TNFR2-targeting peptide for cancer immunotherapy

There is compelling evidence that tumor necrosis factor receptor type II (TNFR2) is preferentially expressed by highly immunosuppressive CD4+Foxp3+ regulatory T cells (Tregs), especially those present in tumor-infiltrating lymphocytes (TILs). These findings led us and others to propose and experimentally proved that targeting TNFR2 with antibodies could induce anti-tumor immune responses. In this study, we identified a TNFR2-targeting peptide P20 through phage display. P20 had in vitro activity to block TNF-TNFR2 interaction and inhibit TNFR2-mediated activation/expansion of Treg cells. The in vivo effect of P20 on tumor growth was examined with mouse tumor models including CT26 colon cancer and OVA-EG7 lymphoma. The results showed that the treatment with P20 (i.p.) resulted in a marked inhibition of tumor growth, accompanied by a reduced number of Tregs and an increased number of IFN-γ+ CD8+ cytotoxic T lymphocytes in the tumor microenvironment. Furthermore, P20 could markedly enhance the efficacy of anti-PD-L1 in the inhibition of tumor growth in a syngeneic MC38 mouse colon cancer model. Thus, P20 may be a useful anti-tumor immunotherapeutic agent and merits further investigation.