

IMMUNOMODULATORY AND ANTITUMOR EFFECTS OF BAICALEIN IN HUMAN NEUROBLASTOMA CELL LINES

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Introduction: Neuroblastoma (NB) is the third most common solid tumor in children, originating from neural crest cells and associated with the peripheral sympathetic nervous system. This pediatric neoplasm is highly aggressive and heterogeneous, with clinical outcomes ranging from spontaneous regression to fatal outcome. Despite therapeutic advances, conventional multimodal treatments remain insufficient, especially in high-risk cases characterized by resistance and poor prognosis. The immunosuppressive tumor microenvironment in NB contributes significantly to treatment resistance, highlighting the need for more effective therapeutic alternatives. In this context, natural compounds have emerged as promising antitumor agents. Baicalein, a flavonoid extracted from the dried roots of *Scutellaria baicalensis* Georgi, has remarkable pharmacological properties. Previous studies have shown that baicalein exerts antitumor effects through the induction of autophagy, inhibition of angiogenesis, and suppression of cell proliferation. Although its efficacy has been reported in various cancers, the mechanisms underlying its action and therapeutic potential in NB are not yet fully. **Objective:** The aim of this study was to investigate the effects of baicalein on two human NB cell lines (IMR-32 and SHSY-5Y) and on the normal lung fibroblast cell line (MRC-5). **Methods:** Cell viability was assessed using the resazurin assay after 24, 48, and 72 hours of baicalein exposure. The Cytometric Bead Array (CBA) Human Inflammatory Cytokines Kit was used to quantify seven inflammatory cytokines (IL-2, IL-4, IL-6, IL-10, IL-17, IFN- γ , and TNF) in all three cell lines. **Results:** Our results show that baicalein significantly inhibited cell proliferation of the IMR-32 cell line in a dose- and time-dependent manner. The SHSY-5Y cell line exhibited greater resistance to baicalein, with significantly higher IC50 values compared to the other cell lines. In addition, baicalein modulated the expression of several cytokines, with a marked, concentration-dependent suppression of IL-6 observed across all cell lines. For other cytokines, baicalein showed selective modulation, with IMR-32 cells showing increased sensitivity in the regulation of inflammatory mediators. **Conclusions:** These results suggest that baicalein has the potential to be used as an adjuvant therapeutic for NB. The consistent reduction of IL-6 levels in all cell lines suggests a possible inhibition of the *JAK/STAT* pathway, which is crucial for IL-6 production and is often hyperactivated in tumors. Thus, baicalein may contribute to the

suppression of tumor growth and modulation of the inflammatory microenvironment in NB, and may represent a promising alternative for future therapeutic strategies.

Keywords: Inflammatory cytokines; flavonoids; baicalein; neuroblastomas.