KIR2DL1

KIR2DL1 (Killer Cell Immunoglobulin-like Receptor 2DL1) is a type of cell surface receptor found on natural killer (NK) cells, a subset of white blood cells that are part of the immune system. KIR2DL1 belongs to a family of receptors known as killer cell immunoglobulin-like receptors (KIRs). These receptors play a crucial role in regulating the activity of NK cells.

KIR2DL1 is known for its ability to recognize and interact with specific molecules on the surface of target cells. In particular, KIR2DL1 binds to human leukocyte antigen-C (HLA-C) molecules that carry a specific subset of HLA-C alleles known as HLA-C2. The interaction between KIR2DL1 and HLA-C2 helps NK cells distinguish between healthy cells and cells that may be infected with viruses or transformed into cancer cells.

Here's how KIR2DL1 works:

Recognition of HLA-C2: KIR2DL1 recognizes and binds to HLA-C2 molecules expressed on the surface of various cells in the body, including both healthy and abnormal cells.

Inhibition of NK Cell Activity: When KIR2DL1 binds to HLA-C2 on healthy cells, it delivers an inhibitory signal to the NK cell. This signal prevents the NK cell from attacking the healthy cell, maintaining immune tolerance and preventing the immune system from attacking the body's own cells.

Activation in the Presence of Abnormal Cells: In the presence of cells that have reduced or altered HLA-C2 expression (such as virus-infected cells or cancer cells), the inhibitory signal from KIR2DL1 is weaker or absent. This reduction in inhibition allows NK cells to become activated and target the abnormal cells for destruction.

The balance of inhibitory and activating signals mediated by KIR2DL1 and other KIR receptors helps NK cells identify and eliminate cells that pose a threat to the body while sparing healthy cells.

KIR2DL1 and other KIR receptors play a crucial role in immune surveillance and the regulation of NK cell activity. Variations in KIR genes and their interactions with HLA molecules can influence an individual's immune response and susceptibility to various diseases, including viral infections and certain types of cancer. Understanding the genetics and function of KIR receptors like KIR2DL1 is important for studying immune responses and developing therapies, especially in the context of immunology and transplantation medicine.

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].

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.