

# OBITUARY

## Tony Pawson 1952–2013

The scientific community has been saddened by the untimely passing of Tony Pawson, a pre-eminent investigator in the signal transduction field over the past three decades. He was born in Maidstone, Kent, UK, in 1952 and went to school at the Winchester College. After reading biochemistry at Clare College, University of Cambridge, he obtained his PhD in molecular virology from Imperial Cancer Research Fund Laboratories under the supervision of Alan E. Smith. In 1976 Tony moved to North America, initially working with Steve Martin at the University of California, Berkeley, USA, on molecular and cellular aspects of cell transformation. These studies fostered in him a longstanding interest in the molecular origins of cellular transformation and cancer progression. They also laid the foundation for his own independent research program that began in the early 1980s at the University of British Columbia in Vancouver, Canada, and moved in 1985 to the Samuel Lunenfeld Research Institute at the Mount Sinai Hospital in Toronto. He remained there for the rest of his life and was instrumental in invigorating Canadian cellular biochemistry through his many discoveries, prudent recruitment and mentoring of junior colleagues. His tireless efforts to promote science in Canada have shaped the region and helped to make Toronto a world-renowned centre for cell signalling research.

Tony's most important discovery was discerning a molecular mechanism of signal transduction that involves the establishment of complexes of signalling molecules that are held together by specific protein–protein interaction domains. Tony unravelled this mechanism by studying the oncogenic tyrosine kinase v-Fps. He found that this enzyme contains structures outside the kinase domain that are necessary for its transforming activity. This finding led to the discovery of the SH2 and SH3 domains that are found in a broad range of signal transduction molecules, including protein kinases, phosphatases and adaptors. Furthermore, Tony showed that the SH2 domain binds tyrosine-phosphorylated residues in proteins, and that, for instance, phospholipase C- $\gamma$  and Ras-GAP use their SH2 domains to bind to specific phosphorylated tyrosine residues in the activated platelet-derived growth factor and epidermal growth factor receptors. He also provided important insights into the structural basis for the selectivity of SH2 binding, which is crucial for specificity in signal transduction.

The SH2 and SH3 domains were the first protein interaction domains shown to be involved in signal transduction; we now know of many more different types of domains mediating specific interactions during signal transduction. Tony Pawson's work also shed light on the important function of adaptor molecules in signalling. These molecules lack enzymatic activity, but are equipped with different types of protein interaction domains that act as bridges between other molecules to organize and facilitate signal transduction. The new concept that Tony formulated — that signal transduction is governed by modular interactions between molecules — represented a paradigm shift in the field. Before this insight, there was no clear idea of how signals pass through the cytoplasm; the view was that signal transduction operated by random diffusion, a scenario that was efficiently disproven by Tony. Importantly, the concept of modular signal transduction, originally formulated for tyrosine kinase receptors, has been found to have general applicability for signal transduction through a number of different types of receptors.

Tony Pawson's elegant combination of genetic, cellular, structural

biological and biochemical techniques has contributed immensely to our understanding of the roles of signalling complexes in the control of cell growth, migration, polarity, axonal guidance and targeted protein degradation. These concepts also greatly influenced the burgeoning field of systems biology. Genome-wide interaction screens from yeast to mammals have uncovered scaffolding and adaptor proteins composed of modular domains that function as interaction hubs that assemble multi-protein signalling complexes. These studies not only underscore the simplicity of the protein–protein interaction model but also emphasize the importance of local modular interactions as a means to mechanistically and spatially control cell-signalling events. Tony's many discoveries and insights provided a molecular understanding that has formed a core of this new biology. They also have vast implications for our understanding of mechanisms involved in the development of cancer and other diseases.

Tony was an eloquent advocate of his findings and enthralled audiences all over the world with his energetic and engaging lectures. His animated renditions, theatrical flair and well-developed sense of humour made him a most popular speaker. His enthusiastic delivery and constant motion was frequently referred to as the 'Pawson Road Show'. Someone fondly suggested that filming a Tony Pawson lecture would not only intellectually inspire the viewer, but could also be used as an exercise video.

Tony's outstanding scientific contributions have been recognized by many prestigious awards, including the Kyoto Prize (2008), the Wolf Prize in Medicine (2005), the Pezcoller-AACR International Award for Cancer Research (1998) and the Gairdner Award (1994). Tony was also a Fellow of the Royal Society of London and the Royal Society of Canada, and an Associate Member of the National Academy of Sciences (US). In 2007, he was invested by Queen Elizabeth II to the Order of the Companions of Honour. Despite all these well-deserved recognitions, Tony remained a humble and unassuming person who was well known for his generosity and kindness. He was also blessed with a loving and supportive family. Maggie, his wife of 36 years, was always by his side until her death from cancer in 2011. Her devotion and encouragement paved the way for Tony's accomplishments. Likewise, his three children, Nick, Catherine and Jeremy, were partners in Tony's success. Tony is also survived by his granddaughter, Millicent, who was born earlier this year.

Tony Pawson was a scientific role model, combining brilliance and creativity with leadership skills and a tremendous ability to motivate people around him. A giant among scientists and an adored colleague has passed away. He will be sorely missed.

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