Killer Cell Immunoglobulin-Like Receptor (KIR) Immune Pathway

About KIR

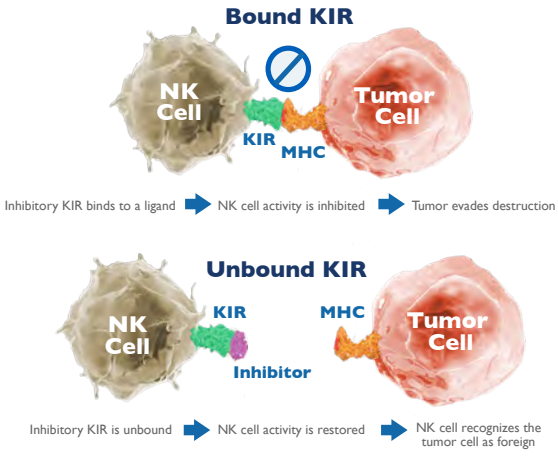
Inhibitory killer cell immunoglobulin-like receptors (KIRs) are immune checkpoint receptors expressed on the surface of natural killer (NK) cells and cytotoxic T cells.[1,2] NK cells and T cells are a type of white blood cell that are part of the immune system. Activation of these cells enables them to kill unhealthy or foreign cells.[1,2]

Involvement in regular immune function

- KIRs are an important regulatory component of the immune system.[1]
- On NK cells, KIRs mediate recognition of healthy cells through interactions with the major histocompatibility complex I (MHC I) on the surface of most healthy cells. This interaction informs the NK cells that the cell is healthy and should not be destroyed.[1]
- Most KIRs are inhibitory, meaning they suppress the killing activity of NK cells so they don't attack healthy cells.[1]

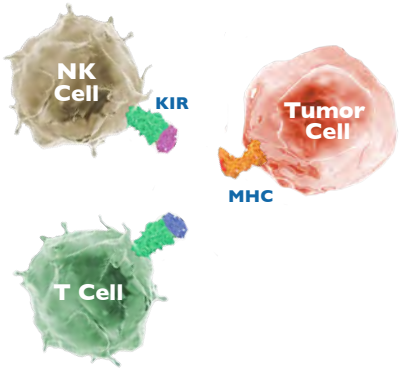
Hypothesis for involvement in tumor growth

- Tumors have developed mechanisms to hide from immune system detection by mimicking the MHC I profile of a healthy cell. This process allows tumor cells to evade NK cell-mediated recognition and destruction.[1,3]
- In preclinical studies, blockade of inhibitory KIRs has been shown to help restore NK cell-mediated immune activity which can help NK cells recognize tumor cells.[4,5]



Interaction with other pathways

- Preclinical studies also suggest that targeting the KIRs pathway in combination with other immune pathways may be a key strategy to more effectively activate the antitumor immune response by targeting two complementary tumor immune escape mechanisms.[6]



The KIR pathway is just one of many immune pathways under investigation at Bristol-Myers Squibb. Learn more about our work in Immuno-Oncology by visiting:
www.immunooncology.bmsinformation.com

[1] Campbell KS, Purdy AK. Structure/function of human killer cell immunoglobulin-like receptors: lessons from polymorphisms, evolution, crystal structures and mutations. Immunology. 2011;132(3):315-325.
[2] Björkström NK, Béziat V, Cichocki F, et al. CD8 T cells express randomly selected KIRs with distinct specificities compared with NK cells. Blood. 2012;120(17):3455-3465. [3] Carbone E, Neri P, Mesuraca M, et al. HLA class I, NKG2D, and natural cytotoxicity receptors regulate multiple myeloma cell recognition by natural killer cells. Blood. 2005;105:251-258. [4] Waldhauer I, Steinle A. NK cells and cancer immunosurveillance. Oncogene. 2008;27(45):5932-5943. [5] Romagné F, André P, Spee A, et al. Preclinical characterization of 1-7F9, a novel human anti–KIR receptor therapeutic antibody that augments natural killer–mediated killing of tumor cells. Blood. 2009;114(13):2667-2677. [6] Antonia SJ, Larkin J, Ascierto PA. Immuno-Oncology Combinations: A Review of Clinical Experience and Future Prospects. Clin Cancer Res. 2014;20(24):6258-6268.

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