

Natural killer (NK) cells are classically associated with immune surveillance and destruction of tumor cells. Consistent with this finding, NK cells cultured under hypoxia demonstrated limited cytotoxicity capacity, but augmented production of vascular endothelial growth factor (VEGF). Gene expression analysis revealed that angiogenic and inflammatory genes were significantly increased for RCC TiNK versus RCC pNK populations, with enrichment of genes in the hypoxia inducible factor (HIF) 1 pathway. NK cells with non-classical phenotypes (CD56+CD16dim/neg; termed decidual NK (dNK) cells) accumulate at the maternal-fetal interface during embryo implantation. As similarities between embryo implantation and tumor growth exist, we tested the hypothesis that an analogous shift in NK cell phenotype and function occurs in RCC tumors.