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(54) Title: TRIPLE COMBINATION THERAPIES FOR TARGETING MITOCHONDRIA AND KILLING CANCER STEM CELLS

(57) Abstract: Cancer stem cells (CSCs) may be eradicated through a novel therapeutic strategy involving, in some embodiments, FDA-approved antibiotics and dietary supplements. The present approach effectively results in the synergistic eradication of CSCs through inhibiting mitochondrial biogenesis in CSCs during induced mitochondrial oxidative stress, without inhibiting normal cells. Embodiments may include a therapeutic agent that inhibits mitochondrial biogenesis and targets the large mitochondrial ribosome, a therapeutic agent that inhibits mitochondrial biogenesis and targets the small mitochondrial ribosome, and a therapeutic agent that behaves as a pro-oxidant or induces mitochondrial oxidative stress. Compositions according to the present approach inhibited CSC propagation by ~ 90% in MCF7 ER(+) cell lines during preliminary studies, with confirmed reduction in mitochondrial oxygen consumption and ATP production. Some embodiments include sub-antimicrobial antibiotic concentrations, thereby minimizing antibiotic resistance concerns. In some embodiments, one or more therapeutic agents are conjugated with a targeting signal.

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