

Thioridazine kills cancer stem cells in human while avoiding toxic side-effects of conventional cancer treatments

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A team of scientists at McMaster University has discovered a drug, thioridazine, successfully kills cancer stem cells in the human while avoiding the toxic side-effects of conventional cancer treatments.

"The unusual aspect of our finding is the way this human-ready drug actually kills cancer stem cells; by changing them into cells that are non-cancerous," said Mick Bhatia, the principal investigator for the study and scientific director of McMaster's Stem Cell and Cancer Research Institute in the Michael G. DeGroote School of Medicine.

Unlike chemotherapy and radiation, thioridazine appears to have no effect on normal stem cells.

The research, published today in the science journal *Cell*, holds the promise of a new strategy and discovery pipeline for the development of [anticancer drugs](#) in the treatment of various cancers. The research team has identified another dozen drugs that have good potential for the same response.

For 15 years, some researchers have believed stem cells are the source of many cancers. In 1997, Canadian researchers first identified cancer stem cells in certain types of leukemia. Cancer stem cells have since been identified in blood, breast, brain, lung, gastrointestinal, prostate and [ovarian cancer](#).

To test more than a dozen different compounds, McMaster researchers pioneered a fully automated robotic system to identify several drugs, including thioridazine.

"Now we can test thousands of compounds, eventually defining a candidate drug that has little effect on normal stem cells but kills the cells that start the tumor," said Bhatia.

The next step is to test thioridazine in clinical trials, focusing on patients with [acute myeloid leukemia](#) whose disease has relapsed after chemotherapy. Bhatia wants to find out if the drug can put their cancer into remission, and by targeting the root of the cancer (cancer [stem cells](#)) prevent the cancer from coming back. Researchers at McMaster have already designed how these trials would be done.

Bhatia's team found thioridazine works through the dopamine receptor on the surface of the cancer cells in both leukemia and breast cancer patients. This means it may be possible to use it as a biomarker that would allow early detection and treatment of breast cancer and early signs of leukemia progression, he said.

The research team's next step is to investigate the effectiveness of the drug in other types of cancer. In addition, the team will explore several drugs identified along with thioridazine. In the future, thousands of other compounds will be analyzed with McMaster robotic stem cell screening system in partnership with collaborations that include academic groups as well as industry.

"The goal for all of the partners is the same – to find unique drugs to change the way we tackle and treat cancer," he said.

The research was supported by grants from the Canadian Institute of Health Research (CIHR), the Canadian [Cancer](#) Society Research

Institute (CCSRI) and the Ontario Ministry of Economic Development and Innovation (MEDI)'s Ontario Consortium of Regenerating inducing Therapeutics (OCReT).

"This large scale research endeavor would have been impossible without the active support and vision of the Canadian and Ontario governments along with private donors," said Bhatia.

More information: Sachlos et al.: "Identification of Drugs Including a Dopamine Receptor Antagonist that Selectively Target Cancer Stem Cells." *Cell*.

Provided by McMaster University

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