

AUTOPHAGOSOME BIOGENESIS IN IRRADIATED COLON CANCER CELLS INVOLVES ERK 1/2, SRC AND PI3K

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Introduction: Autophagy can be induced by amino acid privation, hormone and drug treatment and radiation. In cancer, autophagosome biogenesis has been associated with radio-resistance, invasiveness and multidrug resistance.

Objective: To analyze the biogenesis of autophagosomes induced by ionizing irradiation in a highly invasive cell line of human colon adenocarcinoma, HCT-116 and cell signaling pathways involved.

Results: Cells were irradiated with 8.45 Gy and autophagosome formation monitored. We observed no difference at levels of death by apoptotic between irradiated and control cells, as analyzed by flow cytometry. Also, as seen by electron microscopy, irradiated cells did not display characteristic morphological related to apoptosis. Autophagosomes were characterized by electron microscopy based on their inner content and by its acid nature using the acridine orange staining and Bafilomycin A1, a specific inhibitor of proton vacuolar pump. The biogenesis of autophagosomes was monitored using BSA-Au, a well-known marker of endocytic and autophagic pathways. Furthermore, we demonstrated that Erk 1/2, Src and PI3K are involved in autophagosome biogenesis as observed by immunoblotting and by the use of specific inhibitors of these cell signaling pathways.

Conclusion: Our results demonstrated that irradiation induced autophagosomes formation in HCT-116 cells and that these process is mediated by Erk 1/2, Src and PI3K.

Keywords: autophagy; cell signaling; colon cancer; ionizing radiation.

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