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Reversal of TAM resistance by calcitriol and tretinoin combined therapy is mediated mainly by induction of surviving

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Objective: To investigate the role of single and combined therapeutic effect of tretinoin and calcitriol in reversal of tamoxifen resistance in LCC2, doses were determined by MTT assay.

Materials & Methods: The study included eight groups (triplicates), control group (1% v/v of DMSO), 100 nM 4-OH TAM, 250 nM calcitriol, 1mM tretinoin, tretinoin+calcitriol, TAM+calcitriol, TAM+tretinoin, TAM+calcitriol+tretinoin. After 72 hours, CCND1 was assayed by qRT-PCR while, ERα, survivin, Her-2, and IGF-1R were detected by ELISA.

Results: TAMR was represented by a significant decrease in ERα and significant increase of Her-2, survivin, and EGF-1R in TAM group. Tretinoin significantly increased Her-2, survivin, and IGF-1R while, calcitriol significantly increased ERα. Combined calcitriol and tretinoin treatment significantly increased ERα, Her-2, survivin, and IGF-1R than control. Addition of calcitriol to TAM significantly normalized Her-2, survivin, EGF-1R, and ERα. However, addition of tretinoin significantly lowered Her-2, survivin, and EGF-1R and increased significantly ERα to a normalized level. TAM plus both vitamins significantly increased ERα than TAM alone and even more than the control level, normalized Her-2, and IGF-1R, and significantly lowered survivin than control. Addition of tretinoin to TAM significantly increased CCND1 than TAM and control. A significant reversal correlations was detected between ERα and survivin. A direct significant correlation was also detected between survivin and both IGF-1R and Her-2. Her-2 significantly correlated directly with IGF-1R.

Conclusion: Combined therapy alleviate TAMR via cross-talk of ERα with Her-2, survivin, and IGF-1R with survivin being the most affected effector.

Biography

Eman El-Abd, Ass. Prof. in radiation sciences department, Medical research institute (MRI), Alexandria University, Egypt, grew up in Egypt and received her Bachelor's degree from Biochemistry department, Faculty of science, University of Alexandria in 1991. She received a training fellowship at University of Torvergata, Rome, Italy 1992, Mario Negri sud institute, Chieti, Italy 1992-1993, and Mario Negri institute, Bergamo, Italy 1993-1995. She awarded her MSc in Medical applied chemistry (radiation chemistry), MRI, Alexandria University 1996. After she obtained her Ph.D degree from the school of biological sciences, University of Liverpool, UK in 2002, she joined the MRI as a lecturer in 2002. She established the molecular biology unit in the medical technology center as a part of the MRI. She investigated the role of genes in diagnosis and prognosis of cancers. She was promoted to Ass. Prof. at MRI in 2008. In 2010 she was classified as Number 59 among top 100 health professionals.

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