Joy Delhanty

Personal Details

Name	Joy Delhanty
Dates	Born 1937
Place of Birth	UK
Main work places	Galton Laboratory, London
Principal field of work	Cytogenetics, Preimplantation diagnosis
Short biography	See below

Interview

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Personal Scientific Records

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Biography

Professor Joy Delhanty (b. 1937) graduated in zoology (with special emphasis on genetics) at University College London, University of London, gaining a doctorate in human genetics at UCL. She worked at the Galton Laboratory, UCL, under Lionel Penrose in the pioneering days of human cytogenetics. She has held academic posts at UCL from 1961, becoming professor of human genetics in 1998, until her retirement in 2003, later emeritus. She directed the clinical cytogenetics unit of University hospital (1994-99) and has been director of the UCL centre for preimplantation genetic diagnosis since 1997.

INTERVIEW WITH PROFESSOR JOY DELHANTY, 1st NOVEMBER 2004

PSH. It's Monday 1st November 2004 and I am talking with Professor Joy Delhanty at University College Hospital London, or is it just University College now?

JD. University College London. .

PSH. Joy, I would like to start right back near the beginning and ask when was it you first went to work at the Galton lab?

JD. In 1959, when I had just graduated with my BSc degree and I went to work at the Galton as a PhD student with Lionel Penrose.

PSH. So did you do your undergraduate degree here at UCL?

JD. Yes I did, in the zoology department, specialising in genetics.

PSH. So Haldane was there, just about?

JD. No he wasn't there then, he had actually gone to India.

PSH. He must have just gone the year before that.
So can I ask, was there any special reason that got you interested in genetics at undergraduate level, or was it during that time that your interest in it appeared?

JD. My interest in genetics actually arose before I went to University, because I left school undecided whether to go to University and I got a job as a laboratory technician at part of the Institute for Cancer Research, which was an outstation called Pollards Wood in Buckinghamshire, and I was taken on to work with a couple there called the Fahmys, O J Fahmy, and his wife and they were working on Drosophila, looking at the effects of agents that were carcinogens, which they also had the idea might be mutagens. So I was meant to be looking at the chromosomes of these, or making preparations of the chromosomes of these Drosophila, so that they could be studied to see if there were any changes in the banding patterns, but nearly everybody who went there actually got involved in just breeding the flies for a while. I ended up breeding the flies for a bit and I really didn't know much about it, because you know school level science didn't include much genetics in those days. And then I began to hear them talking about these creatures and they talked about attached X and that sort of thing, so I got interested in it then really.

PSH. Did you actually have a chance to do practical chromosome set-ups at all?

JD. Well, I did migrate into the laboratory where they made the chromosome preparations, so I got to the stage of making the preparations, but I didn't acquire the skills to actually be able to distinguish the banding patterns because I wasn't there long enough basically. Because I decided, it was quite obvious in those days that there was a great distinction between technical people and scientists and it was very obvious to me that I wasn't going to be

able to get anywhere unless I went to university. Then I tried to set up little experiments of my own, you know with these flies to see what would happen and that sort of thing, but I couldn't really interpret the results because I didn't know enough about it. So I left. I was only there for one year and I left and went to University College then, so I already had an interest in genetics and embryology actually. I couldn't decide which I was interested in in the beginning.

PSH. That's interesting. So you really went back over a long way. Can I just ask, the people you were working with how do you spell it f .a.r.m?

JD. No. F.A.H.M.Y. O. J. and his wife was Myrtle Bird.

PSH. I don't think they are folk I have ever encountered their work.

JD. Well you probably wouldn't, I mean it was really based in cancer research. It was just that he had this idea they also caused mutation, which of course it did you know, but it was before the genetic theory of cancer really took hold.

PSH. So you then went on to do your undergraduate?

JD. To do my undergraduate yes, but obviously it wasn't until the third year we did any genetics, any significant amount of genetics.

PSH. Who were the main teachers then?

JD. John Maynard-Smith was my main, he was my tutor and mentor really. [Hans Grüneberg gave inspiring lectures on mouse genetics]. There were some lectures given in the Galton by Lionel Penrose and we did attend them, but they were very mathematical type human genetics. I did learn something from them. They were good, but obviously in human genetics there wasn't a lot to go on then.

PSH. Did you encounter Kalmus at all?

JD. Yes, Kalmus was in the Galton at that time. I don't think he taught very much at that stage.

PSH. So did you do a special project as an undergraduate?

JD. No, I was doing it under very old regulations. We didn't do projects and things.

PSH. OK.

JD. But I remember, actually what I said to you is wrong, isn't it. No that's right, 1959 that's right. So it was in the summer, when I was about to graduate, that the first description of a chromosome abnormality was described, the 47 chromosomes associated with Down's syndrome by Lejeune, and I can remember showing this to John Maynard-Smith and saying "this is interesting". So he said, I wonder if Lionel Penrose is thinking of taking

on someone, you know to pursue this. So I went to see Lionel Penrose and he was certainly interested in taking on someone and he had an MRC studentship, so I went that autumn to set up chromosome studies, somatic chromosome studies I suppose, because Ursula had been working on meiotic material. So I set up the somatics and

PSH. So that was the end of . . .

JD. '59. 1959 .

PSH. And was there really anything apart from Ursula Mittwoch's meiotic studies, was there in existence what you might call a recognisable chromosome lab, or did you really have to start from scratch?

JD. No, I started from scratch. Very much started from scratch, yes. I was given a room, probably a room about this size and it was completely empty. There was nothing in it you know, except a desk I think, and that was it basically. Then on another floor there were various laboratories where things like the blood grouping was going on, you know Sylvia Lawler, and Ursula Mittwoch was there of course and there were various people doing some kind of biochemical genetics.

PSH. Probably Harry Harris was there.

JD. No, he wasn't there, no.

PSH. Or had he moved across to Kings.

JD. He'd gone to Kings. He only came back after Lionel retired, as the new Galton Professor. So I was sent for, not very long, a week or two I think, to David Harnden's lab to learn the basics of setting up tissue cultures and preparing chromosomes from them.

PSH. Was David Harnden by then back in Edinburgh?

JD. No, he was at Harwell.

PSH. He was at Harwell.

JD. And then I came back to the Galton with a long list of things that were essential, because nobody was doing tissue culture or anything, they knew nothing about that. I mean they did have a very ancient and I'm sure it would be considered now very highly dangerous, autoclave. It scared me stiff. Great big thing and there was a lady who knew how to operate it, but that was about all really. They had no facilities for tissue culture really. No equipment at all.

PSH. And was there much in the way of microscope experience apart from Ursula Mittwoch? Were people doing microscope work or, I got the feeling perhaps that there wasn't very much.?

JD. Not really, no. They would have had low power microscopes perhaps, for some of their blood group work, but not really. Ursula was the only person. Well I had had a bit of experience remember, before I went to university using a microscope, so that wasn't a problem really.

PSH. Did they have

JD. I didn't have a microscope.

PSH… a decent microscope.

JD. No, I said they didn't, no. So I had to persuade Lionel that I couldn't do this without a microscope.

PSH. Was that easy?

JD. Yes, because he was very interested. He was really interested, because he had all these interesting families lined up that he wanted to investigate and he was really keen on the work.

PSH. So it was possible to get reasonable equipment once you asked for it?

JD. Yes, well the microscope anyway, otherwise, I mean tissue culture was just done on a bench with a Bunsen burner, just on a table actually, not even a bench, a table which we cleaned down with alcohol.

PSH. And what kind of material were you starting with, was it bone marrow?

JD. No, no, it was skin biopsies

PSH. Skin biopsies.

JD. That was the whole basis of the technique, fibroblast culture got from skin biopsies.

PSH. So this was what David Harnden had got going.

JD. That's what he'd set up, yes. That's what he had got going.

PSH. And where did the biopsies come from? People in the labs to start with as volunteers?

JD. No.

PSH. Or were they patients? I suppose patients with Down's and things?

JD. Patients. I mean it was Lionel who brought in the biopsies initially.

PSH. One of the things which, talking to a few people, I have asked about, I mean Lionel Penrose had been the main authority on Down's for many years and yet he wasn't involved in the very first discoveries, and several people have said that he found it quite a shock, and was kind of upset that after all,

Down's was a chromosome abnormality and perhaps quite upset that the Galton hadn't been involved in this very first discovery. Did you ever sense that?

JD. No, I don't think so, no and if you look back in the literature he in fact suggested the possibility of a chromosome abnormality to explain some of the oddities about the inheritance pattern, the running in families and that sort of thing.

PSH. I had the feeling that he had done that and then, perhaps the very limited study that Ursula was able to do had suggested perhaps there wasn't anything and that therefore it had gone out of his mind and then suddenly came back as a result of other people's work.

JD. As I say, it was really only Lejeune. He was keen to get someone to work on it. Lejeune had the only publication before I started. Obviously it was then followed by Klinefelter mongolism as it was called, wasn't it?

PSH. Yes.

JD. That was quite early on, the Edinburgh Group.

PSH. So by the time you'd got going, I suppose it would have been really end of 1959, would it?

JD. 1960 was the first publications, but some of the things were found, you know, that first year.

PSH. And were you put on to anything specific, or was it a question very much of getting cytogenetics going and looking at Down's in all its aspects?

JD. Looking at Down's and anything else that came along that was of interest. I mean it wasn't very long before he brought some material from UCH, from these spontaneous abortions.

PSH. Was that when the triploidy . . . ?

JD. Yes, that was what led to the triploid, that was the first description of the human triploid, yes.

PSH. Just sticking with Down's for a minute, Penrose must have had access to an unrivalled series of Down's patients. Had the concept of the translocation actually arisen when you were doing your work, or was your paper the first demonstration of a translocation?

JD. Well I think Polani's group found the first case of Down's with a translocation and then, what we found as a result of Penrose having these interesting families, was in a family with two cases of Down's in one sibship, then we were able to demonstrate the inheritance of this centric fusion through the generations, through an unaffected carrier. That was the first demonstration of that.

PSH. One thing which I found interesting when I was talking with Pat Jacobs was, she described to me how they'd asked Penrose up to Edinburgh to look at their series, and how unhesitatingly when he saw the patients he was able to say this one's Down's; this one definitely isn't, and it made a lot of sense out of their results. So I suppose from your point of view if you got a sample in as Down's you could be absolutely sure that it would be Down's.

JD. That's right, yes. I wasn't engaged in finding out whether it was Down's or not. It wasn't like that . No it wasn't that sort of thing really.

PSH. So the Down's work, that was really at an early stage and then the triploidy was all in the same year. Was there anything else in these early years of cytogenetics, the very early years that stands out in your mind as things that happened at the Galton?

JD. Well, a discovery was actually made if you like by one of the other people who was also a student at the Galton and that was Kusum Lele. She found a deleted chromosome in a patient with retinoblastoma.

PSH. I'd forgotten that completely.

JD. And that actually was the very beginning of tumour suppressor genes really, although of course we didn't realise the significance for some time.

PSH. So that must have been quite a big deletion.

JD. Yes, and it would have been associated obviously with all sorts of other congenital abnormalities as well. As you say, if it's a cytogenetically visible deletion it's a huge thing.

PSH. So would it be fair to say then that your lab, by 1960, had really got set up to be able to identify any major chromosome abnormality that was around?

JD. Was around, yes with techniques as they were, obviously pre-banding and that sort of thing yes.

PSH. Because the numerical changes were one thing, but actually identifying deletions must have been at that point quite tricky.

JD. Yes, well that was probably a little bit later than when we are talking about. Probably it was a bit later than when I was doing my PhD. A few years later.

PSH. You did your PhD, was that mainly on Down's or was it on cytogenetics in general?

JD. It was on cytogenetics in general really.

PSH. The trouble about PhDs in this country is that they are not cited in the same way, so that whereas you can get a nice list of everybody's papers, things like books or PhDs or anything like that don't appear, and are yet often some of the most important works in those theses.

JD. I'm sure those things were published anyway. The main findings were published. You could get things published quite quickly in those days.

PSH. Did you publish most of your things in Annals of Human Genetics?

JD. Well, the Lancet it was mainly.

PSH. The Lancet seemed to have a whole wealth of things coming in.

JD. Yes. Penrose seemed to have a hot line to the Editor at the Lancet.

PSH. So after your PhD then, am I right you stayed on?

JD. I stayed on, yes. In fact I started off with an MRC studentship, then after probably about a year and a bit the MRC decided that anyone who was married shouldn't have a full MRC studentship, and since I was married they were going to reduce my studentship to even more of a pittance than it was already.

PSH. That seems rather bizarre doesn't it?

JD. And my husband had decided to go back to college and study for another degree, so we were actually living on this studentship. This was an impossible situation and Lionel Penrose was extremely annoyed with the MRC, so he said that they had to provide a grant for me to study translocations, so in fact he got for me a better deal in fact, a research assistant grant, after all I was only about half way through my PhD and that was on the basis of having found this translocation, this Down's translocation. So I stayed on for a few years afterwards.

PSH. I'm trying to think what year was it Lionel Penrose retired. Was it '74 or something like that?

JD. No, it was longer ago than that. It was about 1965.

PSH. Yes, it must have been. So you would have had about 5 or 6 years at the Galton before Penrose retired from the Chair?

JD. Yes, at the most.

PSH. And then, can I ask, after he retired and moved out to the Kennedy Galton, am I right you stayed in the main Galton rather than move out to that unit.

JD. Yes I did, because Harry Harris came, as you say, and he offered me a lectureship. He said there were some vacant lectureships and he wanted to keep the tissue culture and the cytogenetics going. So he offered me the lectureship.

PSH. So how did the work change from when Penrose retired and Harry Harris came in, because there must have been quite a big change in emphasis overall in what the unit was doing?

JD. Yes, very much, obviously there was a lot more tissue culture was carried on then for purposes of biochemical genetics and there were a lot of people, part of Harry Harris's unit. Because he came not only as a Galton Professor but he brought the MRC unit with him, biochemical genetics unit you know, so that people who were students or employed as members of the unit staff, a lot of them were doing tissue culture, providing cells for biochemical analysis.

PSH. So were you providing really a facility, for other folk?

JD. Yes, I was sort of running it. I mean I wasn't doing the work. I was responsible for running the facility, yes.

PSH. How about hybrid cells, had they got going then or did that come in later?

JD. That came in later really.

PSH. One of the things I have noticed from quite an early stage, looking at the papers, two themes seem to appear. One was the early chorion villous sampling, but the other was colon cancer and I was intrigued. Now how did the colon cancer get going at the Galton?

JD. How did the colon cancer get going? As you know, at the Galton people used to come from all over the world, and quite sort of mature people to be PhD students, clinicians to get their training in human genetics, but they did do PhDs and that sort of thing in those days. One of them was somebody called Arthur Veale.

PSH. Ah yes, from New Zealand.

JD. Yes, and he was interested in polyposis, familial polyposis and other aspects of hereditary colon cancer, and he used to go down to St Mark's Hospital, which was near the Angel Islington in those days, and for quite a long time afterwards, and he used to bring back pieces of material from these polyps and bits of tissue from the gut and things and give them to me, and I would see if I could culture them. But the problem was, in those days we were setting up the cultures in these clots, plasma clots and that was attaching the tissue to the glass sufficiently long enough for the cells to grow out from explants, and then when the cell had grown out we would remove them with trypsin and make a sub culture. That was the basis of the technique, which in my experience up to then had worked, you know for all these fetal tissues and things and that sort of thing, but it didn't really work with these bits of gut, because I suppose they were digesting themselves out of this. But I did get one or two quite interesting results, you know, not publishable but some interesting results as far as I was concerned, which showed that the chromosomes of these bits, they were all over the place, although what he had given me was not malignant tissue, if anything it was

pre malignant, but nevertheless the chromosome changes were quite widespread, so that sort of sparked my interest.

PSH. That's interesting, I perhaps rather imagined that what you would end up culturing might have been be the normal cells, the fibroblasts in between, rather than the tumour cells.

JD. I think later on, later when we tried to do it by, we no longer used plasma clots we put things in flasks and they grew, when we had plastics and things it was easier, we did try to disassociate the tissue and set it up, and as you say what grew then was fibroblasts, because it is much more difficult to grow the epithelial tissues, you know; they need special techniques and that sort of thing. But no, even growing the fibroblasts and then growing the skin fibroblasts from those patients provided interesting results and things, which actually now as I said the wheel has gone full circle. Now they are saying the APC gene is to do with chromosome instability and I thought, I know that.

PSH. That's interesting. Just thinking about other people from elsewhere at the Galton. You are absolutely right, it seems to be that the Galton kind of attracted people from all kinds of countries, and often like you say, people who were already well established in the field. Are there any people during those years that stand out in your mind, the ones coming from elsewhere, because it was a remarkable collection of folk.

JD. Yes. Well O. J. Miller, he was there.

PSH. He was there right at the beginning?

JD He was there right at the beginning.

PSH. Am I not right that his name is on one of those very first papers, to do with, I forget if it was Downs or triploidy, but something very early?

JD. Not one of my very early ones no, it may have been one of the others, maybe Penrose did it with somebody else. Certainly not the very early Down's ones or the triploid, no.

PSH. So where was he from, was it New York?

JD. Yes I think so, something like that.

PSH. I get confused, because I believe there are two O. J. Millers, somebody told me, but it's quite interesting that he was there, because there seemed to have been very little in America at the beginning of cytogenetics. It all seemed to happen in Europe in the first few years and I suppose he must have then gone back and set it up, I mean do you remember what he was actually working on or was he just around?

JD. He was just kind of around as far as I was concerned, but I was fairly junior.

PSH. What about Marco Fraccaro, was he around when you were there?

JD. Not really no, but he was one of the visitors, but he wasn't actually working there. There was Smith wasn't there? I can't remember his first name. He worked with Penrose for a long time.

PSH. Are you thinking of Cedric Smith?

JD. No, not Cedric Smith, no.

PSH. Oh, there was a Smith involved in the Downs.

JD. Yes that's right, from the States.

PSH. I know nothing about him I'm afraid. I didn't even know he was from America

JD. I forget his first name.

PSH. Was he a clinician or a scientist?

JD. I think he was basically a clinician, yes. I mean his name is on one of the books isn't it. Down's Anomaly, Smith and Penrose. Penrose and Smith.

PSH. Yes, that's the only thing I know about him.

JD. Well he worked alongside Penrose for a long time. They were here for a long time, the whole family, loads of children. He was very nice.

PSH. Did you see much of Penrose's dermatoglyphics work? I'm never quite sure who was involved doing that particularly.

JD. Mrs Holt.

PSH. Was that Sarah Holt?

JD. Sarah Holt, yes.

PSH. Because, that seems to be an area which at the time a lot of people felt was important, but it's sort of vanished.

JD. Penrose, I've seen him pick up the hand of a baby in a cot in UCH and say Down's, but with a lens you know, you've got to look at the pattern not just the line. He certainly thought it was important, yes.

PSH. What was Penrose like as a person to work with, I'm thinking not so much as, well I suppose you were a student when you started off.

JD. I was a student, very much, and you see the Galton didn't have a tradition then of taking students as I was, straight from undergraduate, so there were all these other people there who were students, but they were far older and more senior than I was.

PSH. Did you feel you were rather left on your own to sink or swim?

JD. Not really, no, it was quite a friendly place and people like Sylvia Lawler and that sort of thing were very helpful.

PSH. A lot of people I have spoken to said that at first they wondered what they were meant to be doing, but then they asked around and everybody directed people to the right direction and helped them.

JD. Well I think that might be true for these visitors coming from abroad, but basically they had come to learn about human genetics, hadn't they. The fact that they wanted to get a PhD or something was kind of incidental, so I suppose they had to be found a project or something, but really they had just come to learn about modern day human genetics I suppose, but for me it was different because I was really taken on for this project and sent off to Harwell for a couple of weeks to learn how to grow cells and that sort of thing. But I remember when I was still an undergraduate and John Maynard-Smith arranged for me to go to see Penrose, he said I have talked to Penrose. Go to see him. And I went to see him the first time and I said to John, well I have no idea whether he wants me to come or what he wants me to do or anything, and John said Oh it will be alright, go back and see him again, and eventually it sort of crystalised.

PSH. How much contact did you have with the other folk involved in London in genetics? Was there much contact with Paul Polani's group?

JD. No no, not as far as I was concerned, not as a student. No very little.

PSH. I'm never quite sure whether that was because there was a bit of rivalry between Polani and Penrose over things like Down's, or whether it was just geography or what.

JD. Obviously there is always some rivalry, in those days there wasn't nearly as much overt rivalry as there is nowadays, I don't think. It was probably just that both Penrose and Polani were the head of a group, extremely busy I suppose with all sorts of things.

PSH. Yes.

JD. There weren't nearly as many meetings and things arranged then as there are now. In fact I think I seem to remember going to more international meetings than meetings in London. There weren't very many genetic meetings in London.

PSH. You must have had a lot of people giving talks as they visited or passed through?

JD. Yes there were people, certainly plenty of people doing that sort of thing, yes.

PSH. Tell me when it was that you started to get interested in the prenatal area, because up until the early 70s there wasn't anything very practical to do in that area. How did you kind of get into that work?

JD. CVS work?

PSH. Yes, or even were you involved in prenatal work before the CVS side?

JD. No no, I can remember when there were first publications about it and saying to Harry Harris, you know, that I thought we should be doing something about this, but he was dead against it.

PSH. Any reason?

JD. I think he thought we were a research outfit and we shouldn't be, or I as a lecturer, shouldn't be doing clinical diagnostic work.

PSH. I suppose he might have thought it would swamp the proper research.

JD. Yes, I suppose there is some justification yes, so in fact he completely discouraged me from getting involved in that side of it then.

PSH. It's quite interesting that the Galton as a whole never really seemed to develop a strong service alongside it.

JD. No, although you see I mean there were people, there was Martin Crawfurd who was there for a bit.

PSH. Yes that's interesting, because didn't he then go off and join one of the other, the Northwick Park ?

JD. Yes that's right. When Harry Harris first came we were in the old building over Gower Street and we had very little space there. I had this little room as a lab and then they built this new building in the 1960s, Wolfson House, so when we went there as I say, Martin Crawfurd didn't come there. He went off to Northwick Park. But Harry Harris then appointed Mary Lucas, who came as the clinical person and that was basically running a cytogenetic service lab. By then you could use blood cultures and didn't have to do all these skin biopsies and things.

PSH. So were you able then really to develop other fields without feeling you had to be responsible for service cytogenetics?

JD. Yes that's right. I wasn't really involved, although we were then in the new building we were all one big lab you know, we were all in the lab together you know, the service people in one part of it and researchers in another part.

PSH. Now when you started working on CVS material, was this around the time that people like Bernadettte Modell and others were getting involved, or was it before that?

JD. It was around the early 1980s wasn't it, about 1983/84.

PSH. I seem to remember that Bernadette was involved with using this in thalassaemias.

JD. But that didn't really involve us. That was a separate world, as it were. I really got involved because there was a young medic who came to the Galton called Richard Penketh.

PSH. I know him well, because he's now at the Heath in Cardiff.

JD. He is now in Cardiff yes. A consultant in Cardiff isn't he, yes. So he came to do an MD basically and he was supposed to be attached to Mary Lucas in the clinical side, but somehow because it was research really he needed to do, and Mary Lucas was definitely not a research person, never was involved in research, somehow it fell to me to be involved and that's why I got involved and began to get involved in the CVSs and things.

PSH. But did that lead on, imperceptibly, to the pre-implantation work.

JD. Yes it did, in the end yes. Because Richard and I were trying to get the various non radioactive in-situ hybridisation techniques to work, so that we could use them partly for prenatal diagnosis, but also with the idea that it could be used for pre-implantation work as well.

PSH. When was it that that really turned into a reality?

JD. At the end Richard really finished his work for his MD. It took him some time to write it up, but he did get the MD in the end, and so he left and went to Northwick Park initially.

PSH. Did he end up at the Hammersmith at some point, with Robert Winston?

JD. Yes. I'm trying to remember which order of events, because he was at Northwick Park, the clinical research centre for a bit, but I don't think it worked out very well, probably ended up at the Hammersmith, and that's when I was still involved and then he realised the potential of all this material like oocytes and things that were just being thrown away. You know, started to work on chromosomes and oocytes and things and then as you say, Alan Handyside decided they were interested in getting the PGD going. It really took off towards the end of the 1980s when the fluorescent in-situ hybridisation had been described by Pinkel and others. But really I had only seen abstracts, I hadn't seen any papers published, but I had an application from a person called Darren Griffin, who was just finishing his degree at Manchester and he was unusually interested in cytogenetics, whereas most people were not interested in scientific research and cytogenetics, but he was, so I thought it would be worth trying to see whether this FISH technique could really be got to work and whether it would be useful for the embryos. It seemed too good to be true. So he came and he got the technique working at the Galton and it had fantastic benefits for the preimplantation work, because the non radioactive in-situ hybridisation techniques that Richard and I had been trying, they took too long and there was just too much background and that sort of

thing. They just weren't precise enough, but it became clear at least for sexing, which we started off doing, that it [the FISH] was going to be good.

But initially we thought we had been overtaken by the PCR technology, as I said in that Witness Seminar thing; because Alan Handyside and Rob Winston, (really Alan Handyside in the laboratory) got this PCR method going for sexing embryos and that seemed to be so much quicker and simpler, and the first cases were done and they got pregnancies and that sort of thing, but then of course in the early days we were all completely ignorant of the all the problems there were going to be with single cell analysis and then they had a misdiagnosis which turned out to be due to amplification failure, because they were only amplifying the sequence on the Y chromosome, so they didn't see that, then they assumed the embryo was female when in fact it wasn't. So then FISH really came into its own.

PSH. Do you see preimplantation diagnosis ever becoming alongside things like CVS and prenatal diagnosis, or do you think it's likely to remain as a relatively selective approach.

JD. I don't think it will ever be as commonly used as CVS in routine prenatal diagnosis, but there are obviously an increasing number of couples that for one reason or another don't want to go down that route. Either they are infertile so they need to have IVF anyway, or they've tried standard prenatal diagnosis and maybe they've had to have several terminations of pregnancy and they feel they can't face that any more, or some of them are totally opposed to termination of pregnancy on moral or religious grounds to start with; but then there is also the category where, even if you do molecular tests you can't necessarily predict the severity of the condition and some people find that, especially if they've already got a child that's affected with a condition but possibly not too severely affected, they feel they would be killing a child like their own child, you know, if they had termination. So quite often they come and ask for PGD. But also now there's this application that has been taken up hugely in the United States, not so much until recently here, that's for couples going through routine IVF and who for one reason or another they are not achieving a pregnancy, so for these routine IVF patients, this screening of embryos for common aneuploidies is being used more and more, and the IVF specialist here. Paul Serhal thinks that one day more or less all IVF patients will be having their embryos screened.

Well I doubt it personally, because as you know if you read all the literature since starting the PGD, and sometimes when I give talks I always say I would never have started this if I had realised what was going on with these human embryos and how chromosomally mosaic they are. I mean it was all based on the assumption if you took a single cell that would tell you what was going on in the rest of the embryo. Certainly as far as the chromosomes were concerned that's not true at all, so we've actually just started doing the aneuploidy screening ourselves here since the beginning of the year, since January. It's very interesting but a lot of these couples, their embryos are so chromosomally mosaic and so abnormal in that sense, that I'm not surprised they're not getting pregnant, not by IVF anyway. So I suppose they do find it helpful, they say they find it helpful to have an explanation, but there isn't

really anything we can do for them, so from that point of view I am not sure whether its going to be applied to all patients, I don't know.

PSH. Looking back on things, I have been asking everybody I have been seeing two questions. One of these is, is there anybody that stands out in your mind in terms of having had a particular influence on your career, or the way things went. Is there anyone you can sort of pinpoint that you feel helped you along?

JD. Well obviously there was John Maynard-Smith in the beginning, because he pointed me in the right direction, he knew I wanted to do a PhD, but his work was almost entirely mathematical and I had a great problem not so much in doing it but with accepting the way they did their mathematical genetics. I couldn't accommodate their statistical approach, so when this opportunity arose he obviously thought it was perfect for me, which it probably was. The other person who helped me a lot and I shall always be very grateful to is Bette Robson.

PSH. I'm glad you mentioned her because she was a very important part of the Galton.

JD. Yes. So when Harry Harris came and I am grateful to him, he gave me my first academic post you know, he started me off in an academic life in that sense, but his main interests were always focused on the unit really, and so it wasn't really until he left and Bette took over that things changed and really started to take an interest in the other people on the college staff, because then the head of the unit and the Galton professorship were separated and Hoppy became head of the unit and Bette was Galton professor and that really worked much better. So she encouraged me on both the teaching side, I had become quite involved with the teaching, but she was very keen to develop it further by offering degrees in genetics and human genetics. We ran specialised courses and that sort of thing. But she also encouraged me in terms of pursuing other research and applying for grants and that sort of thing. In fact in between, there was Cedric Smith who was briefly Head of Department after Harry went and before Bette was appointed, briefly Cedric Smith was head of the Galton lab and I think I got my first grant then under him and that was for the polyposis work.

PSH. The other thing I have been asking everybody is, whether there is any particular piece or area of work that looking back on, they feel they most specially identify with over their career. Is there anything that stands out as you have a particular fondness for or feel, well that was something you did that really made a bit of a mark?

JD. Well obviously, I think the inherited translocation predisposing to Down's was one and also the triploidy you know, because one of the things that is typical, isn't it, that people in the UK, you discover these things and then it's not developed and in fact it was David Carr, wasn't it, who developed the work on the miscarriage data and that sort of thing and people often said to me, why didn't I do it. Well I wasn't in a position to do it. I was only half way through my PhD.

PSH. And Carr was an obstetrician.

JD. I was pretty dependent on what Penrose brought along, I couldn't initiate a study on spontaneous abortions. I wasn't really in a position to do it.

PSH. But both those pieces of work, triploidy and the translocation, were really landmark discoveries.

JD. I think they were yes.

PSH. And one of the things which interests me when I'm talking with people, is how often, in fact how usually, they name something at the very beginning of their career, because they did it themselves so to speak, without a whole team of folk, and I think that makes a big difference.

JD. But also I would say the polyposis work, describing the chromosome instability in the polyposis, because I actually did the cytogenetics. I did most of that myself really. And the ataxia telangiectasia work you know, very much hands on work all that was.

PSH. Yes.

JD. Then again, the beginning of the FISH work really, although I wasn't actually doing it in my hands then, but I was analysing all the data and that sort of thing, I first noticed the mosaicism in the embryos. I suppose those are the things that stand out so far. I'm emeritus as well now you know, for 2 years.

PSH. Me too. Well thank you very much, Joy. I will stop that there. Very interesting. I am most grateful.