Malcolm Ferguson-Smith

Quite often some of the most innovative and productive scientists are those with extremely varied backgrounds. Malcolm Ferguson-Smith, the first scientist to be honored in this series, is such a person. Purely on the basis of his publications few would realise that Malcolm has been a pathologist all his working life. It was his early interest in the pathology of human sexual development and the possible role of the Barr body which first led him into human cytogenetic studies in the late 1950s. That interest in sex determination has continued for nearly 50 years up to the present day, as we see from his last listed publication on the complex X-Y chromosome constitution of the duck-billed platypus. The difference between visualizing the humble Barr body and the breath-taking magnificence of the multi-chromosome and multi-fluor images of the platypus sex chromosomes is indeed a life-time apart and Malcolm Ferguson-Smith has been central in those developments. It was he who first recognised the potential of flow cytometry for isolating individual chromosomes to address the clinical problems of particular patients. At that time, during the mid-1980s, the conventional wisdom was that chromosomes could only be efficiently sorted using the especially developed and super-expensive high-speed sorters at the Los Alamos and Lawrence Livermore laboratories in the USA. However, several groups in Europe, including that of Malcolm, Brian Young and others, demonstrated that commercially available cell sorters could also be successfully used, if somewhat more slowly, for the same purpose. In parallel to the sorting, FISH methods were being developed by others, but notably the introduction of PCR protocols which could be used for amplifying DNA from sorted chromosomes was a break-through (Telenius et al., 1992) and essential to developing chromosome-specific paints from sorted chromosomes on a large scale. Malcolm and his group went on to use sorted chromosomes in reverse painting, i.e. hybridizing DNA from sorted aberrant human chromosomes back onto normal metaphases to demonstrate the origin of the aberration (Carter et al., 1992). Malcolm's group proceeded to sort the chromosomes of other species to produce chromosome-specific paints with the mouse being the most notable (Liyanage et al., 1996). Undoubtedly, one of the most extraordinary developments was the discovery that chromosome-specific

paints of one species could be successfully hybridized to the chromosomes of another to demonstrate homology (Mueller et al., 1998; Yang et al., 1999; Yang et al., 2000) facilitating wide-scale evolutionary studies in vertebrates. For the true aficionados of meiosis three articles (Ferguson-Smith and Page, 1973; Winsor et al., 1978; Brown et al., 1998) are gems and deal with

aspects that have both fascinated and frustrated human cytogeneticists for decades. Perhaps Malcolm's most sanguine contribution and for which he will be rightly remembered for the longest is his 1966 letter to the *Lancet* (Ferguson-Smith, 1966a) in which he proposed that the XX male phenotype derives from an unequal meiotic exchange between the X and the Y chromosome resulting in transfer of the male-determining factor from the Y to the X. This was at a time when it was not even known which arms of the X and Y paired with each other or the extent of the pairing segment and predated the use of XX males with differing levels of XY interchange to dissect and map the Y chromosome by some 20 years. Amongst his many career activities Malcolm has been a member of the editorial board and regular contributing author of this journal.

On behalf of the Editorial Board
Peter Pearson

Curriculum vitae

Malcolm Ferguson-Smith is currently Research Professor in the Department of Veterinary Medicine, University of Cambridge, UK. He was born in Glasgow in 1931, graduated in medicine at Glasgow University in 1955 and, while undertaking postgraduate training there in pathology, was introduced to research on sex chromatin under Bernard Lennox. Their buccal smear surveys revealed for the first time the high frequency of Klinefelter's syndrome among subfertile males and among those with learning difficulties. Unsuccessful efforts to undertake chromosome analysis in these patients in 1957–58 led to an appointment as Fellow in Medicine at John's Hopkins in 1959 and he remained there working on chromosomes for nearly three years. During this time he established the first chromosome diagnostic service in the USA and undertook cytogenetic research into the Turner syndrome and true hermaphroditism. Returning to Glasgow University in late 1961, he was appointed successively, Lecturer, Senior Lecturer and Reader before becoming Professor of Medical Genetics in 1973. His duties included teaching genetics to first and fourth year medical students and the establishment of a Regional Genetic Service for the West of Scotland comprising counselling clinics, diagnostic laboratories, prenatal diagnosis and screening. The clinical cytogenetics service provided opportunities for contributing to the human gene map using familial chromosome polymorphisms, deletion mapping, in situ hybridisation and chromosome sorting by flow cytometry. In all these aspects of diagnosis and research he was ably supported by his wife, Marie, and an exceptional team of post-docs and technicians. Grant support was provided by the MRC, the Scottish Home & Health Department, the Scottish Hospitals Endowment Trust and the Medical Charities. An initiative by Action Research for the Crippled Child led to the building of the Duncan Guthrie Institute of Medical Genetics in Glasgow in 1980. In 1987 he was appointed Head of Pathology at Cambridge University and Director of the East Anglia Regional Genetics Service. Research continued on gene isolation, fluorescence in situ hybridisation, reverse chromosome painting and studies in karyotype evolution using cross-species chromosome painting. On retir-

ing from the headship of Pathology in 1998, Professor Ferguson-Smith and his small team moved to labs in the Cambridge University Centre for Veterinary Science, to establish the Cambridge Resource Centre for Comparative Genomics supported by the Wellcome Trust. During his long and happy career in medical genetics he has had a number of honorary administrative duties including Vice-President of the Genetical Society and President of the Clinical Genetics Society, President of the European Society of Human Genetics, President of the International Society for Prenatal Diagnosis and is currently President of the Association of Clinical Cytogeneticists. He was elected Fellow of the Royal Society of Edinburgh in 1978, the Royal Society of London in 1983, the Royal College of Obstetricians & Gynaecologists in 1993 and the Academy of Medical Sciences in 1998. He is a Foreign Member of the Polish Academy of Science and of the National Academy of Medicine of Buenos Aires and is an Honorary Associate of the Royal College of Veterinary Surgeons. He has Honorary Doctorates in Science from the Universities of Glasgow and Strathclyde. His editorial duties have included membership of the Board of Cytogenetics from 1961 to 1971 and of its successor from 1972 to 1982; in 1980 he became the founding editor of *Prenatal Diagnosis*. With J.M. Connor his undergraduate textbook "Essential Medical Genetics" has run to five editions.

50 selected publications in chronological order, 1957–2004

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