Professor Jeffrey C. Watkins FRS

1929 – 2023

Jeff was born in Perth, Australia in 1929 and, from his school days, demonstrated a great enthusiasm for Chemistry. He attended the University of Western Australia, studying Organic Chemistry which was followed by a PhD and then postdoctoral fellowships at Cambridge and Yale.

In the 1950s, very little was known about chemical processes in the nervous system, and the concept of chemical transmission was not universally accepted. The offer of a fellowship to join the Physiological lab of John (Jack) Eccles, in Canberra, set the scene for Jeff's future scientific life. Working with electrophysiologists, David Curtis and John Phillis, they set about identifying potential, hitherto unknown, neurotransmitters. L-glutamate proved to be a potent excitant of most neurones with its actions being mimicked by other acidic amino acids such as aspartate. Because of its seemingly ubiquitous effects, this led to their concluding that glutamate was probably a "non-specific" neuronal excitant. The synthesis of N-methyl-D-aspartate (NMDA) changed this perception as it proved to be a potent excitant, much more so than its L-form, implying that a discrete membrane receptor site was involved.

Continuing his extensive synthetic chemistry work at Babraham and then at Carshalton, Jeff came to the University of Bristol in 1973, and began collaborating with Dick Evans, Tim Biscoe and others. A pivotal discovery was that of potent and selective NMDA receptor antagonists, such as D-2-amino-5-phosphonopentanoate (D-AP5) which were able to block both the excitatory action of glutamate on neurones and of excitatory synaptic transmission. At last, glutamate's important neurotransmitter function was recognised. Discovery of the NMDA receptor was rapidly followed by the realisation of the existence of multiple glutamate receptors due to the actions of two glutamate analogues: the dicarboxylic acid, kainic acid (first isolated in Japan from red algae in the 1950s) and, secondly a new, synthetic amino acid, AMPA (by P. Krogsgaard-Larsen, in Denmark). Thus, the terms kainate and AMPA receptors came into existence. In the 1990s, several labs discovered that glutamate could also interact with a distinct group of G-protein-coupled receptors (so-called metabotropic glutamate receptors) that were linked either to PLC activation or the inhibition of adenylyl cyclase. Once again, Jeff's synthetic chemistry group successfully identified selective agonists and antagonists for these novel receptor subtypes.

Jeff's extraordinary enthusiasm for the elucidation of structure-activity relationships led to the synthesis of a phenomenal array of important glutamate agonists and antagonists. As might be expected, neuroscientists around the world were keen to utilise his compounds to investigate diverse physiological and neuropathological processes, such as long term potentiation and synaptic plasticity, epilepsy, stroke, Parkinson's and Alzheimer's diseases and several psychiatric disorders.

Jeff licensed his potent NMDA receptor antagonist, D-CPPene, to Sandoz who took it into phase 3 clinical trials for the treatment of stroke. Although the trial was ultimately unsuccessful, the principle that NMDA receptor antagonists are neuroprotective served as an inspiration for the development of the uncompetitive antagonist memantine, which is in the clinic for treatment of cognitive impairment in Alzheimer's disease.

Those of us who were fortunate to work or collaborate with Jeff knew what a kind, modest and generous person he was. He was always fascinated by the scientific research of other investigators, even if it was way outside the work of his own laboratory. He would give freely of his precious new compounds to facilitate the research of others.

During the 1980s, requests for Jeff's "standard" compounds had become so extensive that he founded the very successful neurochemicals company, Tocris Neuramin. In 1994 Tocris Cookson was formed, following the merger with Cookson Chemicals, founded by Prof Richard Cookson of Southampton University. In 2002, the company was awarded The Queen's Award for Enterprise in International Trade. The company has gone from strength to strength in the succeeding years and today the Tocris catalogue lists over 4000 chemicals. In 2016 the company moved to a purpose-built facility in Bristol, appropriately named The Watkins Building.

Jeff's enormous achievements resulted in his being awarded numerous prizes and international awards and fellowships of the Royal Society and of the British Pharmacological Society.

Jeff started his career in neurochemistry with a mission to discover how the myriad of chemicals in the brain might be involved in neurotransmission. He certainly succeeded on a grand scale, opening the doors to much of what we know today about excitatory transmission in the CNS.

Peter Roberts & David Jane