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CANCER RESEARCH

Cell Membrane Fatty Acid Composition Differs Between Normal and Malignant Cell Lines

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Twenty-eight fatty acids (C8:0 to C24:1 n-9) were measured by gas chromatography in four normal cell lines (C3H/10T1/2, CCD-18Co, CCD-25SK and CCD-37Lu) and seven cancer cell lines (C-41, Caov-3, LS-180, PC-3, SK-MEL-28, SK-MES-1 and U-87 MG). Results show differences in the content and proportions of fatty acids when comparing cancer cell lines with their normal counterparts. Cancer cell lines showed lower C20:4 n-6, C24:1 n-9, polyunsaturated fatty acids (PUFA's) and ratios of C20:4 n-6 to C20:5 n-3 and C16:0 to C18:1 n-9 and stearic to oleic (SA/OA) than their normal counterparts. All cancer cell lines had SA/OA ratios lower than 7.0 while normal cell lines had ratios

greater than 0.7 ($p < 0.05$). In addition, the ratios of total saturated fatty acids (SFA) to PUFA'S and the concentration of C18:1 n-9, C18:2 n-6, C20:5 n-3 were higher in cancer cell lines as compared to normal cell lines. A positive correlation was detected between C16:0 and longer SFA'S ($r = +0.511$, $p < 0.05$) in normal cell lines whereas a negative correlation ($r = 0.608$, $p < 0.05$) was obtained for malignant cell lines. Moreover, cancerous cell lines exhibited a particular desaturation defect and an abnormal incorporation of C18:2 n-6 and C20:4 n-6 fatty acids.

Key words: Fatty acid composition, Cell membrane and cancer

It is well recognized that exogenous fatty acids may be toxic to cultured cells at high concentrations¹. In blood, the highest solubility of free fatty acids is ~ 1 μ m above this concentration free fatty acids may act as detergents and disrupt protein and membrane architecture. Saturated fatty acids can be synthesized from acetyl-CoA and malonyl-CoA up to palmitic acid, then elongated and desaturated to longer chain fatty acids. Although mammalian systems possess four desaturases ("9, "6, "5 and "4); they are unable to insert double bonds into positions beyond "9.

Previous in vitro studies have demonstrated that the capacity of various polyunsaturated fatty acids (PUFA'S) of killing cancer cells was associated to their ability to generate free radicals that stimulate the production of secondary products of lipid peroxidation (2,3). These

studies have been further validated in an in vivo system utilizing human mammary carcinoma cell lines (MDA-MB 231 and MCF-7) transplanted to nude mice (4, 5). This growth inhibitory PUFA effect can be blocked by the addition of antioxidants such as vitamin E (5). However, one study showed that C20:5 n-3 had 60% cell growth inhibition of human lung, breast and prostate carcinoma cells, while C22:6 n-3 had only 30% (6). In another study C12:0 and C16:0 inhibited the growth of colon cancer cells (HT-29), in more significant manner than 18:2 n-6 and this inhibitory action was not blocked by vitamin E (7). These studies suggest yet another mechanism in addition to lipid peroxidation that may be operating in the fatty acid effect upon cell proliferation.

Differences in prostaglandin metabolism have been suggested (8). Nevertheless it seems paradoxical that the same fatty acid could be either a promoter of tumorigenesis and/or an antitumor agent. It has been reported that linoleic acid (LA), an essential fatty acid, can be an effective promoter of mammary tumorigenesis (9). In contrast, it has also been reported that LA suppressed malignant cell line proliferation in culture (10). While we have tackled this issue previously (11), we speculate that fatty acids influence upon cell metabolism can be different in different types of cell. We also believe that by balancing fatty

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