The NFL-TBS.40-63 Anti-Glioblastoma Peptide Disrupts Microtubule and Mitochondrial Networks in the T98G Glioma Cell Line

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The NFL-TBS.40-63 Anti-Glioblastoma Peptide Disrupts Microtubule and Mitochondrial Networks in the T98G Glioma Cell Line

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Despite aggressive therapies, including combinations of surgery, radiotherapy and chemotherapy, glioblastoma remains a highly aggressive brain cancer with the worst prognosis of any central nervous system disease. We have previously identified a neurofilament-derived cell-penetrating peptide, NFL-TBS.40-63, that specifically enters by endocytosis in glioblastoma cells, where it induces microtubule destruction and inhibits cell proliferation. Here, we explore the impact of NFL-TBS.40-63 peptide on the mitochondrial network and its functions by using global cell respiration, quantitative PCR analysis of the main actors directing mitochondrial biogenesis, western blot analysis of the oxidative phosphorylation (OXPHOS) subunits and confocal microscopy. We show that the internalized peptide disturbs mitochondrial and microtubule networks, interferes with mitochondrial dynamics and induces a rapid depletion of global cell respiration. This effect may be related to reduced expression of the NRF-1 transcription factor and of specific miRNAs, which may impact mitochondrial biogenesis, in regard to default mitochondrial mobility.

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