Introduction

MICA and MICB, along with ULPBs, are ligands for the activating receptor NKG2D expressed on NK cells and subsets of T cells in Human. NKG2D ligands are induced by cellular stress and pathogen infections. Their expression is tightly regulated by complex mechanisms both at the mRNA and protein levels. In the case of MICA and MICB, more than 65 and 30 alleles respectively were described with different properties regarding to their cellular location adding to the complexity of this recognition system. Nevertheless, as markers of cellular stress, in particular in tumorigenesis, MICA and the closely related MICB proteins are candidates of choice to be targeted by a cytotoxic therapeutic antibody.

We have generated a panel of anti-MICA mAbs with diverse functional properties. Ongoing work aims to choose the single antibody with highest ADCC and NKG2D blocking capacity.

Results

MICA is a tumoral antigen

Chemotherapeutic agents upregulate MICA expression

Characterization of new anti-MICA/B monoclonal antibodies

Anti-MICA/B mAbs in vitro efficacy

ADCC

CDC

NGK2D blocking capacity

Anti-MICA/B mAbs in vivo efficacy in xenograft models

Preventive setting (IV model)

Curative setting (SC model)

Conclusions

MICA can be targeted by therapeutic antibodies in cancer

- MICA is specifically expressed on many tumors and not in normal tissues
- Chemotherapeutic agents upregulate MICA expression
- Newly generated anti-MICA mAb display high affinities, are pan-alleles and can mediate direct cytotoxic effect through ADCC and/or CDC and demonstrate in vivo efficacy
- Additional modes of action of anti-MICA mAb are currently investigated including:
  - Neutralization of soluble MICA (direct effect or inhibition of shedding)
  - Restoration of NKG2D expression and function
  - Associated biomarker strategy: MICA expression on tumor, sMICA in serum