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Genes up- and down-regulated by dermcidin in breast cancer: a microarray analysis

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ABSTRACT. Dermcidin (DCD) is a human gene mapped to chromosome 12q13 region, which is co-amplified with multiple oncogenes with a well-established role in the growth, survival and progression of breast cancers. Here, we present a summary of a DNA microarray-based study that identified the genes that are up- and down-regulated in a human MDA-361 pLKO control clone and three clones expressing short hairpin RNA against three different regions of DCD mRNA. A list of 235 genes was differentially expressed among independent clones (>3-fold change and $P < 0.005$). The gene expression of 208 was reduced and of 27 was increased in the three DCD-RNAi clones compared to pLKO control clone. The expression of 77 genes (37%) encoding for enzymes involved in amino acid metabolism, glucose metabolism and oxidoreductase activity and several genes required for cell survival and DNA repair were decreased. The expression of EGFR/ErbB-1 gene, an important predictor of outcome in breast cancer, was reduced together with the genes for betacellulin and amphiregulin, two known ligands of EGFR/ErbB

receptors. Many of the 27 genes up-regulated by DCD-RNAi expression have not yet been fully characterized; among those with known function, we identified the calcium-calmodulin-dependent protein kinase-II delta and calcineurin A alpha. We compared 132 up-regulated and 12 down-regulated genes in our dataset with those genes up- and down-regulated by inhibitors targeting various signaling pathway components. The analysis showed that the genes in the DCD pathway are aligned with those functionally influenced by the drugs sirolimus, LY-294002 and wortmannin. Therefore, DCD may exert its function by activating the PI3K/AKT/mTOR signaling pathway. Together, these bioinformatic approaches suggest the involvement of DCD in the regulation of genes for breast cancer cell metabolism, proliferation and survival.

Key words: Dermcidin; Oncogene; Breast cancer; ErbB receptors

