



SELECTED OPPORTUNITY IN ONCOLOGY

ANTI-CATHEPSIN D HUMAN ANTIBODY FOR TRIPLE NEGATIVE BREAST
CANCER TREATMENT

(BIO14138 & BIO18300)

Product factsheet

Stage : *in vivo* PoC

▶ Target:

- ◆ Cathepsin D (Cath-D) a ubiquitous, lysosomal, aspartic endoproteinase that is proteolytically active at low pH

▶ Product:

- ◆ Cross reactive (human/murin) Anti-CathD human antibody (hlgG1)

▶ Application:

- ◆ Breast cancer notably TNBC

▶ Rational :

- ◆ Cath-D is overexpressed and abundantly secreted by human epithelial breast cancer cells, with levels which correlates with poor prognosis. → marker of poor prognosis
- ◆ Cath-D affects both cancer and stromal cells in the tumor microenvironment by increasing the proliferation of cancer cells, stimulating fibroblast outgrowth, angiogenesis, and metastasis. → Oncogenic roles of extracellular Cath-D
- ◆ Anti-cath-D autoantibodies have been detected in the early stages of breast, melanoma, ovarian and lung cancers, indicating that cathepsin D released in tumor may be considered as a tumor-associated antigen (TAA)

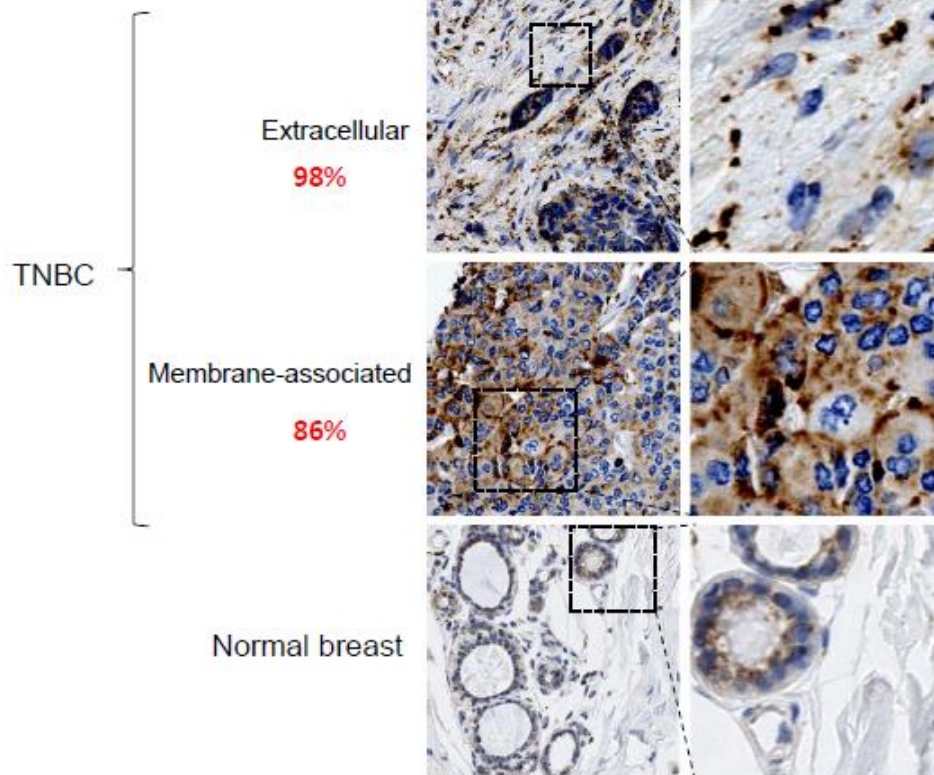
▶ Patent and publication:

- ◆ WO/PCT/EP2016/061454 : HUMAN MONOCLONAL ANTIBODIES FRAGMENTS INHIBITING BOTH THE CATH-D CATALYTIC ACTIVITY AND ITS BINDING TO THE LRP1 RECEPTOR
- ◆ PCT/EP2019/085833: METHODS AND COMPOSITIONS FOR TREATING CANCERS BY IMMUNO-MODULATION
- ◆ Immunotherapy of Triple-Negative Breast Cancer With Cathepsin D-targeting Antibodies. Ashraf Y.* , Mansouri H.* et al, **J Immunother Cancer** **2019** Feb doi: 10.1186/s40425-019-0498-z
- ◆ Nuclear Cathepsin D Enhances TRPS1 Transcriptional Repressor Function to Regulate Cell Cycle Progression and Transformation in Human Breast Cancer Cells *Oncotarget* 015 Sep 6 (29), 28084-103 29 doi : 10.18632/oncotarget.4394
- ◆ Proteolysis of cystatin C by cathepsin D in the breast cancer microenvironment. Laurent-Matha V. et al., **FASEB J.** **2012** Dec;26(12):5172-81. doi: 10.1096/fj.12-205229.
- ◆ Pro-cathepsin D interacts with the extracellular domain of the beta chain of LRP1 and promotes LRP1-dependent fibroblast outgrowth. Beaujouin M, et al.**J Cell Sci.** **2010** Oct 1;123(Pt 19):3336-46. doi: 10.1242/jcs.070938.

Rational

Cath D is a tumor cell associated extracellular biomarker in TNBC

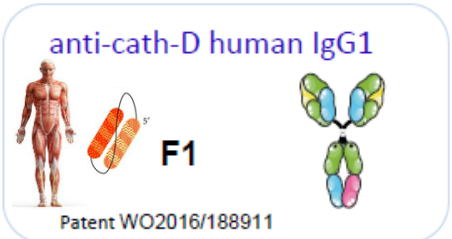
Anti-cath-D immunohistochemistry in TNBC TMA (n=123)



Products

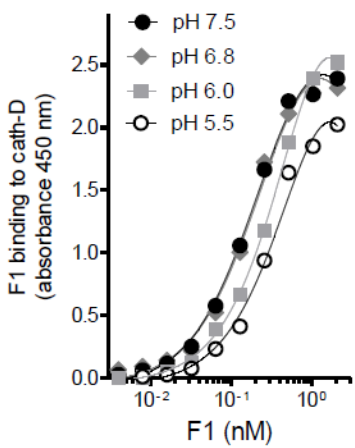
Cross-reactive human anti-cathD Antibody

Selection of human anti-cath D scFv fragments by phage display from HUSC1 library

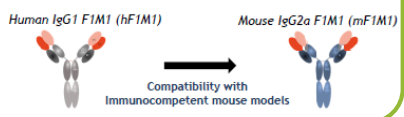
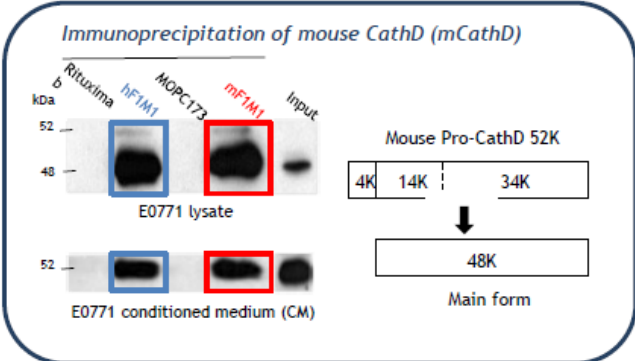
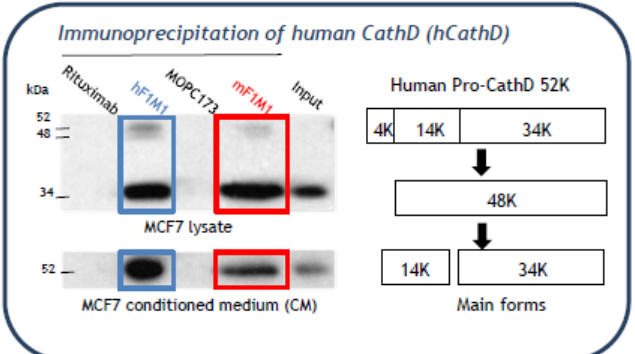


F1 hmAb binding to cath-D secreted by MDA-MB-231 TNBC cells

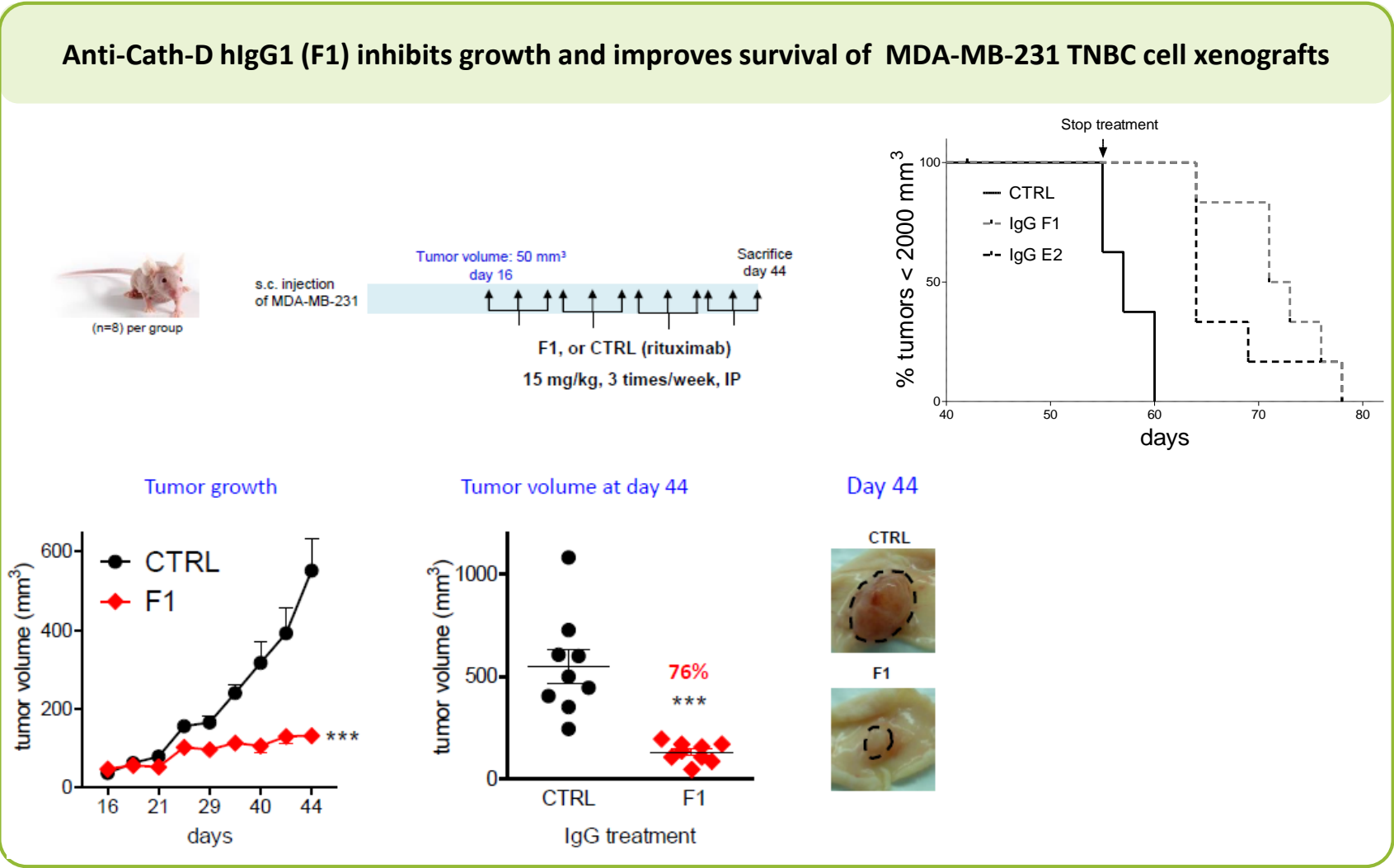
ELISA at acidic pH



F1 hmAb recognizes human & mouse CathD

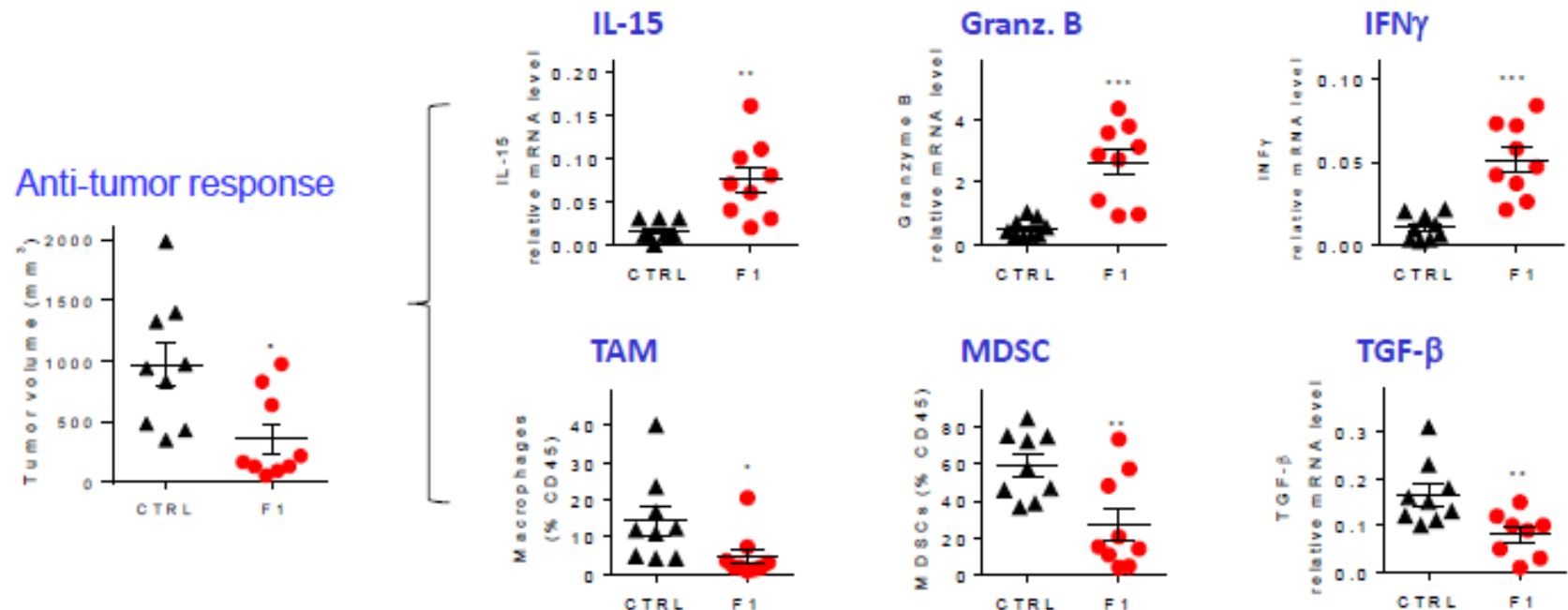


Proof of concept



Proof of Concept

Anti-CathD Ab (F1) modulates immune cell activation and recruitment in MDA-231 xenografts



hAnti-CathD Ab (F1) anti-tumor response :

- Activation of NK (+ IL-15, + Granzyme B, +Perforin, + IFN γ)
- Inhibition of M2-like TAM and MDSC recruitment
- Less immunosuppressive microenvironment (- TGF β)

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