LDHA-Mediated Metabolic Adaptations in the Response of Breast and Prostate Cancer to [C16Pyr][Amp]

Irene Magalhães[1]*, Ludmila Tavares [1], Filipa Vieira [1,2], Regina Silva [1,2], Ricardo Ferraz [2,3,4], Sara Granja [1,2]

[1] *Department of Pathological, Cytological and Thanatological Anatomy, ESS|P.PORTO, 4200-072 Porto, Portugal*
irene_mag@hotmail.com
[2] *REQUIMTE/LAQV, School of Health, Polytechnic of Porto, Rua Dr. António Bernardino de Almeida, Porto 4200-072, Portugal*
[3] *RISE-Health, Center for Translational Health and Medical Biotechnology Research (TBIO), ESS, Polytechnic of Porto, Porto, Portugal*
[4] *Scientific and Technical Area of Chemical and Biomolecular Sciences, ESS, Polytechnic of Porto, Porto, Portugal*

Background: Cancer cells exhibit reprogrammed metabolism that supports uncontrolled proliferation and therapeutic resistance, with high glycolytic activity as a cancer hallmark. Lactate dehydrogenase A (LDHA) plays a key role in cancer metabolism by catalyzing the conversion of pyruvate to lactate, sustaining glycolysis and promoting tumor growth and metastasis. LDHA is frequently overexpressed in breast and prostate cancers and is associated with tumor progression and therapy resistance, making it an attractive metabolic target. Ionic liquids have emerged as innovative compounds in cancer research due to their tunable physicochemical properties and potential biological activity. Prior studies indicate that the novel compound [C16Pyr][Amp] exhibits anticancer activity by reducing cell viability and colony formation and inducing apoptosis. However, its effects on tumor metabolism remain poorly understood. **Objective:** This work aims to clarify the metabolic mechanisms underlying the anticancer effects of [C16Pyr][Amp] and to evaluate LDHA as a potential biomarker and therapeutic modulator in breast and prostate cancer. **Methods:** The impact of [C16Pyr][Amp] on LDHA expression and metabolic responses in breast (MDA-MB-231, T47D) and prostate (22Rv1, DU145) cancer cell lines. LDHA expression was evaluated by immunocytochemistry and metabolic alterations assessed through lactate production and glucose consumption. **Results:** Treatment with [C16Pyr][Amp] led to an overall decrease in LDHA expression, particularly at earlier time points (24 and 48 hours), although increased nuclear staining was observed at 72 hours in MDA-MB-231 cells. An increase in lactate production was observed in all cell lines, along with a reduction in glucose consumption in MDA-MB-231 cells, while no significant changes in glucose consumption were detected in prostate cancer cell lines. **Conclusions:** Overall, LDHA expression was reduced following treatment. [C16Pyr][Amp] did not attenuate glycolytic activity in breast and prostate cancer models; instead, the metabolic profile observed suggests an adaptive response rather than direct modulation of LDHA, warranting further molecular and metabolic investigation.

Keywords: breast cancer; cancer metabolism; ionic liquids; LDHA; prostate cancer

Acknowledgements
InnovHealth scholarships supported by the Young STEAM Impulse Program of the Resilient P.PORTO Program (02/C06-i03.03/2021.PID-15), co-funded by the Next Generation EU funds under the Recovery and Resilience Plan (PRR).

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