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Obituary

Professor Michael John Reed, BSc, MSc, PhD, DSc, FRCPath (1944–2009)

Our scientific community lost a prominent and inspiring scientist, Michael John Reed, who died suddenly on 6th April 2009.

Mike Reed was born on 30th May 1944 in Corringham, Essex. In 1967, Mike obtained a BSc in Zoology from the University of London, and a MSc in Biochemistry from Imperial College in 1969. For the next 4 years Mike worked diligently as a research assistant to Professor Ken Fotherby at the Royal Postgraduate Medical School, London where he completed his research for a PhD, which was awarded in 1973. This research involved an investigation of the mechanisms of action and metabolism of ethinyl oestradiol and norethisterone in women. This sealed his interest in steroid biochemistry and oestrogens remained his favourite steroids throughout his outstanding career.

In 1976 Mike moved to the Department of Chemical Pathology at St. Mary's Hospital Medical School as a Research Fellow with Professor Vivian James. St. Mary's is where he spent the rest of his distinguished career. In 1978 he was appointed as a Lecturer in Chemical Pathology, being promoted to Senior Lecturer in 1983, Reader in Chemical Pathology in 1992 and he was appointed to a Personal Chair of Steroid Biochemistry in 1995; the same year he became a Fellow of the Royal College of Pathologists.

At St. Mary's Mike quickly established a research programme to study the role of oestrogens in the development and growth of tumours in hormone responsive tissues. To examine the production and origin of oestrogens in postmenopausal women with breast or endometrial cancer, a number of sensitive assays were established, including techniques to measure transfer constants and metabolic clearance rates. These *in vivo* methods, using radioactive substrate infusions to calculate the extent of aromatisation in postmenopausal women with breast cancer, earned him international recognition.

The early 1990s marked significant changes and challenges. Firstly, the retirement of Professor Vivian James in 1990 led to the merger of two departments, Chemical Pathology and Clinical Endocrinology to form the Department of Endocrinology and Metabolic Medicine, headed by Professor Desmond Johnston. Secondly, St. Mary's Hospital Medical School merged with Imperial College and brought with it the need for commercially viable research projects, which could potentially be exploited in Imperial spin-out companies. By this time several growth factors and cytokines had been identified by his group as important regulators of the aromatase complex in breast tumours. Initial attempts were therefore made to block the action of these cytokines, IL-6 in particular, with small peptide inhibitors.

With my (AP) interest in the steroid sulphatase (STS) enzyme and Mike's interest in the synthesis of oestrogenic steroids, we pioneered the rationale for the development of STS inhibitors for therapeutic use in hormone-dependent cancers. In a highly synergistic collaboration of some 18 years with Professor Barry Potter and his team of medicinal chemists at the University of Bath, and following early 'proof of concept' research from a subsidiary of 3i plc, Imperial College, Bath University and grants from the Cancer Research Campaign a series of highly potent and "first-in-class" STS inhibitors was synthesised. One inhibitor, oestrone-3-*O*-sulphamate (EMATE) was the first ever active site-directed irreversible inhibitor of the STS enzyme. As this compound possessed oestrogenic properties it was not of interest for oncology applications, but was licensed to a major pharma company for clinical development as a potential HRT regimen. This licensing agreement allowed the formation of a "spin-out" start-up company between Imperial College and the University of Bath, Sterix Ltd., that was allowed to develop gradually before £8M was secured from a syndicate of four venture capital companies to expand the company's university-based R&D and take a second drug into clinical trials. Sterix was subsequently acquired by the Ipsen Group in 2004. Mike exploited his entrepreneurial ability to the maximum. He took full advantage of this commercial funding and built up a significant research group. Mike became a CSO and Director of Sterix from 1998. Further work led to the identification of 667 COUMATE (STX 64, now BN83495), a non-steroidal, non-oestrogenic STS inhibitor which was used for the first ever phase I trial of this class of drug in postmenopausal women with advanced metastatic breast cancer, in collaboration with Professor Charles Coombes and overseen by the charity Cancer Research UK. The drug was well-tolerated, with some patients all of whom had previously progressed on other therapies, showing evidence of stable disease and is currently in four clinical trials for both breast and prostate cancer. The ground-breaking innovation and identification of the active pharmacophore for STS inhibition as a sulphamoyl aryl ester provided an international lead in the field of STS inhibitors that has been maintained and such clinical translation of drug candidates

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is a very rare achievement for academic groups. Numerous patents were granted for this work and a very large portfolio developed from the basic concept. By this time the research group had acquired an enhanced international reputation. In addition to continuing to develop STS inhibitors, compounds were synthesised to inhibit the other enzymes of steroidogenesis as potential drug targets, namely aromatase, 17β-HSDs (1 and 3) and 11β-HSD-1 and this work is continuing strongly.

Since starting the sulphatase inhibitor research programme, several other novel therapeutic targets were identified using this technology. These ranged from dermatology indications, autoimmune diseases and diabetes to endometriosis and BPH. Recently, a number of sulphamoylated steroidal and non-steroidal potent microtubule disrupting compounds were synthesised and identified that also inhibit angiogenesis. These compounds are highly active against a wide range of hormone-independent cancers and importantly are active on drug-resistant cell lines and tumour xenografts. Thus, Mike's research started with hormone-dependent cancer and progressed to the development of novel therapeutic agents for the treatment of hormone-independent cancers. It was his intention to enter one of these potent microtubule disrupting compounds (STX140) into clinical trial when he met his untimely death.

Throughout Mike's commercially funded activities, he still continued to wear his "academic hat" and pursue pure academic interests. He was involved in teaching steroid endocrinology to pre-clinical and clinical students (BSc) and lecturing to postgraduate students undertaking the MSc or the MRCPath examination in Chemical Pathology. He continued to support PhD students and was an examiner for a number of PhD students nationally and internationally. Mike was on the editorial board of several journals and also played an active role in the Society for Endocrinology. Margaret Ghilchik and Dennis Wang were his constant source of strength and inspiration. Lenus Kloosterboer, Jos Thijssen, Luigi Castagnetta, Guiseppe Carruba, Shiuan Chen and Frank Stanczyk were among his most valued international collaborators. Mike was invited to many international meetings as a speaker, where he left a warm and professional impression. He was a most welcome speaker in specialised workshops on steroid metabolism and action organised by Jerzy Adamski. In his outstanding scientific career, Mike published over 275 papers. The impact of this work is now becoming well recognised academically, as well as commercially. Shortly before his death he received news that he had shared in the award of a prestigious interdisciplinary medal for the work on STS inhibitors that sadly he never received formally. In December 2000, Mike was honoured as one the leading breast cancer investigators of the 20th century. He was proud of his team and was very supportive of students and colleagues. He was kind and generous. To his colleagues he was a friend, always ready to give help and advice based on his wide experience. He was also an avid fan of cricket and opera.

Mike is survived by his wife Gill, daughter Julie and son John. He will be remembered as an exceptional academic teacher, an innovative scientist and a passionate humanist. Mike's generosity of sprit and inspiration as a scientist will be greatly missed by all who knew him.

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