TISSUE-SPECIFIC ANTI-TUMOR NK CELL ACTIVATION & EFFECTOR FUNCTIONS

Zerick Dunbar*, Anil Shanker. *Meharry Medical College, Nashville, TN, United States*

Background Natural killer (NK) cells play significant roles in cancer immunity largely due to their direct cytolytic and indirect immune regulatory functions. Clinical studies have demonstrated the role of NK cells in controlling cancer. The number of infiltrating NK cells in tumor tissues has also been shown to be a significant relation to cancer prognosis. However, NK cells have yet to be fully harnessed in immunotherapy partially due to the extensive heterogeneity and plasticity seen among them. For example, the origin, phenotype, and functions of tissue-resident vs circulating NK cells remains controversial. The objective of this study is to elucidate NK cell activation and effector function diversity in solid lung and breast tumor microenvironments. We hypothesize that NK cells from different tissue locations display unique genetic and functional profiles that can predict NK effectiveness in these solid tumor microenvironments. Here, we show the biological diversity that exists among NK cells from distinct locations plus and minus interaction with solid lung and breast murine tumors.

Methods We include the heterogeneity of NK cell specific cluster of differentiation markers and gene expression perspectives based on flow cytometry, qPCR, cytotoxicity, and bioinformatics analyses in conjunction with C57BL/6 $\pm$ LL/2 and BALB/c $\pm$ 4T1.2-HA mouse tumor models, respectively.

Results Thus far we see significant varied expression of the activating and costimulatory NKG2D receptor both across tissue locations and in response to these solid tumors in vivo and ex vivo. We also see varied cytotoxicity and tumor infiltration of NK cells from different tissue locations.

Conclusions Understanding NK cells in solid tumor microenvironments will help answer critical NK cell research questions and lead to advancements in NK-based cancer immunotherapy applications, ultimately helping to mitigate discrepancies between resources applied towards cancer treatment and patient outcomes.

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