A new class of alkaloids with potent and selective targeting of pancreatic cancer in vitro

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Technology description

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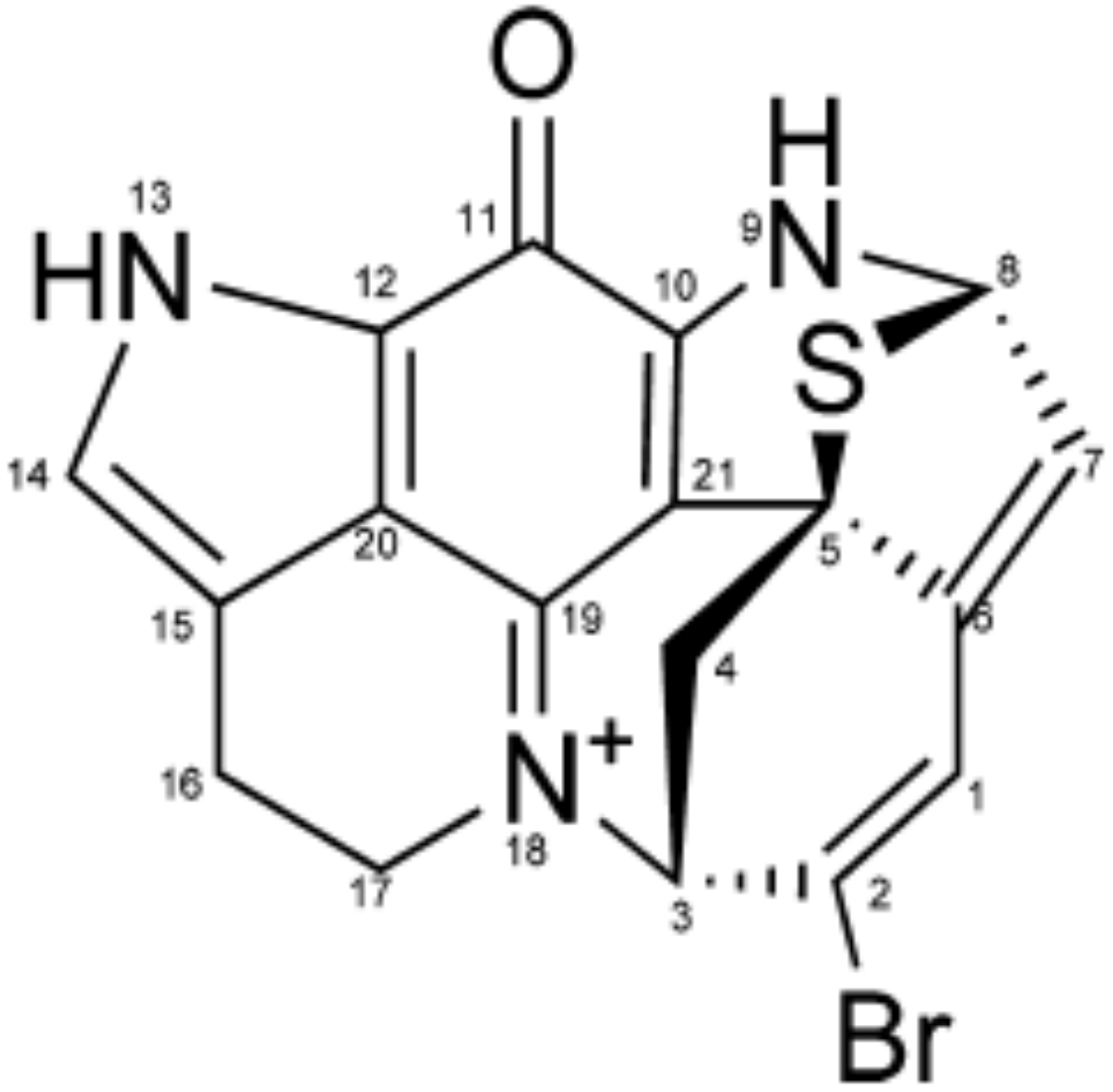
Inventors from MUSC have identified a class of brominated alkaloid compounds, including aleutianamine, which has potent bioactivity across multiple cancer cell lines in vitro. Extraction and purification of specimens of Latrunculia austini, led to isolation of a potential target mass m/z 398 that resulted from MS/MS molecular ion networking-MoIN analysis (vide supra) as a green-yellow solid with the molecular formula of C18H13BrN3OS generated by high-resolution mass spectrometry analysis (Figure 1). Aleutianamine, with its unique ring system, showed anti-cancer selectivity in a differential cytotoxicity zone assay. Aleutianimine selectively killed pancreatic cancer PANC-1 cell line and murine colon cancer 38, human breast cancer cell line MCF-7, human prostate cancer LNCaP. The IC50 value for aleutianamine tested against human HCT-116 colon cancer cells was 1 μM and against PANC-1 pancreatic cancer cells were 25 nM, indicating significant potency and selectivity towards pancreatic cancer. Overall, this new compound class provides a new opportunity to treat cancers, including difficult to treat pancreatic cancer.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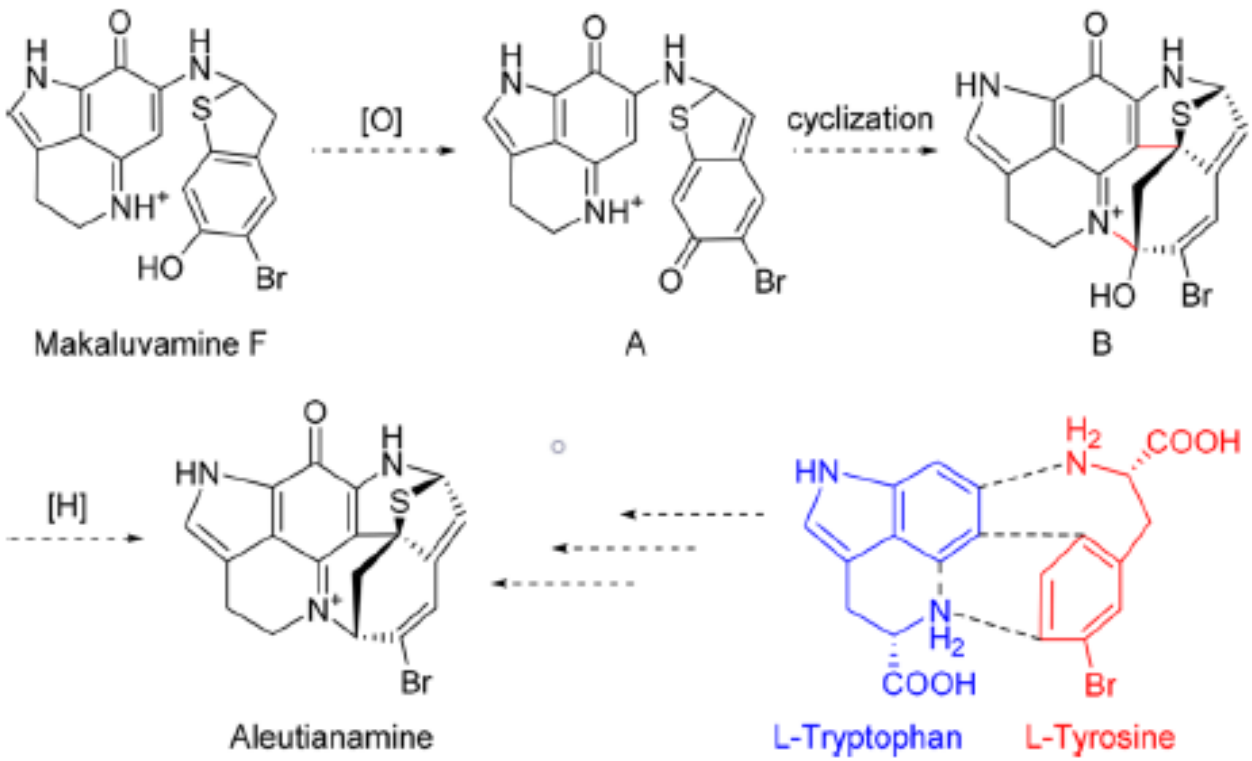

Overview

Pancreatic cancer is one of the deadliest cancers with a 5-year survival rate of less than 8%. The only curative therapy is surgery for which only 15–20% of patients are eligible and of those about 20% are long-term survivors. Hence there is an urgent need for novel therapeutic approaches for pancreatic cancer treatment. Currently, Gemcitabine and Abraxane among other chemotherapeutic drugs are used against pancreatic cancer treatment with limited success. Although standard chemotherapeutic treatments for pancreatic cancer add months to a patient’ s overall survival time, there is little improvement in survival rates. Using computational and mass spectroscopic methods, MUSC inventors have identified a novel aleutianamine compound with effective cell killing against PANC-1 cancer cells. Aleutianamine showed significantly higher cytotoxicity than discorhabdin A (precursor in the biosynthesis of Aleutianamine) toward cancer cell lines and demonstrated selective inhibition to pancreatic cancer cell lines. Thus, developing an aleutianamine based compound could be an effective strategy for treating pancreatic cancer.

Key Words:Pancreatic cancer, aleutianamine, alkaloids, Abraxane, Gemcitabine, PANC-1.

Publication: Zou Y, Wang X, Sims J, Wang B, Pandey P, Welsh C, Stone RS, Avery MA, Doerksen RJ, Ferreira D, Anklin C, Valeriote FA, Kelly M, Hamann MT. Computationally-Assisted Discovery and Assignment of a Highly Strained and PANC-1 Selective Alkaloid from Alaska's Deep Ocean. J Am Chem Soc. 2019 Feb 13 .

Application area

A novel therapeutic approach that could improve chemotherapy for treating pancreatic cancer.
A new alkaloid isolated from Latrunculia austini could be a novel therapeutic compound against pancreatic cancer.

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