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# Resveratrol Reduces the Invasive Growth and Promotes the Acquisition of a Long-Lasting Differentiated Phenotype in Human Glioblastoma Cells.

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### Abstract

Malignant glioblastoma represents a challenge in the chemotherapy of brain tumors, because of its aggressive behavior characterized by chemoresistance, infiltrative diffusion, and high rate of recurrence and death. In this study, we used cultured human U87MG cells and primary human glioblastoma cultures to test the anticancer properties of resveratrol (RV), a phytoalexin abundantly present in a variety of dietary products. In U87MG cells, 100  $\mu$ M RV elicited cell growth arrest by 48 h and bax-mediated cell toxicity by 96 h and greatly limited cell migration and invasion through matrigel. Both in U87MG cells and in primary glioblastoma cultures, the chronic administration of RV (100  $\mu$ M for up to 96 h) decreased the expression of nestin (a brain (cancer) stem cells marker) but increased that of glial acidic fibrillary protein (a mature glial cell marker) and of  $\beta$ III-tubulin (a neuronal differentiation marker). Chronic treatment with RV increased the proportion of cells positive for senescence-associated  $\beta$ -galactosidase activity. This is the first report showing the ability of RV to induce glial-like and neuronal-like differentiation in glioblastoma cells. The beneficial effects of chronic RV supplementation lasted up to 96 h after its withdrawal from the culture medium. The present findings support the introduction of pulsed administration of this food-derived molecule in the chemotherapy regimen of astrocytomas.

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