Synthesizing Anti-cancer Alkaloid Compounds and Derivatives

Technology #16016

Applications

This technology may be used in treatment of a wide range of cancer types by inducing selective cell death.

Problem Addressed

ETP alkaloids are a class of natural products that have been shown to have potent anticancer activity. Until now, there has not been a systematic study of the structure-activity relationship (SAR) of natural and synthetic ETP compounds as it pertains to the compounds' activity against cancer cell lines in culture due to lack of easy availability.

Technology

The inventors have synthesized a set of structurally diverse natural and synthetic ETP alkaloids to study the SAR of ETP-containing natural products and their synthetic cognates and to determine which ETP derivatives demonstrate the most potent anticancer activity. Monomeric and dimeric ETP alkaloid derivatives were created by constructing compounds that varied in the substituents about the hexa-hydropyrroloindoline carboskeleton and the nature, extent and configuration of sulfuration. Sixty natural alkaloids and their derivatives were then tested for their ability to induce cell death in two human cancer cell lines: U-937 (leukemic monocyte lymphoma) and HeLa (cervival cancer). The most potent derivatives from this primary screening were tested in vitro against a panel of three supplementary human cancer cell lines: H460 (lung carcinoma), 786-O (renal carcinoma) and MCF-7 (breast carcinoma). Representative compounds from the monomer and dimer classes were shown to induce caspase-dependent apoptosis. The potent and broad anticancer activity of ETP-containing alkaloids suggests that they have considerable translational potential in treating cancer.

Advantages

- Concise and effective synthetic access to a wide range of products
- Potent induction of apoptotic cell death
- Activity against a wide range of cancer types
- Broad tolerance for modifications at multiple sites that should facilitate small-molecule drug development, mechanistic studies and evaluation *in vivo*

Categories For This Invention:

Life Sciences

255 Main Street, room NE 18-501
Cambridge, MA 02142-1601
Phone: 617-253-6966 Fax: 617-258-6790
http://tlo.mit.edu
Contact the Technology Manager: tlo-inquiries@mit.edu

Clinical Applications
Oncology

Intellectual Property:

Compounds, conjugates and compositions of epipolythiodiketopiperazines and polythiodiketopiperazines
Issued US Patent
9,353,150
Substituted pyrazino[1',2':1,5]prrrolo[2,3-B]indole-1,4-diones for cancer treatment
Issued US Patent
Substituted pyrazino[1',2':1,5]prrrolo[2,3-B]indole-1,4-diones for cancer treatment
US Patent Pending
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Inventors:

Mohammad Movassaghi
Nicolas Boyer
Justin Kim

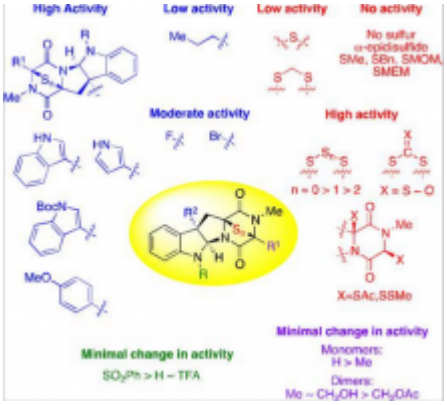
Publications:

Synthesis and Anticancer Activity of Epipolythiodiketopiperazine Alkaloids
Chemical Science
April 1, 2013
Research Update: Chemists Find Help from Nature in Fighting Cancer
MIT News
February 27, 2013

External Links:

Movassaghi Group
http://web.mit.edu/movassag/www/

Image Gallery:



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