Natural killer (nk) cells in adoptive cell therapy: A new era of cancer treatment.

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Introduction

Cancer remains one of the leading causes of mortality worldwide, necessitating the development of innovative and effective treatment modalities. Adoptive cell therapy (ACT) has emerged as a promising immunotherapeutic strategy, harnessing the body's immune system to fight malignancies. Among the various immune cells employed in ACT, Natural Killer (NK) cells have garnered significant attention due to their potent anti-tumor capabilities and reduced risk of graft-versus-host disease (GVHD). This article explores the role of NK cells in ACT, their advantages over other cell-based therapies, and the future of NK cell-based cancer treatment [1].

Natural Killer (NK) cells are a subset of lymphocytes that play a crucial role in the innate immune response. Unlike T cells, NK cells do not require prior sensitization to recognize and eliminate tumor cells. They exert their cytotoxic effects through several mechanisms, including direct cell lysis via perforin and granzyme release, antibody-dependent cellular cytotoxicity (ADCC), and cytokine production (Caligiuri, 2008). The ability of NK cells to distinguish between normal and malignant cells is governed by a balance between activating and inhibitory receptors [2].

The use of NK cells in adoptive cell therapy presents several advantages: Unlike T cells, NK cells do not rely on antigen-specific T cell receptors, making them safer for allogeneic transplantation. NK cells can target a wide range of tumor types without prior sensitization [3].

NK cells can work synergistically with monoclonal antibodies like Rituximab and Trastuzumab to enhance ADCC. NK cells can be engineered to express chimeric antigen receptors (CARs) to enhance tumor specificity and persistence [4].

NK cells for adoptive therapy can be derived from multiple sources NK cells can be isolated from donor blood and expanded ex vivo. A rich source of naïve NK cells with high proliferative potential [5].

NK cells generated from iPSCs offer a renewable and customizable option for therapy. Genetically modified cell lines, such as NK-92, provide an off-the-shelf alternative. Several clinical trials have demonstrated the efficacy of NK cell-based therapies against hematological malignancies and solid tumors [6].

NK cell therapy has shown promising results in AML patients, leading to durable remission. The combination of NK cells with monoclonal antibodies enhances tumor clearance. Challenges such as the immunosuppressive tumor microenvironment are being addressed through genetic modifications and combination therapies [7].

Despite their potential, NK cell-based therapies face several challenges: Enhancing NK cell survival and proliferation in vivo is critical for sustained therapeutic effects [8].

The immunosuppressive nature of solid tumors hinders NK cell function, necessitating strategies to enhance infiltration and activity. While CAR-T cells have demonstrated success, optimizing CAR-NK cells for improved persistence and specificity is an ongoing area of research [9].

As advancements in NK cell expansion, persistence, and engineering continue, NK cell therapy is poised to revolutionize cancer treatment, offering hope to patients with refractory malignancies [10].

Conclusion

NK cell-based adoptive cell therapy represents a promising frontier in cancer treatment. Their innate cytotoxic capabilities, reduced GVHD risk, and potential for genetic modifications make them an attractive option for immunotherapy.

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