John Robert Stanley Fincham

The death of John Robert Stanley Fincham on February 9th 2005 marked the passing of an exceptional academic who will be remembered for his extraordinary dedication and intellectual contribution to science, most particularly to genetics.

John's university career began at Peterhouse College Cambridge. He graduated in Botany in 1946 and remained at Cambridge to complete his PhD in 1950. From the outset of his career, John was recognised as having an outstanding intellect. In 1948 he went to the California Institute of Technology as an Agricultural Research Council Scholar where he worked with George Beadle, Norman Horowitz and Sterling Emerson in what was a stronghold of *Neurospora* genetics. Shortly after he married Sterling Emerson's daughter, Ann, so John's visit was productive on both a scientific and personal level. He was appointed to a lectureship in the Botany Department of Leicester University in 1950 and was made a Reader four years later. A year as an Associate Professor in the Massachusetts Institute of Technology preceded his appointment as Head of the Genetics Division of the John Innes Institute in 1961. He remained at John Innes until 1966 when he was appointed as Professor and Head of the newly established Department of Genetics at Leeds. In 1976, John was appointed to the Buchanan Chair of Genetics in Edinburgh and was head of the Department of Genetics until 1984 when he moved to take up the Balfour Chair in Cambridge. He is the only person to have held both of these prestigious chairs. On his "retirement" from Cambridge in 1991, John returned to Edinburgh where he continued to take an active part in teaching and research.

The disruption that each new appointment must have brought to John's research did not inhibit his publications and writing. He published well over 100 journal articles from 1949 until 2004. In addition he found time to write major monographs and textbooks. His first, *Fungal Genetics*, originally written with Peter Day, remains the yardstick by which all other texts on this subject are judged, and went through several editions and major revisions as the subject expanded. Four other books followed; all single author works, including a textbook on Genetics. He also edited symposium volumes and wrote influential reviews on several quite different topics.

John published on a variety of topics, including unstable pigmentation genes and transposons in *Antirrhinum*, but his main research interest remained focussed on genetics of fungi and on the model organism *Neurospora crassa* in particular. His research began with his doctoral work in the laboratory of David Catcheside in 1946. John's initial work demonstrated that several species of *Neurospora* all had seven chromosomes. At this time the groundbreaking experiments of Beadle and Tatum, which led to the 'one gene-one enzyme' hypothesis, were pointing the way towards a combined biochemical and genetical approach to the analysis of metabolic pathways, and John was quickly involved in the analysis of mutants that were deficient in the enzyme glutamate dehydrogenase. These mutants identified the *am* locus. In 1957, he and his former student John Pateman made the unexpected discovery that some combinations of alleles at the *am* locus were able to complement each other and restore enzyme function. John Fincham provided the correct explanation for this observation, and subsequent experiments from his group showed that the active enzyme was a hexamer of identical subunits. Allelic complementation could occur if the aggregation of two different types of alleles of defective polypeptides generated hexamers with some enzyme activity.

The discovery of allelic complementation was the start of an in-depth investigation of the *am* gene using traditional genetics and biochemistry. Many mutants were isolated and analysed and the amino acid sequence of the wild-type enzyme was determined.

In 1982 John went on to clone the gene using what was, at that time, a novel approach. He used information from compensatory frameshift mutations, and the fact that his group had determined the amino acid sequence of the enzyme, to deduce a 17 base pair nucleotide sequence. This was used to probe the *Neurospora* genome and isolate and identify the *am* gene. The discovery that the stretch of DNA was interrupted by a sequence of bases that did not encode amino acids identified an intron in the *am* gene. This was only the second example of an intron in a protein-encoding gene from a lower eukaryote. John went on to characterise further *am* mutants by integrating what was known from earlier studies with the DNA sequence information obtained following the successful cloning of the gene. This provided gratifying verification of earlier conclusions based on complementation and enzyme assays. Latterly, John was anticipating the elucidation of the three-dimensional structure of glutamate dehydrogenase so that amino acid interactions he had predicted from his earlier work would be verified.

In *Neurospora*, transformants that contain duplicate DNA segments undergo frequent mutation of these repeat sequences when any transformant is crossed to another strain. This phenomenon, called Repeat Induced Point mutation (RIP), was discovered by Eric Selker. John, who had always had an interest in gene instability, was intrigued by RIP and investigated the phenomenon. He analysed disruption of the *am* gene in transformants that contained three copies of the gene. He found that RIP tended to disrupt 2 out of the 3 copies but there were some cases where all three copies had been disrupted, leading to the conclusion that there could be multiple rounds of disruption during the sexual cycle. In addition to gene disruption which

produced non-functional alleles, John demonstrated that RIP could produce new functional alleles, which specified glutamate dehydrogenase with altered heat sensitivity and enzyme kinetics.

John always had a very range of interest in many aspects of genetics, and stimulated discussion over a wide range of science issues with his penetrating questions and insightful analysis. This talent was never more evident than after seminars when John, almost invariably, led off a discussion by a succession of stimulating questions. He was a geneticist of the old school; his diligent reading of the literature often resulted in his alerting colleagues to publications in areas of genetics that were quite remote from his primary interests.

John was elected a Fellow of the Royal Society in 1969 and made a Fellow of the Royal Society of Edinburgh in 1978. He was President of the Genetical Society of the UK from 1978 to 1981. In 1977 he was awarded the Emil Christian Hansen medal for his contribution to research into fungi.

Outside science, John had an interest in music, mountaineering and many sports. He played rugby, cricket, and squash and he continued playing the latter despite the handicap of a hip replacement that affected his ability, but not his enthusiasm, for chasing the little ball about the court. An incident at the time he underwent the hip replacement operation illustrates his dedication to science. John cycled to the Princess Margaret Rose Hospital and, after undergoing the pre-operation tests, persuaded the medical staff that he was quite capable of not eating and obeying any other strictures placed upon him just as well if he was in the library as in the hospital bed. So he was allowed to cycle away from the hospital to return a few hours later when the operation was more imminent!

John leaves a wife, Ann, a son and three daughters.

Dr. Jeff Bond, Professor Noreen Murray

John Robert Stanley Fincham, BA, PhD, ScD(Cantab), FRS. Born 11 August 1926; FRSE 6 March 1978; died 9 February 2005