CURCUMIN, OXIDATIVE STRESS AND BREAST CARCINOGENESIS

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Abstract. Human breast cancer is a major cause of global morbidity and mortality in women and it is a process that involves numerous molecular and cellular alterations attributed to environmental substances and agents such as hormones. Oxidative stress is one of the important pathogenic factors of cancer development. Among the antioxidants, curcumin (1, 7-bis (4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione; diferuloylmethane) is a dietary natural yellow pigment derived from the rhizome of the herb Curcuma longa (Zingiberaceae). It exerts anti-proliferative, anti-migratory and apoptotic effects. The aim of this study was to evaluate genes that could be targeted by curcumin in a breast carcinogenesis in vitro model induced by radiation and estrogen. Such model was developed with a normal immortalized breast epithelial cell line, MCF-10F that was exposed to low doses of high LET (linear energy transfer) alpha particles (150 keV/μm) of radiation, and cultured in presence of 17β–estradiol. This model consisted of the following cell lines: i) MCF-10F, ii) Alpha3, a malignant non-tumorigenic, iii) Alpha5, a tumorigenic one and iv) Tumor2, derived from Alpha5 injected into the nude mice. Previous results showed that Alpha5 and Tumor2 increased cell proliferation, presented anchorage independency, invasive capabilities and tumor formation in nude mice in comparison to control. Curcumin decreased such characteristics and gene expression of mutant p53, c-Ha-ras, Rho-A, catalase, metastatic genes as Serpin-1, Caveolin-1, epithelial mesenchyme transition-related genes as E-Cad, N-Cad, Beta Cat, Fibronectin, Twist, Slug, Axl, Vimentin, Stat-3, ZEB2 and others as Cyclin-D1, related to mechanism as NFκB, Caspase-3, Caspase-8. It can be concluded that curcumin interferes with multiple genes that promote carcinogenesis and therefore affecting genomic instability. It seems that curcumin as a pleitropic molecule may impinge upon several processes related with cell proliferation, invasion and metastasis by inducing apoptosis in breast carcinogenesis in vitro.

Key words: curcumin, breast carcinogenesis, gene expression, radiation, estrogen

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