Investigating the role of Gβγ subunits in Kv7 dependent relaxations

Jennifer B Stott and Iain A Greenwood

Vascular Research Group, Institute of Molecular and Clinical Sciences, St George's University of London, London, UK

Questions: Kv7 channels are important regulators of vascular tone. Recently, native vascular Kv7 channels were shown to be regulated by Gβγ subunits. Here, we aim to establish the functional implications of G protein βγ subunits in Kv7 dependent relaxations of the rat vasculature

Methods: Relaxations to isoproterenol and calcitonin gene related peptide (CGRP) of the rat mesenteric and renal arteries were assessed by myography. Localisation of Kv7.4 and Gβ was studied using proximity ligation assay.

Results: Relaxations to isoproterenol in MA and RA, and CGRP in MA are Kv7 dependent. Relaxations to isoproterenol in rat renal, but not mesenteric arteries, were impaired in the presence of Gβγ inhibitors (gallein, M119K and Grk2i). Relaxations to CGRP in mesenteric arteries were sensitive to Gβγ inhibition. In MA myocytes treated with isoproterenol or CGRP there was an increase in Kv7.4-Gβ PLA puncta. Treatment of cells with gallein inhibited this increase, but did not affect basal puncta levels. In RA myocytes there is a higher level of basal Kv7.4- Gβ, but this does not increase with isoproterenol treatment. Gallein treatment decreases basal puncta levels in the RA.

Conclusions: Gβγ subunits are required for CGRP relaxations in MA and isoproterenol relaxations in RA, but not MA. The Kv7.4-Gβ interaction is implicated in mediating some vasorelaxant signals.

Keywords: Vascular, Kv7, G protein beta gamma