セミナー開催のお知らせ

日時：2019 年 1 月 23 日（水），13:00-14:30

場所：自然科学本館 104 講義室

題目：**CGRP and its receptors as novel targets for migraine**

講師：Prof. Debbie Lucy Hay

所属：School of Biological Sciences, The University of Auckland, Auckland 1142, New Zealand, The Maurice Wilkins Centre for Molecular Biodiscovery, The University of Auckland, Auckland 1142, New Zealand

Email: dl.hay@auckland.ac.nz

要旨：

Headache disorders are a major cause of disability. Of these, migraine makes the biggest impact. This condition is characterised by severe head pain, often accompanied by visual and gastric disturbances. A sensory neuropeptide that is found in the pain-sensing nerves of the face and head – calcitonin gene-related peptide (CGRP) – is heavily implicated in contributing to migraine pathophysiology. In 2018, three new drugs (monoclonal antibodies) have been approved in the USA and Europe that reduce the activity of CGRP, and thus prevent migraine. This seminar will explain the importance of CGRP and outline the current understanding of CGRP receptors. It is commonly thought that there is only one important receptor but discoveries in the Hay lab have shown that a second receptor, known as AMY_1, is potently activated by CGRP can be found in the sensory trigeminal ganglia (Figure). CGRP receptors are unusual for G protein-coupled receptors because they require an accessory protein, receptor activity-modifying protein 1 (RAMP1), to function. This seminar will describe the CGRP receptors and the role of RAMPs in CGRP biology. This will include discussion of the recent cryo-EM structure of the canonical CGRP receptor[1]. The current status of the pharmacology of CGRP receptors will be discussed, including that of small molecule CGRP receptor antagonists that are currently in phase 3 clinical trials. The approval of the new drugs against the CGRP system is a landmark for the field but there are likely to be other opportunities to exploit CGRP biology.

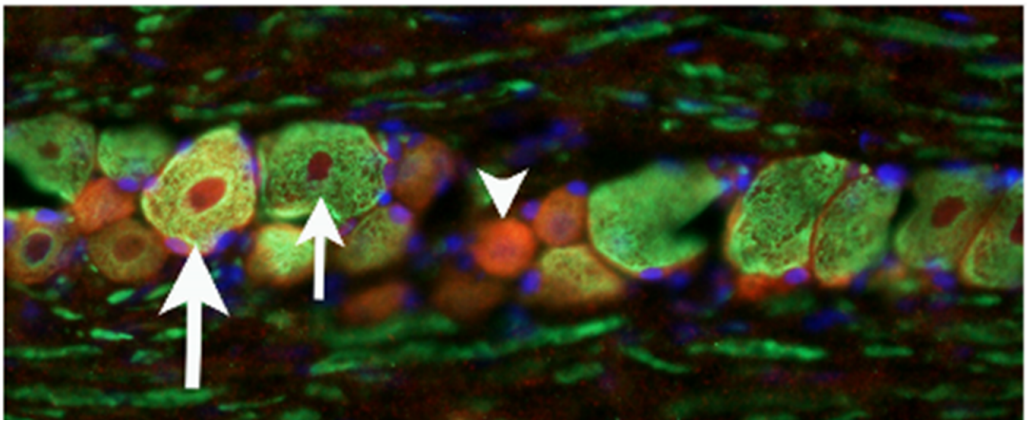

Figure. Immunofluorescence image of rat trigeminal ganglia showing co-expression of RAMP1 with the calcitonin receptor, forming the AMY_1 receptor, in a neuronal cell body (yellow, large arrow). Nuclei are blue. Image adapted from [2].

[1]Liang *et al*., Cryo-EM structure of the active, Gs-protein complexed, human CGRP receptor. *Nature*. 561(7724):492-497, 2018.

[2]Walker *et al*., A second trigeminal CGRP receptor: function and expression of the AMY_1 receptor. *Ann Clin Transl Neurol.* 2(6):595-608, 2015.

問い合わせ先：**環日本海域環境研究センター臨海実験施設　関口俊男**
Mail: t-sekiguchi@se.kanazawa-u.ac.jp, Tel: 0768-74-1151