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ROS and Nf-κB role in repurposed drugs treatment of hamster fibrosarcoma

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The NF-κB activity in cancer cells promotes tumor growth by stimulation of cell proliferation, neoangiogenesis and by inhibition of apoptosis and ROS activity[1]. Anticancer combinations of two repurposed drugs: metformin[2] with 2-deoxy-*D*-glucose, deoxycholic acid, caffeine, itraconazole or disulfiram (< 50% LD_{50}, equivalent to usual human dose) mechanism of action was investigated by rescuing treated BHK-21/C13 fibrosarcoma growth in hamsters with ROS inhibitor nitroglycerin and NF-κB stimulator mebendazole. 19 days after inoculation, anticancer effects were assessed by biophysical measurements of fibrosarcoma growth and immunohistochemical markers of tumor proliferation (Ki-67, PCNA), neoangiogenesis (CD34, CD31), glucose metabolism (GLUT1), NO metabolism (iNOS) and apoptosis (COX4, Cytochrome C). The combinations have shown significant antitumor effects ($P < 0.05$) which were inhibited partly by addition of ROS inhibitor nitroglycerin and completely by NF-κB stimulator mebendazole. Results indicate the key role of NF-κB in anticancer action of investigated drug combinations of non-oncological drugs and their potential to be used in oncology.

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