Natural killer cells

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Natural killer cells are a type of white blood cell that plays a crucial role in the innate immune system, which is the body's first line of defense against infections and cancer. NK cells are unique because they can recognize and destroy infected cells and cancer cells without prior exposure or activation, unlike other immune cells that require prior sensitization.

Natural killer (NK) cells are immune cells that attack cancer cells directly and produce antitumor immunity-related cytokines.

The adoptive transfer of expanded and activated natural killer (NK) cells is a form of immunotherapy in which NK cells are isolated from a patient or a donor, expanded or activated in the laboratory, and then infused back into the patient. This approach is being investigated for its potential in cancer treatment and other medical conditions.

Here's how the process typically works:

Isolation of NK Cells: NK cells can be collected from the patient's own blood (autologous) or from a donor (allogeneic). Donor-derived NK cells are often used when there is a need for a larger quantity of NK cells or when the patient's own NK cells are not sufficiently active against the disease.

Expansion and Activation: The isolated NK cells are cultured and expanded in the laboratory to increase their numbers. During this process, they may also be activated to enhance their cytotoxic (cell-killing) abilities. Various techniques, such as cytokine stimulation or genetic modification, can be used to activate and expand NK cells.

Quality Control: The expanded and activated NK cells undergo rigorous quality control testing to ensure their safety and efficacy. This includes checking for cell purity, viability, and functionality.

Infusion: Once the expanded and activated NK cells meet quality standards, they are infused back into the patient through intravenous (IV) administration. This infusion typically takes place in a clinical setting, such as a hospital or a specialized treatment center.

Monitoring and Follow-Up: After the infusion, patients are closely monitored for any adverse reactions and to assess the therapeutic effects. Follow-up assessments may include blood tests, imaging studies, and clinical evaluations.

The goal of adoptive NK cell transfer is to harness the potent cytotoxic abilities of NK cells to target and destroy cancer cells or other disease-related cells. NK cells are known for their ability to recognize and attack abnormal cells without the need for prior sensitization, making them attractive candidates for immunotherapy.

This approach is an active area of research and clinical trials, and its effectiveness is being studied in various cancer types and other diseases, including hematological malignancies, solid tumors, and infectious diseases. The field of NK cell-based immunotherapy continues to advance, and it holds promise as a potential treatment option for patients who may not respond well to conventional therapies.

The adoptive transfer of expanded and activated NK cells is expected to be a promising glioblastoma immunotherapy. Maeoka et al. previously established an efficient expansion method that produced highly purified, activated primary human NK cells, which they designated genuine induced NK cells (GiNKs). The GiNKs demonstrated antitumor effects in vitro and in vivo, which were less affected by blockade of the inhibitory checkpoint receptor programmed death 1 (PD-1). They assessed the antitumor effects of GiNKs, both alone and combined with an antibody targeting killer Ig-like receptor 2DLs (KIR2DL1 and DL2/3, both inhibitory checkpoint receptors of NK cells) in vitro and in vivo with U87MG GBM-like cells and the T98G GBM cell line. Impedance-based real-time cell growth assays and apoptosis detection assays revealed that the GiNKs exhibited growth inhibitory effects on U87MG and T98G cells by inducing apoptosis. KIR2DL1 blockade attenuated the growth inhibition of the cell lines in vitro. The intracranial administration of GiNKs prolonged the overall survival of the U87MG-derived orthotopic xenograft brain tumor model. The KIR2DL1 blockade did not enhance the antitumor effects; rather, it attenuated it in the same manner as in the in vitro experiment. GiNK immunotherapy directly administered to the brain could be a promising immunotherapeutic alternative for patients with GBM. Furthermore, KIR2DL1 blockade appeared to require caution when used concomitantly with GiNKs [1)].

Key characteristics and functions

Surveillance and Defense: NK cells continuously patrol the body, scanning for cells that display abnormal proteins on their surface. This includes cells infected with viruses, bacteria, or other intracellular pathogens, as well as cancer cells. When they identify such abnormal cells, NK cells can initiate a rapid response to eliminate them.

Lack of Specificity: Unlike T cells and B cells of the adaptive immune system, NK cells do not have receptors specific to a particular antigen (molecule). Instead, they recognize a broad range of abnormal or “stressed” cells by assessing the balance of activating and inhibitory signals on the target cell's surface. Healthy cells typically display inhibitory signals that prevent NK cell attack, while infected or cancerous cells may have reduced inhibitory signals and/or increased activating signals.

Immune Response Regulation: NK cells help regulate the immune response by releasing cytokines and chemokines that can influence the activity of other immune cells. They can also enhance or dampen the immune response depending on the context.

Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC): NK cells can also participate in antibody-mediated immune responses. They can recognize antibodies bound to target cells and induce their destruction through a process known as ADCC.

Role in Pregnancy: NK cells play a unique role in maintaining a healthy pregnancy. They help in regulating the growth and development of the placenta and are involved in the implantation process. Abnormalities in NK cell function have been associated with certain pregnancy complications.

Immunotherapy: NK cells have been investigated for their potential in cancer immunotherapy. Techniques such as adoptive NK cell therapy involve isolating and expanding NK cells from a patient's own or a donor's blood, which can then be infused back into the patient to target and destroy cancer cells.

In summary, natural killer cells are a critical component of the innate immune system, serving as a rapid and versatile defense against infected cells and cancer. Their ability to recognize and eliminate abnormal cells makes them essential in maintaining overall health and immune surveillance. Researchers continue to study NK cells and their potential applications in various aspects of medicine, including cancer treatment and immunotherapy.

Natural killer cells safeguard against early tumor formation by destroying transformed target cells in a process referred to as NK immune surveillance. However, the immune escape mechanisms used by malignant brain tumors to subvert this innate type of immune surveillance remain unclear.

Natural killer (NK) cells are innate lymphoid cells with robust antitumor functions rendering them promising therapeutic tools against malignancies. Despite constituting a minor fraction of the immune cells infiltrating tumors in the brain, insights into their role in central nervous system (CNS) pathophysiology are emerging. The challenges posed by a profoundly immunosuppressive microenvironment as well as by tumor resistance mechanisms necessitate exploring avenues to enhance the therapeutic potential of NK cells in both primary and metastatic brain malignancies. In a review, Balatsoukas et al. summarized the role of NK cells in the pathogenesis of tumors in the brain and discuss the avenues investigated to harness their anticancer effects against primary and metastatic CNS tumors, including sources of therapeutic NK cells, combinations with other treatments, and novel engineering approaches for augmenting their cytotoxicity. We also highlight relevant preclinical evidence and clinical trials of NK cell-based therapies [2].

1)
Maeoka R, Nakazawa T, Matsuda R, Morimoto T, Shida Y, Yamada S, Nishimura F, Nakamura M, Nakagawa I, Park YS, Tsujimura T, Nakase H. Therapeutic Anti-KIR Antibody of 1-7F9 Attenuates the Antitumor Effects of Expanded and Activated Human Primary Natural Killer Cells on In Vitro Glioblastoma-like Cells and Orthotopic Tumors Derived Therefrom. Int J Mol Sci. 2023 Sep 16;24(18):14183. doi: 10.3390/ijms241814183. PMID: 37762486; PMCID: PMC10531877.
2)
Balatsoukas A, Rossignoli F, Shah K. NK cells in the brain: implications for brain tumor development and therapy. Trends Mol Med. 2022 Jan 22:S1471-4914(21)00325-7. doi: 10.1016/j.molmed.2021.12.008. Epub ahead of print. PMID: 35078713.