Autophagy in the hematopoietic system and development of novel autophagy detection assay

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My lab is interested in the role of autophagy in the hematopoietic system. Autophagy is responsible for degradation of cellular proteins and organelles via the lysosomal degradation pathway. The induction or suppression of autophagy has been linked to diverse physiological and pathophysiological conditions such as nutrient starvation, stress, circadian rhythm maintenance, exercising, hypoxia, cancer, neurodegeneration, cardiac myopathies, infections, inflammation and ageing. Taking advantage of our extensive experience of *in vivo* models, we deleted a core autophagy gene in mice in the haematopoietic system only. We found that adult mice develop lethal anaemia with an arrested red blood cell development. Immature red blood cells are prone to caspase 3- dependent cell death. Cell death is caused by an inability to remove mitochondria during red blood cell development leading to accumulation of reactive oxygen species (ROS), autophagy being essential in this step. (1). Other hematopoietic lineages were also affected by the loss of autophagy, in particular the hematopoietic stem cells. Absence of autophagy led to accumulation of damaged mitochondria and ROS followed by DNA mutations and development of leukemia (2).

We are now investigating whether autophagy plays a role in human leukemia. we have therefore developed a novel assay using an imaging flow cytometer (Image stream), allowing the detection of autophagy in primary cells. This assay detects autophagy in cells derived from blood and or digested tissue from patients with diverse diseases such as cancer, neurodegeneration immunodeficiency and mitochondrial disease.

References:

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