CD38 Identifies a Subset of Natural Killer Cells With Differential Phenotype and Function

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Natural killer (NK) cells are involved in surveillance and killing of tumor cells. Although classically part of innate immunity, I and others have identified a subset of NK cells with adaptive properties that are present in many healthy individuals, which are longer lived and possess enhanced antitumor activity. Studies have previously identified that adaptive NK cells express lower levels of CD38. Therefore, I hypothesize that CD38 regulates NK cell function. To study the functionality of these cells, I compared the activation of NK cells with low CD38 expression (putative adaptive NK cells) vs those with high CD38 expression (i.e. canonical NK cells) present in healthy blood donors. I used flow cytometry to measure NK cell degranulation by CD107a staining and cytokine production (IFN-γ and TNF) when co-cultured with leukemia (K562) and lymphoma (Raji +/- rituximab) tumor target cells. I also measured the expression of perforin and granzyme b, proteins involved in direct tumor cell killing. I found that CD38 low/negative NK cells express higher levels of granzyme b, but lower levels of performance. This subset also demonstrated decreased activation markers when co-cultured with tumor cells. Future studies aim to characterize other modes of NK cell activation, phenotype, and tumor cell killing using NK cells with varying expression of CD38.