

Endoplasmic reticulum stress is activated after epibrassinolide treatment leading autophagy in wild type and Atg5^{-/-} mouse embryonic fibroblasts: a survival mechanism in non-malignant cells.

P.4.3.B-008

K. Adacan¹, P. Obakan Yerlikaya¹, E. Damla Arisan¹, A. Coker Gurkan¹, N. Palavan Unsal¹

¹ISTANBUL KULTUR UNIVERSITY, Istanbul, Turkey

Autophagy is a process of cellular self-degradation during which macromolecules, damaged/aged organelles and proteins are delivered to the lysosome by engulfment within double-membrane vesicles. The accumulation of un/misfolded proteins in the ER can activate ER stress leading unfolded protein response (UPR) resulting autophagy. Beclin-1, LC3 and Autophagy Related Genes (Atg) play key roles in formation of autophagosome membrane, which are triggered by Ulk-1 signaling through AMPK (AMP-activated protein kinase). Conversely, autophagy is inhibited by the mammalian target of rapamycin (mTOR), a central cell-growth regulator that integrates growth factor and nutrient signals.

Epibrassinolide (EBR) is a member of brassinostereoids plant hormones with a structural similarity to mammalian steroids. Our previous work demonstrated that EBR treatment caused ER stress and UPR which resulted in caspase-dependent apoptosis in SW480, DLD-1, HT-29 and HCT116 colon carcinoma cell lines.

Here, we demonstrate that EBR treatment activates UPR by inducing ER stress-related proteins in wild type (wt) MEF (mouse embryonic fibroblast) cells. In contrary to our previous results in malignant cells, MEF cells do not undergo apoptosis after EBR treatment in stead autophagy is activated causing cell survival. We used Atg5^{-/-} MEF cells to understand the correlation between ER stress and autophagy. Surprisingly, we observed a significant downregulation of p62/SQSTM1 protein, which is known as one of the autophagy marker, in Atg5^{-/-} MEF cells. ER stress was also triggered in these cells. Therefore, we conclude that autophagy is a key mechanism to promote cell survival after EBR treatment against ER stress in both wt and Atg5^{-/-} MEF cells. These findings suggested that EBR as an ER stress inducer, is able to activate autophagy in order to promote cell survival in non-malignant cells.