LYSATES OF GLIOMA CELLS, GLIOMA-CONDITIONED OR NORMAL ASTROCYTES DIFFERENTLY INFLUENCE DENDRITIC CELL FUNCTION

Introduction: The main goal of this research was to study the diverse influence of rat glioma, glioma-conditioned (reactive) and normal astrocyte cell lysates on the immunogenicity level of lysate-pulsed dendritic cells.
Materials and methods: Astrocyte conditioning was achieved by indirect co-culturing of rat astrocytes with C6 glioma cells. Cell lysates were prepared from conditioned astrocytes, glioma cells, and normal rat astrocytes and were used separately to pulse dendritic cells derived from rat splenic mononuclear fraction. Dendritic cells were then administered subcutaneously to rats. The immune response was assessed by measuring serum interferon-γ (IFN-γ) levels and levels of cytokines produced by splenic mononuclear cells of immunized rats. Antigen concentrations in lysates and cytokine concentrations in culture medium supernatants were defined by ELISA. Dendritic cell immunophenotype was defined by flow cytometry.
Results: Glial fibrillary acidic protein (GFAP) and connexin 43 (Cx43) concentrations in lysates differed between the groups, with the highest values in reactive astrocytes. Immunophenotyping revealed no significant difference between percentage of CD83 and CD86-positive cells in all groups but showed that significantly less cells pulsed with lysates of reactive astrocytes exposed CD11b/c in comparison with other groups. Conversely, dendritic cells pulsed with lysates of reactive astrocytes secreted the highest amount of interleukin (IL)-12.
The serum level of IFN-γ in rats was the highest after administration of glioma cell lysate-pulsed dendritic cells with no difference between groups of dendritic cells pulsed with either of two astrocytic lysates. After injections of reactive astrocyte lysate-pulsed dendritic cells, lower IFN-γ and higher IL-10 production by mononuclear cells was detected in comparison with glioma lysate pulsing group.
Conclusion: Despite promoting IL-12 secretion, lysates of glioma-conditioned reactive astrocytes induced less marked dendritic cell maturation and immunogenicity in vivo than lysates of glioma cells or astrocytes.
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Keywords : dendritic cells, immunogenicity, glioma, reactive astrocytes, co-culture
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