF.

PSH. So he would have been at that point there with Peter Goodfellow?

SP. That's right yes and Ellen Solomon.

PSH. And Ellen Solomon yes, because I don't think either of them were in Oxford with him to my knowledge.

SP. Oh I think Ellen was, yes.

PSH. I could be completely wrong.

SP. I think they were both, well Peter Goodfellow was a PhD student of Walter Bodmer in Oxford and Ellen was with Walter. I think they were all in Oxford then. And of course John Edwards was at Birmingham at that time I think.

PSH. I think he was at Birmingham and then went to Oxford after Walter Bodmer moved to London.

SP. And he was always interested in mapping. My first introduction to him was going to a meeting in Birmingham which he organised, presenting something on ovarian teratomas.

PSH. Can I ask how you got involved with the ovarian teratoma work. Was that with Sylvia Lawler or was it separate from that?

SP. It was separate from Sylvia Lawler. I can't quite remember who got me into it. It had been suggested by, (oh how could I forget his name, from Seattle, no not from Seattle, further north than that, Portland. It will come to me). David Linder from Portland, Oregon.

PSH. It will come Sue, don't worry.

SP. He suggested that they could be used for mapping because they might be a product of meiosis and Harry I think was interested in this and said to me, would you like to take this on? It was not my initiative. I think it was Harry Harris' initiative and so then I made contact with people that were doing surgery on ovarian tumours at the Elizabeth Garret Anderson, the affiliated hospital to UCH, and also the Marsden and tried to find ovarian teratomas which, although they are common, the pre-operative diagnosis of them is not terribly accurate unless they happen to have teeth in them. So it was quite hard collecting them but they were very interesting

PSH. When did you start, may I ask, to focus on chromosome 9?

SP. My favourite chromosome, yes.

PSH. I got to see a paper on that from 1978 but presumably there were things which were pointing in that direction before then.

SP. Well we mapped, at the same time as Meera Khan actually, we mapped adenylate kinase by linkage, we mapped it to chromosome 9 and it had already been shown in the lab that AK1 was linked to the ABO blood group. But Peter Cook had very much developed what he called desperation mapping from the families, which was that although it was almost hopeless to try and put things anywhere, you could exclude them from large bits of the chromosome, and he had actually excluded the ABO blood group from everywhere on chromosome 9 apart from right at the two ends which were not very informative and so this was a very interesting discussion in the lab, because I was quite sure that AK1 was on 9, and I couldn't test the ABO and he was quite sure that AK1, if it was on 9 it had to be right on the end and there was no evidence for it being on 9, and so we just got interested in chromosome 9 really and we found one or two other things, something on the short arm of 9, the mitochondrial form of aconitase. And then of course eventually tuberous sclerosis.

PSH. Now by this point the gene mapping workshops had got going I suppose. Were you in on them from the very beginning?

SP. No the first one I went to was Baltimore for meeting number 3 and I remember Bette saying to me 'You've got quite a lot of data. Would you like to go to Baltimore?' And it was very exciting.

PSH. And since that meeting I guess probably you were involved in the entire cycle?

SP. Yes I was more or less yes. I just missed one because I was ill but all the others I was at.

PSH. I mean, those were fascinating meetings, what was your impression of those meetings in terms of particularly going to one of them for the first time? What struck you about those workshops?

SP. Well I suppose I had so little experience of meetings at all that I didn't realise at the time how unusual they were. The only thing I had been to before I think was the Paris meeting in 1970; I think there was a Paris genetic meeting wasn't there?

PSH. That was a big one

SP. Which I must tell you that I recall something Harry Harris said there, which someone else might have said to you, because I would like to record this. There was some discussion about Tay Sachs disease and about prenatal diagnosis and what this would do to the frequency of Tay Sachs disease and he stood up and said 'I can suggest another way of reducing the

frequency of Tay Sachs disease. I think all Jews should marry non Jews. This is what I did myself.' So that was quite a startling pronouncement really.

PSH. Yes; did he get any comments from that?

SP. Oh yes he did, yes. So the gene mapping workshop was very different from that meeting because of the participation and the actual development of the work during the meeting. I very much enjoyed that and I remember somebody saying, somebody gave a short presentation which said adenosine deaminase may be on chromosome 20 and Frank Ruddle after that presentation said "can anyone support that?" And without having thought about it at all beforehand I said "I can support that yes." And so it was amazing that you could feel you could make a little contribution and that was always the thing about those meetings, you really thought people cared about your data because they really wanted to know.

PSH. They were very special.

SP. They were very special, yes.

PSH. And I suppose in a way the philosophy had taken a lot from the HLA workshops.

SP. Yes it had, yes. Not that I went to them but I can see from what I know about the HLA workshops. And of course originally all the autosomes other than 1 and 2 I think, were all in one group and then gradually as there were more and more genes found, the great achievement of the 70s, by the end of the 70s we did at least have one thing on each chromosome.

PSH. And you came onto the chromosome 9 committee, am I right.

SP. Yes. I moved around a bit. I was co-chair of chromosome 1 and then I was chair of 1 and then I was chair of 2 and then I was chair of 9. Yes I did move around a bit.

PSH. At what point then did tuberous sclerosis come into the equation as a rather specific disorder to be mapped?

SP. I think it was about 1985, which was the year in which it really became clear that we were really going to be able to find genes by where they were. Actually Duchenne and a few things were found so the whole mapping was definitely looking up.

PSH. This was after RFLPs.

SP. This was after RFLPs and our lab was quite slow changing to RFLPs and that was partly because a lot of the interest had been in the enzymes themselves, in the markers themselves and I do remember a group of us going to a talk in the main college where someone described RFLPs and we were really gobsmacked. I can't remember what date that was. As we walked back we thought this is going to revolutionise the world.

PSH. It might have been Bob Williamson talking, or Kay? [Davies]

SP. Yes it might well have I can't remember who it was. So John Osborne approached me and said "would you be interested in trying to find tuberous sclerosis and we've got a few families who have got a bit of a collaboration with Glasgow going but I've got some more families and you could do a much wider range of enzymes here." So he came and talked and everyone from the unit came and so everyone agreed they would do their pet enzyme and see if we could find tuberous sclerosis. And of course there was already just a slight hint about the ABO but it was nothing like significant. But indeed we did get a lod score of over 3 with ABO but we were very lucky.

PSH. I always feel a bit embarrassed about that initial paper because I was editor of Journal of Medical Genetics when it was sent in and the data weren't that convincing and we rejected it. Then it turned out that it was all correct.

SP. Yes but it was really lucky that it was correct. We had 14 families I think and we had a lod score of just over 3 for the ABO blood group and we also had an additional family which was not informative of the ABO blood group but which was informative for AK1 which was also contributed, and AK1 is really quite close to ABO so that increased our confidence in it. However there were many uninformative families and several of those subsequently turned out to be on chromosome 16. Had they all been informative we wouldn't have got a positive lod score and indeed only about three weeks after, I think, that paper came out we found a big family from Manchester which had 5 phase known recombinants with ABO. So we would not have published at all if we had had that. So that was lucky. You have to have a bit of luck sometimes. It was a long time before we had any more luck with TSC1. It took us a long time. It was ten years before anyone saw a mutation in TSC1.

PSH. That was the same with Huntington's wasn't it?

SP. Yes.

PSH. But did you have any idea that it was likely to be heterogeneous at that point or did that come later?

SP. No we didn't. I think that was quite a surprise because it is such a funny disease and it is so weird. It has such weird manifestations and these weird manifestations could be in any family. There was tremendous variation within families but it just seemed very likely that it was one gene in those days. And in fact the variation in severity is something that Penrose had considered in 1935 as to what that could be. It was very far sighted of him.

PSH. That's interesting. In tuberous sclerosis?

SP. In tuberous sclerosis yes.

PSH. And what did he think?

SP. Well he was in charge of the mental deficiency hospital in Colchester and together with Mavis Gunther they described the new mutations in tuberous sclerosis and they discussed, how the variation within the family arose because it was the same mutation and was it variation in the normal allele or was it unlinked variation and could you tell something about whether they were more similar between a parent and a child or between sibs. So they had to try to sort that out and they realised they couldn't really sort it out because I suppose there is so much ascertainment bias in the parent being mild or they wouldn't have had children. But it was very interesting they considered it.

PSH. It is interesting and in a way it is not dissimilar to the arguments that Penrose later used for anticipation in myotonic dystrophy and I'm pretty certain that tuberous sclerosis was one of the disorders he gave in that paper where he had a table of anticipation showing that it existed in most of these diseases but a lot more in myotonic dystrophy.

SP. And we still don't know in tuberous sclerosis what accounts for the variation. It is still something I'm very interested in.

PSH. Yes.

SP. So I've got off the track there I think. What were you asking me about?

PSH. No, you didn't get off the track at all, but what I was going to ask next was, at what point did you start getting interested and involved in nomenclature?

SP. Well yes, I can remember that. Cathy Abbot was a post doc with me and she was very upset about the terrible nomenclature for the transcription factors that we were thinking about to do with liver disease. We were by then working on alpha 1 - antitrypsin deficiency. So she said you should do something about those and of course I did know Phyllis quite well because Phyllis McAlpine had been here as a student and then went back to Canada and took over in nomenclature. So I wrote to Phyllis and I started. We never did sort out the transcription factors. I had an early realisation that nomenclature is not as easy as you might think, because the first expert I wrote to to help with naming these transcription factors, wrote back and said the whole subject was much too sensitive for him to get involved in. I can't remember the exact date that that was but I then just helped a little bit with nomenclature for various things with Phyllis and it was only, I didn't really seriously get involved until 1996.

PSH. But am I right that from quite an early stage, the nomenclature committee did have 'teeth' so to speak? It was regarded as a body that had a fair amount of power in what it decided rather than everybody ignoring it.

SP. Yes certainly in the human genetics community it did and in mapping meetings there was a nomenclature room which was looked after by Tom Shows and Phyllis and people with a new gene had to go and get an approved name for that and you couldn't proceed until you had done that, and that was very well accepted in the human genetics community. The difficulty

really was getting that to apply to other communities. They didn't see the authority. They didn't accept the authority of the human gene mapping meetings because there were votes at the Human Gene Mapping meeting which gave the committee authority to decide on gene names.

PSH. But even so, I think the importance of what the nomenclature committee has done is underestimated, because if you look at some other fields as being persisting in chaos, really that was pretty well avoided for human genes.

SP. Yes I think it was. There are many names one doesn't like. There are many names nobody likes but on the whole there is a recognised, approved abbreviation for each thing that's been recognised as a gene and so there is much less confusion I think about genes than there would have been otherwise.

PSH. When you became involved with that committee, was there still quite a lot of trauma around in terms of people feeling desperately upset that their own system wasn't the one or do you think that had been worked through a bit earlier?

SP. It had been worked through I think with the Human Geneticists, people who sort of supported the Human Gene Mapping meetings, but still and to this day people are very frequently annoyed about gene names. One of the turning points for the nomenclature was when Nature Genetics decided that they would insist on correct nomenclature and that was just really fortunate in that they allowed two unfortunate things to go through which were very confusing and so they saw that this needed standardisation. One was the haemochromatosis gene which they allowed somebody to call HLAH even though there was already an HLAH which was very not far away, which was nothing to do with this gene and also there was, I think in the same issue, there was the PEX genes which can be peroxisomal genes or something else. There's some confusion about the PEX gene and so then they [Nature Genetics] became very strongly supportive and we had many many phone calls from people who had never heard that there was a standard in nomenclature and they were horrified to be told by the journal that they couldn't publish there unless they got approval for their gene name, and of course they didn't want it to delay their publication. And of course they wanted to publish in Nature Genetics so that was very helpful to the nomenclature committee I must say. But some of them were pretty cross. People have threatened to sue us but nobody actually has.

PSH. I hadn't realised it had got that bad?

SP. But of course there are still some journals who don't insist on nomenclature so people can publish. Often people who really hate the name, publish under their own preferred name but I think increasingly they do mention the approved name somewhere because databases like standardisation, so on the whole the major databases just take the name from us. If people don't put the database name in, people may be confused so I think we've turned the corner really.

PSH. When the gene mapping workshops made the transition into chromosome specific workshops and HUGO were getting going, were you involved with HUGO from its start?

SP. I wasn't a founding member of HUGO, no. I think you had to be fairly distinguished to be a founding member of HUGO in the original. Bette is a founding member.

PSH. But then am I right that HUGO then developed its own, I mean the nomenclature committee had an extended life under HUGO. Was it the same as it had been before?

SP. Yes. When Phyllis was head of the nomenclature committee, she never felt very happy about the relationship with HUGO, I don't think. She didn't think that they particularly supported nomenclature but by the time I was involved, they were supportive and we just regarded ourselves as a subcommittee of HUGO and it has kept that way and the council have been supportive. For many years they have been supportive of nomenclature.

PSH. So you must have had about 10 years as being the person mainly running that?

SP. For nomenclature yes, '97 to 2007.

PSH. And what has happened to it now?

SP. Elspeth Bruford is now in charge. Over the years there have been several people sort of running the project. I was always more hands off than Phyllis. I mean Phyllis really approved every name herself and there were 7,000 genes named by the time we inherited it. That was an awful lot of genes, an awful lot. She ran herself into the ground doing it and I was really determined I wasn't going to do that and there was money available to have support. So we absolutely discovered that you had to have post doc people doing it. It just didn't work with anyone below the level of post doc. Partly because of the knowledge required but also because of the authority required to deal with quite eminent persons. So Elspeth Bruford was the latest person in charge of the project. There have been several very good people who have moved on to other things and about two years ago we began thinking what should happen to the nomenclature committee and we felt that perhaps they had more in common with the database people than people in the biology department, even though I think now, the biology department has recognised that it's a loss that it went, and so we sort of explored a little bit who was interested to host the nomenclature committee and several people on the Hinxton site were interested and there were other universities that were interested as well. But we went and talked to Ewan Birney and to Richard Durbin and it was decided that Elspeth would write a grant with Ewan Birney as being the named PI because she was paid from the grant so she didn't have an established position, Elspeth Bruford wrote this grant for a continuation of the work and from NIH NHGRI and the Wellcome Trust she got money, 5 people for 5 years and that started September last year. And two people went with her to Cambridge and they are currently advertising for the other two posts.

PSH. That's good.

SP. So that's under control. And is extending now to more other animals and there has been a lot more involvement with the other species and a lot of collaboration with other nomenclature groups

PSH. Sue, coming back to some of the other people now who were involved. What about Peter Cook, because I always feel he was a huge loss dying so young?

SP. He was a dreadful loss yes. He was really the life and soul of the linkage and so enthusiastic and absolutely the right hand man of Bette Robson and he would sit up all night calculating, feeding these old computers that you had to feed with cards to calculate lod scores and he had a very good, I mean he started very early in his contribution to linkage in that he was still a medical student when he noticed the recombination in males was less than in females. Most of us were a very long way off noticing anything like that when we were students. And he was a very central, pivotal figure of the unit really and he was a tremendous loss. We were devastated. It was also just a week before the quinquennial review so that was not very good but that was the least of the worries. We were so upset about it.

PSH. In terms of a person to work with, how did you find David Hopkinson, what sort of person was he as a leader of the group and the unit?

SP. Oh I think he was very good at managing staff. He was much loved by the staff I would say and he very much looked for careers of junior people and he was very very bright. The last project he got involved with was the genetics of facial features, was perhaps a project a little before its time and I think that was a bit unfortunate although he was nearly 65 so he was retiring. He would have liked the unit to continue I think and he also would have liked to get more funding for the facial features but the MRC were not really encouraging about the facial features so that didn't go very far but he had many original ideas that were very very good technically and he inspired a lot of young people.

PSH. How far was Harry Harris still actively involved with that work at the time, the early years you were here or was it really David Hopkinson that was . . .

SP. Both of them were very active really. Harry would come around, he had a tremendously good memory. He could remember everybody's experiments better than they could themselves which was really very embarrassing. He would drop his ash from his pipe onto your best gel, but I think by that time Hoppy was probably better at the practical advice, but both of them were very very inspirational really.

PSH. The other group or sort of allied group which I always remember myself which must have really been of great importance was the blood group people with particularly Ruth Sanger and then Patricia Tippet.

SP. Ruth Sanger, Race and Sanger yes, Patricia Tippet, yes they were very close associates of the unit and all the samples that came into the unit which were always blood grouped upstairs, there were a lot of blood groups with a linkage analysis and that continued until Pat's group left and by then we were not doing so many family studies. And there was also of course, the other people here I still keep up with were the people doing chromosomes, Joy Delhanty and Jenny Parrington in the unit was a chromosome person and that was also very synergistic, the chromosome analysis. And a clinician Mary Lucas, who retired some time ago now but was running the NHS side.

PSH. Can I ask you, at what point did you become Haldane Professor?

SP. Oh that was just a name made up by Jerry [Jerry Hyams, head of Department of Biology at the time].

PSH. A very good name.

SP. It's not all very appropriate. I'm not mathematical enough to be a Haldane Professor. I think it was probably, because I did have a personal chair, an honorary chair when I was in the MRC unit and then I did apply for the Galton chair and they interviewed two people. They interviewed Ellen and myself, Ellen Solomon and not surprisingly they offered it to Ellen Solomon. And she said, 'well what space would you offer me if I came', and they said 'we don't know yet' and she said, 'well when you know what space you would offer me, ask me again'. And this went on for about two years and then she took the post of head of Guys which nobody could blame her for and this problem has remained to this day actually, getting a Galton professor. So then I suppose they thought I should have an also-ran prize so they said they would call me the Haldane Professor. I think that's really a summary of what happened and then they appointed David Goldstein, but not as the Galton Professor, just in a professorial chair. I think he was really thought of a Galton professor and he was very good but he was offered much better facilities at Duke and he went to Duke. So they are trying to reorganise genetics again, about to try and hopefully advertise yet again for somebody and yet again they haven't sorted the space question.

PSH. And Steve Jones' post, how does that relate to what you might call the overall Galton structure?

SP. Well he has a personal chair and the Galton is a bit of a difficult word and some of the young people feel it has eugenic implications and don't use it and I think Penrose coined it really to avoid calling it the Department of Eugenics before it got properly renamed as the Department of Human Genetics and then of course it got changed into Genetics and then eaten by the Biology Department. So it's only the old-timers really use the word Galton laboratory, because actually it is part of the, it's the sort of north end of the Biology Department but the Biology Department has just been dissolved so the whole structure of life sciences is being reformulated, so I believe it's official title at the moment is the Biology Department Legacy. So I am not sure what is going to happen. There is an effort to reconstitute Human Genetics more, to involve people doing Human Genetics all over the Greater UCL and I've tried that before and failed although we got to know each other

quite well but it didn't ever crystallise into a unit, or crystallise into a building but maybe this time it will. There are new people trying it.

PSH. Sue, having been very busy indeed all these years, are there things that you are planning to continue now that you are in formal terms retired? Any lab projects or are you going to leave that now?

SP. I would like to continue a little bit with tuberous sclerosis but probably not as a lab based thing. I certainly will continue the mutation database and I will have a bit of funding for that going on to pay somebody one day a week to keep that up. Also I have got involved in worrying about the ethics of locus specific databases and Dick Cotton asked me to chair a working group on that because it would be so valuable to get the data from the diagnostic laboratories and indeed the Cardiff laboratory has supplied diagnostic data and it is a really an important part of the database. But some other laboratories were reluctant because they felt that not everybody had given explicit consent and so we are trying to sort out some guidelines about that and to get some general policy which it could apply to; there are about 500 locus specific databases and of course they collect data from all over the world so it was quite difficult to get a unified set of guidelines but that is something I'm trying to do.

PSH. That would be very valuable.

SP. Yes.

PSH. That would be very good.

SP. I hope soon to circulate a very preliminary document to people about that. The other thing I am still interested in is the variation in severity in tuberous sclerosis and a sort of related question which it's just related because of its variation in severity is the variation in severity of alpha l -antitrypsin deficiency.. My family had a child who died after two failed liver transplants, needed because of a severe form of alpha-1-antitrypsin deficiency; although virtually all patients have the same mutation only about 10% get liver disease. I don't know if I will ever continue anything with that but it's a great sadness to me that we never got anywhere with that. We just never got anywhere with that. But tuberous sclerosis, I'm still hopeful we might get somewhere with that.

PSH. I've been asking everybody I've seen two specific questions. The first one I have been asking is, is there any one person in particular that stands out as having been particularly influential in the way your career developed, either as a mentor or colleague?

SP. It's difficult to say between Harry and Hoppy. I think Hoppy really because he was a very wise counsellor I think. He would always take a problem very seriously and think very hard about it and be very very helpful. I think he was, he never thought about gain for him. He always thought about what was best for you if you asked him about things. I think it was mostly him. But I have had tremendously valuable support from lots of colleagues and Dallas Swallow and I are very close and think in many ways the same

way. Of course it is hard to pick out really the main person. It was Stuart Spicket who was the one in Cambridge. He was very influential in telling me I should do research.

PSH. The other question Sue, I have been asking everybody is if you had to choose one piece of work or area of work which you had been involved in over these years which you feel you identify particularly with, is there one area or piece of work you would choose from all the others?

SP. It's quite difficult because I really enjoyed almost all of it. You know for many years I kept thinking, it's wonderful somebody pays me to do this. I think the tuberous sclerosis was the most exciting but I was very fond of chromosome 9.

PSH. Sue, I have been kind of selective in the areas I have touched on, particularly in terms of your own work because there are lots and lots of things you have done and been involved with which I haven't said a word about. But are there any particular things you would like to bring up and say which you think are important that I haven't mentioned?

SP. I don't think so really, I think you've covered most things. The alpha 1 trypsin deficiency was interesting because we did develop the prenatal diagnosis for that, not that it's a difficult prenatal diagnosis but it hadn't actually been done before and it was interesting that there was quite a demand for it in the beginning because there were people who hadn't had children because they couldn't be sure.

PSH. Well Sue, thank you very much. I am going to turn the machine off now.

End of recording.