

# New therapeutic monoclonal antibody and fragments anti-MICA for cancer treatment

University of Chile has generated a recombinant human antibody and fragment able to neutralize soluble MICA protein and opsonize tumor cells, for treating several types of cancer

## THE CHALLENGE

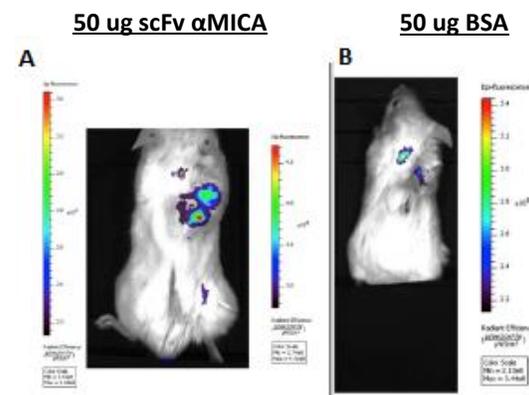
Protein MHC class I polypeptide-related sequence A (MICA) is a danger signal expressed in the surface of several epithelial tumor cells which interacts with the receptor of activation of cytolytic lymphocytes NKG2R. Although initially this interaction has an important role in the control of tumor progression, it later contributes to tumor immune evasion: high levels of soluble and surface MICA negatively regulates NK cell activation, allowing tumor growth. Thus, MICA has become an interesting therapeutic target for cancers expressing this protein.

## THE TECHNOLOGY

**New recombinant human monoclonal antibody and fragments (scFv, Fab) against the ectodomain  $\alpha$  of MICA protein**, derived from a gene library of University of Chile. The antibody and fragments form complexes with soluble MICA, inhibiting its binding to NKG2DR which leaves it free to bind to other ligands present in the tumor cell surface, reverting the NK cell inactivation and improving the immune response to tumors. The antibody would also form complexes with cell surface MICA, activating effector functions of antibodies, activating CDC and inducing ADCC.

## STAGE OF DEVELOPMENT

- **In vitro validation** with tumor cells and recombinant MICA proteins
- **In vivo studies in humanized mouse model for gastric adenocarcinoma (Fig. 1)**
- **Epitope validated with >50 samples of gastric cancer patients**, via massive sequencing analysis
- **Optimized sequence to increase target affinity** – Directed mutagenesis



**Figure 1. Fluorescence emission in NOD-SCID-IL-null mice (NSG) with MKN-45 cell tumors. (A) scFv- $\alpha$ MICA-Dylight 650, 20 min post-inoculation. (B) BSA-Dylight 650, 20 min post-inoculation (control).**

## COMPETITIVE ADVANTAGES

- Unique sequence
- Targets all 92 MICA protein variants
- No crossed-reactivity against MICB

## APPLICATIONS

- Treatment for gastric cancer and other cancers expressing MICA (prostate, breast, lung, etc.)
- Complementary to surgery or other cancer treatments

## OPPORTUNITY

University of Chile is searching for industry partners for **out-licensing** this technology and/or **collaborating** in its further development.

## INTELLECTUAL PROPERTY/REFERENCES

- Chilean patent application 201703503; WO/2018/000105