OBITUARY

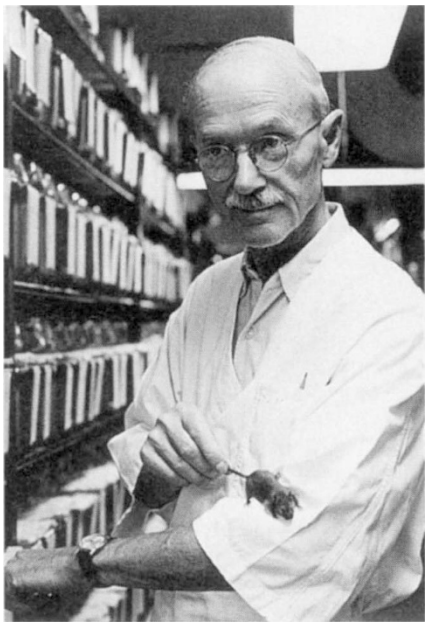
George D. Snell (1903–96)

GEORGE Snell is dead. But — to paraphrase what was said about another man at another time — if I choose, I do not have to believe it. So profound has been his influence on an entire scientific discipline, that for as long as immunologists use congenic strains in their experiments, as long as the major histocompatibility complex continues to absorb us, indeed, as long as immunogenetics continues to exist, George Snell will remain with us in spirit.

Snell once remarked that had a course in astronomy been offered at the Harvard Medical School, where he enrolled in 1926, he might have become an astronomer. Instead, he was caught up in the enthusiasm of William E. Castle, a pioneer in mammalian genetics. At the Bussey Institute, an old mansion donated to Harvard by a wealthy family, Castle lived with his students and scores of rats, mice, guinea-pigs and rabbits. Snell was assigned the task of measuring linkage between the *dilute* and *short ear* genes in the house mouse. This assignment was the second decisive moment in Snell's career because — except for a brief period in which he studied the genetics of social behaviour in the parasitic wasp *Habrobracon* — he remained faithful to the mouse until he retired from experimental work.

Upon earning his PhD in 1930, Snell was granted a postdoctoral position with Hermann J. Muller at the University of Texas at Austin. A few years earlier, Muller had discovered that X-rays induced mutations in *Drosophila* and Snell proposed to test whether they did so in the mouse as well. Snell's two years at Austin proved, on the one hand, to be disappointing: he saw little of Muller, who spent part of the time on sabbatical leave in the Soviet Union, and he was unable to induce mutations in mice. On the other hand, he was exposed to *Drosophila* genetics and he discovered that X-rays induced translocations. Snell's work established that, at least in mammals, X-rays caused chromosomal aberrations rather than point mutations, it generated the methodological and conceptual basis for mammalian cytogenetic studies, and it produced several translocation strains (some still extant) that later proved useful in mapping studies.

Snell left Austin, was unemployed briefly, and then taught for a time before joining Clarence C. Little at the Jackson Laboratory, Bar Harbor, Maine, in 1935. Little, also a former student of Castle's, had founded the laboratory only six years earlier to study the genetics of cancer, using mice as experimental animals. One of Snell's first tasks was to edit a book summarizing the available knowledge about the laboratory mouse. Because little was known about mouse embryology, and there was no one who could write this part of the book, Snell characteristically decided to research the area himself. The result was a chapter that



some 40 years later would become the foundation of the burgeoning discipline of mammalian developmental biology.

The editing of the *Biology of the Laboratory Mouse* had, however, another, more far-reaching effect on Snell's scientific career. Little contributed to the book a chapter entitled "The genetics of tumor transplantation", in which he summarized studies begun at the turn of the century and in which he had become involved while at the Bussey Institute. The studies stemmed from the observation that a spontaneously arisen tumour in a mouse of one inbred strain could be transplanted successfully to same-strain individuals but not to different-strain mice. Breeding experiments revealed the transplanted tumour growth to be controlled by multiple, but still unidentified, genes. Upon reading this chapter, Snell became fascinated by the mysterious tumour-resistance genes. He realized, however, that if he was to understand the nature of the histocompatibility genes, as he had begun to call them, they would have to be separated from one another, and he began to consider how this could be done.

His earlier contact with the *Drosophila* geneticists may have given him the advantage here. In 1948, he published a paper in which he described a method for developing congenic mouse strains, each of which would differ from an inbred strain at a single histocompatibility locus. He developed the mathematical theory of the underlying process, estimated how many years it would require and then began the work. Although a fire at the laboratory a couple of years later destroyed his initial efforts, he nevertheless began anew and ultimately produced the basic stock of mouse congenic strains differing at individual histocompatibility loci. Testing of the strains soon convinced him that the loci fell into two different categories — major and minor — depending on their effect on transplant survival.

Collaboration with Peter A. Gorer, who was visiting Jackson Laboratory on leave from Guy's Hospital in London, resulted in establishing that the major locus was identical to a locus encoding antigen II, identified earlier by Gorer. Snell and Gorer named the locus histocompatibility 2, or H–2. When further analysis revealed the locus to be complex genetically, the concept of the major histocompatibility complex, or MHC, was born. Although Snell followed several other leads stemming from his work with tumours (for example, he discovered independently the phenomenon of immunological enhancement), he and his co-workers focused mainly on further characterization of the H–2 immunogenetic complex. Much of the current knowledge concerning it derives from this work.

The concept of congenic strains and the discovery of the MHC has had a profound effect on the development of the entire field of immunology over the past 25 years. For these contributions Snell was awarded, together with Jean Dausset and Baruj Benacerraf, the Nobel Prize for Medicine in 1980.

George D. Snell died on 6 June. To future generations, he has left his scientific legacy; to those of my generation who knew him personally, he has bequeathed warm memories of a man modest to a fault, a man of the highest personal integrity, and one whose friendship brightened our lives. Jan Klein

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