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Pharmacological interventions that target flexible metabolism of cancer cells

Amir Abrishami[1], Fatemeh B. Rassouli[1,2*]

[1]Department of Biology, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran
[2] Novel Diagnostics and Therapeutics Research Group, Institute of Biotechnology, Ferdowsi University of Mashhad, Mashhad, Iran
First author's e-mail: amir.abrishami25@gmail.com
Corresponding author's e-mail: behnam3260@um.ac.ir

Abstract

Introduction: Metabolic flexibility of cancer cells, which is mediated by oncologic changes during carcinogenesis, enables them to switch between oxidative phosphorylation and glycolysis to maintain homeostasis. Metabolism-targeting pharmacological therapies aim to disrupt metabolic pathways in normoxic or hypoxic niches of tumor cell population. In this regard, vital biomolecules that provide energy and metabolites required for maintenance and self-renewal of cancer cells are at the center of attention.

Methods: We searched for recent articles including key words *cancer cell*, *flexible metabolism*, and *metabolic targeting* in databases Web of Science, PubMed and Scopus.

Results: In the continuously expanding list of chemicals targeting cancer cell metabolism, metformin and aspirin are those with available preclinical/clinical data regarding tolerability and efficacy. Metformin can potentially target different metabolic pathways linked to cancer progression, including mTOR signaling, fatty acid, cholesterol and acetyl-CoA carboxylase synthesis, and fatty acid β-oxidation. Therefore, shift from anabolic to catabolic processes, along with energetic stress caused by reduced ATP levels resulted in metformin-inhibited proliferation, and even –induced apoptosis. The main aspirin metabolite in human blood, sodium salicylate, also inhibits mTOR and fatty acid synthesis, as well as cyclooxigenase 1. Interestingly, brief exposures to aspirin is not only tolerable by cancer patients, also induces strong synergistic anticancer effects with metformin.

Conclusion: Due to promising effects of metformin and aspirin in targeting altered metabolism, cancer patients may benefit from combination of these pharmaceutical agents on the basis of their systemic metabolic state.

Key words: Flexible metabolism, Cancer therapy, Metabolic targeting.