Mary Lyon

Mary Lyon graduated from Girton College, Cambridge in 1946 and obtained her Ph.D in 1950 as a student of R.A (later Sir Ronald) Fisher. She then joined Toby Carter's MRC group at the Institute of Animal Genetics, Edinburgh to assess through work on the mouse the genetic risks to man of exposure to ionising radiation. Shortly after she moved with the group to its ultimate home at the MRC Radiobiological Research (now Mammalian Genetics) Unit at Harwell. She became head of the Genetics Division in 1962 and propelled it to one of the leading mouse genetics laboratories in the world before her official retirement in 1990.

Mary's career has spanned the meteoric rise in the interest and knowledge of mouse genetics and its application to human medicine. Perhaps more than any other she spearheaded this advancement. Her first major contribution was surely her formulation of the X-chromosome inactivation hypothesis in 1961, which alone may be regarded as the most significant advance in modern mammalian genetics. It was clear virtually from the beginning that "Lyonization" was not specific to the mouse but rather a mammalian phenomenon. As such it has proved of great significance in human clinical genetics and it continues to serve as a model system for gene regulation. The mechanism by which one of the two X chromosomes becomes inactivated and how almost all its genes become transcriptionally repressed has been, and continues to be, the subject of intense investigation in laboratories throughout the world, verifying and extending the further concepts introduced by Mary over the years.

A further personal triumph for Mary has been her success in unravelling the mysteries of the enormously 'complex' *t*-complex. Her long-term research on this intriguing region of mouse chromosome 17 has led to major advances in the understanding of its genetic structure and function. It can now be regarded as perhaps the best-known segment of the mouse genome becoming among the first targets for intensive molecular investigation.
Mary Lyon's contributions to the core radiation studies at Harwell and her treatises on radiation genetic risk assessment, later expanded to include risks from chemical mutagens, have been extensive. She has been responsible for major advances in the field, these including comparative aspects, effects of low radiation doses, and mutational responses in female germ cells, and she devised new ways of assessing risks from chemical mutagens that became internationally applied. Perceptive reports bearing upon genetic risk characterised her chairmanship of Committee 4 of the International Commission for Protection against Environ-mental Mutagens and Carcinogens.

However, her firm convictions on the importance of formal mouse genetics have perhaps had the greatest long-term impact. She was among the first to recognise the importance of mouse mutants both as potential models of human disease and for investigating biological processes. Accordingly, it became standard practice at Harwell to characterise all new mutations, map them wherever possible expanding the linkage map, and exploit them, as appropriate, for investigating such events and phenomena as non-disjunction, sex determina-tion, genomic imprinting.

Accompanying this overall philosophy have been her efforts over the years to disseminate relevant scientific information. This was first achieved through Mouse News Letter and its successor, Mouse Genome, which she edited from 1956 to 1970. Her personal contributions with her Chromosome Atlas of the Mouse showing homologies with human chromosome regions has been of immense value. And editions of the 'bible' of mouse genetics, Genetic Strains and Variants of the Laboratory Mouse, to which she contributed as well as co-editing, have been the keystone for mouse geneticists everywhere. Beyond this, her vigilance, foresight, powers of persuasion and sheer hard work on the Committee for Standardised Nomenclature for Mice has brought mouse genetic nomenclature to its present clear state without any of the confusion and uncertainty that could easily have dogged a rapidly expanding science.

The generation of characterised mouse mutants, combined with the use of embryo freezing for storing valuable stocks that she initiated, made Harwell with its expertise in mouse genetics the leading European mouse genetics resource by the 1990s. This contributed substantially to the case for the establishment of the Harwell Genetics Division as an independent Mammalian Genetics Unit in the 1990s. Its new 'Mary Lyon' Centre is currently under construction.

Although she officially retired in 1990, Mary has continued with her research at Harwell, new work including characterisation of a series of eye and other mutations, updating and further contributing to the understanding of the *t*-complex, and predicting elements of genomic imprinting based upon X-chromosome inactivation. In addition, she has presented a further intriguing hypothesis on the role of interspersed repetitive LINE elements, in which the X-chromosome is very rich, proposing that they serve as booster elements to promote the spread of *Xist* mRNA inactivation.

Mary Lyon's scientific achievements led to her election in 1973 as Fellow of the Royal Society, which also awarded her a Royal Medal in 1984. In 1979 she was elected a Foreign Associate of the National Academy of Sciences, and in 1980 she was elected an Honorary Fellow of the American Academy of Arts and Sciences. She is also an Honorary Fellow of her old College, Girton, and has received many other honours and awards.