Chocolate compound stops cancer cell cycle in lab experiments

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Researchers from the Lombardi Comprehensive Cancer Center at Georgetown University have shown how an ingredient found in chocolate seems to exert its anti-cancer properties -- findings that might be used one day to design novel cancer treatments. The study, published in the April issue of the journal Molecular Cancer Therapeutics, explains how pentameric procyanidin (pentamer), a natural compound found in cocoa, deactivates a number of proteins that likely work in concert to push a cancer cell to continually divide.

"There are all kinds of chemicals in the food we eat that potentially have effects on cancer cells, and a natural compound in chocolate may be one," said the lead author, Robert B. Dickson, Ph.D., professor of oncology. "We need to slowly develop evidence about the selectivity of these compounds to cancer, learn how they work, and sort out any issues of toxicity."

Chocolate, like many other foods, is the source of many possible anti-cancer compounds, but Dickson stresses that this research, which is part of a series of studies conducted at Georgetown on the chocolate-cancer connection, does not mean that people who eat chocolate will either reduce their cancer risks or treat a current case. Although the study was conducted in breast cancer cell cultures, the finding could potentially apply to other cancers, Dickson said. (The studies are being funded by MARS Incorporated.)

Chocolate is made from the beans of cacao trees, and, like some other plants, are rich in natural antioxidants known as flavonoids. These antioxidants may protect cells from the damage caused by unstable molecules known as free radicals, which are thought to contribute to both heart disease and cancer development. The primary family of flavonoids contributing to the antioxidant benefit in chocolate is the procyanidins, and of the various types of procyanidins, pentamer seem to be strongest, according to a number of studies.

Given this, the Georgetown researchers looked at what happened when they used a purified preparation of pentamer on a variety of breast cancer cells, compared to treatment on normal breast cells. They used a variety of tests to find and identify proteins that were deactivated in the cancer cells.

What they located were two well known tumor suppressor genes as well as two other proteins known to be involved in regulating the "cell cycle" -- the progression of a cell from a state of being "quiet" into division and growth. They specifically found that the breast cancer cells stopped dividing when treated with pentamer and that all four proteins were inactivated. Furthermore, expression of one of the genes was reduced.

Dickson notes that "the novel aspect here is that a pattern of several regulatory proteins are jointly deactivated, probably greatly enhancing the inhibitory effect compared to targeting any one of the proteins singly. That is also why the compound seems to work on cancer cells, irrespective of whether any of these single genes are mutated, which often happens in cancer cells."

He adds that the researchers don't know why pentamer deactivates these proteins simultaneously, stopping the cell cycle. "We don't know at a fundamental level whether a master switch that triggers cell growth is turned off, or whether the chocolate compound exerts multiple independent effects on diverse cellular processes. That will be the subject of future studies here."

Co-authors of the study from Georgetown University are first author Danica Ramijak, Nicole Thompson, and Linda Metheny-Barlow. Leo Romanczyk from Masterfoods, USA, and other collaborators also contributed.

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