

Magnolia compound hits elusive target in cancer cells

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A natural compound from magnolia cones blocks a pathway for cancer growth that was previously considered "undruggable," researchers have found.

A laboratory led by Jack Arbiser, MD, PhD, at Emory University School of Medicine, has been studying the compound honokiol, found in Japanese and Chinese herbal medicines, since discovering its ability to inhibit tumor growth in mice in 2003.

Arbiser's team's results were published in the July issue of *Clinical Cancer Research*. The research was a collaboration with the laboratory of David Foster, PhD, at Hunter College of the City University of New York. Hunter graduate students Avalon Garcia and Yang Zheng are the first authors of the paper. The collaboration also involved the lab of Dafna Bar-Sagi at New York University School of Medicine.

"Knowing more about how honokiol works will tell us what kinds of cancer to go after," says Arbiser, who is an associate professor of dermatology. "We found that it is particularly potent against tumors with activated Ras."

Ras refers to a family of genes whose mutation stimulates the growth of several types of cancers. Although the Ras family is mutated in around a third of human cancers, medicinal chemists have considered it an intractable target.

Honokiol's properties could make it useful in combination with other antitumor drugs, because blocking Ras activation would prevent tumors from escaping the effects of these drugs, Arbiser says.

"Honokiol could be effective as a way to make tumors more sensitive to traditional chemotherapy," he says.

One of the effects of Ras is to drive pumps that remove chemotherapy drugs from cancer cells. In breast cancer cell lines with activations in Ras family genes, honokiol appears to prevent Ras from turning on an enzyme called phospholipase D, Arbiser and his colleagues found. It also has similar effects in lung and bladder cancer cells in the laboratory. Phospholipase D provides what have come to be known as "survival signals" in cancer cells, allowing them to stay alive when ordinary cells would die.

Emory University is in the process of licensing honokiol and related compounds so that they can be tested in people in cooperation with industry partners.

Source: Emory University

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