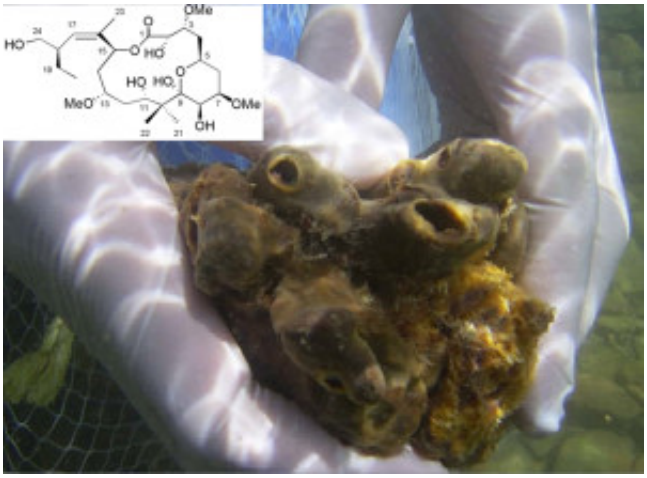
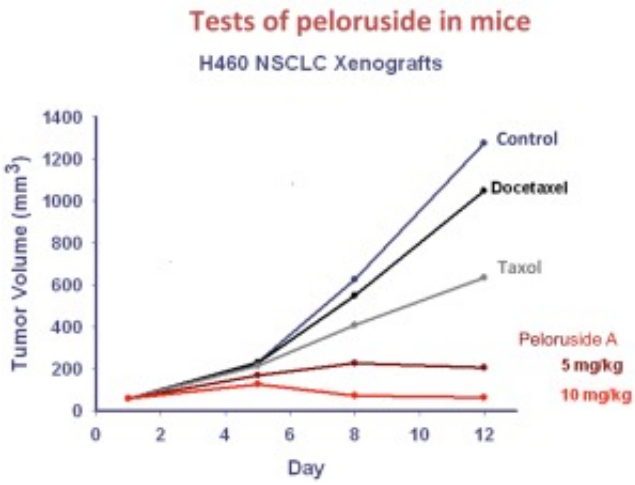
Sponge toxin kills lung and breast cancer cells in mice

Peloruside A is a potent toxin that was isolated from a New Zealand marine sponge. It has a similar mechanism of action to the commonly used taxane-type anticancer drugs, including paclitaxel and docetaxel, that block the action of microtubules in cells. The taxanes are clinically effective in preventing growth of solid tumours of the lung, breast, and ovary. The target of peloruside and paclitaxel is the microtubule, an structural protein inside the cell that is needed for cell division, proliferation, and intracellular transport.



Peloruside binds to a unique site on microtubule protein that differs from that of the taxanes. Another marine sponge natural product, laulimalide, is the only known compound that also binds to this non-taxane site. Peloruside at low nanomolar concentrations prevents growth in culture of a panel of cancer cell lines, including cell lines that are resistant to the front line taxane drugs. Because the taxane drugs have toxic side effects in the clinic, including peripheral neuropathy, nausea, muscle pain, joint pain, and low white blood cell levels, new anticancer agents are being sought. Using an immunodeficient mouse model of cancer, the efficacy of peloruside was tested against the standard taxane anticancer drugs: paclitaxel and docetaxel. Peloruside inhibited growth of human non-small cell lung cancer cells by 84% to 95% compared to paclitaxel and docetaxel (50% and 18%, respectively). In a second study also using lung cancer cells and varied schedules of dosing, peloruside again showed better activity than the taxanes with inhibitions ranging from 51 to 74%, compared to 44% and 50% inhibition.



A third study was conducted in a mouse model using breast cancer cells, and peloruside was better tolerated than either paclitaxel or doxorubicin. Doxorubicin is widely used in anticancer therapy but targets the genetic material of the cell - the DNA. It was concluded from the above preclinical studies in mice that peloruside was highly effective in preventing the growth of human lung and breast cancer cells in mice and that further therapeutic development of peloruside as a potential new anticancer agent is warranted. This research was conducted in association with the University of Texas Southwestern Medical Center (Dallas), Reata Pharmaceuticals, Inc (Dallas), and the CTRC Institute for Drug Development (San Antonio).

Publication

Peloruside A Inhibits Growth of Human Lung and Breast Tumor Xenografts in an Athymic nu/nu Mouse Model.
Meyer CJ, Krauth M, Wick MJ, Shay JW, Gellert G, De Brabander JK, Northcote PT, Miller JH
Mol Cancer Ther. 2015 Aug