PBD-based anti-MICA/B antibody drug conjugate with a dual mechanism of action: direct tumor cell killing and restoration of NKG2D-mediated immunosurveillance

Florence Lhospice1, Stéphanie Cornen1, Laurent Pouyet2, Ester Morgado2, Romain Remark1, Delphine Brégone1, Adeline Montbel1, Nadia Anceriz1, Mathieu Bléry1, Ariane Morel1, Manel Kraiem1, Kenneth Crook1, Yannis Morel1, Eric Vivier1. 1 Innate Pharma, 117 Av de Luminy – 13009 Marseilles, France; 2 MI-MAbs, 117 Av de Luminy-13288 Marseilles, France.

Background

MICA and MICB can be expressed at the surface of a wide variety of tumor cells, while having a limited expression on healthy tissues. This expression pattern makes MICA/B promising targets for the development of antibody drug conjugates (ADC). In addition, MICA and MICB serve as ligands for T cells. As a consequence, the expression of MICA and MICB promotes recognition in vivo. Dual mechanism of action: disrupting the interaction between MICA/B and NKG2D that induces impaired immunosurveillance. Tumor direct targeting and immunoactivation

Anti-MICA/B-PBD is site-specifically conjugated

Anti-MICA/B-PBD is potent against various cell lines

Anti-MICA/B-PBD cures mice in B16.F10-MICA syngeneic melanoma model and protects via tumor-specific immunological memory

MICA/B molecules are attractive targets for an ADC approach based on their selective expression in a wide range of malignancies while showing restricted expression in healthy tissues. The anti-MICA/B-PBD shows efficacy both in vitro and in vivo, paving the path for further evaluation towards clinical development.