
Lunenfeld-Tanenbaum Research Institute

Tony Pawson 1952–2013

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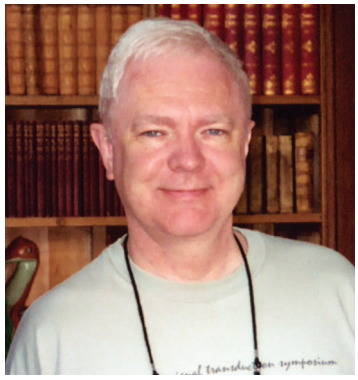
Charisma is an enigmatic characteristic that few possess. Likewise, creativity is an ordained rather than a learned skill. But when combined with natural curiosity, hard work and a measure of good fortune, it paves the way for exceptional scientific discovery. This was exemplified by Tony Pawson, one of the most extraordinarily gifted and celebrated molecular and cellular biologists of our time. Unfortunately, Tony died suddenly in Toronto on 7 August 2013.

Tony was born in Maidstone, Kent, UK in 1952 into an influential English family of eminent sportsmen and actors. He was educated at the Winchester College before reading biochemistry at Claire College, Cambridge. After a successful PhD under the supervision of Alan E. Smith at the Imperial Cancer Research Fund Laboratories (now called the London Research Institute), he moved to the laboratory of G. Steven Martin at the University of California, Berkeley. His postdoctoral experience nurtured a longstanding interest in the molecular mechanisms of cellular transformation and cancer progression. He continued this work when he took up a faculty position in the Department of Microbiology at the University of British Columbia, Vancouver, in 1981. In 1985, Tony was recruited to the Samuel Lunenfeld Research Institute at the Mount Sinai Hospital, Toronto, and was director of the institute from 2002 to 2005. He was also a senior fellow of Massey College at the University of Toronto. Tony was a passionate supporter of colleagues and trainees and an eloquent advocate for Canadian science. He was hugely influential within the international cell-signaling community and attracted many recognized leaders of this field to the University of Toronto and its affiliated research institutes.


Lorene Langeberg

Tony at Kinfauns Castle, Scotland, 2003.

Tony's principal discovery was the Src homology 2 (SH2) domain, a noncatalytic segment of protein that folds to form a phosphotyrosine-recognition motif. This provided a simple and elegant means to recruit SH2 domain–containing proteins to sites of tyrosine phosphorylation. In a seminal paper (Sadowski, I., Stone, J.C. and Pawson, T., *Mol. Cell. Biol.* **6**, 4396–4408, 1986), Pawson and colleagues showed that the SH2 domain modifies kinase function and the transforming activity of Fujinami sarcoma virus. Soon afterwards, they and others showed that many oncogenic tyrosine kinases, scaffolding and adaptor proteins contain SH2 domains. This early work culminated in the structural elucidation of SH2 domains, detailed mutagenic investigation of this common polypeptide fold and the realization that phosphotyrosine signaling proceeds through 'protein-interaction modules' to facilitate the assembly of macromolecular complexes. These findings not only provided the context for the initial discovery of phosphotyrosine by Tony Hunter but also offered a first glimpse of a molecular language that cells use to relay intracellular signals.

Emboldened by his early discoveries, Tony embarked on a systematic analysis of protein-interaction modules. He published a series of influential papers that charted the identification, structure and function of several modular domains. These works were augmented by proteome-wide analysis of interaction networks and the development of genetically modified–mouse models to test the physiological role of modular scaffolding and adaptor proteins. Tony's boundless curiosity also led him into the burgeoning field of bioinformatics. He was a proponent for the use of algorithms to catalog modular protein-interaction domains, and he helped develop a procedure called protein domain profiling, which orders proteins in the entire proteome by hierarchical clustering based on domain composition and linkage. There are now about 90 defined distinct protein-interaction modules. His collective work of over 400 articles illustrates how signaling through protein-interaction modules provides precise spatial and temporal control of the cell.

Not surprisingly, Tony's outstanding scientific contributions were internationally recognized. He was invested by Queen Elizabeth II to the Order of the Companions of Honor and the Order of Canada, elected to the Royal Society London and the Royal Society of Canada and became an Associate Member of the US National Academy of Sciences. He was the recipient of several prestigious prizes including the Canada Gairdner Award, the Heineken Prize for Biochemistry, the Wolf Prize in Medicine and the Kyoto Prize. Tony garnered this recognition while remaining an approachable and unassuming individual who cared deeply for his friends and colleagues.

My personal recollections of this gentle giant of science came from sharing the podium with him at numerous cell-signaling conferences and from our frequent walks in various parts of the world. Tony's inherent theatrical flair and quick wit made him a popular and entertaining speaker who enthralled audiences with animated and engaging lectures. Tony also had an amazingly well-developed sense of humor that often came to the fore during our one-on-one interactions. I fondly recall one spring day in Alberta as we walked across a frozen Lake Louise, marveling at the iconic view of the Canadian Rockies. As we shuffled toward the shore, we inspected magnificent ice sculptures of a moose and a grizzly bear. Tony turned to me and quipped that he was "so proud to live in a country where ice sculptures could be created in October and still be enjoyed the following April."

Tony was also blessed with a loving and affirming family. They were the core of his being and provided him with the support and security to live out his extraordinary life. Maggie, his wife of 36 years, was his continual companion until her untimely death. Her steadying influence paved the way for each of Tony's accomplishments. Likewise, Tony was particularly proud of his three children—Nick, Catherine and Jeremy—each of whom played their part in Tony's success. Son-in-law Tyler Westcott and granddaughter Millicent also survive Tony.

Tony was my friend, my confidant and my most frequent collaborator. His influence on cellular biochemistry was enormous, and his enduring legacy will be the future discoveries of his many trainees and the fond memories that remain with his family, friends and colleagues.

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