UNIVERSITÄTSMEDIZIN BERLIN

Technology Offer

Novel Imidazol-Based HDAC Inhibitors for the Treatment of Cancer

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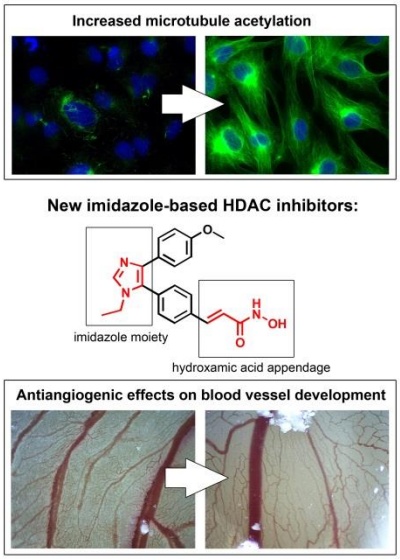

Background

Histone deacetylases (HDACs) are implicated in the control of cell proliferation and differentiation and have been shown to be overexpressed in cancer cells of several tumor types such as breast-, liver- and bladder cancer. HDAC inhibitors are promising candidates for the treatment of cancer as well as for the treatment of protozoal diseases and psoriasis. The currently known HDAC inhibitors are categorized in pan- and class-specific inhibitors in dependence of their inibititory properties regarding the different HDAC isoforms. The hydroxamic acid derivative Vorinostat e.g. is a pan-HDAC inhibitor approved for clinical applications. However the clinical effectiveness of currently approved HCAC inhibitors are unsatisfactory in patients with solid tumors due to resistance properties. Furthermore some of them seem to induce adverse stem cell-like characteristics in prostate cancer cells.

Technology

Novel imidazole-based hydroxamic acid derivatives have been generated which show higher cytotoxic properties in resistant cancer cell lines compared to state of the art HDAC inhibitors such as SAHA (e.g. IC50 of 0,95 µM vs. 1,51 µM (SAHA) in a melanoma cell line and IC50 of 2,9 µM vs. 7,9 µM (SAHA) in a resistant cervix carcinoma cell line). Lower concentration of novel inhibitor are necessary to show inhibitory function in a cell-line based metastasis assay (matrigel migration assay): The percentage of invasive tumor cells is more reduced as in the presence of SAHA, even if SAHA is used in a two-fold concentration. Furthermore the novel compounds have better anti-angiogenic properties compared to SAHA, proven in an *in vitro assay.* The anti-angiogenic efficience could also be verified in an *in vivo* model of fertilized chicken eggs (CAM-Assay). Biocompatibility could be proven in mice.

Benefits

- ✓ Higher effectiveness in many resistant cancer cell lines
- ✓ Higher cytotoxicity (lower IC50) compared to other HDAC inhibitors
- ✓ Biocompatible and oral applicable
- ✓ Variable optimization possible re. effectiveness and pharmacology, also pro-drugs and conjugation systems possible

Application

Novel compounds as therapeutic agent for cancer therapy

Commercial Opportunity

In-licensing or industrial cooperation for further development

Key words

Hydroxamic acid derivatives, histone deacetylases inhibitor, HDAC inhibitor, cancer, tumor, anti-angiogenic

Developmental Status

in vivo (mouse)

IP Status

EP patent application (07/2014)

Patent Owner

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