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Content

RESCUING HAMSTER FIBROSARCOMA GROWTH BY STIMULATION OF DIFFERENT PROONCOGENIC SIGNALING PATHWAYS RELATIVE TO REPURPOSED ANTICANCER DRUG MECHANISMS

Kosta J. Popović,[1] Dušica J. Popović,[2] Dejan Miljković,[3] Dušan Lalošević,[3] Ivan Čapo,[3] Mihalj Poša,[1] Zana Dolićanin,[2] Jovan K. Popović[4]

[1]Department of Pharmacy, Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia;
[2]Department of Biomedical Sciences, State University of Novi Pazar, Novi Pazar, Serbia;
[3]Department of Histology and Embryology, Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia;
[4]Department of Pharmacology, Toxicology and Clinical Pharmacology, Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia.

Introduction: Many drugs registered for various non-oncological indications influence tumor metabolic processes, signaling pathways, enzymes, proteins, tumor receptors and genes that regulate proliferation, neoangiogenesis, apoptosis and necroptosis, without affecting these activities in healthy cells. The aim: Detecting underlying anticancer mechanism of metformin in two-drug combinations with other repurposed drugs (2-Deoxy-D-glucose, deoxycholic acid, caffeine, itraconazole or disulfiram) by rescuing BHK-21/C13 hamster fibrosarcoma growth with glucose, vitamin C, nitroglycerin or mebendazole.

Methods: The anticancer mechanisms of examined drug combinations, <50% LD_{50} (equivalent to usual human dose), were determined by rescuing fibrosarcoma growth with addition of aforementioned agents in treatment. Immunohistochemical markers (Ki-67, PCNA, CD34, CD31, GLUT1, iNOS, COX4, Cytochrome C) in control and experimental groups were assessed 19 days after BHK-21/C13 tumor inoculation. Tumors were excised, measured and blood collected. Biophysical, pathohistological, toxicological, hematological, biochemical and statistical analyses were performed.

Results: Only addition of NF-kB stimulator mebendazole to effective two-drug combinations containing metformin rescued cancer growth, indicating that this pathway may be responsible for antitumor action.

Conclusion: NF-kB signaling pathway downregulation plays an essential role among anticancer mechanisms of investigated metformin combinations in hamster fibrosarcoma treatment.

Key words: fibrosarcoma; hamster; repurposed drugs; anticancer mechanism

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