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Cancer Immunotherapy: Chapter 9. Immunological Sculpting: Natural Killer-Cell Receptors and Ligands

Sarah S. Donatelli, Julie Y. Djeu

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Natural Killer (NK) cells are a unique subset of lymphocytes genetically programmed to locate and destroy cellular malignancies. They accomplish this through unique cell surface receptors that, upon contacting a target cell, transmit either inhibitory or activating intracellular signals, ultimately determining whether the target cell will be killed or spared. Acquisition of the capacity to kill comes only after the NK cell is rendered tolerant to healthy self cells through interaction with naturally expressed MHC I molecules. The resulting functional NK cell is endowed with both repressive and stimulatory receptors that recognize MHC I or MHC I-related proteins, and stress-induced proteins that are not normally expressed by healthy cells, respectively. The respective signaling pathways are generally conserved among receptors; consequently, mechanisms that dysregulate NK-cell surface receptor density may directly impair NK responsiveness towards cancerous cells by affecting the ratio of inhibitory-to-activating signals. Furthermore, activating receptors can be downregulated, suggesting a targeted evasion strategy that specifically converts the NK cell towards an inhibitory phenotype.

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