A novel family of functional cardiac G protein-coupled receptors with potential roles in nutrient sensing and contractility

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G protein-coupled receptors (GPCRs) are seven transmembrane-spanning proteins that mediate cellular and physiological responses – they are critical for cardiovascular function and are targeted by frontline therapies for the treatment of hypertension and heart failure. Nevertheless, these therapies only target a small fraction of the cardiac GPCR repertoire, indicating that there are many opportunities to investigate unappreciated aspects of heart biology. Moreover, the majority of studies have excluded the large families of odorant and taste receptors, despite the fact that these account for more than half of the human GPCR superfamily.

We have previously elucidated the expression of a subset of odorant and taste receptors in rodent hearts, some of which were up-regulated in cellular and *in vivo* models of starvation, indicating potential roles in nutrient sensing. We have also demonstrated profound bitter ligand-induced and G protein–dependent effects on cardiac contractility in mouse hearts (Foster *et al.*, 2014). These taste receptors are also expressed in human hearts, where some (*e.g.*, TAS2R14) are of comparable abundance to the β1-adrenoceptor. To extend these findings, we have accessed a large collection of human heart samples from the Sydney Heart Bank, enabling us to investigate the taste receptor expression profile in healthy and diseased failing hearts (of various aetiologies and ages).

Our data suggest that a similar repertoire of taste receptors are expressed in healthy and failing hearts, whereas there are interesting patterns of taste receptor regulation in the heart with age. In our preliminary observations in functional experiments using explanted human right atrial tissue, we have observed profound negative inotropic effects of bitter ligands that specifically activate TAS2R14. Taken together, these data foreshadow novel roles in heart for a previously unappreciated family of cardiac GPCRs.

Foster SR, Blank K, See Hoe LE, Behrens M, Meyerhof W, Peart JN, Thomas WG. (2014) Bitter taste receptor agonists elicit G-protein-dependent negative inotropy in the murine heart. *FASEB Journal* **28**: 4497-4508.