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Mitochondrial estrogen receptors and endocrine therapy response

A Giray Kurt¹, B Karakas², S G Temel^{3,4}, H Basaga² and O Kutuk¹¹Baskent University, Turkey²Sabanci University, Turkey³Uludag University, Turkey⁴Near East University, Northern Cyprus

Breast cancer is the most common malignancy in 2015 in Europe. Estrogen receptors (ERs) and estrogen signaling regulate key molecular events in breast cancer development and progression. Estrogen receptor status is an important prognostic factor. BCL-2 protein family members regulate mitochondrial apoptotic pathway and impaired cell death signaling promotes cancer cell survival in response to chemotherapy, hypoxia or oncogenic stress. BH3-only proapoptotic BCL-2 proteins integrate cellular damage into mitochondrial apoptotic pathway either by selectively interacting with antiapoptotic BCL-2 proteins or by directly activating multidomain proapoptotic BCL-2 proteins. Here in this study, we evaluated the how estrogen receptors' intracellular localization affects mitochondrial cell death priming and endocrine therapy response in breast cancer cells by using CellTiterGlo cell viability assay, confocal immunofluorescence microscopy, immunoblotting, qPCR and BH3 profiling technique; which is a functional mitochondrial cell death assay for assessing apoptotic blocks employed by cancer cells. We found that ER-alpha is selectively expressed in breast cancer cell lines, but in contrast ER-beta is ubiquitously found in all breast cancer cells. Moreover, both ER-alpha and ER-beta in breast cancer cells are partially localized to mitochondria. We determined the BH3 profiles of breast cancer cells as well as EC50 values for tamoxifen, anastrozole and fulvestrant to evaluate how mitochondrial estrogen receptors affect mitochondrial cell death priming and endocrine therapy response. Our work highlights the promising potential of using BH3 profiling assay in predicting breast-cancer endocrine therapy response and the contribution of mitochondrial estrogen receptors in endocrine therapy-induced cell death in breast cancer cells.

Biography

A Giray Kurt has completed her PhD from Inonu University in Turkey and Post-doctoral studies from Baskent University, School of Medicine in Turkey. She has published more than 7 papers.

asligk44@gmail.com

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