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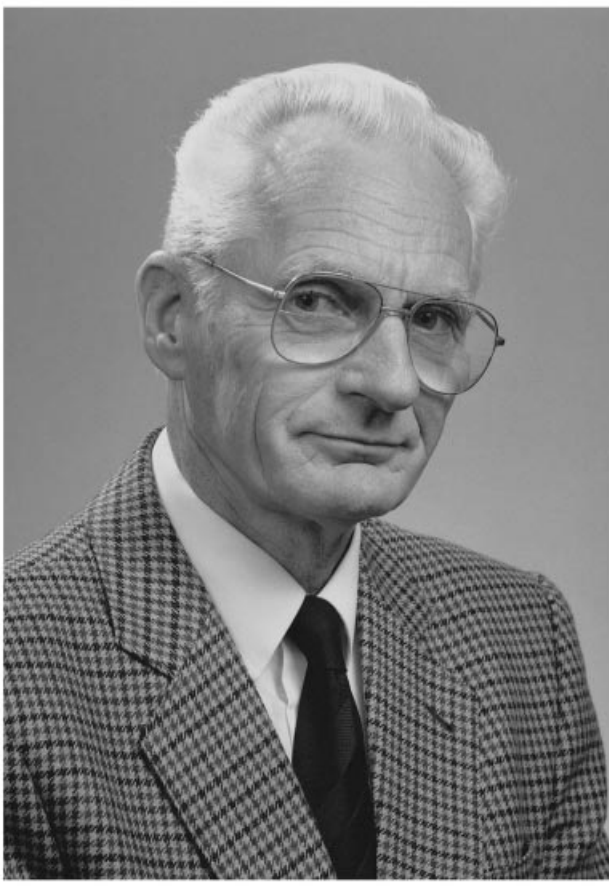
Bruce Cattanach: Mutagenesis and where it can lead you

This Special Issue of *Genetical Research* constitutes a tribute to the work and achievements of Bruce Cattanach on the occasion of his official retirement. Bruce began his career working on mutagenesis in mice. His interest in mutagenesis continued throughout his career but through it he was led to a wide range of major discoveries in mammalian genetics. The contributions from his colleagues in this issue provide a flavour of the various fields his work has covered.

Bruce was born on 5 November 1932. According to the story, when asked as a child what he would like to do when he grew up, he said that he would like to grow cows in test-tubes. Nevertheless, his first degree involved plants, being in Agricultural Botany at Durham University. However, he had already acquired his lifelong interest in breeding and showing pedigree dogs. Thus, animal genetics captured his attention and he moved to the Institute of Animal Genetics in Edinburgh, where he became a PhD student in the group of Charlotte Auerbach, the discoverer of chemical mutagenesis. He started as he meant to go on and his second paper was a letter to *Nature* in which he described the induction of translocations by triethylenemelamine (TEM), the first instance of chemical mutagenesis in a mammal.

Among the translocations induced by TEM was what later came to be known as Cattanach's translocation, involving the X chromosome and chromosome 7. Mice heterozygous for this translocation show variegation due to X chromosome inactivation. This led him to an interest in X-inactivation, then a new idea. He showed that variegation due to autosomal genes involved in translocations with the X chromosome could in part be explained by variable reversal of previous inactivation. With his keen eye for detail he noticed different levels of variegation in different crosses, and this led to the discovery of the *Xce* locus. He showed that alleles at this locus affected the choice of X-chromosome for inactivation, and probably formed part of the X-inactivation centre, now a topic of great interest.

After his PhD at Edinburgh Bruce spent two years at Oak Ridge, again working on mutagenesis, alongside Bill and Lee Russell, two pioneers of mutagenesis work with mammals. He then returned to Charlotte Auerbach's Unit in Edinburgh. His interest in X chromosomes was by then as great as in mutagenesis, and his next move was to the City of Hope in California, to join Susumu Ohno who had made the key finding underlying the discovery of X chromosome inactivation. In the course of his X-chromosome work there Bruce found an inherited type of XX maleness in the mouse. This proved to be due to the *Sxr* sex reversal factor, which later became important in the understanding of sex determination in the mouse. Thus began another of Bruce's interests, in sex determination. *Sxr* involved a transposition of the sex-determining region of the Y chromosome from the short arm to the pseudoautosomal region. Bruce used it to provide evidence of meiotic crossing-over between X and Y. On being transferred to the X chromosome *Sxr* was variably subject to X inac-



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tivation, resulting in female, hermaphrodite or male phenotypes.

After three years in California, Bruce returned to Britain to work in the Genetics Division of the MRC Radiobiology Unit at Harwell, now the Mammalian Genetics Unit. He became head of the Division in 1987, the same year that he was elected a Fellow of the Royal Society. At Harwell he was able to pursue all his various research interests, from mutagenesis to sex determination and to include new interests. In mutagenesis he continued his earlier work on chemical mutagenesis, showing the extreme variation in sensitivity of different stages of spermatogenesis to various chemical mutagens. He also made extensive studies on changes in the spermatogonial stem cell population after various radiation or chemical treatments, and the effects of these changes on the mutation rate. Mutants he discovered in this work were of interest in numerous ways. In particular he found the recessive mutation hypogonadal, *hpg*, deficient in gonadotrophin-releasing factor, which has been a valuable tool in studies of the hypothalamic gonadotrophin releasing system. Another major finding was that of numerous large cytogenetically visible deletions among the offspring of irradiated males. He devised a new method of measuring non-disjunction in mice, using Robertsonian translocations. His lynx-eyed ability to detect abnormalities in mice, together with his remarkable perception of their biological significance, led him to notice differences in young mice according to the parental origin of specific chromosomes. Thus, he discovered autosomal imprinting in mammals. His mutagenesis work once again proved valuable in unravelling a biological phenomenon. He had an extensive stock of chromosomal translocations and deletions, which provided a resource for generating maternal and paternal disomies. With the aid of these he was able to make a detailed imprinting map of the mouse genome, showing that only certain specific small regions of the chromosomes carry imprinted genes. This map has been very important in the identification of the particular genes concerned. Its construction has come despite Bruce's strong dislike of mapping in general.

Despite all his major achievements Bruce has remained completely unassuming. His lively sense of humour helps to keep the lab very cheerful. He is a stimulating colleague ready to listen to and criticize new ideas, and, as most of the authors who have contributed to this issue will know, he collaborates readily. Also as his collaborators will know, he is meticulous in writing papers, and frequently goes through several drafts before he is satisfied. He has his strong dislikes and, in particular, he has never been a committee man.

On his way to California in 1966 he married his wife Margaret and they had two daughters, Jean and Susan. Margaret tragically died suddenly in 1996. He is athletic and in his younger days was a keen squash player. His interest in breeding as well as judging dogs remains as strong as ever and the whole lab has followed with delight his successful project to breed genetically short-tailed boxers. He also has a strong interest in genetic disease in dogs, and in control schemes to eliminate particular diseases from certain breeds.

It has been a privilege to have known and worked with Bruce. Let us hope that he has a long and happy future, and that his scientific contributions long continue.

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