Skysong Innovations
Advancing the Arizona State University Knowledge Enterprise

1475 N. Scottsdale Road, Suite 200
Scottsdale, AZ 85287-3538
Phone: 480 884 1996 Fax: 480 884 1984

Case ID:M07-064LC^
Published: 2/26/2020

Cyclodepsipeptide compounds presenting anti-cancer and anti-infective activity, and their synthesis

Inventors

George (Bob) Pettit
Rui Tan
Robin Pettit

Contact

Jovan Heusser
jovan.heusser@skysonginnovations.com

The actinomycete genus Kitasatospora has a prominent history of producing bioactive compounds, including bafilomycin B1 and bafilomycin A1. One particular compound isolated from Kitasatospora, respirantin, is a cyclodepsipeptide with potential cancer cell growth inhibitory and antifungal/antimicrobial properties. A need exists to isolate and modify these unique anticancer and antifungal/antimicrobial compounds.

Prof. George (Bob) Pettit, and his team at Arizona State University have isolated respirantin as well as other related molecules possessing both anti-cancer and anti-microbial activities. These additional related compounds include kitastatin 1 and a valeryl homologue of respirantin. All three of these compounds exhibit potent anti-cancer cell growth properties (GI50 ~ 0.0006 µg/mL), in addition to excellent anti-microbial and anti-fungal properties.

Moreover, these researchers have also realized the total synthesis of the respirantin compound. This approach should offer ready access to the scale-up synthesis of respirantin, kitastatin 1 and a variety of their structural analogs.

Potential Applications

- Respirantin, Kitastatin & analogs for:
  - Inhibiting carcinoma cell growth (leukemia, pancreas, breast, CNS, Lung-NSC, colon and prostate cancer)
  - Inhibiting microbial and fungal growth activity (Cryptococcus neoformans, Enerococus faecalis, Micrococcus luteus, Stenotrophomonas maltophilia, Micrococcus luteus, Staphylococcus aureus, Escherichia coli, Enterobacter cloacae, Steptococcus pneumoniae, Neisseria gonorrhoeae, or Candida albicans, Cladosporium cucumerinum, Epidermophyton floccosum, and Microspermum ypseum)

Benefits and Advantages

- These compounds are synthetically available and easy to produce in large scale

- Fermentation production, requiring only a few additional post-production modifications (2.6 mg to 10.8 mg production values depending on the desired compound)
- Impressive spectrum of activity against a panel of human cancer cell lines
  - Special selectivity against the pancreas BXPC-3 human cancer cell line

In Vitro and/or In Vivo Data

Against human cancer derived cell lines (NCI's standard sulforhodamine B assay), these cyclodepsipeptide compounds showed cancer cell growth inhibition against P388 murine leukemia, PXPC-3 pancreas, MCF-7 breast, SF268 CNS, NCI-H460 lung, KM20L2 colon and DU-145 prostrate cell lines.

Against Cryptococcus neoformans, cyclodepsipeptide 1 has a minimum inhibitory concentration (MIC) of 2 μg/mL, against Micrococus luteus, cyclodepsipeptide 2 had marginal activity (MIC of 64 μg/mL), and against C. neoformans and Enterococcus faecalis, Kitastatin 1 had marginal activity (MIC of 64 μg/mL).

Stage of Development

Structural modifications of kitastatin 1 are in progress as well as preclinical development.

Lead Structures