Background

Tumor metastasis is the main cause of death for patients with triple-negative breast cancer (TNBC), and the identification of metastasis drivers in TNBC is an urgent therapeutic need. Here, expression of target molecules in primary tumors and metastases and their pro-metastatic impact were assessed.

Pathophysiology

**TROP-2 DETACHES E-CADHERIN FROM THE β-ACTIN CYTOSKELETON, WITH LOSS OF CELL-CELL ADHESION AND ACTIVATION OF β-CATENIN**

A. Immunoprecipitation assays show that Trop-2 interacts tightly with E-cadherin and severely impairs E-cadherin binding to the actin cytoskeleton (high Trop-2 and decreased β-catenin in the E-cadherin immunoprecipitate).

B. Trop-2 expression induces decreased cell-cell adhesion.

C. Trop-2 expression-induced hormetic cell-cell adhesion associates to a shift of aggressive skin toward smaller cell diameter and latency.

D. Transcriptionally active β-catenin is increased by Trop-2, as shown by the increase of GFP fluorescence in cancer cells transfected with Trop-2 and a GFP-expressing β-catenin-responsive reporter gene.

**THE TROP-2/E-CADHERIN/β-CATENIN MODULE DETERMINES THE DISEASE-FREE SURVIVAL OF TNBC PATIENTS**

![Graph showing disease-free survival (DFS) of TNBC patients with different Trop-2 expression levels.]

Conclusions

We have identified functional inactivation of E-cadherin by Trop-2 as a pivotal driver of EMT-less metastatic diffusion in TNBC. The Sacituzumab govatrecan-hzly anti–Trop-2 antibody has been shown to be effective in metastatic TNBC. Our findings provide support for a driving role and key therapeutic relevance of Trop-2 in TNBC.

References