



Introduction to the Special Issue in Honor of Graham L Collingridge

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It is my greatest pleasure to serve as the guest editor of the special issue of *Neurochemical Research* dedicated to Professor Graham L. Collingridge. While Graham's immense contributions to neuroscience is wide ranging, he is probably best known for the seminal discovery that long-term potentiation (LTP) in area CA1 of the hippocampus is mediated by the *N*-methyl-D-aspartate (NMDA) subtype of ionotropic glutamate receptors. LTP is a form of synaptic plasticity, which underlies learning and memory. This pioneering research heralded the beginning of studies in the neuropharmacology and cellular mechanisms of synaptic

plasticity, a field in which Graham is internationally recognized as a leader. The papers in this special issue of *Neurochemical Research* were contributed by Graham's long-standing friends and collaborators. The topics of the original studies and review articles are relevant to Graham's research interests: mechanisms of synaptic plasticity in health and disease, in particular, understanding synaptic plasticity in molecular terms and how pathological alterations in these processes may lead to major brain disorders, such as Alzheimer's disease and epilepsy.

Graham was educated at George Spicer Primary School and Enfield Grammar School in Enfield, North London, England. He studied pharmacology at the University of Bristol. As a PhD student, Graham studied the effect of tetanus toxin on GABA-mediated synaptic inhibition in the rat substantia nigra at the School of Pharmacy, University College London. He was a postdoctoral fellow in the Department of Physiology at the University of British Columbia

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(Vancouver, Canada) and in the Department of Physiology and Pharmacology at the University of New South Wales (Sydney, Australia). In 1983 he was appointed to a lectureship at the Department of Pharmacology at the University of Bristol. From 1990 until 1994 he was the Departmental Chair in Pharmacology at the University of Birmingham (UK). In 1994 he returned to the University of Bristol as Professor of Neuroscience in Anatomy. There he served as Departmental Chair of Anatomy (1997–1999) and then as the Director of the MRC Centre for Synaptic Plasticity (1999–2012). Graham has held visiting Professorships at the University of British Columbia and at Seoul National University. Since 2015 he is the Ernest B. and Leonard B. Smith Professor and Chair of the Department of Physiology at the University of Toronto. He is also a Senior Investigator at the Lunenfeld-Tanenbaum Research Institute, Mount Sinai Hospital in Toronto. Graham maintained his collaborative links with the School of Physiology, Pharmacology and Neuroscience at the University of Bristol, UK.

Graham's career was fundamentally defined by two major discoveries. The discovery of LTP [1] and the identification of L-glutamate receptor subtypes, such as NMDA receptors, using selective agonists (e.g. NMDA, [9]) and antagonists (e.g. D-(-)-2-Amino-5-phosphonopentanoic acid (D-AP5), [5]). The development of new pharmacological tools enabled him to identify a role for the NMDA receptor in the process of LTP. As a postdoc in Vancouver, Graham observed that when he blocked the activity of the NMDA receptor with an antagonist such as D-AP5, it prevented the induction of LTP, suggesting that this was the trigger mechanism for this process [3]. His work has revealed multiple aspects of NMDA receptor function and uncovered unexpected complexity in the mechanisms of LTP [8]. Graham's early work is reviewed in this issue by his collaborators [6]. His subsequent studies dissected regulatory mechanisms and intracellular signalling pathways that are relevant to learning, memory and neurodegeneration [4]. One fundamental question was how α -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors are altered at synapses following LTP induction. The notion that these receptors are rapidly moved into and out of synaptic membranes had profound implications for our understanding of the mechanisms of LTP and long-term depression [2]. More recently, Graham and his collaborators showed that calcium-permeable AMPA receptors can also trigger synaptic plasticity at hippocampal CA1 synapses [7].

Graham's contributions to neuroscience is recognized by numerous prestigious awards and fellowships. For example, the Sharpey-Shafer Prize (The Physiological Society 1992), Gaddam Memorial Prize (The Pharmacological Society 2003), The Santiago Grisolia Prize (2008) and The Feldberg Prize (2013). He is also a co-winner of The Brain Prize 2016 with Timothy Bliss and Richard Morris, which was awarded

for their “*ground-breaking research on the cellular and molecular basis of LTP and the demonstration that this form of synaptic plasticity underpins spatial memory and learning*”. In 1997 he was elected as Founder Fellow of the European DANA Alliance for the Brain, which coordinates the annual Brain Awareness Week for an audience that includes the general public. In 1998 he was elected as Founder Fellow of the Academy of Medical Sciences (UK), which aims to advance biomedical and health research and its translation into benefits for society. In 2001 he was elected as Fellow of The Royal Society. The Fellowship is made up of the most eminent scientists, engineers and technologists from the UK and the Commonwealth.

Graham has an international reputation of research excellence and leadership in the field of synaptic plasticity, neuropharmacology and neurochemistry. He served on the Editorial Boards of several neuroscience journals and he was the Editor-in-Chief of Neuropharmacology from 1993 until 2010. From 2007 until 2009 he served as President of the British Neuroscience Association. In addition to serving the wider neuroscience community, Graham has an impressive track record in training and mentoring students and young scientists and helping them to succeed in their careers. Many of his previous student and postdocs pursue highly successful careers in research, higher education and industry. Several of them contributed to this special issue, and I am very grateful for their input.

Together with all the other contributors to this special issue in your honor, I wish you all the best for the future. We look forward with great anticipation to the next scientific discovery that you will make in the coming years.

Elek Molnár
Guest Editor

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