

# METABOLIC REWIRING IN PROSTATE CANCER VIA ZINC-INDUCED MITOCHONDRIAL ACONITASE INHIBITION: PERSPECTIVES FOR POST-ONCOLOGICAL TISSUE TRANSPLANTATION

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**Introduction:** Prostate epithelial cells exhibit unique biochemical specialization, accumulating high levels of zinc (Zn) to inhibit mitochondrial aconitase (m-aconitase) and facilitate citrate secretion. During malignancy, zinc dyshomeostasis triggers metabolic rewiring, reactivating the tricarboxylic acid (TCA) cycle to fuel tumor progression. For tissue transplantation and engineering, understanding these zinc-dependent metabolic signatures is essential for developing biomimetic scaffolds and regenerative strategies aiming to restore cellular homeostasis and prevent recurrence post-oncological resection.

**Materials and Methods:** To evaluate the biochemical dynamics of Zn in prostatic tissue, data were aggregated from experimental studies analyzing mitochondrial extract preparations derived from rat ventral prostate models. The analysis prioritized the stoichiometric shift of the citrate/isocitrate ratio at equilibrium under the inhibitory influence of 7-10 micromolar ( $\mu\text{M}$ ) concentrations of Zn. Research was synthesized through a comparative analysis of primary sources retrieved from the National Center for Biotechnology Information (NCBI) PubMed, ResearchGate, and Google Scholar, covering 1998 to 2025.

**Results:** This framework allowed for an in-depth assessment of the inhibitory kinetics of mitochondrial aconitase (m-aconitase) and the functional downregulation of the zinc-regulated, iron-regulated transporter-like protein 1 (ZIP1). These metabolic trends were subsequently mapped against cellular bioenergetics in prostate cancer to establish their clinical relevance for tissue engineering and post-resection regenerative medicine. Findings demonstrate that 7-10 micromolar ( $\mu\text{M}$ ) Zn maintains a unique 13.5:1 citrate/isocitrate ratio by inhibiting mitochondrial aconitase (m-aconitase), a process mediated by a mitochondrial "citrate factor protein". In prostate cancer, the downregulation of zinc-regulated, iron-regulated transporter-like protein 1 (ZIP1) causes a 60-80% intracellular zinc depletion. This loss reactivates the tricarboxylic acid (TCA) cycle and oxidative phosphorylation, providing the bioenergetic fuel necessary for tumor progression.

**Conclusions:** The investigation underscores that the zinc-regulated, iron-regulated transporter-like protein 1 (ZIP1) and mitochondrial aconitase (m-aconitase) regulatory axis is fundamental for preserving prostatic metabolic homeostasis. Since Zn depletion acts as a critical metabolic switch for prostate cancer progression, targeting this pathway offers significant therapeutic potential. Future research should prioritize the development of zinc-enriched biomimetic scaffolds in tissue engineering. Such regenerative strategies could effectively restore cellular stability and minimize the risk of malignant recurrence following post-oncological transplantation.

**Keywords:** prostate cancer, zinc homeostasis, mitochondrial aconitase, metabolic rewiring, tissue engineering.