532 Antibody-based Therapy against ADAM8-expressing Cancers

Asset Overview

Product Type	Antibody
Indication	Oncology
Current Stage	Preclinical
Target(MoA)	Inhibition of activity for both metalloprotease (MP) and disintegrin (DI) domains of ADAM8
Brief Description	• We have generated a panel of highly specific, dual antagonist monoclonal anti-ADAM8 antibodies; each antibody can simultaneously inhibit the MP and DI activities. • Two lead therapeutic candidates, ADP2 and ADP13, significantly reduce tumor growth and metastasis and improve survival in TNBC mouse models when given as monotherapies. • These antibodies also dramatically enhance treatment response when added to chemotherapy. • In the future, we plan to expand to other ADAM8-driven oncology indications beyond TNBC
Organization	Adecto Pharmaceuticals

Differentiation

□ **First-in-class potential**

- Identified the cell surface protein ADAM8 as an important driver of TNBC growth and spread and validated it as a target for treatment.
- High levels of ADAM8 are expressed in 34%of TNBC patient samples and 48% of all breast cancer-derived metastases.
- This expression is an independent predictor of poor prognosis.

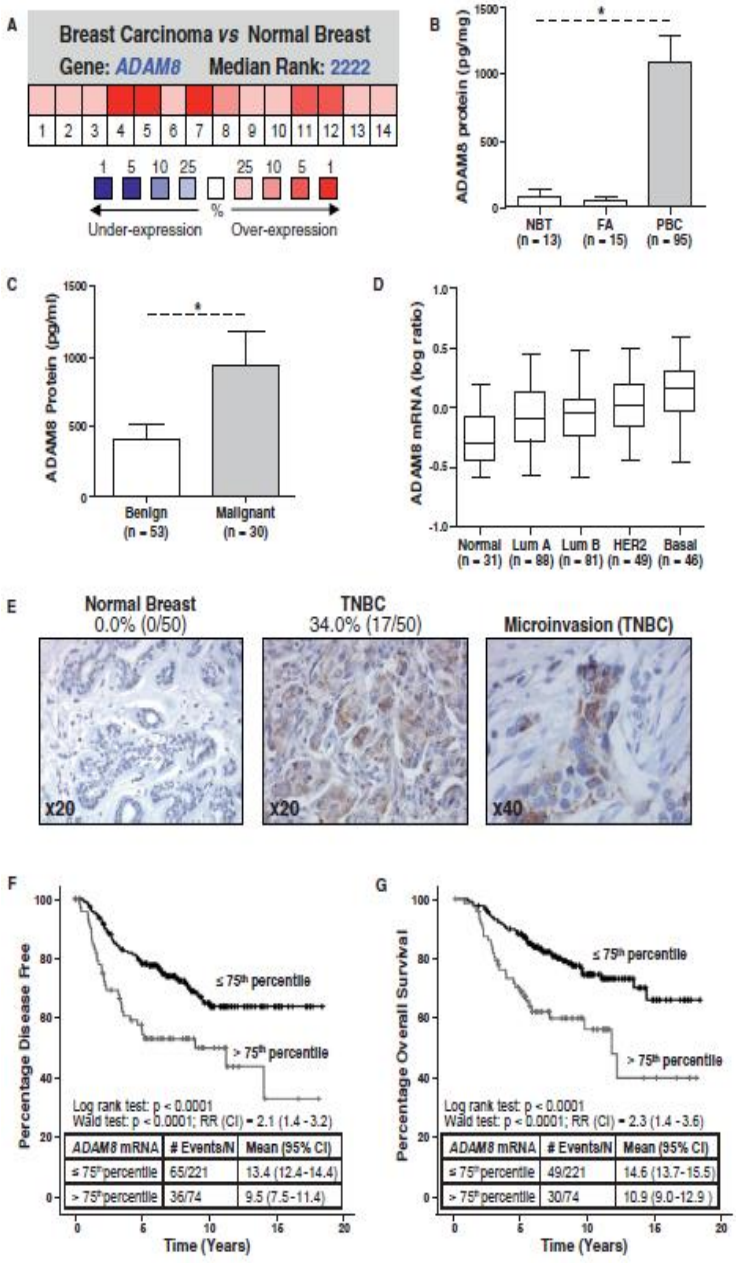
□ **Key role of ADAM8 in the aggressive phenotypes of TNBC cells**

- TNBC cell migratory and invasive properties are maintained by ADAM8.
- ADAM8 expression in TNBC cells is increased in 3D suspension cultures.
- ADAM8 promotes tumor growth, spreading of CTCs and metastasis.
- Knockdown of ADAM8 induces angiogenic tumor dormancy.
- ADAM8 is necessary for release of pro-angiogenic factors.

532 Antibody-based Therapy against ADAM8-expressing Cancers

Key Data

ADAM8 is overexpressed in human breast cancer

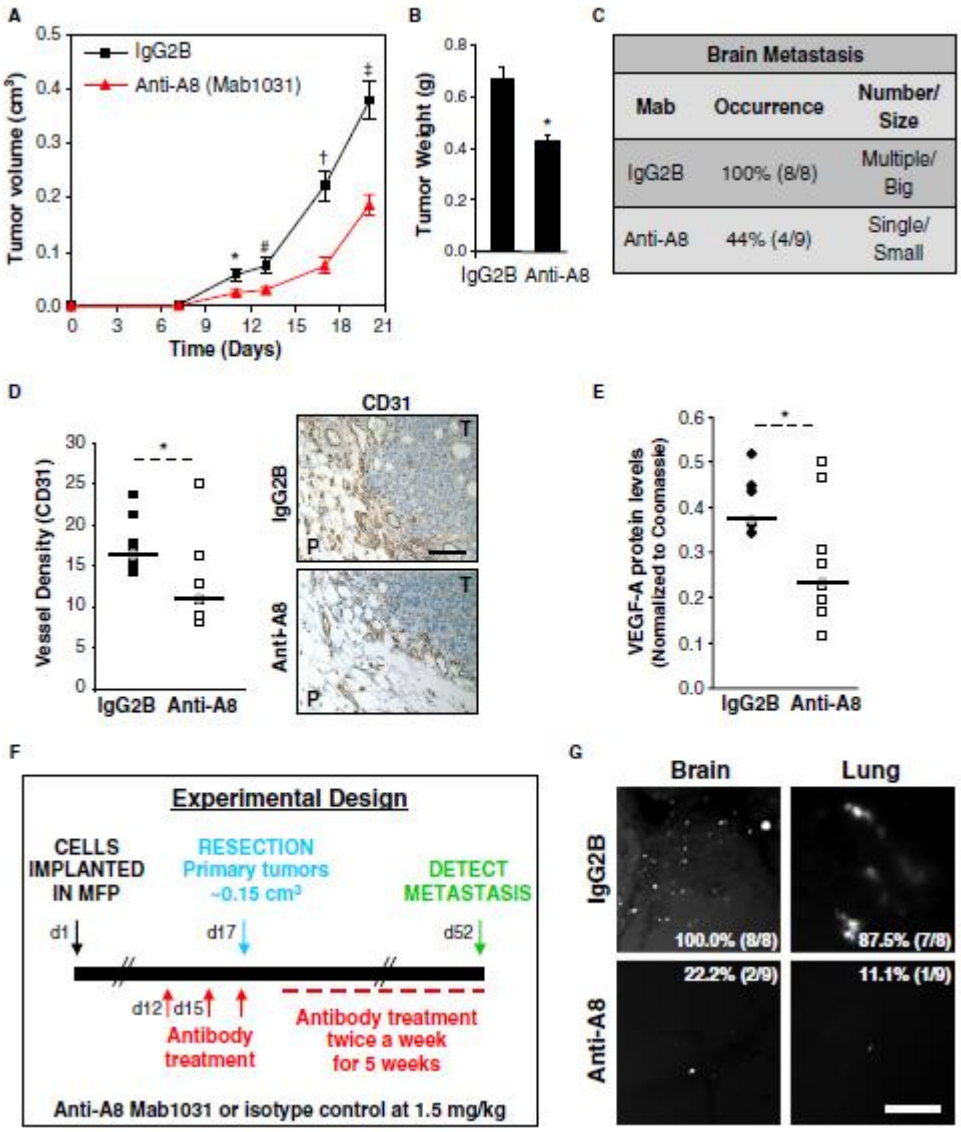


A) ADAM8 mRNA expression in samples from breast tumor and normal breast tissue was analyzed using the Oncomine microarray database. Pooling of 14 analyses from six different microarray studies shows ADAM8 is one of the more highly expressed genes in breast cancer versus normal tissue. B, C) ADAM8 protein levels were measured by ELISA in samples from adjacent normal breast tissue (NBT), fibroadenoma (FA) and primary breast carcinoma (PBC) (B), and in serum of patients with either benign or malignant breast disease (C). D) ADAM8 mRNA expression was analyzed across the different molecular breast cancer subtypes in the van de Vijver microarray dataset, which includes 295 primary breast tumors from normal-like (Normal), luminal A (Lum A), luminal B (Lum B), HER2, and basal-like (Basal) subtypes E) Representative pictures of ADAM8 staining analyzed by immunohistochemistry in adjacent normal epithelial tissue and primary TNBC samples from 50 patients or areas of microinvasion. Percentages of ADAM8-positive samples are given. F, G Kaplan–Meier curves show the percentage of disease-free survival (F) and overall survival (G) for 295 patients with primary breast cancer stratified based on ADAM8 mRNA levels using the 75th percentile.

532 Antibody-based Therapy against ADAM8-expressing Cancers

Key Data

ADAM8 monoclonal antibody decreases orthotopic tumor formation, angiogenesis and metastasis



A–E) MDA-MB-231 shCtrl-3 cells were injected into the MFP of female mice. Animals were treated with either 0.5 mg/kg anti-ADAM8 (anti-A8, Mab1031, n = 9) or isotype-matched control (IgG2B, n = 8) in i.p. injection twice weekly(A). At the end of the experiment, tumors were weighed (B) and the presence of brain metastases was examined by fluorescent microscopy (C). Angiogenesis was evaluated by CD31 immunohistochemical staining of tumor sections. P: Peritumoral area, T: Tumor. Bar: 100 lm(D). VEGF-A levels in the tumor extracts were determined by WB and normalized to Coomassie staining (E). F–G) Scheme of experimental design (F). Metastases to the brain and lungs were examined by fluorescent microscopy. Representative images and frequency of metastases (percentage of animals positive per group: IgG2B, n = 8; anti-A8, n = 9) are presented (G). Bar: 250 lm.

532 Antibody-based Therapy against ADAM8-expressing Cancers

Intellectual Property

Patent No.	PCT/US2014/037857
Application Date	
Status	Application, Pending
Country	US, EP, AU, CA

Contact Information

Contact Person	Martin
Email	Martin.Son@tufts.edu
URL	https://www.adectopharma.com/technology