

Broad-spectrum Metastasis Suppressing Compounds in Human Solid Tumors



Therapeutic Area	Oncology	Indications	Solid Tumors
Modality	Small Molecule	Development Stage	Hit to Lead/Lead Optimization

Overview

Background

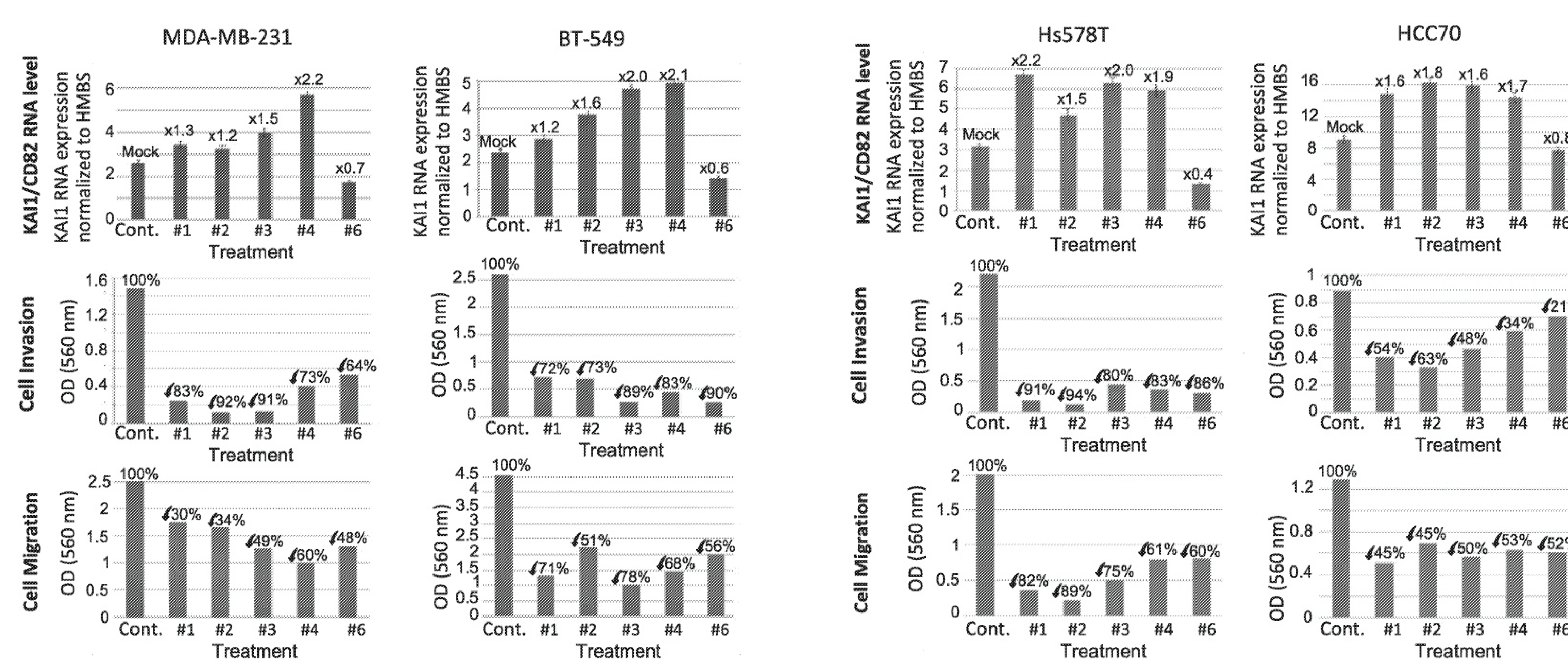
- Despite recent advances in cancer therapy, still malignancy is responsible for 15% of human death. Among these patients having solid tumors, 90% die from metastatic disease. Thus, effective prevention and suppression of metastasis is still an elusive goal. The proposed compounds and/or their derivatives identify a potential novel therapy for a broad-spectrum of the major human solid tumors.
- We have identified six compounds belonging to two chemical groups which inhibit at low concentration metastasis invasion and cell migration in culture without affecting cell proliferation. This was found in the eight types of solid human cancers tested. Currently we start to address the effect of these compounds in Patient Derived Xenografts (PDXs) in mice.

Technology Advantages

- Most current therapies for metastasis address already existing specific metastatic cells via cytotoxic compounds. Our approach tackles the metastasis process itself
- Current metastatic therapies usually address single human metastasis type, whereas ours addresses at least 8 major solid human cancer types.
- Based upon the mechanism of action of several of our compounds, there is a good chance for their activity in at least 5-6 additional solid human cancers.

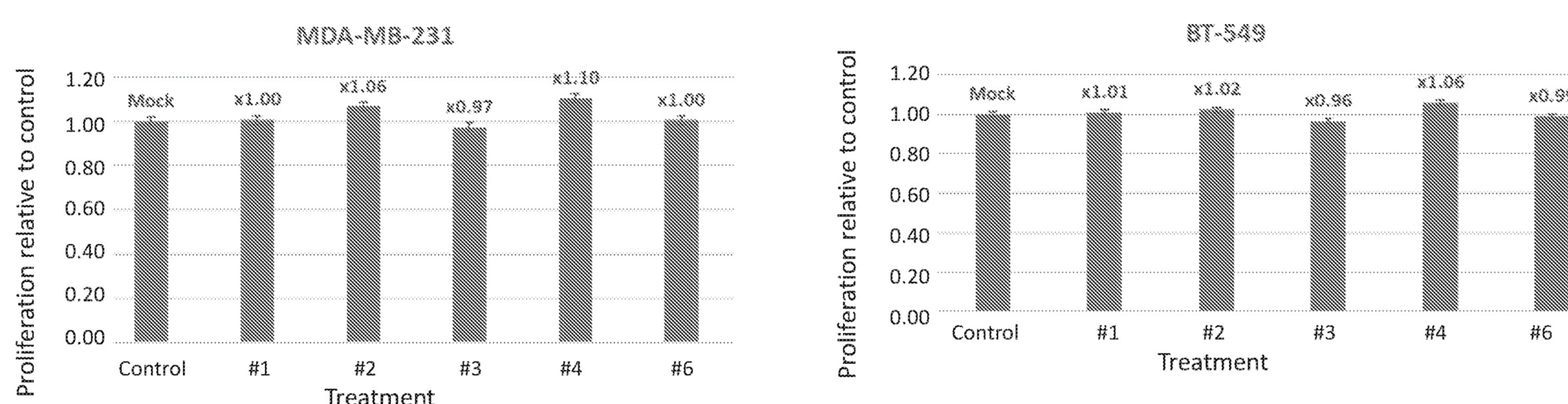
Key Data

Inhibitory effects of cell invasion and cell migration on triple-negative breast cancer cell lines



- KAI1 RNA expression:** The results show that 4 out of the 5 compounds (compounds #1-#4 at 5uM) stimulated KAI1 RNA expression by up to 2.0-2.2-fold in the TNBC MDA-MB-231 and BT-549, HCC70 and Hs578T cell lines.
- Cell Invasion:** Incubation of these four compounds at 5uM for 48 hours with each of these TNBC cell lines resulted in severe inhibition of metastasis cell invasion, typically from 54%-94%.
- Cell Migration:** All four tested TNBC cell lines (MDA-MB-231, BT-549, HCC70 and Hs578T) had their cell migration inhibited (from 30%-89%) by each of the five compounds.
- Further Applications:** Similar effects were observed in 8 types of solid human cancers including breast cancer, melanoma, pancreatic cancer, NSCLC, and liver carcinoma.

Inhibitory effects of cell invasion and cell migration on triple-negative breast cancer cell lines



Compounds effect on TNBC cell lines Proliferation MDA-MB-231, and BT549 cells were counted and seeded evenly into 6-well plates. The cells were incubated with the medium alone or with the addition of 5uM of the different compounds. After 48 h of incubation, the cells were harvested and counted again to assess cell proliferation. Data are presented as the mean +/- standard error of the mean of three independent experiments.

IP Status & Publication(s)

Intellectual Property

Patent Number
PCT application filed

Patent Family
-

Publication(s)

- Under reviewing