Abstract #LB-1320

MOSPD2: A novel target for Bi-specific Ab mediated killing of tumor cells

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BACKGROUND

We have previously described motile sperm domain-containing protein 2 (MOSPD2) as essential for breast cancer metastasis in vitro and in vivo. In this study, we detected high expression of MOSPD2 in different organ tumors and cancer cells, and subsequently developed CD3xMOSPD2 BiTE, a firstly generated bi-specific antibody that directs killing of MOSPD2 expressing cancer cells.

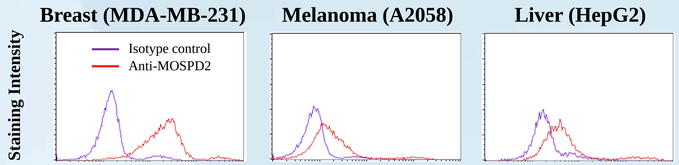
METHODS

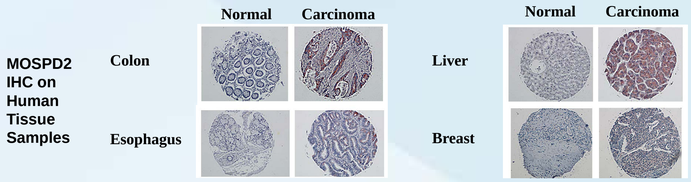
The prevalence of MOSPD2 was evaluated by IHC in tissue microarrays layered with cores, representing multiple organ tumors and normal tissue. Human monoclonal antibody against the extracellular region of human MOSPD2 was generated. To determine the presence of cell surface MOSPD2 expression, FACS analysis was performed on cell lines derived from different tumor origins. BiTE was generated to comprise the scFv region of anti-human CD3 and the scFv region of a human anti-human MOSPD2. Cancer cell lines were co-cultured with freshly isolated T-cells or effector CD8 T-cells in the presence of CD3xMOSPD2. Cancer cell survival rate and T cell activation was determined after 2-3 days by FACS.

RESULTS

MOSPD2 is Expressed on the Surface of Cancer Cells

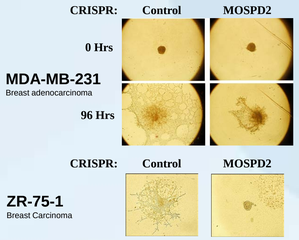
MOSPD2 Cell Surface Staining by FACS



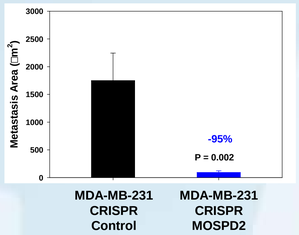


MOSPD2 Promotes Cell Invasiveness in Vitro and In Vivo and Correlates with Invasiveness in Human Tumor Samples

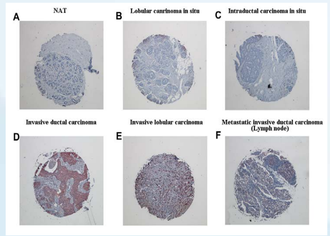
Invasion Assay

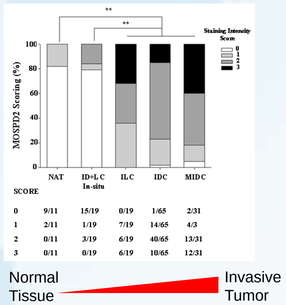


Lung Metastasis in SCID Mice Injected IV with Breast Cancer cells



MOSPD2 Expression is Correlated with Invasiveness in Human Breast Cancer

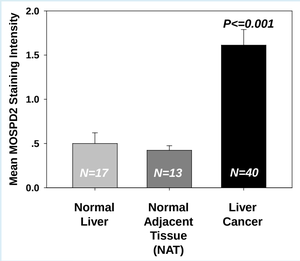


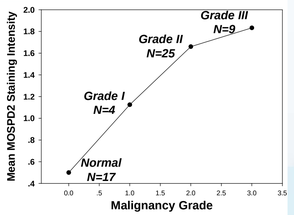


SCORE					
0	9/11	15/19	0/19	1/65	2/31
1	2/11	1/19	7/19	14/65	4/3
2	0/11	3/19	6/19	40/65	13/31
3	0/11	0/19	6/19	10/65	12/31

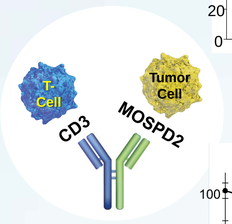
Normal Tissue → Invasive Tumor

IHC staining of Human Liver Samples shows that MOSPD2 Expression is induced In Correlation with Tumor Progression

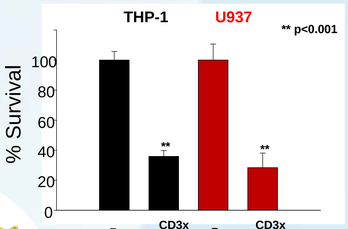




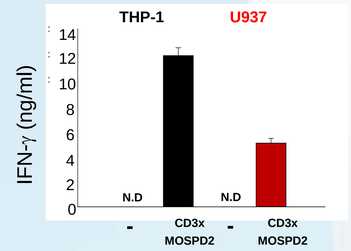
CD3xMOSPD2 Bi-specific Ab mediates Killing of Tumor Cells by T-Cells



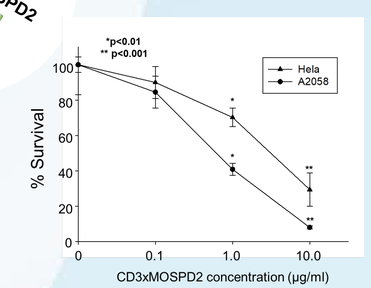
CD3xMOSPD2 Ab mediated killing of Monocytic Cell lines

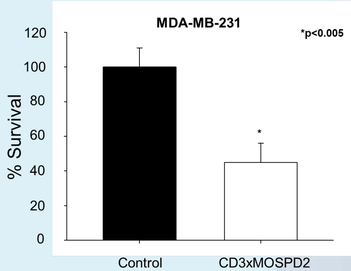


Activation of T-Cell and Secretion of IFN-gamma by the CD3xMOSPD2 Ab



Specific and Dose-dependent Killing of Solid Cancer Cell Lines





CONCLUSIONS

- MOSPD2 is expressed on the surface of multiple tumor cells and promotes tumor cell invasion in vitro and in vivo.
- MOSPD2 expression in human breast cancer and liver cancer specimens shows correlation with tumors progression and invasiveness. Normal tissues show minimal or no expression.
- **Accordingly, MOSPD2 is a novel potential target for the treatment of cancer.**
- **We developed bi-specific antibodies that mediate the killing of myeloid and solid-derived cancer cells by T-cells, and provide proof-of-concept for the therapeutic potential of MOSPD2 as a novel target in oncology.**