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(54) Title: MITOCHONDRIAL ATP INHIBITORS TARGETING THE GAMMA SUBUNIT PREVENT METASTASIS

(57) Abstract: High ATP production by the mitochondrial ATP-synthase is a new therapeutic target for anti-cancer therapy, especially for preventing tumor progression. A mitochondrial-related gene signature for metastasis is described, which features the gamma-subunit of the mitochondrial ATP- synthase (ATP5F1C). Knock-down of ATP5F1C expression significantly reduces ATP- production, 3D anchorage-independent growth and cell migration. Administration of the Bedaquiline, or a Bedaquiline derivative with a TPP moiety, down-regulates ATP5F1C expression in vitro and prevents spontaneous metastasis in vivo. Mitochondrial ATP5F1C is a promising new biomarker and molecular target for future drug development, for the prevention of metastatic disease progression.

WO 2023/119232 A1