**Background** Tumor endothelial cells (TECs) play a crucial role in the development and progression of cancer. TECs also play a role in the way cancer cells interact with and evade the immune system. Targeting TECs with specific therapies has the potential to greatly impact the treatment of cancer by stopping the growth of new blood vessels and improving infiltration and the effectiveness of immunotherapies. The presence of CD8 T cells in several cancer types is associated with better clinical outcomes and while we know that homing receptor ligands (HRL) in the vasculature regulate entry into tumors, the factors that control their local expression are incompletely characterized.

**Methods** To distinguish the regulatory role of pro-inflammatory cytokines (IFNγ and TNFα) in endothelial cells from tumor (TEC) and normal tissues (EC) and its antagonism by the angiogenic factors VEGF and FGF2, we evaluated expression of VCAM-1, ICAM-1, and the chemokines CXCL9 and CXCL10 in cell lines and specific knock out mice in vitro, in vivo, and ex vivo using mainly flow cytometry, immunofluorescence, western blot, and qPCR.

**Results** Consistent with other studies, we found that TNFα alone upregulated VCAM-1 and ICAM-1, and IFNγ alone upregulated CXCL9 in 3 long-term murine EC lines. In contrast, we found that in TEC from B16F1OVA tumors implanted in either IFNγ KO and TNFα receptor KO mice, expression of these HRL was substantially decreased, demonstrating co-dependence on both signaling pathways. In TECs isolated and cultured ex vivo with combination of cytokines, we found that the sustained expression of HRL required IFNγ and TNFα dual treatment. Surprisingly, VEGF had little effect on either cytokine-driven expression of any of these HRL while FGF2 was strongly inhibitory, and dual treatment partially reversed this restriction. Additionally, it compensated the impact of decreased expression of specific transcription factors in TECs. Furthermore, trends in vivo also imply an improved HRL expression in TECs of dual-treated tumors.

**Conclusions** These results demonstrate the complexity of HRL expression in TEC (inadequately recapitulated by EC lines) and that some individual pathways are actively suppressed in tumors. In the long term, a better understanding of these mechanisms will directly lead to improved effectiveness of cancer immunotherapies.

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