Cardiac adventures in autophagy

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Autophagy is a ubiquitous cellular catabolic process responsive to energy stress status. Research over the last decade has revealed that cardiomyocyte autophagy is a prominent homeostatic pathway, important in adaptation to altered myocardial metabolic demand. The cellular machinery of autophagy involves targeted direction of macromolecules and organelles for lysosomal degradation. Autophagy activation has been identified as cardio-protective in some settings (*i.e.* ischemia and ischemic preconditioning). In other situations chronically elevated levels of autophagy have been linked with cardiopathology (*i.e.* sustained pressure overload and failure).

The Cardiac Phenomics Laboratory at The University of Melbourne has significantly advanced understanding of the mechanisms and modulators of autophagy in the cardiac setting – characterizing autophagic perturbations in several disease states. We have demonstrated that myocardial autophagic excess in early development predisposes the heart for later adult hypertrophic pathology. Our work has shown that autophagy is regulated by G-protein coupled receptor signaling processes, and may be modulated by reciprocal receptor actions of GPCR-ligands (*i.e.* angiotensin activation of AT1 and AT2 receptor subtypes). In diabetic cardiomyopathy our investigations have revealed the operation of a glycogen-specific autophagic process. In glycophagy, selective adaptor and scaffolding proteins are involved, and these are different to the homologue proteins important for protein macromolecular breakdown (‘macrophagy’). Ongoing work is directed towards identifying intervention strategies of potential benefit in remediating dysfunctional autophagic states associated with a range of cardiopathologies.