

## ABSTRACT

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Immunological features in de novo and recurrent glioblastoma associate with survival outcomes.

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Glioblastoma (GBM) is an immunologically "cold" tumor characterized by poor responsiveness to immunotherapy. Standard-of-care for GBM is surgical resection followed by chemoradiotherapy and maintenance chemotherapy. However, tumor recurrence is the norm, and recurring tumors are found frequently to have acquired molecular changes (e.g. mutations) that may influence their immunobiology. Here, we compared the immune contexture of de novo and recurrent GBM (rGBM) using high-dimensional cytometry and multiplex immunohistochemistry. Although myeloid and T cells were similarly abundant in de novo and rGBM, their spatial organization within tumors differed and was linked to outcomes. In rGBM, T cells were enriched and activated in perivascular regions and clustered with activated macrophages and fewer regulatory T cells. Moreover, higher expression of phosphorylated STAT1 by T cells in these regions at recurrence was associated with a favorable prognosis. Together, our data identify differences in the immunobiology of de novo and rGBM and identify perivascular T cells as potential therapeutic targets.

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