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Stimulation and inhibition of NF-kB by repurposed drugs – effects on hamster fibrosarcoma

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Background: NF-kB transcription factors are key regulators of apoptosis, autophagy, necroptosis and turns up everywhere in cancer life and death. This study investigated how the regulation of NF-kB by repurposed drugs in oncology affect experimental fibrosarcoma development and progression in hamsters. Material and Methods: Anticancer efficacy of certain drugs was tested on fibrosarcoma experimentally induced by BHK21/C13 cells in Syrian golden hamsters. Used repurposed drugs with in vitro verified NF-kB inhibitory effect were: metformin, caffeine, itraconazole, nitroglycerin. Used drug with known NF-kB stimulatory effect was mebendazole. Tumor biophysical characteristics, histology and immunohistochemistry were assessed. Blood samples were collected for hematological and biochemical analyses and the main organs were toxicologically analyzed. Results: Our study showed that combinations of NF-kB inhibitors: metformin with caffeine, metformin with itraconazole and metformin with nitroglycerin, in human equivalent doses could be efficacious (p < 0.05) against fibrosarcoma growth, which can rescued by mebendazole, without toxicity and influence on biochemical and hematological tests. Conclusion: Combinations of repurposed drugs with NF-kB inhibitory effect: metformin with caffeine, metformin with itraconazole and metformin with nitroglycerin could be an important therapeutic option in oncology. Keywords: BHK-21/C13 cell culture, drug effects, fibrosarcoma, hamsters, NF-kB

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