# Mary Lyon

## Personal Details

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| Name | Mary Lyon |
| Dates | Born 1925 |
| Place of Birth | UK |
| Main work places | Edinburgh, Harwell |
| Principal field of work | Radiation genetics, gene mapping |
| Short biography | See below |

## Interview

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| Recorded interview made | Yes |
| Interviewer | Peter Harper |
| Date of Interview | 11/10/2004 |
| Edited transcript available | See below |

## Personal Scientific Records

Significant Record set exists
Records catalogued
Permanent place of archive
Summary of archive

## Biography

Mary Lyon was born on 15 May 1925 in Norwich, England and educated at Girton College, Cambridge. After her PhD she joined the staff of the Medical Research Council working on mouse genetics. She has published many papers on radiation and chemical mutagenesis and on studies of mutant genes. She was head of the Genetics Section of the MRC Radiology Unit at Harwell from 1962 to 1987.

She is best known for her discovery of X-chromosome inactivation, an important cytogenetic phenomenon. She is a Fellow is the Royal Society and a Foreign Associate of the US National Academy of Sciences.

**INTERVIEW WITH DR MARY LYON, 11th OCTOBER, 2004**

PSH. It's Monday 11 October 2004 and I am interviewing Dr Mary Lyon in her office at the MRC Unit at Harwell. Mary, might I start a bit from the beginning and can I ask you, how did you first really get interested in science?

ML. That's going back an awfully long way, it must have been when I was at school.

PSH. Whereabouts in the country was that?

ML. I was in Birmingham. At a grammar school in Birmingham.

PSH. And did you have a good science or biology teacher?

ML. Yes, she was very good. Her name was Mary Udall, she had a very clear analytical mind, made it all very clear and interesting.

PSH. So that made you feel it was something you wanted to do with your career.

ML. Yes

PSH. May I ask, were you born and brought up in Birmingham?

ML. No, I was born in Norwich.

PSH. In Norwich, yes. And then after your school years, then did you carry on and do biology at university?

ML. Yes, I went to Cambridge and read zoology, physiology and organic chemistry and biochemistry. Zoology was my main subject.

PSH. Were there any special bits that attracted you in those years?

ML. Well, it was experimental embryology. There had been a lot of work. It was in the 1940s that I was at Cambridge and there had been important advances in experimental embryology in the 1930s, and Waddington had written interesting books on the subject; 'An Introduction to Modern Genetics' and I think he had another one called 'Genes and Embryos', or something like that, and it was clear that embryonic development must depend on genes. I mean, now of course that is blindingly obvious, but at the time that was a relatively new idea and very interesting.

PSH. Can you remind me, was Waddington actually at Cambridge at that point, or not?

ML. He had been at Cambridge, but it was wartime when I was there and he was away doing war service, doing war-related research.

PSH. Because an awful lot of departments got completely disrupted in those years, didn't they?

ML. Yes.

PSH. But there was enough teaching going on to make it really interesting and worthwhile.

ML. Yes.

PSH. So after you had done your degree, what came next?

ML. I did a PhD, and I wanted to do a PhD in genetics, and R A Fisher was Professor of Genetics in Cambridge at that time, so I started on a PhD with him. He had mice that he was doing mapping experiments with, and he had 21 lines of mice because he had got 21 genes, and of course the mouse had 20 pairs of chromosomes. He thought there must be at least one linkage among these 21 genes and he was crossing them all against each other, and he had 21 lines, each with a different combination of 5 genes. And he gave research students one of these lines to look after.

PSH. May I ask which one you got?

ML. It was called line 18 and it had in it the 'pallid' gene, and I noticed that the 'pallid' mice tended to tilt their heads on one side, so I worked on that, and it worked out that the 'pallid' mice have the absence of otoliths in the inner ear and the way they tilted their head depended on how many otoliths were missing, because the 'pallid' gene itself had full penetrance in its effect on coat colour but the effect on the otoliths has incomplete penetrance, and so you got some mice with otoliths in one ear and not the other and some mice with all their otoliths absent and so on. I worked out how that particular otolith absence correlated with their postural reflexes, and I also studied what affected the penetrance.

PSH. And am I right, I think you wrote a paper on that around 1950 or thereabouts?

ML. That's right.

PSH. And was that part of your PhD work?

ML. Yes

PSH. And may I ask, at that point did you actually find a linkage with your mutant, or did that only come later?

ML. As far as I remember it was already known, yes it was already known, that pallid was linked with agouti.

PSH. Yes. I always think, and I suppose a lot of people think of R A Fisher as being a theoretical person, and I mean, I don't think of him actually doing experiments with mice.

ML. No, I think the theoretical work was his strength. I don't think he did anything important with the mice.

PSH. But he had a group of people who were actually, like yourself, doing practical breeding experiments and linkage work. That's interesting. Am I right that around that time, or maybe it was a bit later, would it, there were other people with R A Fisher, I think Walter Bodmer was there a bit later wasn't he?

ML. He was a bit later yes.

PSH. And was Anthony Edwards there?

ML. Yes, I think again later.

PSH. So was there anyone else who went on for their, so to speak lifetime work in genetics, at the same time as you?

ML. No, I don't think so. One who did most I think was Norman Bailey. I'm sure he's not a known name in mouse genetics. He was working on theoretical aspects of linkage.

PSH. After you had done your PhD, what was the next step that you took?

ML. I moved in the course of my PhD from Cambridge to Edinburgh. The war was now over and Waddington was in Edinburgh. I finished my PhD there, and then Waddington had got money from the MRC to work on the genetic risks of radiation, because there was concern at that time about weapons testing in the atmosphere, and about nuclear energy and fall-out in the atmosphere from these things, and so Waddington got money from the MRC to investigate the genetic effects of radiation, and he also got money for me to work in that group, so I joined mouse genetics through working on mutagenesis.

PSH. So may I ask, was that actual creation of radiation induced mouse mutants or was it still observation of natural ones.

ML. It was creation of the radiation induced mutations.

PSH. And at that point, were there any particular radiation induced mutants, that either you worked on, or which arose out of that work?

ML. Well, the original idea of the work was to induce inversions in the mouse, so that one could use the inversions to suppress crossing over, over a long distance on the chromosome, so that you could detect lethal mutations in the crossover-suppressed region, and as a matter of fact no inversions came out of that work. What did come out were a number of translocations and those proved valuable later on for working out which linkage groups were on which chromosomes and so on.

PSH. Had the MRC Human Radiation Unit under Court Brown, had that got going at that point or did that come later?

ML. That came later.

PSH. So the cytogenetic side was still, I suppose mouse cytogenetics really was very difficult at that point.

ML. It was. There was a cytogeneticist attached to the group whose name was Slizynski but he didn't get very far with it.

PSH. Was he one of the Poles who had come over to Edinburgh in the war?

ML. That's right.

PSH. Because there was a Polish medical school still there, wasn't there?

ML. Yes

PSH. How long were you in Edinburgh before you moved to Harwell?

ML. 5 or 6 years.

PSH. Then, did you come direct from Edinburgh to Harwell, or was there a stage in between.

ML. I came direct. This unit, the radiobiology unit, existed here at Harwell and at some stage, although Waddington had got this grant up in Edinburgh, the work in Edinburgh was somehow considered the work to be part of this unit at Harwell and at some stage, in the early 1950s, it was decided that the Edinburgh group should move to Harwell, because we could have the facilities here.

PSH. So it wasn't just you on your own that moved, it was the mouse group as a whole.

ML. Yes.

PSH. I see. I didn't know that. Who was director here, was this T C Carter at the time?

ML. He was head of the mouse genetics. The head of the whole unit was John Loutit.

PSH. Yes. I was talking the other day with Ted Evans and he was telling me a bit about John Loutit, but I didn't ask him about T C Carter. I mean, was he also one of the ones that moved from Edinburgh?

ML. That's right yes.

PSH. I see you published a number of papers with him, was his main work then mutagenesis, mouse mutagenesis?

ML. Yes.

PSH. And did he have an interest in specific mutants, or was he more interested in their radiation genesis?

ML. He had an interest, in particular in the luxate mutant, which was a gene that affected the growth of the limbs, and a mutation to that occurred. I think it occurred in Cambridge, I'm not sure, Cambridge or Edinburgh. T C Carter was at Cambridge for a short time before he went to Edinburgh and he found a spontaneous mutation to luxate and he did a lot of work on the inheritance of it and the quality of it.

PSH. Yes. May I ask what point was it that you first encountered the coat colour genes and mutants in mice? Was it when you were in Edinburgh or after you came down here?

ML. Coat colour genes?

PSH. Well, I suppose I am thinking of the X-linked genes.

ML. Oh that was in Edinburgh, yes.

PSH. Then the whole question of the X-linked basis and X-inactivation, am I right that that came when you found a mosaic mouse for one of these mutations?

ML. Yes.

PSH. At this stage, was Charles Ford and his cytogenetic group already down here, or did he arrive later on?

ML. He was already here when we got here. We got here in 1955 and he had arrived I think in about 1949, I would say.

PSH. And when did it become possible to really do useful cytogenetics on these mutants; was this after the new human techniques came in, or did the mice come first?

ML. I think the mice came first. What happened, I think, was that the mouse genetics group came from Edinburgh to Harwell and we had these translocations that were potentially cytogenetically interesting, and Toby Carter wanted them looked at and there was Charles Ford here, and Charles Ford was trying to get methods going for studying mammalian chromosomes and Toby Carter asked him to look at our translocations, which he did. He looked at meiosis in mice carrying translocations and the first major thing that came out of it was his finding of the T6 translocation, which had a small marker chromosome, which was used to show the immuno-suppressive effect of radiation, and very shortly after he discovered that, the authors whose names I forget, discovered that the human chromosome number in cultured cells was 46, and Charles Ford then very quickly confirmed in human meiotic

cells that it was 46 in the body as well. That was the start I think of human cytogenetics.

PSH. Yes. Was one of those translocations that you were studying the one that Tony Searle found or was that a different one?

ML. The one that had Tony Searle's name was a different one.

PSH. Right yes. One of the people, in quite a few of the things you have written, you have said was a big influence, was Ohno and his work, and I was wondering did he ever come and work in Harwell for a spell or not?

ML. No.

PSH. Because you wrote some papers together and it made me wonder whether actually he had come across for a time, but you must have met him several times?

ML. Yes.

PSH. I am intrigued, he always seems to me to have been a very original person?

ML. He was, yes, very original.

PSH. Yes. One of the other pieces of work which seems to have started right back in those early years was your work on the T locus.

ML. Yes.

PSH. How did that come about? Was that a natural mutant it started with, or . . .?

ML. Way back in the 1950s, which was the sort of time I started working on the T alleles, as they were called then, had a set of peculiar properties and one of the properties was thought to be that they had a high mutation rate from one little t to another little t, and I thought from the point of view of mutagenesis it would be interesting to study this high mutation rate and investigate whether it was affected by radiation. So I set up an experiment to look for these mutations from one T allele to another by treating mice with radiation, and what came out of it in fact, was that these changes were not mutations at all, they were crossovers in a region of abnormal chromosomes, and so I worked out what I could at that time of the properties of the different crossovers, but I was trying to work on mutation, but this was not mutation and it was not affected by radiation, so I dropped it after a few years and then I came back to it later in the 1970s, because people had become very interested in little t's and were talking about them being involved, very important in development and involved in immunological reactions and so on, and they were talking as though the whole thing was one locus, and to me it was a whole chromosome region, so I didn't think they could be right in what they were doing, so I got back into it myself to try and sort it out some more.

PSH. I think I'm right that really you followed it all the way through to the molecular characterisation, which now has really answered some of those difficult questions.

ML. Yes.

PSH. If I can just come back to the X chromosome and X inactivation, from my perspective as someone in human and medical genetics, it's been of huge importance. Was that something that you thought about when you first put the idea forward? Did you see that it was likely to be important in terms of human and medical genetic disorders then?

ML. I'm sure I didn't foresee all of the importance of it, but I did think it was going to be important for human genetics, yes.

PSH. Because from a very long time ago, clinicians had recorded patchy changes in heterozygous females for different diseases, and I'd wondered whether that was something which you were aware of at the time you were doing the mouse work?

ML. No. I did the mouse work and then wondered whether it applied to all mammals. I thought it would apply to all mammals, because part of the whole idea of X-inactivation was that the sex chromatin represented the inactive X, and there had been a lot of work on the sex chromatin and it was found in all mammals, so I did think that inactivation would be found in all mammals, so I started reading up all the literature on human X-linked genes, to see what evidence I could find. I did find some, but there was very little known about human genetics in those days.

PSH. That's true. Coming on to your links with human genetics, although you yourself have stuck to the mouse, there have been some wonderful collaborations and one person who I have also seen and talked with, who seems to crop up in the stories in a number of places is John Edwards.

ML. Oh yes.

PSH. And am I right that he linked with people at Harwell from a very early stage?

ML. Yes.

PSH. Because I know he linked with the cytogenetics people, but he must have been a good person to link and discuss things with in terms of X-linked diseases too.

ML. Yes.

PSH. Can I ask you, when was it that you and John Edwards and others started to try to work out the homologies between mice and men?

ML. I think that was in the 1980s sometime.

PSH. Right, so that really came quite a bit after the X chromosome work.

ML. Yes

PSH. Was this ever something that was a planned programme, or did it just sort of happen, the homology side?

ML. Well, John Edwards was very much the motivator of it, the one who drove it forward, and he was very interested in it. He used to have meetings at which we discussed all the various homologies that were known and made tables and
maps of homologous mutants.

PSH. And am I right that Tony Searle was involved in that also?

ML. Yes.

PSH. And then Veronica Buckle, was she working mainly here or in Oxford?

ML. In Oxford, yes.

PSH. Because it does seem to me that all sorts of interesting things can come out of that, which perhaps had been a bit of a forerunner for the more detailed genome projects.

ML. Yes.

PSH. One of the things which I have been asking everybody I see has been, which particular piece of work or part of their work over the years, if you just had to choose one, which would you feel you identify most closely with, or feel most affection for. I know it's difficult to ask, but could you single out an area, or is it really not possible.

ML. I think the X inactivation.

PSH. Yes. Because it has had huge effects, yes. The other thing I have been asking people, is of the various influences on them during their career, is there a particular person they have either worked with or been influenced by, that really stands out?

[Pause]

ML. I don't really know.

PSH. Well no, fair enough. It has interested me that there are some people who can say a specific person, but for others it is more of a combination, and quite a lot of people seem to have rather just done it themselves.

ML. I think it may have been a combination of a lot of people over the years.

PSH. One of the things that I have noticed is how many really thorough reviews you have written on topics. I am always amazed that you have been

able to find both the time and to cover the fields so thoroughly. Is that something you have always enjoyed, writing these reviews?

ML. No, I don't really enjoy writing reviews.

PSH. You've done an awful lot of them, and they are very good reviews; and the other thing which has always impressed me is that, whereas a lot of people have got diverted from their primary work and gone off into committees and running very large departments and all kinds of other things, you have very much stuck to your mouse work haven't you?

ML. I have tried to, yes, at times it's been very difficult, but I have always tried to stick to the mouse work.

PSH. Have you always, in terms of the group of people working directly with you, has it always been a small to moderate size, or have there been times when it got very big and almost, so to speak, out of control?

ML. No, it has always been small to moderate size.

PSH. Yes?

ML. Yes.

PSH. That must be very satisfying in a way that allows you to be really involved in everything.

ML. Yes.

PSH. I think it's wonderful that you are working away here, so long after you came here; have you felt it a very fulfilling career, may I ask?

ML. Oh yes, yes, very much so, yes.

PSH. And there have been an awful lot of changes in MRC and everything else, but they seem to have left you fairly well undisturbed, and seeing the new building and everything, it must be very satisfying seeing it all going ahead.

ML. Yes. Well this mouse genetics unit developed to be, I think, one of the mouse genetics laboratories of the world; the mouse house we had before this new one, although it was smaller and less sophisticated, it was I think about the biggest mouse genetics laboratory in the country, so there was no incentive to go off somewhere else, because here were the best facilities, so you tended to want to stay here, but a lot of people in other departments in the Unit left at various times for pastures new, but in mouse genetics there was a tendency that once you got here you stayed here.

PSH. Yes. One thing I should have asked you at the very beginning, but I didn't, was did you come from a scientific or medical family at all, in terms of possible influences that might have.

ML. No, I didn't. My father was a civil servant. My mother was a schoolteacher before she was married. On my father's side of the family, people were mostly civil servants or teachers, or other kinds of service jobs.

PSH. So really, it wasn't until you got to school and had a good biology teacher that you felt pointed in that direction.

ML. Yes.

PSH. Mary, are there any other things that you would like to bring up, particularly from the point of view of influences on human genetics that your work and the mouse work has had?

ML. Well, there's always been the mutagenesis, and mutagenesis has always been trying to relate itself to human genetics, and I think that the fact that you could show that radiation was mutagenic in the mouse has been an incentive for development of human genetic studies.

PSH. Is it fair to say that human genetics wouldn't have really got the tremendous boost it got in the 1950s, if it wasn't for the radiation risks and dangers?

ML. Well that's my opinion certainly, yes.

PSH. It's actually struck me, meeting a lot of people, that they all say the same and, it's something I didn't fully realise before, but it does seem that it was the spur that got things going.

ML. Yes.

PSH. Mary, thank you very much indeed, and I will turn off the machine now and I am very grateful for you sparing the time.

ML. It's been a pleasure.

**End of tape.**