



NOVEL COMBINATION OF INHIBITORS OF WNT AND MACC1 FOR CANCER THERAPY

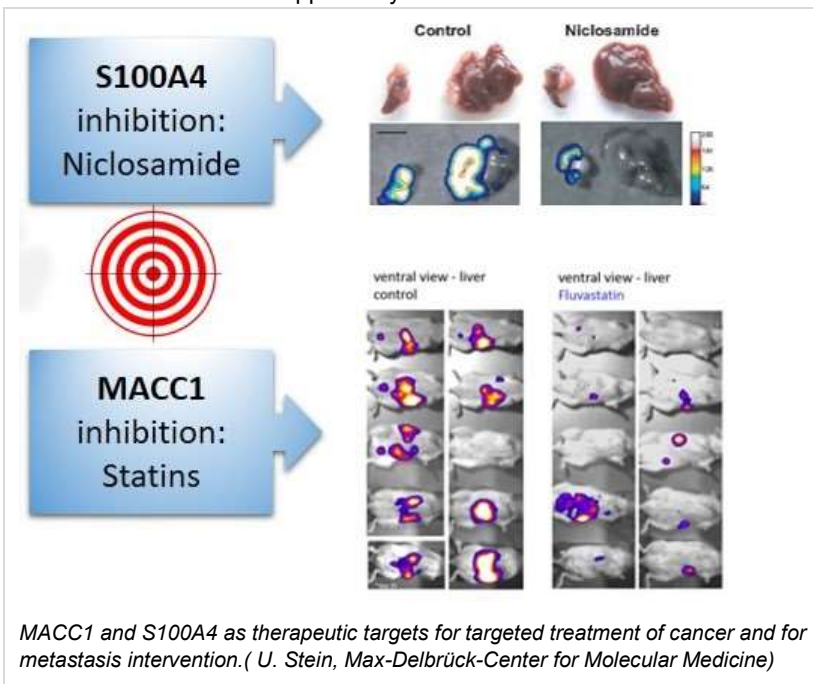
solid tumor therapy, metastasis prevention, synergistic combination, WNT signaling, MACC1, focus: CRC

INVENTION NOVELTY

The discovery of a novel mechanism whereby MACC1 induces migration and metastasis via the Wnt/S100A4 axis has led to a novel combinatorial treatment strategy: inhibition of Wnt/beta-catenin signaling combined with MACC1 inhibition.

VALUE PROPOSITION

Opportunity for strategic repurposing by novel, IP protected combination of established drugs in fixed-dose or single-tablet combinations. Alternative opportunity: combination with novel small molecule MACC1 inhibitors in development.



TECHNOLOGY DESCRIPTION

In vitro proof of concept was achieved for the combination of niclosamide (representing the class of S100A4 transcriptional inhibitors) and either a statin or a MEK1 inhibitor (both representing the class of MACC1 inhibitors). Strong synergistic anti-migratory and anti-invasion effects *in vitro* as well as anti-metastatic effects *in vivo* have been observed. This potentially improves anti-metastatic therapies and allows to dose drugs at significantly lower levels, which reduces potential side-effects of chemotherapy, while simultaneously achieving stronger therapeutic efficacy

DEVELOPMENT STATUS

Preclinical: *In vitro* and *in vivo* data package available.

COMMERCIAL OPPORTUNITY

Available for licensing and co-development partnerships. Strong expertise and know-how for development in CRC and metastatic CRC available to support development partnerships. Development for other indications also supported by broad patent scope.

PATENT SITUATION

Patent applications based on WO2020169812A1 with priority of 2019 are pending in EP, US, CA and JP.

FURTHER READING

Kortüm et al., Combinatorial treatment with statins and niclosamide prevents CRC dissemination by unhooking the MACC1- β -catenin-S100A4 axis of metastasis. *Oncogene*, 2022.

Gohlke et al., Real-world evidence for preventive effects of statins on cancer incidence: A trans-Atlantic analysis, *Clin Transl Med*, 2022.

Kobelt et al., The newly identified MEK1 tyrosine phosphorylation target MACC1 is druggable by approved MEK1 inhibitors to restrict colorectal cancer metastasis, *Oncogene*, 2021.

Juneja et al., Statin and rottlerin small-molecule inhibitors restrict colon cancer progression and metastasis via MACC1, *PLOS Biology* 2017.

Sack et al., Novel effect of antihelminthic Niclosamide on S100A4-mediated metastatic progression in colon cancer, *J Natl Cancer Inst*, 2011.

