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Apoptosis Pathway Targeted by Thymoquinone in MCF7 Breast Cancer Cell Line

Authors : M. Marjaneh, M. Y. Narazah, H. Shahrul

Abstract : Array-based gene expression analysis is a powerful tool to profile expression of genes and to generate information on therapeutic effects of new anti-cancer compounds. Anti-apoptotic effect of thymoquinone was studied in MCF7 breast cancer cell line using gene expression profiling with cDNA micro array. The purity and yield of RNA samples were determined using RNeasyPlus Mini kit. The Agilent RNA 6000 Nano LabChip kit evaluated the quantity of the RNA samples. AffinityScript RT oligo-dT promoter primer was used to generate cDNA strands. T7 RNA polymerase was used to convert cDNA to cRNA. The cRNA samples and human universal reference RNA were labelled with Cy-3-CTP and Cy-5-CTP, respectively. Feature Extraction and GeneSpring software analysed the data. The single experiment analysis revealed involvement of 64 pathways with up-regulated genes and 78 pathways with down-regulated genes. The MAPK and p38-MAPK pathways were inhibited due to the up-regulation of PTPRR gene. The inhibition of p38-MAPK suggested up-regulation of TGF-ß pathway. Inhibition of p38 - MAPK caused up-regulation of TP53 and down-regulation of Bcl2 genes indicating involvement of intrinsic apoptotic pathway. Down-regulation of CARD16 gene as an adaptor molecule regulated CASP1 and suggested necrosis-like programmed cell death and involvement of caspase in apoptosis. Furthermore, down-regulation of GPCR, EGF-EGFR signalling pathways suggested reduction of ER. Involvement of AhR pathway which control cytochrome P450 and glucuronidation pathways showed metabolism of Thymoquinone. The findings showed differential expression of several genes in apoptosis pathways with thymoquinone treatment in estrogen receptor-positive breast cancer cells.

Keywords : cDNA microarray, thymoquinone, CARD16, PTPRR, CASP10
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