NIH researchers identify 22 antioxidants that can kill dividing cells

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(Medical Xpress) -- Researchers at NIH's National Human Genome Research Institute have identified 22 antioxidants out of more than 4000 compounds it has been studying, that are able to cause DNA damage and cell death, a result that could lead to new kinds of less harsh chemotherapy drugs. They group have published the results of their exhaustive study in the *Proceedings of the National Academy of Sciences*.

Antioxidants, such as resveratrol, found in grapes, blueberries and cranberries, which are currently used to treat a variety of ailments ranging from diabetes to heart disease and which some believe reduces the impact of aging, turns on a group of proteins called sirtuins and appears to be able to fix broken DNA and to prevent genes from mutating. This new research shows that they are able to do the opposite as well when administered in higher doses, which would be a good thing if the cells the antioxidants are working on are cancerous. They found that 22 of the antioxidants they studied were able to kill cells that were dividing, two of which have thus far been resistant to current methods of treatment. Specifically, they found that resveratrol and genistein both were able to kill cells that were rapidly dividing, a hallmark of tumor formation and were selective in their killing abilities, meaning they didn't kill the cells around them too.

The team stresses the importance of these findings suggesting that if antioxidants can be used to treat cancers, they would be much safer for patients as they would target only cancer cells, and wouldn't compromise the immune system in the process. They also note that much higher

doses of the antioxidants must be administered to kill dividing cells than people would normally get from drinking wine or taking supplements. And lest anyone grow too excited by their findings, they point out that their research is still in its infancy and that a lot more work will need to be done to discern whether such high doses of antioxidants would be harmful to a patient in ways not yet apparent. They add that they need to find out exactly which types of rapidly dividing cells are killed to figure out if they would be useful in treating just certain kinds of tumors, or a broad spectrum.

More information: High-throughput genotoxicity assay identifies antioxidants as inducers of DNA damage response and cell death, *PNAS*, Published online before print March 19, 2012, doi: 10.1073/pnas.1114278109

Abstract

Human ATAD5 is a biomarker for identifying genotoxic compounds because ATAD5 protein levels increase posttranscriptionally in response to DNA damage. We screened over 4,000 compounds with a cell-based quantitative high-throughput ATAD5-luciferase assay detecting genotoxic compounds. We identified 22 antioxidants, including resveratrol, genistein, and baicalein, that are currently used or investigated for the treatment of cardiovascular disease, type 2 diabetes, osteopenia, osteoporosis, and chronic hepatitis, as well as for antiaging. Treatment of dividing cells with these compounds induced DNA damage and resulted in cell death. Despite their genotoxic effects, resveratrol, genistein, and baicalein did not cause mutagenesis, which is a major side effect of conventional anticancer drugs. Furthermore, resveratrol and genistein killed multidrug-resistant cancer cells. We therefore propose that resveratrol, genistein, and baicalein are attractive candidates for improved chemotherapeutic agents.