Novel Tautomycetin Analogs Specifically Inhibit SHP-2, May Provide New Cancer Treatment

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Technology description

Description

SHP-2 is an oncogene from the protein tyrosine phosphatase (PTP) superfamily. Mutations in SHP-2 can cause multiple forms of leukemia and solid tumors, as well as the autosomal dominant disorders Noonan syndrome and Leopard syndrome, making SHP-2 an attractive drug target. However, it has proven difficult to develop SHP-2 inhibitors with optimal potency and pharmacological properties. Tautomycetin (TTN) may provide a promising lead for the development of new immunosuppressive and anti-tumor agents. TTN is a complex polyketide natural product produced byStreptomyces griseochromogens. It 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.
Researchers at UW–Madison and Indiana University have developed novel TTN analogs that inhibit SHP-2. These analogs can be used to treat diseases related to SHP-2, including Noonan syndrome, Leopard syndrome, leukemia and solid tumors.
The researchers showed that TTN and one of its engineered analogs, TTN D-1, specifically inhibit the activity of SHP-2. They also determined the X-ray crystal structure of SHP-2 with TTN D-1 bound to its active site. Together with the biochemical and cellular data, this structure supports the idea that SHP-2 is a cellular target for TTN and provides new insights for developing novel therapeutics that target SHP-2.

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