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Scientists develop new cancer-killing compound from salad plant

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(PhysOrg.com) -- Researchers at the University of Washington have updated a traditional Chinese medicine to create a compound that is more than 1,200 times more specific in killing certain kinds of cancer cells than currently available drugs, heralding the possibility of a more effective chemotherapy drug with minimal side effects.

The new compound puts a novel twist on the common anti-malarial drug artemisinin, which is derived from the sweet wormwood plant (Artemisia annua L). Sweet wormwood has been used in herbal Chinese medicine for at least 2,000 years, and is eaten in salads in some Asian countries.

The scientists attached a chemical homing device to artemisinin that targets the drug selectively to cancer cells, sparing healthy cells. The results were published online Oct. 5 in the journal *Cancer Letters.*

"The compound is like a special agent planting a bomb inside the cell," said Tomikazu Sasaki, chemistry professor at UW and senior author of the study.

In the study, the UW researchers tested their artemisinin-based compound on human leukemia cells. It was highly selective at killing the cancer cells. The researchers also have preliminary results showing that the compound is similarly selective and effective for human breast and prostate cancer cells, and that it effectively and safely kills breast cancer in rats, Sasaki said.

Cancer drug designers are faced with the unique challenge that cancer cells develop from our own normal cells, meaning that most ways to poison cancer cells also kill healthy cells. Most available chemotherapies are very toxic, destroying one normal cell for every five to 10 cancer cells killed, Sasaki said. This is why chemotherapy's side effects are so devastating, he said.

"Side effects are a major limitation to current chemotherapies," Sasaki said. "Some patients even die from them."

The compound Sasaki and his colleagues developed kills 12,000 cancer cells for every healthy cell, meaning it could be turned into a drug with minimal side effects. A cancer drug with low side effects would be more effective than currently available drugs, since it could be safely taken in higher amounts.

The artemisinin compound takes advantage of cancer cell's high iron levels. Artemisinin is highly toxic in the presence of iron, but harmless otherwise. Cancer cells need a lot of iron to maintain the rapid division necessary for tumor growth.

Since too much free-floating iron is toxic, when cells need iron they construct a special protein signal on their surfaces. The body's machinery then delivers iron, shielded with a protein package, to these signals proteins. The cell then swallows this bundle of iron and proteins.

Artemisinin alone is fairly effective at killing cancer cells. It kills approximately 100 cancer cells for every healthy cell, about ten times better than current chemotherapies. To improve those odds, the researchers added a small chemical tag to artemisinin that sticks to the "iron needed here" protein signal. The cancer cell, unaware of the toxic compound lurking on its surface, waits for the protein machinery to deliver iron molecules and engulfs everything -- iron, proteins and toxic

compound.

Once inside the cell, the iron reacts with artemisinin to release poisonous molecules called free radicals. When enough of these free radicals accumulate, the cell dies.

"The compound is like a little bomb-carrying monkey riding on the back of a Trojan horse," said Henry Lai, UW bioengineering professor and co-author of the study.

The compound is so selective for cancer cells partly due to their rapid multiplication, which requires high amounts of iron, and partly because cancer cells are not as good as healthy cells at cleaning up free-floating iron.

"Cancer cells get sloppy at maintaining free iron, so they are more sensitive to artemisinin," Sasaki said.

Cancer cells are already under significant stress from their high iron contents and other imbalances, Sasaki said. Artemisinin tips them over the edge. The compound's modus operandi also means it should be general for almost any cancer, the researchers said.

"Most currently available drugs are targeted to specific cancers," Lai said. "This compound works on a general property of cancer cells, their high iron content."

The compound is currently being licensed by the University of Washington to Artemisia Biomedical Inc., a company Lai, Sasaki and Narendra Singh, UW associate professor of bioengineering, founded in Newcastle, Wash. for development and commercialization. Human trials are at least several years away. Artemisinin is readily available, Sasaki said, and he hopes their compound can eventually be cheaply

manufactured to help cancer patients in developing countries.

Other authors of the study are Steve Oh, UW medical student; Byung Ju Kim, UW chemistry instructor; and Singh.

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