Autophagy is Involved in Lipid Droplet Breakdown in Serum-Starved Breast Cancer Cells

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Š. Koren[I], E. Jarc Jovičić[I,II], M. Jusović[I,II], P. Starič[I], T. Petan[I]

[I]Jozef Stefan Institute, Department of Molecular and Biomedical Sciences, Ljubljana, Slovenia, [II]Jozef Stefan International Postgraduate School, Ljubljana, Slovenia

Lipid droplets (LDs) are dynamic fat storage organelles present in most eukaryotic cells and involved in the regulation of lipid metabolism, cell signaling and protein trafficking. LDs accumulate in cells deprived of oxygen and nutrients, indicating their involvement in the cellular stress response. Recent studies have shown that LDs are engaged in a complex relationship with autophagy, the major cellular recycling and stress response pathway. Autophagy may participate in both LD biogenesis and breakdown, whereas LDs may provide essential lipids for the initiation of autophagy. It is not yet clear how this complex interplay is regulated and which molecular pathways are responsible for the execution of the multiple possible outcomes. These questions are particularly important in cancer cells, which are often exposed to nutrient and oxygen fluctuations and use both autophagy and LDs for protection against metabolic stress. In this work, we aim to determine if and how autophagy and LDs cooperate in the protection of breast cancer cells against starvation. We found that LD biogenesis is upregulated during severe amino acid deprivation in Hanks' balanced salt solution, whereas milder starvation in the absence of serum induces LD breakdown. The latter was dependent on cytosolic lipolysis mediated by adipose triglyceride lipase (ATGL). Intriguingly, autophagy was active during both severe and mild starvation. Using live-cell confocal imaging we show that autophagosomal and lysosomal structures colocalize with LDs during mild, but not during severe starvation, suggesting the involvement of "lipophagy", an LD-selective form of autophagy, in starvation-induced breakdown of LDs. In accordance, inhibition of autophagic flux with bafilomycin A1 or chloroquine further elevated the colocalization between LDs and autophagosomes. These results suggest that autophagy is active during mild starvation and is involved in the breakdown of LDs in aggressive breast cancer cells.