Autophagy literally means ‘self-eating’ and is generally defined as a lysosome-dependent mechanism of intracellular degradation used for cytoplasmic turnover. The word ‘autophagy’ was coined in 1963 by Christian de Duve, the discoverer of the lysosome, for which he was the joint recipient of the 1972 Nobel Prize in Physiology and Medicine.

Surprisingly, in each of the following 30 years, only a handful of papers on autophagy were published. However, the last ten years has witnessed an enormous expansion in our knowledge of the molecular aspects of autophagy; in 2010, over 1800 publications appeared with autophagy in the title or abstract. The impetus for this can be traced back to the identification of AuTophaGy (ATG) genes in yeast. The ATG genes provided the much-needed tools to investigate both the molecular mechanism and the various roles that autophagy plays in the cell. To date, 34 yeast ATG genes have been identified, many of which have known orthologues in other eukaryotes.

Autophagy is conserved throughout eukaryotes and plays a fundamental role in defense against metabolic stress, recycling cellular components to aid survival. In higher eukaryotes, autophagy plays a role in development, defense against intracellular pathogenic bacteria and viruses, lifespan, and tumour suppression. In addition, it is essential for eliminating large structures such as organelles that are too large for degradation by the proteasome. The field of autophagy research is continually expanding as it becomes implicated in other cellular processes. Understanding the regulation and molecular mechanisms in the many scenarios represents an exciting but daunting task.

Three distinct categories of autophagy have been described: microautophagy, chaperone-mediated autophagy and macroautophagy. Macroautophagy is most studied and best understood, and most people use this word synonymously with autophagy. The key steps of (macro)autophagy are summarised on the cover illustration. After an initiating signal, proteins encoded by ATG genes contribute to the formation of a double-membrane phagophore, which expands to form a vesicle or autophagosome that sequesters the cargo for degradation. Fusion of the autophagosome with a lysosome delivers the cargo in the hydrolytic lumen of the autophagolysosome. Degradation products are then transported into the cytoplasm.

This Showcase on Research features five articles, each from different laboratories focussing on different aspects of autophagy. In addition to being a route for the bulk turnover of cellular contents, a picture is emerging that shows autophagy to be a particularly ‘fussy eater’ that can select specific cargo for degradation. Accordingly, there has been a proliferation of ‘gastronomic’ terms reflecting this selectivity, including nucleophagy (nucleus), ribophagy (ribosome), ERphagy (endoplasmic reticulum), xenophagy (intracellular pathogens) and mitophagy (mitochondrion). It is vital that cells maintain a healthy population of mitochondria, and Alexander May and Mark Prescott look at what we know of how mitochondria are recognised and selected for degradation during mitophagy. This article also highlights the ongoing importance of model organisms such as yeast to autophagy research.

In addition to the protective role of autophagy during nutrient stress, it also impacts on immune function at several levels. Justine Mintern and Jose Villadangos examine the role of autophagy in both innate and adaptive immunity, and highlight links with inflammatory diseases such as Crohn’s disease and autophagy. Tanya D’Cruze and Rod Devenish focus on the theme of autophagy and the innate immune response, providing an excellent overview of how autophagy defends against microbial cellular invaders. In particular, they address how bacterial pathogens interact with autophagic processes, and in doing so, highlight the increasing number of bacterial pathogens that employ a range of countermeasures to avoid elimination and manipulate autophagy for their own benefit. In the fourth article, Pu Xia contrasts the well-established role of autophagy as a pro-survival mechanism with a role for autophagy as a form of programmed Type II cell death. In the final article, Markus Bach and Georg Ramn return to the role of autophagy in metabolic control, and address the existence of other regulatory pathways in addition to the relatively well-established mTOR pathway.

Autophagy is a relatively young, dynamic, continually expanding and exciting field of research with many avenues to be explored. The five articles presented here serve to highlight just some of the research on autophagy undertaken in Australia. The contributing authors have indicated the need for a forum, possibly in the form of a workshop or symposium, to further promote and facilitate research in this field. To be informed of upcoming events, please register your interest by emailing autophagy@monash.edu.

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In the next issue...
In December, the Special Technical Feature will be on Tissue Engineering – Guest Editor: Zee Upton

Australian Biochemist – Editor Rebecca Lew, Editorial Officer Liana Friedman
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Cover Illustration
Macroautophagy is the best understood category of autophagy. The sequential steps of the process are driven by products of the AuTophaGy (ATG) genes, many of which are required for the formation of the double-membrane autophagosome that sequesters the cargo. Fusion of the autophagosome with the lysosome (mammals) or vacuole (yeast) results in degradation of the cargo and transport of the products into the cytoplasm for recycling. Macroautophagy can sequester specific cargoes (e.g., mitochondria) for degradation, the molecular mechanism(s) of which is the focus of much research attention.
Image courtesy of Alexander May, Department of Biochemistry and Molecular Biology, Monash University.