Background: Telomerase (TERT) emerges as an attractive target for immunotherapy in glioblastoma (GBMs), the most common primary brain tumor in adults. High prevalence (~40%) of activating mutations in TERT promoter was found in GBMs. Our aim was to analyze the spontaneous CD4 Th1 response against TERT in patients with GBMs.

Methods: Thirty-seven GBM patients were analyzed in this study. The anti-TERT Th1 response was measured by IFN-γ ELISPOT assay after in vitro stimulation of blood lymphocytes with Th1 epitopes derived from TERT. Peptides mixture derived from Wilms tumor 1 (WT1) was used as second model of GBM-associated tumor antigen. The recall of the antiviral response was also evaluated for each patient by IFN-γ ELISPOT assay. Regulatory T cell (Treg) [CD4+CD25+CD127lowFoxP3+] and monocytic myeloid-derived suppressor cells (M-MDSC) [Lin−HLA-DRhiCD11b+CD14+CD33+] were measured in blood by flow cytometry. TERT promoter mutations (C228T and C250T) were analyzed on brain tumor using DNA sequencing.

Results: The spontaneous anti-TERT Th1 response was detected in 43.2% (16/37) of GBM patients, and 58.1% patients had anti-WT1 Th1 response. A strong correlation was observed between these two antitumor immune responses. However, there was no correlation between the antitumor immunity and the anti-viral response detected in most patients (91%). We found that the frequency of anti-TERT Th1 response decreased in patients exhibiting high circulating level of Treg and M-MDSC. In contrast to anti-WT1 Th1 response, the anti-TERT Th1 response appeared to be positively associated with patients’ overall survival (OS). Interestingly, this association was more pronounced, but non-significant, when focusing on GBM patients exhibiting TERT promoter mutations (median OS: 33.6 vs 16.3 months, in anti-TERT Th1 responders and non-responders respectively).

Conclusions: We report the presence of spontaneous anti-TERT Th1 response in blood of patients with GBM. This response tends to increase patients’ OS suggesting its involvement in GBM immunosurveillance. These results strongly support the rational to develop immunotherapy targeting telomerase in glioblastoma.

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