Technology Overview

New HDAC Inhibitors as Anticancer Agents
OTT#1392

TECHNOLOGY

The inventors have designed, synthesized and screened HDAC inhibitors that have antitumor activity with reduced toxicity in mice. The fragments are designed from previously discovered HDAC inhibitors, thailandepsins (TDP) A and B which are natural analogs of FK228, a cancer drug currently on the market. TDPA and TDPB while potent were also highly toxic to cells and mice. These compounds specifically inhibit HDAC4 or HDAC6 indicating greater specificity than some HDAC inhibitors on the market. The new analogs show promising effects on cervical cancer, breast cancer, colon cancer, and renal cancer cell lines with GI_{50} values in single to sub µM range. The three lead compounds are less toxic than the parental TDPs with MTD values greater than 200 mg/kg. The lead compounds are currently being tested in mouse tumor xenograft models for colon tumor cells versus a SAHA, a drug currently on the market, as a control.

In the past ten years, over 490 clinical trails of more than 20 HDAC inhibitors have been initiated as single agents or in combination with other chemotherapy drugs, with two being approved. The FK228 family of HDAC inhibitors show excessive toxicity and poor solubility that limits their usefulness for treating cancer. Our novel compounds show great promise as anti-tumor therapies with specificity and low toxicity.

FEATURES/BENEFITS

- **Specific –** The lead compounds specifically target HDAC4 or HDAC6
- **Safer –** Lead compounds are less toxic than the parental natural products they were derived from
- **Effective –** Initial cell culture studies show activity against cervical, breast, colon, and renal cancer cell lines
- **Cheaper –** Synthesis of the small molecules is easy and inexpensive
- **Druggable –** The lead compounds are more soluble than FDA approved drugs FK228 and SAH

INTELLECTUAL PROPERTY

A U.S. Provisional Patent Application has been filed.

This technology is part of an active and ongoing research program and is seeking partners for development of the final product. It is available for developmental research support/licensing under either exclusive or non-exclusive terms.

MARKETS

The global market for histone deacetylase inhibitors (HDIs) was valued at $223.2 million in 2012 and was estimated at $361.8 million for 2013. BCC Research expects the market to grow to $954.3 million by 2018, and register a five-year compound annual growth rate of 21.4% from 2013 to 2018. Histone deacetylase inhibitors (HDIs) are promising therapeutics that have already shown potential for oncological applications such as cancer detection, diagnosis, and prognosis. Current candidates are demonstrating successful pre-clinical and clinical trials for various other diseases such as neurologogical ailments, heart diseases, HIV infections, and many others.

To date, there are just two approved HDIs -- vorinostat (Zolinza) from Merck & Co. and romidepsin (Istodax) from Celgene Corporation. Both of these are approved for cutaneous T-cell lymphoma (CTCL) and romidepsin is used for peripheral T-cell lymphoma (PTCL). This presents an enormous prospect for developing curative therapies for fatal diseases through histone deacetylase inhibitors.

INVENTORS

Mahmun Hossain

Dr. Mahmum Hossain is an Associate Professor in the Department of Chemistry and Biochemistry at the University of Wisconsin-Milwaukee. Dr. Hossain's group is interested in developing novel organic reactions that will simplify the synthesis of existing biologically active compounds and also enable the generation of a new class of therapeutics for
human diseases.

Yi-Qiang (Eric) Cheng

Dr. Eric Cheng is currently a Professor of Pharmaceutical Sciences at University of North Texas Health Science Center. He was previously a faculty member at the University of Wisconsin-Milwaukee where he taught microbiology and biotechnology at both the undergrad and graduate levels. His research interests are based around discovering and developing bioactive natural products as drugs or drug leads in the areas of oncology and infectious disease.

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