Sequestration of T cells in bone marrow in the setting of glioblastoma and other intracranial tumors

T cell dysfunction contributes to tumor immune escape in patients with cancer and is particularly severe amidst glioblastoma (GBM). Among other defects, T cell lymphopenia is characteristic, yet often attributed to treatment. Shohei Koyama (Department of Respiratory Medicine and Clinical Immunology, Graduate School of Medicine, Osaka University) and the researchers of Harvard University, Duke University, and the John Hopkins University reveal that even treatment-naïve subjects and mice with GBM can harbor AIDS-level CD4 counts, as well as contracted, T cell–deficient lymphoid organs. Missing naïve T cells are instead found sequestered in large numbers in the bone marrow. This phenomenon characterizes not only GBM but a variety of other cancers, although only when tumors are introduced into the intracranial compartment. T cell sequestration is accompanied by tumor-imposed loss of S1P1 from the T cell surface and is reversible upon precluding S1P1 internalization. In murine models of GBM, hindering S1P1 internalization and reversing sequestration licenses T cell–activating therapies that were previously ineffective. Sequestration of T cells in bone marrow is therefore a tumor-adaptive mode of T cell dysfunction, whose reversal may constitute a promising immunotherapeutic adjunct.

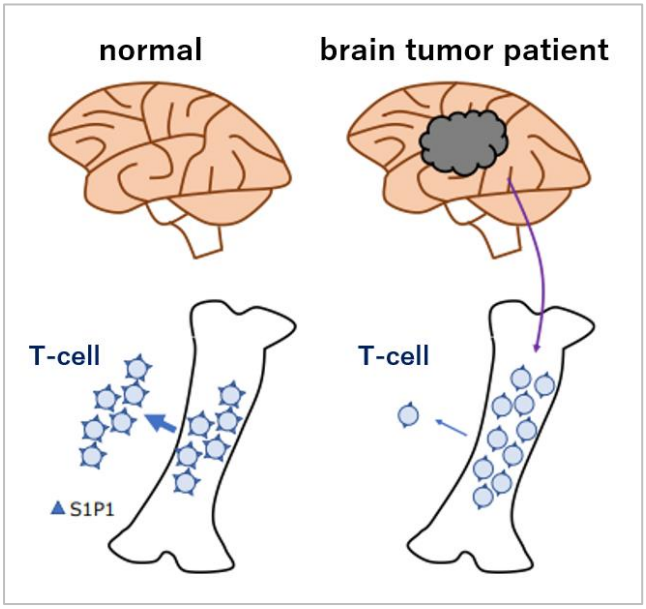

Figure: The brain tumor prevents the migration of T lymphocytes from the bone marrow.
In a patient with a brain tumor (R), T lymphocytes cannot get out from the bone marrow.

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