

Vitamin C, an essential micronutrient and antioxidant, was initially described as an antitumor molecule; however, several studies have shown that it can promote tumor progression and angiogenesis. Thus, considering the high concentrations of vitamin C present in the brain, our aim was to study the effect of vitamin C deficiency on the progression of Glioblastoma using a Glioblastoma model generated by the stereotactic injection of human Glioblastoma cells (U87-MG or HSVT-C3 cells) in the subventricular zone of guinea pig brain. Initial characterization of U87-MG and HSVT-C3 cells showed that HSVT-C3 are highly proliferative, overexpress p53, and are resistant to ferroptosis. To induce intraperiventricular tumors, animals received control or a vitamin C-deficient diet for 3 weeks, after which histopathological and confocal microscopy analyses were performed. We demonstrated that the vitamin C-deficient condition reduced the glomeruloid vasculature and microglia/macrophage infiltration in U87-MG tumors. Furthermore, tumor size, proliferation, glomeruloid vasculature, microglia/macrophage infiltration, and invasion were reduced in C3 tumors carried by vitamin C-deficient guinea pigs. In conclusion, the effect of the vitamin C deficiency was dependent on the tumor cell used for Glioblastoma induction. HSVT-C3 cells, a cell line with stem cell features isolated from a human subventricular Glioblastoma, showed higher sensitivity to the deficient condition; however, vitamin C deficiency displayed an antitumor effect in both Glioblastoma models analyzed ¹⁾.

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Jara N, Ramirez E, Ferrada L, Salazar K, Espinoza F, González-Chavarría I, Nualart F. Vitamin C deficient reduces proliferation in a human periventricular tumor stem cell-derived glioblastoma model. *J Cell Physiol.* 2021 Jan 11. doi: 10.1002/jcp.30264. Epub ahead of print. PMID: 33432597.

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