

A NEW WAY TO IMPROVE THE EFFECTIVENESS OF CHEMOTHERAPY IS DISCOVERED IN COLON CANCER RESEARCH

According to the American Cancer Society, colorectal cancer is the third most common cancer found in men and women in this country, not counting skin cancers. Researchers funded by the Foundation have identified one mechanism that enables colon tumors to flourish by silencing the action of protective genes. Correcting that mechanism can potentially make chemo much more effective in treating colon and other cancers, without the side effects that some current therapies cause.

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It is well established that many important genes which protect our cells against becoming cancerous can be silenced (i.e. "turned off") by an abnormal chemical modification of DNA called "DNA methylation". This allows cancer cells to grow, spread and to become resistant to chemotherapy. Dr. Melnick and his colleagues have explored the mechanism through which abnormal DNA methylation turns off these important protective genes. Specifically, they focused on a protein called "Kaiso", which had been shown to have the ability to attach to methylated genes and turn them off.

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Their research demonstrated:

- Higher levels of Kaiso protein were found in samples of mouse and human colonic tumors versus normal intestinal tissue.
- Kaiso was bound to critical methylated protective genes (i.e. "tumor suppressor genes") in colon cancer cells
- Removing the Kaiso releases these genes from silencing, allowing them to regain their normal protective function.
- Removing Kaiso made colon cancer cells much more susceptible to being killed by chemotherapy drugs.

Although the research was conducted on colon cancer, it appears to be applicable to other types of cancer in humans as well, since Kaiso is widely expressed in tumors.

These findings have important treatment implications. Restoring the tumor suppressor genes makes the colon tumor more susceptible to the impact of chemotherapy. Drugs that block Kaiso functions could thus potentially improve the effectiveness of chemo in treating various kinds of cancer.

Eloisi C. Lopes, Ester Valls, Maria E. Figueroa, Alexander Mazur, Fan-Guo Meng, Gabriela Chiosis, Peter W. Laird, Nicole Schreiber-Agus, John M. Greally, Egor Prokhorchouk, and Ari Melnick **Kaiso Contributes to DNA Methylation-Dependent Silencing of Tumor Suppressor Genes in Colon Cancer Cell Lines**, *Cancer Research*, Sept. 2008; 68: 7258-7263.

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<http://cancerres.aacrjournals.org/cgi/reprint/68/18/7258>

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