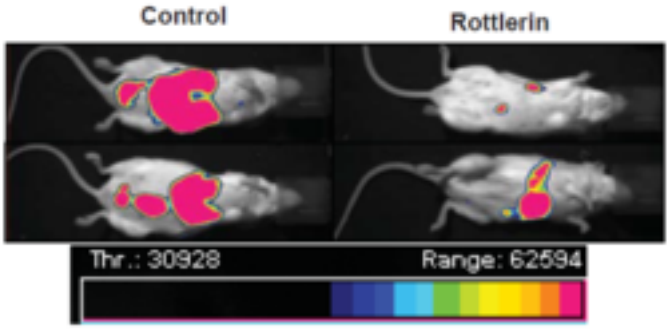
Technology transfer for academic research
A company of the LifeScience Foundation

MACC1 inhibitors for restriction of metastasis and cancer progression

Reference Number: 03-00391/32-00010

Challenge

Colorectal cancer (CRC) is one of the leading causes of cancer-associated death worldwide. Complete surgical resection and subsequent chemotherapy are the first-line therapies of choice. However, CRC can either relapse at the primary tumor site or metastasize to distant organs. Once metastasized, the treatment options available for CRC patients are very limited and survival rates drop significantly. MACC1 (Metastasis-Associated in Colon Cancer 1) has been identified as a key driver for metastasis and studies showed that five-year-survival rates dropped to 15% for patients with high MACC1 expression compared to 80% for patients with low MACC1 expression. MACC1 has also been linked to other solid tumors such as gastric cancer, breast cancer or ovarian cancer. It is therefore an interesting target to treat metastasis and tumor progression.



Bioluminescence signals show significant reduction in tumor burden and metastases formation in animals treated with Rottlerin compared with control animals.

Technology

A MACC1 promoter-driven luciferase reporter gene assay was developed, allowing the first identification of potent MACC1 inhibitors in a high-throughput screening. Among these hits, the natural compound Rottlerin was further profiled and emerged as an effective inhibitor of MACC1 expression.

CHARITÉ
UNIVERSITÄTSMEDIZIN BERLIN

Licensing Contact
Dr Michael Karle
Technology Manager
T: +49 30 948930-02
F: +49 30 948930-00
karle(at)ascenion(dot)de

Ascenion GmbH
Herzogstraße 64
D-80803 München
T: +49 89 318814-0
F: +49 89 318814-20
info@ascenion.de
www.ascenion.de

Berlin
Braunschweig
Hamburg
Hanover
Munich
Neuherberg

Rottlerin reduced proliferation and migration of CRC cells significantly *in-vitro* and was evaluated *in-vivo* in a xenograft mouse model to measure effects on tumor growth and liver metastases via bioluminescence. In comparison with control groups, animals treated with Rottlerin had an increased overall survival rate. Moreover, Rottlerin showed an effective restriction of metastasis formation. Analysis of *in-vivo* MACC1 transcription confirmed the inhibitory effect of Rottlerin and underlined the therapeutic potential of this substance. The subsequent analysis of several active Rottlerin derivates gave a first insight into the structure-activity relationship.

A significantly large number of novel cancer therapeutics is based on structures derived from natural compounds. The identification of Rottlerin as a potent MACC1 inhibitor therefore may serve as an interesting option for the development of novel therapeutics to restrict metastasis and cancer progression.

Commercial Opportunity

Available for licensing or collaboration.

Patent Situation

PCT-application WO2016/020427 pending (priority of August 5, 2014).