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TopBP1 a sweet spot for treatment in multiple cancers

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A compound called calcein may act to inhibit topoisomerase IIβ-binding protein 1 (TopBP1), which enhances the growth of tumors, said researchers from Baylor College of Medicine in a report that appears online in the journal *Nature Communications*.

"The progression of many solid tumors is driven by de-regulation of multiple common pathways," said Dr. Weei-Chin Lin, associate professor of medicine- hematology & oncology, and a member of the NCI-designated Dan L. Duncan Cancer Center at Baylor. Among those are the retinoblastoma (Rb), PI(3)K/Akt and p53 pathways, which, when de-regulated, lead to accumulation and structural alteration of TopBP1.

Previously topoisomerase IIβ-binding protein 1 had been shown by Lin's lab to suppress apoptosis (programmed cell death) in cancer by repressing E2F1 and to mediate effects of p53 mutations. (TP53 is a tumor suppressor gene). When it is mutated or missing, it cannot prevent the formation of tumors. Moreover, mutant p53 proteins gain new functions in promoting cancer progression, and these activities in part depend on TopBP1.)

In studies in cell culture and in mice, Lin and his colleagues at Baylor showed that calcein inhibits these activities of TopBP1.

Here the authors identify calcein as a lead compound to inhibit TopBP1 and show that calcein has anti-tumor activity in mouse cancer models.

A topoisomerase is a class of enzymes that control the number and topology of supercoils in DNA. Type I enzymes cut one DNA strand, rotate it about the other, and reseal the ends. Type II enzymes cut and reseal both ends. TopBP1 is a protein that binds the enzyme.

Provided by Baylor College of Medicine