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Epibrassinolide induced apoptosis via endoplasmic reticulum stress regardless of p53 expression in prostate cancer cells

Pinar Obakan, Elif Damla Arisan, Ajda Coker-Gurkan and Narcin Palavan-Unsal
Istanbul Kultur University, Turkey

Epibrassinolide (EBR) is a member of brassinosteroids a class of plant polyhydroxysteroids, with well-known growth-promoting roles. EBR induces apoptosis in prostate cancer cells both LNCaP expressing functional androgen receptor (AR+) or nonexpressing (AR-) DU146 or PC3 cells. However, the mechanism by which EBR exerts its effects is poorly understood. Our previous SILAC (stable isotope labeling amino acids in cell culture) data suggested that EBR activates endoplasmic reticulum (ER) stress via CHOP translocation to the nucleus. ER stress is induced by cytokines, ischemic injury, and chemicals causing unfolded protein response (UPR) directing cell to apoptosis via different stress sensors such as IRE1 α , ATF4 and PERK. We demonstrated that EBR treatment altered ER stress biomarkers and activated caspases in both AR+ or AR- prostate cancer cells. We also confirmed these results by co-treatment of EBR with rapamycin, a translation inhibitor, or with MG132 (26S proteasome inhibitor). While rapamycin prevented EBR-induced apoptosis, MG132 further increased its apoptotic effect in prostate cancer cells. In addition we also found that p53 expression is not determinative in the decision of apoptosis following EBR treatment. We determined that mutant and wildtype p53 expressing or p53 -/- cell lines underwent apoptotic cell death by dephosphorylating AKT at Ser473 and led to the alterations of glycogen synthase kinase 3 beta (GSK-3 α) at Ser9 which are major cell survival promoting molecules. Therefore we conclude that EBR triggers ER stress-mediated apoptosis regardless of p53 expression via GSK3b dephosphorylation in carcinoma cells.

Biography

Pinar Obakan has completed her MSc. from University Paul Sabatier, Toulouse III and her PhD from Istanbul University. She works in Istanbul Kultur University as Assist. Prof. since 2013. She has published 14 papers in reputed journals.

p.obakan@iku.edu.tr

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