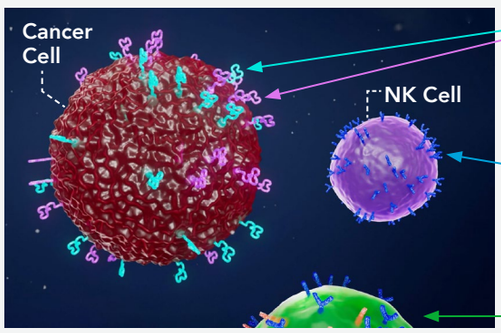
EXPRESSION OF MICA/B

(MHC CLASS I CHAIN-RELATED PROTEIN A and B)

WHAT IS MICA/B?



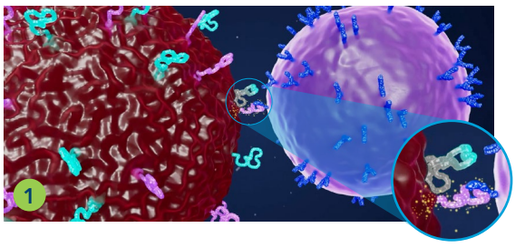
MICA and **MICB** (major histocompatibility complex class I chain-related molecule A and B) are surface proteins that are expressed on many solid tumors and hematological malignancies with limited expression on normal tissue.[1]

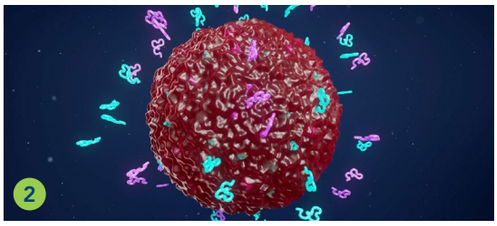
NKG2D (natural killer group 2 member D) ligands, like MICA/B, are upregulated when a cell is stressed or damaged allowing for recognition by NKG2D-expressing cytotoxic immune cells, such as NK and certain subsets of **T cells**.[2]

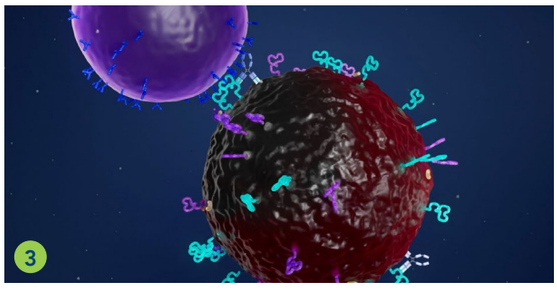
FUNCTION OF MICA/MICB

When MICA or MICB binds to NKG2D-expressing immune cells, a series of intracellular signaling pathways are triggered. This activation results in 1 secretion of cytokines and release of cytotoxic granules containing perforin and granzymes to induce cell death of target cells expressing MICA or MICB.[3]

However, cancer cells have established mechanisms to evade NKG2D-mediated destruction by 2 shedding of MICA/B from their cell surface.[4]







RESEARCH IMPLICATIONS AND INTERACTIONS

Restoring MICA/B on the surface of cancer cells is a novel therapeutic strategy to enable 3 immune-mediated killing of cancer cells, while leaving healthy tissue unharmed.[2,3]

MICA/B is one of the pathways currently being investigated by Cullinan Therapeutics as part of our modality-agnostic, targeted approach to discover and develop molecules with the potential to make a meaningful difference in patients' lives.

Learn more about our research by visiting: https://cullinantherapeutics.com/pipeline

REFERENCES:

1. Zhao Y, Chen N, Yu Y, et al. Prognostic value of MICA/B in cancers: a systematic review and meta-analysis. *Oncotarget*. 2017;8:96384–95.
2. Whalen KA, Rakhra K, Mehta NK, et al. Engaging natural killer cells for cancer therapy via NKG2D, CD16A and other receptors. *MAbs*. 2023;15(1):2208697.
3. Ferrari de Andrade L, Tay RE, Pan D, et al. Antibody-mediated inhibition of MICA and MICB shedding promotes NK cell-driven tumor immunity. *Science*. 2018;359(6383):1537-1542.
4. Xing S, F de Andrade L. NKG2D and MICA/B shedding: a 'tag game' between NK cells and malignant cells. *Clin Transl Immunology*. 2020;9.

Mechanism descriptions are based on pre-clinical data.