



UNIVERSITÀ DEGLI STUDI DI SALERNO



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Coordinatore: Chiar.mo Prof. *Antonietta Leone*

***Nuove prospettive terapeutiche del glioma:
N6-isopenteniladenosina
ed
SR141716***

settore scientifico disciplinare di afferenza: MED/04

Dottorando

Dott.
*Antonio Christian
Pagano Zottola*

Tutore

Chiar.mo Prof.
Antonietta Leone

Co-tutore

Chiar.mo Prof.
Patrizia Gazzero

Abstract

Glioma is a fatal disease characterized by uncontrolled cellular proliferation and it is the most common primary brain malignancy in adults. Despite years of research, malignant glioma remains one of the most aggressive cancer, with an average expectancy of life of 12-15 months after resection, radiotherapy and chemotherapy.

N6-isopentenyladenosine (iPA) is a modified nucleoside with a pentaatomic isopentenyl moiety, derived from mevalonate, that induces inhibition of cell proliferation in several tumor cell lines. It has been shown that iPA modulates the expression of several proteins involved in the promotion of tumor growth, but only recently, our studies suggested bone morphogenetic protein 4 (BMP4), part of the transforming growth factor beta superfamily, as potential iPA target. According to preliminary results, in fact, iPA, in several human colorectal cancer and glioma cell lines, is able to inhibit cell proliferation and to modulate, in a tumor specific way, the expression of BMP4, involved in the migration, invasion and differentiation of tumor cells.

SR141716 is an antagonist of cannabinoids receptor type 1 (CB1), involved in the regulation of cellular processes linked to survival, proliferation, invasion and angiogenesis in physiopathological conditions.

Our group showed that a majority of human glioma cell lines overexpresses CB1, compared to normal human astrocytes, and that, in this cancer model, SR141716 is able to induce apoptosis via G1 phase stasis. This study demonstrates also that SR141716 increases the functional and selective expression of MICA/B on the surface of malignant glioma cells through a mechanism that involves STAT3 inhibition. This makes SR141716 treated-glioma cells, a potent target for allogeneic NK cell-mediated recognition through a NKG2D restricted mechanism. Although further studies will be necessary to investigate the mechanism of action of these molecules, these results shed new light on the oncogenic networks in the complex biology of glioma.