

Chris Marshall 1949–2015

The scientific community is mourning the loss of Chris Marshall, a pre-eminent molecular, cell and cancer biologist who died on 8 August. Chris was an exceptional scientist, inspirational mentor and a dear friend to many.

Born in the Midlands, England in 1949, he attended the King Henry VIII grammar school before reading genetics at Cambridge. His PhD studies in the laboratory of Henry Harris in Oxford were followed by postdoctoral work with Sammy Franks at the Imperial Cancer Research Fund (ICRF; later the Cancer Research UK (CRUK) London Research Institute and now part of the Francis Crick Institute), and Ruth Sager at the Sidney Farber (now Dana–Farber) Cancer Institute in Boston. Prior to the advent of molecular biology, he explored the dominance of the cancer phenotype by cell fusion experiments between transformed and non-transformed cells, and highlighted the existence of both oncogenic and tumour-suppressor genes.

Appreciating his sharp mind, Robin Weiss hired Chris as a team leader at the Institute of Cancer Research (ICR) in 1980. A few months later Alan Hall was recruited as a budding molecular biologist. Uniting Chris and Alan under one roof resulted in an astonishing scientific partnership and a deep friendship that lasted until Alan's unexpected death earlier this year. In a series of ground-breaking papers, they determined that a mutant *RAS* gene, *NRAS*, was responsible for transforming sarcoma cell lines; showed how carcinogens mutate *RAS* genes; and determined the prevalence of these mutations in specific cancers. In these early days of molecular biology, this type of analysis was far from trivial, and their success reflected how Chris and Alan embraced the latest technologies. Through a collaboration with Frank McCormick, Chris's group was amongst the first to perform PCR in the UK — the sound of a robot shifting tubes between water baths was characteristic of his lab at the time. The expertise of Hugh Paterson also ensured that Chris and Alan's groups fully exploited micro-injection and time-lapse microscopy using analogue VHS video recording.

Chris next focused on understanding the mechanism of *RAS* action. In contrast to today, little was known about how signals are transmitted from the plasma membrane to the nucleus. His team, together with other research groups, delineated the mitogen-activated protein kinase (MAPK) cascade. He determined how *RAS* was targeted to the plasma membrane, and showed that this was critical for its function. He further showed that both *RAS* and its effector, *RAF*, can activate *ERK*/*MAPK* signalling, and in a series of beautiful experiments demonstrated that *RAS* regulated *RAF* by recruiting it to the plasma membrane. The clinical use of both *RAF* and *MEK* inhibitors to treat cancer patients today can be traced to these seminal experiments. Chris's group also showed that *RAS*–*MAPK* signalling wasn't just for driving proliferation, but could also drive cell differentiation. This raised the question of how one pathway could induce such different outcomes. Chris proposed that the duration of the signal was critical; a beautifully simple idea that still resonates in our understanding of signal transduction two decades later. Following his work on the *MAPK* cascade, he became interested in the metastatic behaviour of cancer cells and the biology of the tumour as a whole. Contemporaneously with Peter Friedl, he began investigating



the mechanisms that underlie the phenotypic plasticity of cancer cell invasion. He documented how the antagonism between *RAC* and *RHO* GTPases enables cancer cells to adopt different migratory behaviours, and contributed to our understanding of how crosstalk between cytoskeletal regulators affects tumour angiogenesis.

Unsurprisingly, this body of work led to his election to the European Molecular Biology Organization in 1993, the Royal Society in 1995, a Gibb Life Fellowship from the Cancer Research Campaign (which later formed CRUK with the ICRF) in 1992 and numerous other distinctions, including the Novartis Medal of the Biochemical Society, the Buchanan Medal of the Royal Society and a CRUK Lifetime Achievement in Cancer Research Prize. He was also a founding member of the Academy of Medical Sciences and chaired CRUK's science funding committee.

These decades of scientific excellence are remarkable, and yet only tell part of what made Chris such a cherished member of the scientific community. Chris was concerned not only about the science, but cared deeply about his colleagues and laboratory members. Over the 35 years of his tenure at the ICR, he created a flourishing research environment characterized by excitement and commitment. Ideas were encouraged and discussed for hours, and rigour was the underlying expectation. It was also fun — Chris possessed a unique sense of humour and was wonderful company. For his students and postdocs, of whom we are two, he was often the major influence of their scientific lives. These qualities ensured that he headed the highly productive Division of Cell and Molecular Biology, latterly the Division of Cancer Biology, and served as director of research at the ICR with great success. He also imparted sage advice to many colleagues. Most notably he played a significant role in the identification of *BRAF* as a major oncogene in melanoma, the first oncogene identified by 'big cancer genomics', and even returned to the bench to help with the focus formation assays required for the study. During his career, he became passionate about the need to move these findings into the clinic as quickly as possible, and was a strong advocate for ensuring that basic research was translated towards new treatments for patients.

Chris was an inspiration, both for his talent and passion for science and for his humanity, and was loved and respected by many in the scientific community. Outside the lab, Chris loved cycling, romantic comedies and the blues. Most of all, Chris was devoted to his family. He is survived by his wife Lesley, his children Joe, Lucy, and Francis, from his first marriage to Viv, and four grandchildren. He will be greatly missed.

Alison Lloyd and Erik Sahai

Alison Lloyd is at the MRC Laboratory for Molecular Cell Biology, UCL, London, WC1E 6BT, UK. Erik Sahai is at the Francis Crick Institute, 44 Lincoln's Inn Fields, London, WC2A 3LY, UK.
e-mail: alison.lloyd@ucl.ac.uk; erik.sahai@crick.ac.uk