

Endogenous Mediators: The Double-Edged Swords of the Myocardium



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Short summary:

Endogenous mediators play a crucial role in both pathological and protective mechanisms in ischaemic heart disease. This talk will focus on two endogenous systems, the endothelin (ET-1) system and the lysophosphatidyl (LPI)/GPR55 receptor system, in the setting of cardiovascular disease, highlighting the two-sided roles that they play. In terms of ET-1, I will show evidence that, depending upon which receptor it activates it has either a pro-arrhythmic or anti-arrhythmic effect. In terms of the orphan receptor GPR55 I will explore the duplicitous role that it, and its natural ligand LPI, appears to play in both the response to acute myocardial ischaemia and in cardiometabolic control.

Short Biography:

Professor Wainwright graduated from the University of Aberdeen with a BSc (Hons) in Pharmacology and subsequently the University of Strathclyde with a PhD in Cardiovascular Pharmacology. Cherry spent over 20 years at Strathclyde University as an academic involved in both teaching and research, before moving to the Robert Gordon University in Aberdeen in 2003 as a Research Professor, where she spent 8 years as the Director of the multi-disciplinary Institute for Health & Wellbeing Research (2007-2015) and was subsequently Lead Cardiometabolic Health Research and Co-Director of the Centre for Natural Products in Health. She has held the position of Professor Emeritus since August 2023. Throughout her career Cherry's research has focused on mechanisms underlying the pathophysiology and the identification of novel therapeutic targets of cardiovascular diseases; and one of the main threads has been the evaluation of the role of endogenous biological mediators as both the perpetrators of, and protective substances against, cardiovascular disorders. For the last 20 years her emphasis has been on the role of the endocannabinoid system in cardiac (ischaemia/reperfusion) and vascular (atherosclerosis, restenosis) injury and energy regulation in the cardiovascular system. Cherry has published over 90 full original articles and invited reviews, 6 book chapters and edited a book on myocardial preconditioning. She also has 3 patent applications and has given over 40 invited symposium lectures. She is a Fellow of the British Pharmacological Society and the Higher Education Academy, a member of the IUPHAR Natural Products Section Committee, sits on Scientific Advisory Boards for several organisations and is currently President Elect for the British Pharmacological Society.

Recent Publications:

1. Wainwright CL, Tiexiera M, Adelson, D, Buenz E, Bruno D et al. Future Directions for the Discovery of Natural Product-Derived Immunomodulating Drugs. *Pharmacol Res* 2022 177: 106076.
2. Walsh SK, Lipina C, Ang S-Y, Sato M, Chia L-Y, Kocan M, Hutchinson DS, Summers RJ, Wainwright CL. GPR55 regulates the responsiveness to, but does not dimerise with, α 1A-adrenoceptors. *Biochem Pharmacol* 2021 188:114560. (doi: 10.1016/j.bcp.2021.114560.)
3. Bermano G, Stoyanova S, Hennequart F, Wainwright CL. Seaweed-derived bioactives as potential energy regulators in obesity and type 2 diabetes. *Adv Pharmacol.* 2020 87: 205-256. doi: 10.1016/bs.apha.2019.10.002.

4. Skene K, Walsh SK, Okafor O, Godsman N, Barrows C, Meier P, Gordon MJ, Beattie JH, Wainwright CL. Acute dietary zinc deficiency in rats exacerbates myocardial ischaemia/reperfusion injury through depletion of glutathione. *Br J Nutr.* 2019 121: 961-973. (doi: 10.1017/S0007114519000230).
5. Robertson-Gray OJ, Walsh SK, Ryberg E, Jönsson-Rylander A-C, Lipina C, Wainwright CL. l- α -Lysophosphatidylinositol (LPI) aggravates myocardial ischaemia/reperfusion injury via a GPR55/ROCK-dependent pathway. *Pharmacol Res Perspect* 2019 7: e00487. (doi: 10.1002/prp2.487).
6. Lipina C, Walsh SK, Mitchell SE, Speakman JR, Wainwright CL & Hundal HS. GPR55 deficiency is associated with increased adiposity and impaired insulin signaling in peripheral metabolic tissues. *FASEB Journal* 2019 33:1299-1312. (doi: 10.1096/fj.201800171R).
7. Walsh S K, Hepburn C Y, Keown O , Åstrand A , Lindblom A , Ryberg E , Hjorth S , Leslie SJ, Greasley P J & Wainwright C L. Pharmacological profiling of the haemodynamic effects of cannabinoid ligands: A combined in vitro and in vivo approach. *Pharmacol Res Perspect* 2015 3: e00143.
8. 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.