

Separating a cancer prevention drug from heart disease risk

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Several clinical studies have shown that taking the anti-inflammatory drug celecoxib can reduce the risk of developing polyps that lead to colon cancers, at the cost of increasing the risk of heart disease. But what if this tradeoff was not necessary?

Researchers at Winship Cancer Institute of Emory University have identified a way that celecoxib (<u>Celebrex</u>) pushes cancer cells into suicide, separately from its known effects. The Winship team's results outline a route to alternatives to celecoxib that keep its cancer-preventive properties while avoiding its risks.

Celecoxib's risk profile has confined its use to people who have inherited <u>cancer risk</u> or those who have had cancer already. Its effectiveness at stopping <u>tumor progression</u> and recurrence is being tested in several clinical trials for people who have had lung, head and neck and other <u>types of cancer</u>.

Shi-Yong Sun, PhD, and colleagues report in an upcoming issue of the journal <u>Cancer Research</u> that celecoxib inhibits an enzyme called GSK3 (glycogen synthase kinase 3) in <u>lung cancer cells</u>. This causes the disappearance of a protein called c-FLIP, which usually staves off apoptosis, a form of cellular suicide.

"We have been focusing on how celecoxib induces c-FLIP degradation and apoptosis in cancer cells, independent of COX-2 inhibition," Sun says.



Scientists think that celecoxib's ability to inhibit COX-2 enzymes is the basis for its anti-inflammatory properties as well as its influence on heart disease.

Sun is professor of hematology and medical oncology at Emory University School of Medicine and a Georgia Cancer Coalition Distinguished Cancer Scholar. The first author of the paper, postdoc Shuzhen Chen, is now at the Chinese Academy of Medical Sciences' Institute of Medicinal Biotechnology in Beijing. Fadlo Khuri, MD, deputy director of Winship Cancer Institute, is a co-author on the paper.

The result was surprising partly because until a few years ago, scientists thought that inhibiting GSK3, while possibly helpful in diseases such as diabetes, could promote cancer. However, recent results suggest that blocking GSK3 may stop cell growth in prostate, pancreatic and colon cancers and some types of leukemia.

Sun cautions: "We do not know whether GSK3 inhibition by celecoxib has anything to do with celecoxib's cardiovascular risk."

Provided by Emory University

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