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ANALYSIS OF ALLELIC IMBALANCES AND PROTEIN EXPRESSION IN HUMAN HIGH-GRADE ASTROCYTOMAS

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Although it is clear that genetic alterations in malignant gliomas affect cell proliferation and cell cycle control, the molecular mechanisms that mediate glioma invasion are still poorly understood. The G protein-coupled and cell surface chemokine receptor CXCR4, and the transcription factor Twist have been proposed as potential brain tumor-associated genes implicated in the invasiveness and proliferation of glioma cells. The study of genetic alterations and the search for new prognostic protein markers have been of longstanding interest in the characterization of aggressive behavior of these tumors and may be useful for their molecular classification, in the future.

In this work, we studied the genetic alterations exhibited by a group of human high-grade gliomas (glioblastomas or astrocytomas grade IV), obtained from 12 patients diagnosed with glioblastoma, and by a human high-grade astrocytoma cell line (U-118 MG). We carried out interphase fluorescence in situ hybridization (iFISH) to evaluate the allelic imbalances corresponding to numerical abnormalities of the following chromosome regions: 1p36, 19q13, 7q11, 9p21, 9q34, 10q23, 13q14, 17p13 and 22q11. We also studied the density of the chemokine receptor CXCR4 and of the transcription factor Twist, using western blot and immunocytochemistry assays.

The results showed huge genetic aberrations in all the chromosome regions analyzed, both in the fresh tumor samples and in the cell line, as well. Additionally, this astrocytoma cell line expressed the proteins CXCR4 and Twist which density was modified by the immunomodulator lipopolysaccharide and by immunosuppressive drugs.

These results confirm the existence of complex cytogenetic abnormalities in high-grade gliomas, that are characterized by tumoral genetic heterogeneity and which magnitude could be unveiled by these findings. Moreover, this could give some specific biological cues in the modulation of protein expression related to the invasive capacity of astrocytic cells.

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