

RNA Interference of the Caspase Inhibitors XIAP and Survivin Modulate Apoptosis in Glioma

Lopez, P.L.C.¹, Silva, A.O.¹, Chiela, E.C.F.¹, Vargas, J.E.¹, Zamin, L.L.¹, Lenz, G.¹

¹Departamento de Biofísica, Instituto de Biociências, Universidade Federal do Rio Grande do Sul, Rio Grande do Sul, Brazil.

Background: Gliomas are the most common tumor on CNS with prognostic lower than one year. Modulation of the expression of proteins that regulate apoptosis may lead to a better understanding of gliomas resistance to chemotherapics and to potentially sensitize these cells to drugs used on cancer treatment. **Objectives:** To sensitize gliomas to chemotherapeutic agents by silencing the caspase inhibitors XIAP and Survivin. **Methods and Results:** XIAP and Survivin were silenced in gliomas cell line U87 MG using stable RNA interference expression by lentiviral vector. Glioma with silenced XIAP presented 44% less viability when compared to control cells when treated with 1 μ M of Doxorubicin, and 57% to 1 μ M with Etoposide. Silenced cell presented reduced proliferation, although preliminary characterization did not show evident cell cycle alterations by flow cytometry or increase in senescence, as analyzed by β -Gal Senescence Assay. **Conclusions:** Silencing of caspase inhibitors is a strategy for sensitizing cells to chemotherapeutic agents and at least some of the resistance of gliomas cells may be due to over-expression of these genes. Senescence result should be reconsidered and caspase assay performed to explain phenotypic alterations by silencing of XIAP and Survivin.

Key words: glioma, apoptosis, lentiviral vector

Supported by: Instituto Milênio de Terapia Gênica (CNPq), CAPES, FAPERGS