THE JOURNAL OF IMMUNOLOGY

Reporter Cell Lines

HOME | ABOUT | SUBMIT | AUTHOR INFO | ARCHIVE | SUBSCRIBE | PERMISSIONS | ADVERTISE |

Institution: NSTL China Trial

The Journal of Immunology, 2013, 190, 53.26
Copyright © 2013 by The American Association of Immunologists, Inc.

53.26

TNF signaling drives myeloid-derived suppressor cell accumulation (P2051)

Zhihai Qin[1]

[1]Institute of Biophysics, CAS, Beijing, China

TNF, an inflammatory cytokine that is enriched in the tumor microenvironment, promotes tumor growth and subverts innate immune responses to cancer cells. We previously reported that tumors implanted in TNF receptor-deficient (Tnfr-/-) mice are spontaneously rejected; however, the molecular mechanisms underlying this rejection are unclear. Here we report that TNF signaling drives the peripheral accumulation of myeloid-derived suppressor cells (MDSCs). MDSCs expand extensively during inflammation and tumor progression in mice and humans and can enhance tumor growth by repressing T cell-mediated antitumor responses. Peripheral accumulation of MDSCs was drastically impaired in Tnfr-/- mice. Signaling of TNFR-2, but not TNFR-1, promoted MDSC survival through upregulation of cellular FLICE-inhibitory protein (c-FLIP) and inhibition of caspase-8 activity. Loss of TNFRs impaired the induction of MDSCs from bone marrow cells, but this could be reversed by treatment with caspase inhibitors. These results demonstrate that TNFR-2 signaling promotes MDSC survival and accumulation and helps tumor cells evade the immune system.