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The role of the GPR55/LPI system in cardiovascular physiology and pathology

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GPR55 is a recently de-orphanised receptor, whose endogenous ligand is the lysophospholipid, lysophosphatidyl inositol (LPI). GPR55 has been implicated to play a role in numerous physiological and pathophysiological processes such as cancer and diabetes, but to date relatively little is known about its involvement in the cardiovascular system. My group has been studying the GPR55/LPI system in cardiovascular physiology and our recently published data has shown that a dysfunctional GPR55/LPI system results in reduced cardiac systolic function and contractile reserve, an effect that may be related to impaired sympathetic nervous activity. More recently we have shown that LPI exacerbates the extent of injury following acute myocardial ischaemia and reperfusion, signalling via the RhoA/ROCK pathway. We have also explored the role of GPR55 in the development of obesity and metabolic syndrome, and the impact of this on cardiovascular function and injury sustained following myocardial ischaemia/reperfusion. In terms of the vasculature, we have also investigated the importance of GPR55 in the setting of atherogenesis, in terms of vascular endothelial function, atheroma development and dyslipidaemia-induced cardiac impairment. In my lecture I will summarise this data and provide evidence for an essential role of the GPR55/LPI system in cardiovascular and metabolic physiology.

Curriculum Vitae

Qualifications:

1981BSc (Hons) Pharmacology,University of Aberdeen, Scotland.

1984 PhD Cardiovascular Pharmacology, University of Strathclyde, Scotland.

FESC (1988), FHEA (2001), FBPharmacolS (2005)

Academic appointments:

1984-1988 Postdoctoral Research Fellow, Department of Physiology & Pharmacology, University of Strathclyde, Glasgow

1988 - 1993 Janssen Foundation Research Lecturer, Department of Physiology and Pharmacology, University of Strathclyde.

1993 - 1994 Lecturer, Department of Physiology & Pharmacology, University of Strathclyde.

1994-2000 Senior Lecturer, Department of Physiology & Pharmacology, University of Strathclyde.

2000-2003 Reader, Department of Physiology & Pharmacology, University of Strathclyde.
2003-2008 Faculty Professor of Cardiovascular Pharmacology, School of Pharmacy, The Robert Gordon University, Aberdeen.

2009-2015 Director, Institute for Health & Welfare Research, Robert Gordon University, Aberdeen

2015-Present Director, Centre for Cardiometabolic Health and Co-Director, Centre for Natural Products in Health, Robert Gordon University

Publications:

Published ~ 80 full original papers in peer reviewed journals, in excess of 200 conference abstracts, 12 invited reviews, 3 book chapters, edited 1 book and published 2 patents.

Selected Recent Publications:

1. Walsh S K, Hepburn C Y, Keown O , Åstrand A , Lindblom A , Ryberg E , Hjorth S , Leslie SJ, Greasley P J& **Wainwright CL.** Pharmacological profiling of the haemodynamic effects of cannabinoid ligands: A combined *in vitro* and *in vivo* approach. *Pharmacol Res Perspect* 2015 Jun;3(3):e00143..

2. Walsh SK, Hector EE, Andreasson AC, Jonsson-Rylander AC, **Wainwright CL**. GPR55 deletion in mice leads to age-related ventricular dysfunction and impaired adrenoceptor-mediated inotropic responses. *PLoS One* 2014; 9: e108999.

3. Curtis MJ, Hancox JC, Farkas A, **Wainwright CL**, Stables CL et al., (2013). The Lambeth Conventions (II): Guidelines for the study of animal and human ventricular and supraventricular arrhythmias. *Pharmacol Ther*. 139 (2):213-248.

4. Markos F, RuaneO'Hora T, **Wainwright** CL, Noble MI (2012). Dependence of smooth muscle tone upon pulsatility in the iliac artery of the anaesthetised pig. *Pflugers Arch*.463(5):679-84..

5. McGrath JC, Drummond GB, McLachlan EM, Kilkenny C, **Wainwright** CL (2010). Guidelines for reporting experiments involving animals: the ARRIVE Guidelines. *Br J Pharmacol*. 160(7):1573-6.

6. Hector, EE, Robins, SP, Mercer, DK, Brittenden, J & **Wainwright**, CL, (2010). Quantitative measurement of mature collagen cross-links in human carotid artery plaques. *Atherosclerosis,* 211(2), pp. 471-474

7. Keown, OP, Winterburn, TJ, **Wainwright**, CL, Macrury, SM, Neilson, I, Barrett, F, *et al.*, (2010). 2-Arachidonyl Glycerol Activates Platelets Via Conversion to Arachidonic Acid and Not by Direct Activation of Cannabinoid Receptors. *Br J Clin Pharmacol,* 70(2), pp. 180-188

8. McDonald, RA, Pyne, S, Pyne, NJ, Grant, A, **Wainwright**, CL & Wadsworth, RM (2010). The sphingosine kinase inhibitor N,N-dimethylsphingosine inhibits neointimal hyperplasia. *Br J Pharmacol*, 159(3), pp. 543-553

9. Walsh, SK, Hepburn, CY, Kane, KA &**Wainwright**, CL (2010). Acute administration of cannabidiol in vivo suppresses ischaemia-induced cardiac arrhythmias and reduces infarct size when given at reperfusion. *Br J Pharmacol*, 160(5), pp. 1234-1242

10. Walsh, SK, Kane, KA & **Wainwright**, CL (2009). Mast cell degranulation--a mechanism for the anti-arrhythmic effect of endothelin-1? *Br J Pharmacol* **157**: 716-23