Astrocytes protect glioma cells from chemotherapy and upregulate survival genes via gap junctional communication.

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Abstract

Gliomas are the most common type of primary brain tumor. Using current standard treatment regimens, the prognosis of patients with gliomas remains poor, which is predominantly due to the resistance of glioma cells to chemotherapy. The organ microenvironment has been implicated in the pathogenesis and survival of tumor cells. Thus, the aim of the present study was to test the hypothesis that astrocytes (the housekeeping cells of the brain microenvironment) may protect glioma cells from chemotherapy and to investigate the underlying mechanism. Immunofluorescent and scanning electron microscopy demonstrated that glioma cells were surrounded and infiltrated by activated astrocytes. In vitro co-culture of glioma cells with astrocytes significantly reduced the cytotoxic effects on glioma cells caused by various chemotherapeutic agents, as demonstrated by fluorescein isothiocyanate-propidium iodide flow cytometry. Transwell experiments indicated that this protective effect was dependent on physical contact and the gap junctional communication (GJC) between astrocytes and glioma cells. Microarray expression profiling further revealed that astrocytes upregulated the expression levels of various critical survival genes in the glioma cells via GJC. The results of the present study indicated that the organ microenvironment may affect the biological behavior of tumor cells and suggest a novel mechanism of resistance in glioma cells, which may be of therapeutic relevance clinically.

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