Australian National University

Ligand-biased signaling by the calcium-sensing receptor. How a gut amino acid sensor can also mediate feedback control of calcium metabolism

Thursday 14 November 2013 1 – 2pm

Arthur Conigrave Professor, School of Molecular Bioscience, University of Sydney

Slatyer seminar room R.N. Robertson Building (Bldg. 46), Linnaeus Way, ANU

Taste receptors belonging to G-protein coupled receptor Class C support the sensing of multiple nutrients. The calcium-sensing receptor is a particularly interesting example. It mediates amino acid sensing in the gut as well as $Ca2^{+}$o-dependent feedback control of whole body calcium metabolism. Recent work suggests that the receptor adopts distinct ligand-dependent conformations in favour of signaling by distinct pathways. The underlying mechanisms and the physiological significance of a receptor that lies at the cross-roads between macro- and micro-nutrient metabolism will be discussed.

Prof Arthur Conigrave MD PhD FRACP, Deputy Dean, Faculty of Medicine, University of Sydney is an Endocrinologist and Molecular Pharmacologist (School of Molecular Bioscience and Department of Endocrinology, Royal Prince Alfred Hospital). He demonstrated that the calcium-sensing receptor is a sensor of L-amino acids (PNAS 2000) and went on to define a broad-spectrum L-amino acid-sensing subgroup of the Class C GPCRs (TiPS 2000, TEM 2006; Pharm Therap 2010). He is interested in the molecular basis of nutrient sensing including its roles in protein nutrition, the interface of between protein nutrition and mineral metabolism (Ann. Rev Nutr 2008), how hormone-secreting cells convert nutrient signals into functional outcomes (JBC. 2004; JCEM 2009), and identifying novel modulators (JBC 2011). His work on the CaSR has contributed to the recognition that, arising from its pluripotency of sensing and signaling (Endocrin 2012; AJP 2013), it not only coordinates macro- and micro-nutrient metabolism but also determines cell fate in the context of development, tissue maintenance (JBC 2011) and cancer. He is the author of over 100 original and review articles and chapters, and is currently Marie Curie Visiting Scientist to the EU Research Consortium entitled 'The multi-faceted calcium-sensing receptor'.

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