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CELLULAR GLYCOLYSIS AND THE DIFFERENTIAL SURVIVAL OF LUNG FIBROBLAST AND LUNG CARCINOMA CELL LINES

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Abstract: Tumor growth and abnormal cell survival were shown to be associated with a number of cellular metabolic abnormalities revealed by impaired oral glucose tolerance, depressed lipoprotein lipase activity leading to hypertriglyceridemia, and changes in amino acid profile as evidenced by increased plasma free tryptophan levels in patients with breast, lung, colon, stomach, and other cancers from various origins. The above findings seem to relate to or indicate a shift to non-oxidative metabolic pathways in cancer. In contrast to normal cells, cancer cells may lose the ability to utilize aerobic respiration due to either defective mitochondria or hypoxia within the tumor microenvironments. Glucose was shown to be the major energy source in cancer cells where it utilizes aerobic /anaerobic glycolysis with the resultant lactic acid formation. The role of energetic modulations and use of glycolytic inhibitors on cancer/normal cell survival is not clearly established in the literature. We hypothesize that natural intermediates of glycolysis and the citric acid cycle will differentially and negatively impact the cancer phenotype in contrast to their no effects on the normal cell phenotype. Therefore, the purpose of this study was to evaluate six potential glycolytic modulators namely, Pyruvic acid, oxalic acid, Zn acetate, sodium citrate, fructose diphosphate (FDP) and sodium bicarbonate at µM concentrations on growing A549 (lung cancer) and MRC-5 (normal; human lung fibroblast) cell lines with the objective of determining their influence on visual impact, cell metabolic activity, cell viability and end-point cell survival. Exposed and non-exposed cells were tested with phase-contrast micro-scanning, survival/death and metabolic activity trends through MTT-assays, as well as death end-point determinations by testing re-growth on complete media and T4 cellometer counts. Results showed that oxalic acid and Zn acetate both influenced the pH of the medium and resulted in differential massive cell debris within the exposure period. Pyruvic acid, sodium citrate, sodium bicarbonate and FDP did not cause pH changes; however, they caused detectable cell disfigurement and loss of metabolic activity, viability and survival/ death end points with the resultant death of the A549 cell line. The MRC-5 cell line was differentially unaffected by exposure to pyruvic acid, sodium citrate, sodium bicarbonate, FDP and Zn acetate, underwent complete recovery and remained both attached and healthy for 6 weeks upon subculture when transferred to a new complete medium. Oxalic acid did not show differential modulation with the consequent loss of survival and death of the MRC-5 cell line. Phase contrast, metabolic activity, cell counts as well as death end-point findings confirmed our hypothesis. These studies show the potential possibly for exploiting cellular metabolic differences in cancer control.

Keywords: Energetics, MRC-5, A549, Cancer, survival, modulation, glycolytic inhibitors, mitochondria

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