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Title: Metabolic modification as a potential therapeutics approach in lung cancer

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Body: Background: It is well established that cancer cells can activate their glycolysis pathway in order to survive in hypoxia micro-environment. Tumors cells show a high rate of glycolysis and lactate production, even in the presence of oxygen. Importantly, some cancer cells demonstrate impaired mitochondria respiration and high glycolysis, namely Warburg effect. Objective: Our overall goal is to target Warburg phenomenon as a treatment approach for lung cancer and to reverse the metabolic activity towards its normal glycolysis/mitochondrial ratio. Methods: We used adenocarcinoma cell lines (A549, H1650, H1563, and H2030), large cell tumor (H1299) and small cell lung cancer (SCLC, SHP77). We quantified the lactic acid production using a colorimetric assay. Dichloacetate (DCA) was used to induce mitochondrial activity and 2-deoxyglucose (2-DG) was used to inhibit the glycolysis pathway. Western blot analyses were performed to determine the protein expression level of glycolysis markers, GAPDH and PKM2, and an oxidative phosphorylation marker ATP5B. Results: We demonstrated that Warburg Effect (aerobic glycolysis) occurs only in A549 and H2030 lung cancer cells. A549 and H2030 cells produce high quantity of lactic acid and were sensitive to glycolysis inhibition. H1650, which represents a higher mitochondrial activity, was more sensitive to DCA, an enhancer of oxidative phosphorylation. Impact: Glycolysis shut-down and mitochondrial activation induce cell death in lung cancer cell lines. This research is a proof of concept for the feasibility of metabolic modification as an anti cancer therapy in lung cancer.