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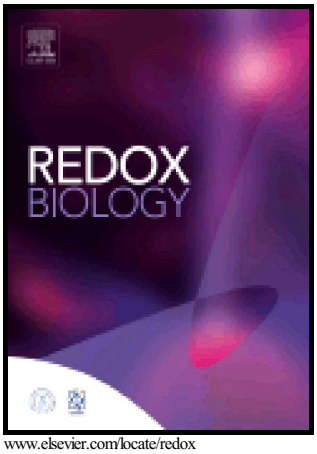

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REDOX MECHANISM OF LEVOBUPIVACAINE CYTOSTATIC EFFECT ON HUMAN PROSTATE CANCER CELLS

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REDOX MECHANISM OF LEVOBUPIVACAINE CYTOSTATIC EFFECT ON HUMAN PROSTATE CANCER CELLS

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Running title: Levobupivacaine REDOX properties

ABSTRACT : Anti-cancer effects of local anesthetics have been reported but the mode of action remains elusive. Here, we examined the bioenergetic and REDOX impact of levobupivacaine on human prostate cancer cells (DU145) and corresponding non-cancer primary human prostate cells (BHP). Levobupivacaine induced a combined inhibition of glycolysis and oxidative phosphorylation in cancer cells, resulting in a reduced cellular ATP production and consecutive bioenergetic crisis, along with reactive oxygen species generation. The dose-dependent inhibition of respiratory chain complex I activity by levobupivacaine explained the alteration of mitochondrial energy fluxes. Furthermore, the potency of levobupivacaine varied with glucose and oxygen availability as well as the cellular energy demand, in accordance with a bioenergetic anti-cancer mechanism. The levobupivacaine-induced bioenergetic crisis triggered cytostasis in prostate cancer cells as evidenced by a S-phase cell cycle arrest, without apoptosis induction. In DU145 cells, levobupivacaine also triggered the induction of autophagy and blockade of this process potentialized the anti-cancer effect of the local anesthetic. Therefore, our findings provide a better characterization of the REDOX mechanisms underpinning the anti-effect of levobupivacaine against human prostate cancer cells.

Keywords : prostate cancer ; levobupivacaine ; glycolysis ; oxidative phosphorylation ; Wortmannin.
Visual abstract (submitted as separate file).

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