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Identification and Cytolytic Function of a Novel NK Cell Surface Receptor that Binds Haymaker on the K562 Leukemia Cell Line

Natural killer lymphocytes (NK cells) are the first line of defense (innate immunity) against viral infections and cancer since they do not require activation to deliver a lethal hit to infected/aberrant cells. In contrast, T lymphocytes require stimulation by a foreign/neo-antigen, which may take days before they are active against the pathogen (adaptive immunity). Although numerous NK cell receptor-coreceptors (ligands) have been revealed, the exact mechanism by which unstimulated (naive) nNK cells lyse the prototypical leukemia target cell line (K562) has not been fully characterized. I identified the nNK cell receptor that interacts with the Haymaker (HYMKR) ligand on K562 cells. Our laboratory previously determined that HYMKR is the translocase of the outer membrane of mitochondria (TOMM40). Pull-down experiments with HYMKR polypeptide affinity resins, peptide sequencing, and flow cytometry results provided evidence that moesin is the nNK cells receptor for the HYMKR ligand. Moesin is a protein that typically links the inner leaf of the plasma membrane to the cytoskeleton; additionally, in nNK cells, it localizes to the cell surface, where it binds to HYMKR on leukemia cells. Moesin was not found on the surface of freshly isolated unstimulated T lymphocytes from healthy subjects and is, therefore, a marker that distinguishes unstimulated NK cells from unstimulated T cells.