

3 bromopiruvato no glioblastoma multiforme, antagoniza efeito do piruvato e provoca estresse oxidativo

## **3-Bromopyruvate antagonizes effects of lactate and pyruvate, synergizes with citrate and exerts novel anti-glioma effects.**

[El Sayed SM](#), [El-Magd RM](#), [Shishido Y](#), [Chung SP](#), [Diem TH](#), [Sakai T](#), [Watanabe H](#), [Kagami S](#), [Fukui K](#).  
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### **Source**

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### **Abstract**

Oxidative stress-energy depletion therapy using oxidative stress induced by D-amino acid oxidase (DAO) and energy depletion induced by 3-bromopyruvate (3BP) was reported recently (El Sayed et al., *Cancer Gene Ther.*, 19, 1-18, 2012). Even in the presence of oxygen, cancer cells oxidize glucose preferentially to produce lactate (Warburg effect) which seems vital for cancer microenvironment and progression. 3BP is a closely related structure to lactate and pyruvate and may antagonize their effects as a novel mechanism of its action. Pyruvate exerted a potent H<sub>2</sub>O<sub>2</sub> scavenging effect to exogenous H<sub>2</sub>O<sub>2</sub>, while lactate had no scavenging effect. 3BP induced H<sub>2</sub>O<sub>2</sub> production. Pyruvate protected against H<sub>2</sub>O<sub>2</sub>-induced C6 glioma cell death, 3BP-induced C6 glioma cell death but not against DAO/D-serine-induced cell death, while lactate had no protecting effect. Lactate and pyruvate protected against 3BP-induced C6 glioma cell death and energy depletion which were overcome with higher doses of 3BP. Lactate and pyruvate enhanced migratory power of C6 glioma which was blocked by 3BP. Pyruvate and lactate did not protect against C6 glioma cell death induced by other glycolytic inhibitors e.g. citrate (inhibitor of phosphofructokinase) and sodium fluoride (inhibitor of enolase). Serial doses of 3BP were synergistic with citrate in decreasing viability of C6 glioma cells and spheroids. Glycolysis subjected to double inhibition using 3BP with citrate depleted ATP, clonogenic power and migratory power of C6 glioma cells. 3BP induced a caspase-dependent cell death in C6 glioma. 3BP was powerful in decreasing viability of human glioblastoma multiforme cells (U373MG) and C6 glioma in a dose- and time-dependent manner.

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