Therapeutics & Vaccines

Novel Tautomycetin Analogs Provide Potential Natural Products for the Treatment of Cancer or Autoimmune Disease

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WARF: P100341US02

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The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in developing novel tautomycetin analogs that may be useful in the treatment of several types of cancer and other disorders.

Overview

Tautomycetin (TTN) is a complex polyketide natural product produced by *Streptomyces griseochromogens*. It specifically inhibits the protein phosphatases PP1 and PP2A, which are two of the four major serine/threonine phosphatases that regulate an array of cellular processes. Because many human diseases are characterized by an altered interplay between phosphatases and kinases, compounds that selectively inhibit PP1 and PP2A may be useful in the treatment of diseases like cancer.

In contrast to other naturally occurring PP1 and PP2A inhibitors, TTN is highly selective for PP1. Thus, it represents both an attractive drug lead and a powerful tool for understanding the role of PP1 in various biological pathways. TTN has been identified as a potent immunosuppressor of activated T cells in organ transplantation and also has been shown to inhibit growth of colorectal cancer cells and induce apoptosis.

The Invention

A UW–Madison researcher has developed novel TTN analogs, which may be potentially useful for the treatment of cancer or autoimmune disorders. The researcher previously cloned and sequenced the biosynthetic gene cluster for TTN. He discovered that inactivating two genes, *ttnD* and *ttnF*, abolishes production of TTN and leads to the production of five new TTN analogs.

WARF reference number P100290US03 describes the use of the analogs to inhibit the oncogene SHP-2. In addition to autoimmune disorders, the analogs can be used to treat diseases related to SHP-2, including Noonan syndrome, Leopard syndrome, leukemia and solid tumors.

Applications

- Provides novel natural products that may be useful therapeutics for cancer or autoimmune disorders
- Provides a tool to improve understanding of TTN biosynthesis and the role of PP1 in various pathways

Key Benefits

- Highly selective for PP1
- TTN is a natural product of microbial origin and can be produced by large-scale fermentation
- May be administered in combination with other anticancer therapeutics from different pathways

Additional Information

Related Technologies

- WARF reference number P100290US03 describes the use of the analogs to inhibit SHP-2.

Publications

- Luo Y., Li W., Ju J., Yuan Q., Peters N.R., Hoffmann F.M., Huang S.X., Bugni T.S., Rajski S., Osada H. and Shen B. 2010. Functional Characterization of TtnD and TtnF, Unveiling New Insights into Tautomycetin Biosynthesis. J. Am. Chem. Soc. 132, 6663–6671.

Tech Fields

- Therapeutics & Vaccines : Autoimmune disorders
- Therapeutics & Vaccines : Oncology

For current licensing status, please contact Rafael Diaz at rdiaz@warf.org or 608-960-9847