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School of Medical Sciences Seminar Series

Wednesday the 10th of November 2021

3:00 – 4:00pm on Microsoft Teams

We ask all attendees to mute and turn off their video

Associate Professor Wendy Imlach

Monash Biomedicine Discovery Institute & Department of Physiology, Monash University, Melbourne Australia.

'Targeting spinal adenosine signalling to treat neuropathic pain.'

Bio: Associate Professor Wendy Imlach is head of the Pain Mechanisms lab in the Department of Physiology at Monash University and the Deputy Head of the Neuroscience Program in the Monash Biomedicine Discovery Institute. Her research is focused on neural circuits in the spinal cord that are activated in chronic pain, in an effort to identify new therapeutic targets. She obtained her PhD in Pharmacology in New Zealand from the University of Otago and held postdoctoral positions at Columbia University in New York, and in Australia at the University of Queensland and University of Sydney. Wendy has a background in neuropharmacology, synaptic physiology and neural circuitry and her laboratory investigates spinal dorsal horn circuitry and nociceptive signalling.

Abstract: Neuropathic pain, one of the most intense types of chronic pain, is caused by malfunction of the nervous system and involves persistent changes in pain signalling. We have shown that there is an increase in endogenous adenosine in the spinal cord in chronic pain states, which is accompanied by increased sensitivity of adenosine A1 receptors in the spinal dorsal horn. These adaptations produce anti-nociceptive activity that can be further enhanced by positive allosteric modulation of the adenosine A1 receptor. In this talk, I will describe our work investigating the effects of allosteric modulation of the adenosine receptor on spinal circuit activity in pain states. We have used patch-clamp electrophysiology to study changes in synaptic input and intrinsic activity of spinal nociceptive neurons in both primate and rodent to understand the analgesic mechanism of A1R allosteric modulators at a circuit level. These findings are supported by our behavioural data using preclinical pain models that show a decrease in neuropathic pain with minimal side effects, and an increased level of effectiveness as the pain signals in the spinal cord get stronger. This work was recently published in Nature as part of a large multidisciplinary study which includes the high-resolution structure of the A1 receptor bound to both adenosine and an analgesic allosteric modulator, providing the first atomic level snapshot of where these drugs bind. Our findings provide proof of concept that disease- and tissue-specific selectivity can be achieved through exploiting the cooperativity between an allosteric GPCR modulator and an endogenous agonist.

School of Medical Science Seminar Co-convenors

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