Curry-derived molecules might be too spicy for colorectal cancers

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Curcumin, the yellowish component of turmeric that gives curry its flavor, has long been noted for its potential anti-cancer properties. Researchers from Tohoku University in Sendai, Japan, report on an apparent improvement upon nature: two molecular analogues of curcumin that demonstrate even greater tumor suppressive properties. The team presented their findings from the first test of these molecules in a mouse model of colorectal cancer today at the American Association for Cancer Research Centennial Conference on Translational Cancer Medicine.

According to Tohoku University researcher Hiroyuki Shibata, M.D., curcumin is one of the most widely studied plant-based chemicals with anti-cancer properties. Research has associated curcumin with several distinct actions, including the suppression of genes that promote cell growth (for example, the destruction of the pro-cancerous protein â catenin), and induction of programmed cell death (apoptosis) in colorectal cancer.

Unfortunately, natural curcumin has what researchers term “low bioavailability” -- the molecule quickly loses its anti-cancer attributes when ingested, Shibata says. With the aim of improving the therapeutic potential of curcumin, Shibata and his colleagues synthesized and tested 90 variations of the molecule’s structure. Two, GO-Y030 and GO-Y031, proved to be more potent and bioavailable, than natural curcumin.

“Our new analogues have enhanced growth suppressive abilities against

colorectal cancer cell lines, up to 30 times greater than natural curcumin," said Shibata, associate professor in the Department of Clinical Oncology at the Institute of Development, Aging and Cancer at Tohoku University. "In a mouse model for colorectal cancer, mice fed with five milligrams of GO-Y030 or GO-Y031 fared 42 and 51 percent better, respectively, than did mice in the control group."

In 2006, the researchers published basic safety and structural data for GO-Y030 and GO-Y031 in Molecular Cancer Therapeutics, a publication of the American Association for Cancer Research, and they continue to study the mechanisms behind the molecules' apparent potencies. In its natural form, the curcumin molecule is composed of two ring structures linked by a chain of seven carbon atoms. The active ring structures of GO-Y030 and GO-Y031, however, are linked by a shorter, five-carbon chain, which Shibata says might – for reasons still under investigation –account for their enhanced potency.

Like curcumin, the researchers believe the new analogues have clinical potential that extends beyond colorectal cancer. "In addition to colorectal cancer, the â catenin-degrading abilities of these molecules could apply to other forms of cancer, such as gastric cancer," said Shibata. "Like curcumin, these analogues also down-regulate a number of gene products, such as NF-kappa B, ErbB2, K-ras, that are also implicated in breast, pancreas and lung cancers among other diseases."

"In addition to their chemopreventative abilities, these molecules might also form the basis of a potent chemotherapy, either alone or in combination with other modes of therapy," said Shibata.

According to Shibata, the next step for the researchers is to further examine the drug delivery mechanisms, toxicology and pharmacokinetics of these analogues, before extending the research to clinical trials. Their studies were funded by the Japanese Society for the

Promotion of Science and the Miyagi Health Service Association.

Source: American Association for Cancer Research