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OSMR controls glioma stem cell respiration and confers resistance of glioblastoma to ionizing radiation

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Glioblastoma is the most malignant primary brain tumor in adults. The median survival rate is ~16 months, even after surgery, radiation and chemotherapy. There is, therefore, an urgent need for better treatment options.

Glioblastoma contains a rare population of self-renewing brain tumor stem cells (BTSC) which are endowed with properties to proliferate, spur the growth of new tumors, and, at the same time, evade ionizing radiation (IR) and chemotherapy. However, the drivers of BTSC resistance to therapy remain unknown. The cytokine receptor for oncostatin M (OSMR) regulates BTSC proliferation and glioblastoma tumorigenesis. In this paper, the researchers report their discovery of a mitochondrial OSMR that confers resistance to IR via regulation of oxidative phosphorylation, independent of its role in cell proliferation. Mechanistically, OSMR is targeted to the mitochondrial matrix via the presequence translocase-associated motor complex components, mtHSP70 and TIM44. OSMR interacts with NADH ubiquinone oxidoreductase 1/2 (NDUFS1/2) of complex I and promotes mitochondrial respiration. Deletion of OSMR impairs spare respiratory capacity, increases reactive oxygen species, and sensitizes BTSCs to IR-induced cell death. Importantly, suppression of OSMR improves glioblastoma response to IR and prolongs lifespan.

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