Dissecting NK Cell Profiles at Single Cell Resolution: A Comparative Transcriptomic Analysis Across Liver, Spleen, Bone Marrow, and Peripheral Blood

George, Anjali (School: University School of Milwaukee)

Natural Killer (NK) cells are an essential component of innate host defense against Hepatocellular Carcinoma (HCC). A central determinant of NK cell function is their tissue residency. I hypothesized that comparing the gene expression profiles (GEP) of NK cells in the peripheral blood (PB), bone marrow (BM), and spleen with NK cells in healthy as well as HCC liver will delineate their functional differences and therapeutic potential against HCC. Leveraging single-cell RNA-sequencing data, we analyzed the transcriptional profiles of NK cell subsets across the liver, spleen, bone marrow, and peripheral blood. Concurrently, the gene expression profiles (GEP) of NK cells in healthy and HCC livers were compared. Eight distinct NK cell clusters were identified, reflecting differences in phenotype and maturity. GNLY, a cytolytic marker, was upregulated in PB and BM NK cells compared to healthy liver and spleen NK cells. The checkpoint gene LAG3 was upregulated in healthy liver NK cells compared to PB, BM, and splenic NK cells. Numerous Immediate Early Genes (IEGs) were differentially upregulated in splenic NK cells. Additionally, various immunoglobulin chains were upregulated in healthy liver NK cells compared to HCC liver, suggesting a unique phenotype, while checkpoint genes TIGIT and CD96 were upregulated in HCC liver NK cells compared to those in healthy liver. The functional significance of differences in GEP noted between PB, BM and tissue-resident NK cells merit further exploration to elucidate their differential roles in modulating host immune response. Furthermore, the upregulation of checkpoint genes - TIGIT and CD96 - in HCC liver NK cells suggests promising therapeutic opportunities for NK cell immune modulation in HCC.

Awards Won: