Natural Killer Cells dependent inhibition by MHC I molecules

Natural Killer (NK) cells are bone marrow derived lymphocytes, widely distributed both in lymphoid and non-lymphoid tissues. They constitute 5-10% of the lymphocyte population. NK cells play an important role in innate immunity as they can lyse tumor and virally infected cells through the action of perforin and granzymes. NK cells express inhibitory receptors specific for MHC class I molecules. The absence of MHC class I molecules on target cells lead to activation of NK cells, i.e. the NK cells are not inhibited, which can lead to the elimination of cells with low or no expression of MHC class I molecules.

In my project I used TAP deficient tumor cells. Cells that lack TAP molecules cannot load peptides efficiently, resulting in "empty", unstable MHC class I molecules which are denatured during transport to or shortly after arrival to the cell surface. Such cells thus have very low levels of MHC class I molecules at the cell surface. It has been shown that MHC class I expression can be increased by incubation of the cells in medium containing specific, MHC class I binding peptides. This result in stabilization of the "empty" MHC molecules, thus rescuing them from falling apart, gradually increasing the steady state expression.

The objective of my study was to optimize a condition where I stabilize the MHC class I molecules of the TAP deficient tumor cells using MHC class I specific peptides and analyze NK cell inhibition by modulating the expression of MHC class I molecules.

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