

## Alan Hall 1952–2015

Alan Hall's unexpected death on 3 May 2015 shocked and saddened an immense swath of the biological research community. Alan made fundamental contributions to our understanding of how the cellular cytoskeleton is organized and regulated. His pioneering work in cell biology established that Rho family proteins are critical regulators of cell shape, migration, division and polarity, providing an essential framework for understanding the structure and function of normal and malignant cells. But beyond his scientific achievements, and perhaps more importantly, Alan deeply influenced many as a supportive supervisor and mentor, a visionary colleague, a fun and uplifting friend.

Originally from the industrial South Yorkshire town of Barnsley, UK, Alan graduated in 1974 with a chemistry degree from Oxford University. He then joined the laboratory of Jeremy Knowles at Harvard University, where in 1977 he completed his PhD in chemistry, having applied newly emerging molecular biology techniques to study enzyme structure–function relationships. Alan furthered his expertise in recombinant DNA technologies and heterologous protein production with post-doctoral positions in the laboratories of Ken Murray at the University of Edinburgh and Charles Weismann at the University of Zurich.

In 1981, Alan was hired by Robin Weiss, the director of the Institute of Cancer Research in London, to add his expertise in molecular biology to their repertoire. Working at the Chester Beatty Laboratories in Chelsea, Alan quickly established a partnership with Chris Marshall, who had joined the institute several months previously. Together, they applied the strategy of isolating transforming oncogenes through transfection of cancer DNA into mouse fibroblasts, and in 1983 discovered *N-Ras*, the third human oncogene to be cloned. Alan's background in enzymology and recombinant protein production led him to combine biochemical approaches with cell biology to study *N-Ras* function and regulation. His interests soon widened into investigating how *N-Ras* interacting proteins acted as regulators and effectors, and characterizing the signalling pathways responsiveness to active *N-Ras*.

While still at the Institute of Cancer Research, Alan began investigating the — then recently discovered but still poorly understood — Ras homologue (Rho) proteins. At the time, little was known about the signalling pathways that connect external cues to the cytoskeleton, or the molecular mechanisms that enable the cytoskeleton to perform its biological functions. In a pioneering series of experiments performed with Anne Ridley and later with Catherine Nobes, Alan established that three related small GTPases, Rho, Rac and Cdc42 play distinct roles in determining cell shape and movement. Alan's insight provided the field with long-awaited connections between growth factor and G-protein coupled receptors and the cytoskeleton.

In 1993, Alan moved his group across London to the Medical Research Council's new Laboratory for Molecular Cell Biology (LMCB). The creation of this institute, which Alan would head from 2001, generated a surge of excitement and support for British cell biological research. There, Alan explored the numerous cell processes that were regulated by Rho GTPase signalling. Dozens of groups around the world joined the search for connections between Rho proteins, regulators, effectors and cell responses. Highlights from Alan's research at the LMCB include



discovering the connection of Cdc42 with the Wiskott–Aldrich syndrome protein, WASP, and the role of Rho proteins in the activation of the phagocyte oxidase and later of phagocytosis in general. Notably, Alan and colleagues also implicated Rho proteins in cell cycle progression. Later, he ventured into cell polarity research and, together with Sandrine Etienne-Manneville, uncovered how Rho GTPases regulate two seemingly disparate types of cellular organization; epithelial cell planar polarity and cell polarity in migration. Alan's work has triggered an enormous wave of research into how signals from the environment influence cell shape, polarity, motility and proliferation and how these pathways are deregulated in cancer.

During his PhD at Harvard, Alan developed a love for the east coast of the US and sometimes talked of a desire to return there. This likely helped Tom Kelly and Harold Varmus to recruit him in 2006 as chair of the Cell Biology Program at the Memorial Sloan Kettering Cancer Center (MSKCC). Asked during an interview for this position, "What is the next big question in cell biology?", Alan answered "How do we put it all together?" by which he meant how do the cellular pathways and machinery fit together to form and maintain cells and cell populations? Alan eventually oversaw the recruitment of six faculty members to the Cell Biology Program, seeking cell biologists who were interested in answering these bigger questions and whose research would dovetail with existing cell signalling and adhesion expertise in the department. Being deeply aware that progress in cancer research would be limited without a truly mechanistic understanding of normal cell function, and recognizing that much of cell biology remained to be discovered, Alan

recruited investigators examining cell division, cell death, cell movement and cellular homeostasis.

When setting up his own laboratory at MSKCC, Alan brought two students, two postdocs and a lab manager from London. Always self-deprecating, he would joke that he was happy these lab members moved with him, as by himself he might not have known what equipment to buy or how to do the experiments. Many more joined his laboratory in New York, and Alan maintained a large and vibrant group that investigated the establishment of cell polarity and the regulation of cell adhesion by Rho GTPases. During his years in MSKCC, Alan made important insights into how cell division and polarity are coordinated in tissue morphogenesis, how polarity is disrupted by signalling from K-Ras, and how collective cell migration is regulated by the Rac1 activator  $\beta$ -PIX. Alan's body of work has profound implications not only for how cells organize themselves, but also for how tissues are built and how forces and signals (both chemical and spatial) are integrated during development and in cancer. During a career that spanned nearly four decades, Alan placed Rho GTPases on the map as major controllers of cell behaviour and organization, which participate in intricate signalling crosstalk with each other and with Ras proteins, revealing part of the amazing order and complexity of the cell.

Alan maintained broad influence over the cell biology community. He was a senior editor of the *Journal of Cell Biology* for 20 years and became editor-in-chief in 2014. He contributed significantly to setting high standards for research within the cell biology community, putting forward editorials on data presentation and reproducibility. Alan served on the editorial boards of *Cell*, *The EMBO Journal*, *Genes & Development*, *Journal of Cell Science* and *BMC Cell Biology*, and was head of the cell biology faculty for the Faculty of 1000. He participated in numerous grant review committees, including those of the Wellcome Trust on various occasions, and was a member of the HHMI scientific review board since 2008. His seminal scientific contributions were recognised through numerous distinctions: he was elected as a member of EMBO in 1994 and as a Fellow of the Royal Society in 1999, he received the Novartis Medal from the British Biochemical Society, the Louis-Jeantet Prize for Medicine in 2005 and the Gairdner International Award in 2006.

But beyond these accolades, Alan Hall was adored by everybody who knew him. He was known for his humility and is remembered for his generosity. At MSKCC, he invited several other laboratories to join his weekly lab meetings, exerting a supportive influence on the work of Songhai Shi, Michael Overholtzer and Philipp Niethammer. Always checking on junior faculty, or offering advice to students and postdocs, Alan welcomed discussion on any topic, with anyone, at any time. During professional meetings, he was often the wisest, but rarely the loudest in the room. Since his passing, many continue to stop by his office, as if he might still be there, sitting at his desk and facing the door just as he used to, happy to chat about science, or life. Many remember having spoken to him only recently, and now many untold stories are being related: a supervisor with no unkind words; a neighbour and friend, always with a smile and that wonderful sense of humour; a mentor, who once offered his own laboratory's finances to fund the research of another. The stories abound and continue to accumulate. Richard Wong, a surgeon who was invited to attend to Alan's extended lab meetings, commented: "Not many people knew how much Alan has helped me over the years — he never sought any credit for it, and that was his style."

Alan maintained a healthy work-life balance. He loved his family, Italian food and wine, and was a fan of the football team AC Milan. He is survived by his beloved wife, Eileen, and their children, Ali and Graham. Alan and Eileen were excited for the imminent visit of their children, coming over from London, and the joy of being grandparents. With them, we mourn the untimely passing of Alan Hall, a titan of science, and an even better human being.

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