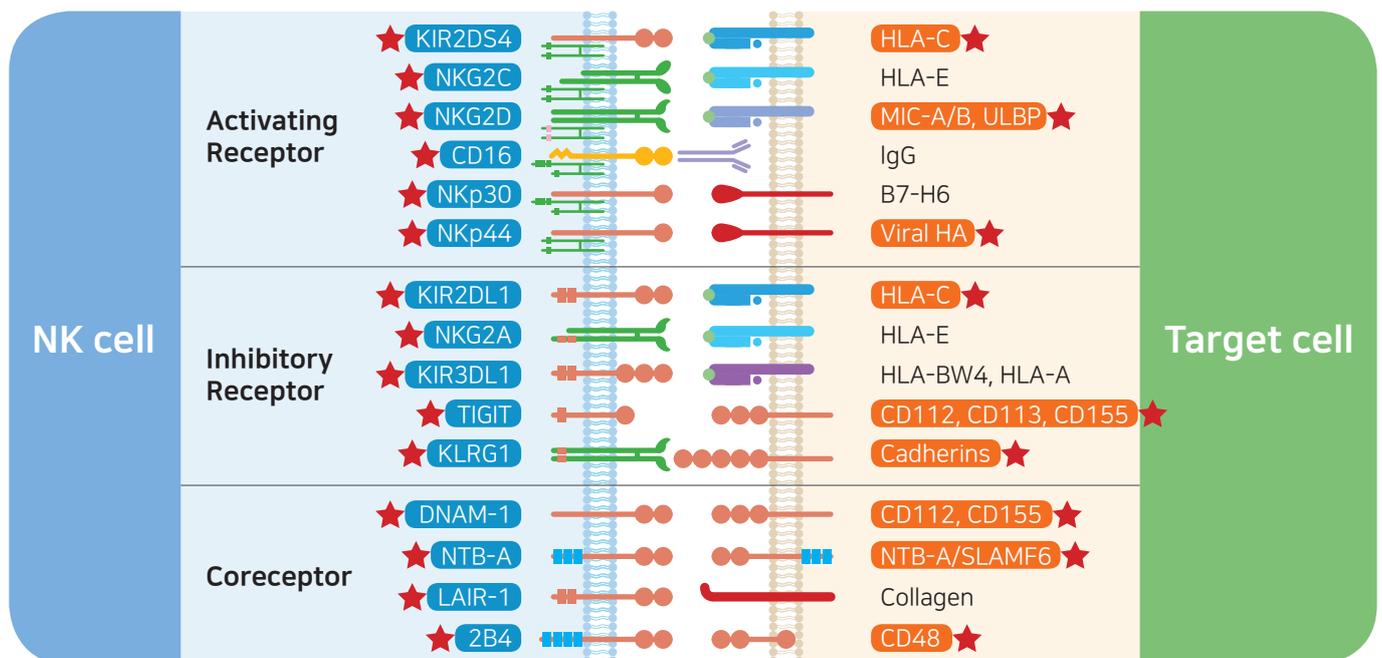


# Natural Killer Cell

Natural Killer (NK) cells are a type of cytotoxic lymphocyte critical to the innate systems that play a key role in the first line of defense against transformed and virus-infected cells. NK cells are now recognized as a separated lymphocyte lineage with both cytotoxicity and cytokine-producing effector functions. NK cells sense their target through a whole array of receptors, both activating and inhibitory. NK cells are unique, as they can discriminate target cell from other healthy 'self' cells and activate to kill cells that are 'missing self' markers of major histocompatibility complex (MHC) class I. This role is especially important because harmful cells that are MHC I marker cannot be detected and destroyed by other immune cells, such as T lymphocyte cells.

## Key Receptors on Human NK cells

The functional outcome of NK cell against the target cell is determined by the balance of signals transmitted from diverse activating and inhibiting receptors. The main activating receptors of NK cell include the cytotoxicity receptor (NCRs; NKp46, NKp30, and NKp44), C-type lectin receptor (CD94/NGK2C, NKG2D, NKG2E/H and NKG2F) and killer cell immunoglobulin-like receptors (KIRs, KIR2DS and KIR3DS), while the inhibitory receptors include C-type lectin receptor (CD94/NGK2A/B) and KIRs (KIR2DL and KIR3DL).

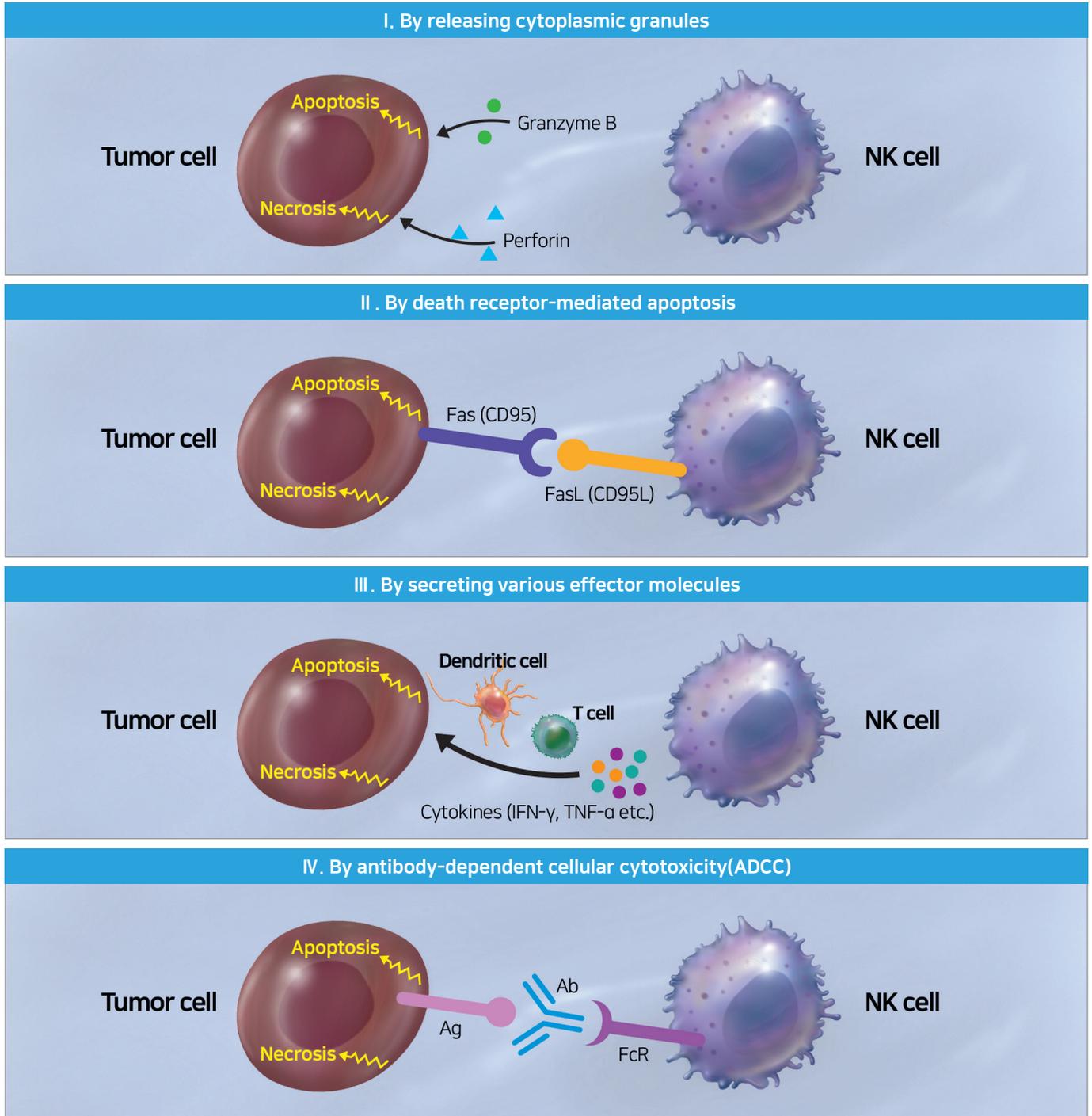


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Also, the intensity and the quality of NK cell cytotoxic and cytokine responses depend on the cytokine microenvironment, as well as on interactions with other cells of the immune system, such as T cells, dendritic cells (DCs) and macrophages. Type I IFN, IL-12, IL-18, and IL-15 are potent activators of NK cell effector function. It is also well known that IL-2 promotes NK cell proliferation, cytotoxicity and, to some extent, cytokine secretion.

## Mechanism

NK cells directly kill target tumor cells through several mechanisms: (i) by releasing cytoplasmic granules containing perforin and granzymes that lead to tumor-cell apoptosis by caspase-dependent and -independent pathways; (ii) by death receptor-mediated apoptosis. Some NK cells express tumor-necrosis factor (TNF) family members, such as FasL or TNF-related apoptosis-inducing ligand (TRAIL), which can induce tumor cell apoptosis by interacting with their respective receptors, Fas and TRAIL receptor (TRAILR), on tumor cells; (iii) by secreting various effector molecules, such as INF- $\gamma$ , that exert antitumor functions in various ways, including restricting tumor angiogenesis and stimulating adaptive immunity; (iv) through antibody-dependent cellular cytotoxicity (ADCC) by expressing CD16 to destroy tumor cell.



## Reference

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