MTOR-independent autophagy induced by interrupted endoplasmic reticulum-mitochondrial Ca2+ communication: a dead end in cancer cells

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 The interruption of endoplasmic reticulum (ER)-mitochondrial Ca2+ communication induces a bioenergetic crisis characterized by an increase of MTOR-independent AMPK-dependent macroautophagic/autophagic flux, which is not sufficient to reestablish the metabolic and energetic homeostasis in cancer cells. Here, we propose that upon ER-mitochondrial Ca2+ transfer inhibition, AMPK present at the mitochondria-associated membranes (MAMs) activate localized autophagy via BECN1 (beclin 1). This local response could prevent the proper interorganelle communication that would allow the autophagy-derived metabolites to reach the necessary anabolic pathways to maintain mitochondrial function and cellular homeostasis. Abbreviations: 3MA: 3-methyladenine; ADP: adenosine diphosphate; AMP: adenosine monophosphate; ATG13: autophagy related 13; ATG14: autophagy related 14; ATP: adenosine triphosphate; BECN1: beclin 1; Ca2+: calcium; DNA: