

# The Biochemical Society

*Presents:*

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### **Research Summary**

Autophagy (from the Greek self-eating) is a cellular mechanism which generates nutrients for the cell, primarily during times of starvation. Autophagy is also used to eliminate cell material that becomes damaged, leading to a periodic clean-up of the cell interior. Although it is a response by single cells, it is also very important for the health of an organism.

When autophagy is suppressed cells exhibit signs of oxidative damage because their dysfunctional mitochondria cannot be removed and continue to produce reactive oxygen species. Similarly, suppression of autophagy causes the build-up of mutant proteins that cause neurodegenerative disorders.

Autophagy is also critical for the neonatal period: animals which lack autophagy die soon after birth because they cannot generate nutrients during that time. Finally, autophagy is critical for the extension of lifespan in all organisms studied, and is therefore a significant factor that affects healthy ageing. The pathway of autophagy starts when a novel double membrane vesicle called an autophagosome is formed in the cell interior.

We have shown that one of the signals for formation of autophagosomes is the synthesis of a lipid called PI3P which leads to formation of omegasomes. These are membrane extensions of the endoplasmic reticulum, from which some autophagosomes emerge. We are studying exactly how this happens, both in terms of signals and of how the intermediate structures eventually lead to an autophagosome.

## Latest Publications

Assembly of early machinery for autophagy induction: novel insights from high resolution microscopy Oncotarget. 2016 Dec 27;7(52):85678-85679

Alpha-synuclein fibrils recruit TBK1 and OPTN to lysosomal damage sites and induce autophagy in microglial cells . J Cell Sci. 2018 Nov 7

Autophagy, Inflammation, and Metabolism (AIM) Center of Biomedical Research Excellence: supporting the next generation of autophagy researchers and fostering international collaborations Autophagy. 2018;14(6):925-929

Correlative Live Cell and Super Resolution Imaging of Autophagosome Formation. Methods Enzymol. 2017;587:1-20

Live cell imaging of early autophagy events: omegasomes and beyond. E Karanasios, E Stapleton, SA Walker, M Manifava, NT Ktistakis. Journal of visualized experiments : JoVE, , 77, , 2013. PMID: 23929131. DOI: 10.3791/50484

How phosphoinositide 3-phosphate controls growth downstream of amino acids and autophagy downstream of amino acid withdrawal. NT Ktistakis, M Manifava, P Schoenfelder, S Rotondo. Biochemical Society transactions, 40, 1, 37-43, 2012. PMID: 22260663. DOI: 10.1042/BST20110684