Metformin, a lipophilic biguanide inhibiting hepatic gluconeogenesis and improving peripheral utilization of glucose, is a well-established medication for the management of type 2 diabetes. Furthermore, metformin has been shown to have pleiotropic effects targeting oxidative phosphorylation via complex I inhibition. Thus, it regulates the energy supply to cells from mitochondrial complex I respiration along with reduced glycolytic metabolism. Several pre-clinical in vitro studies on cell lines derived from pheochromocytoma (PHEO) have suggested anti-proliferative potential of metformin which hints that metformin could be used as a potent candidate for PHEO anti-cancer therapy. However, these results have yet to be confirmed in vivo.

Murine PHEO MPC cells and human progenitor hPheo1 cells were treated with metformin in vitro to study the effect on cell proliferation and ATP production. Mice were injected with MTT cells subcutaneously and when the tumors reached the average volume of $120.2 \pm 48.1 \text{ mm}^3$, they were randomized into 3 groups (n=5) treated with vehicle, 125 mg/kg metformin i.p. daily (6 times a week), or the drug dissolved into drinking water (5 mg/ml). Tumor progression and survival data were collected.

Metformin effectively decreased PHEO cell proliferation and overall ATP production in dose-dependent manner in vitro. Tumor progression was similar in both metformin-