Metabolic Effects of a Lung Cancer Cell Treatment With Sodium Butyrate

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Histone deacetylase inhibitors (HDACi) induce different phenotypes in various transformed cells, including growth arrest, apoptosis, autophagic cell death and senescence. The molecular basis of these pleiotropic effects are largely unknown.
The HDACi sodium butyrate is a short chain fatty acid that affects proliferation and cell cycle of different tumor cells but little is know about its metabolism or about the possible metabolic effects induced by this compound in tumors and normal cells.
In this work, we have analyzed the effects of sodium butyrate on cell proliferation, cell cycle, glucose metabolism and mitochondrial function in lung cancer cell H460 and in normal human lung fibroblast, IMR90 Our results have shown that sodium butyrate produces a time and dose dependent effect on the growth of H460. Fluorescence-activated cell sorting assays, after the incubation of H460 cells with 10 mM sodium butyrate for up to 48 hours, show a decrease in the S phase and an increase in the proportion of cells in G1 phase. Morphological changes could also be observed, suggesting that butyrate-dependent cell differentiation is occurring. In H460 cells, almost all hexokinase activity was shown to be mitochondria-associated, and the treatment with sodium butyrate promoted a decrease in enzyme activity.. Additionally, sodium butyrate treatment reduced the glycolytic flux, when analyzed by lactate production. Results with high-resolution respirometry suggested an increase in oxidative metabolism subsequent to incubation of H460 cells with 10 mM sodium butyrate for 24 hours leading to an increased routine respiration and higher consumption of oxygen associated to ATP synthesis.

Key words: lung cancer, sodium butyrate, hexokinase, mitochondrial physiology