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Halicloic acids A and B as indoleamine 2,3-dioxygenase (IDO) inhibitors

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Immune escape plays an important role in cancer progression. Immune surveillance generates a strong selective pressure for tumor cells that can evade immune destruction. Once the tumors escaped local and peripheral immune surveillance, invasion and metastasis can evolve, leading to lethal cancer progression. Localized IDO-mediated degradation of tryptophan at a tumor site prevents immunological rejection of the tumor. Expression of IDO is constitutively activated in human cancers and also by antigen-presenting cells at the periphery of tumors and in the tumor-draining lymph nodes. Marshalling the immune system against solid tumors is an attractive noncytotoxic approach to treating cancer. Thus, inhibiting IDO has recently attracted much attention as a new strategy for anticancer drug development.

紹介論文

J. Nat. Prod., **2012**, 75 (8), pp 1451–1458
Halicloic Acids A and B Isolated from the Marine Sponge *Haliclona* sp. Collected in the Philippines Inhibit Indoleamine 2,3-Dioxygenase.
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要旨

Indoleamine 2,3-dioxygenase (IDO) is an enzyme in humans that is encoded by *IDO1* gene and it plays a central role in tumor-cell evasion of T cell mediated immune rejection. IDO catalyzes the oxidative cleavage of the 2,3 bond of tryptophan, the first and rate-limiting step in the kynurenine pathway of tryptophan catabolism causing the degradation of L-tryptophan to N-formylkynurenine. Thus, depletion of tryptophan inhibits T-cell proliferation and prevents immunological rejection of the tumor and eventually leads to cancer progression. Silencing of the IDO gene resulted in lower rates of tumor development. In this study, Halicloic acids A and B isolated from *Haliclona* sp. show promising inhibitory results for in vitro inhibition of IDO activity. This finding suggests that they are new target for cancer therapy and serve as a natural product template for synthetic IDO inhibitors' design in the future.

参考論文

J. Nat. Prod., **2006**, 69*,* pp 1496-1499
Indoleamine 2,3-Dioxygenase Inhibitors from the Northeastern Pacific Marine Hydroid *Garviea annulata.*
Alban Pereira, Eduardo Vottero, Michel Roberge, A. Grant Mauk, and Raymond J. Andersen