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Researchers uncover powerful new class of weapons in the war on cancer

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An interdisciplinary team of researchers from the University of Texas Medical Branch, and Winship Cancer Institute of Emory University have identified small molecules that can represent a new class of anticancer drugs with a novel target for the treatment of lung cancer. These findings are detailed in *Nature Communications*. A PCT patent (WO 2013028543 A1) was jointly documented by these two Institutes for the invention.

Survival outcomes remain poor for lung cancer patients in large part because of lung cancer's resistance to conventional therapies. Programmed cell death, or apoptosis, is a natural process within cells that scientists are learning to successfully exploit in cancer therapies. The Bax molecule is required for the decision-making stage for programmed cell death. This research team has previously identified the serine184 site of the Bax molecule as a critical functional switch in controlling its cell death activities. Therefore, the researchers sought to learn how manipulate the Bax molecule at S184 to devise a new strategy for cancer treatment.

In the present study, researchers used the structural pocket around S184 as a docking site to screen about 300,000 small 'drug-like' compounds from the National Cancer Institute's library of small molecules to discover compounds that activate Bax and trigger apoptosis in lung cancer cells. They identified three small-molecule Bax activators that target the S184 site of Bax, activate the cell death machineries of Bax and potently repress lung tumor growth. The researchers also found that application of these compounds to Bax-positive lung cancer tumors did

not have any toxic effects on nearby noncancerous tissues.

"These compounds hold potential as an entirely new class of anticancer drugs with a unique therapeutic target for the treatment of cancers expressing Bax, including lung cancer," said Dr. Jia Zhou, lead UTMB author and associate professor at Department of Pharmacology and Center for Addiction Research. "They induce high levels of cell death in lung cancer cells without triggering cell death in noncancerous cells."

More information: *Nature Communications*, www.nature.com/ncomms/2014/140 … /abs/ncomms5935.html

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