Curcumin blocks the metastasis of colon cancer by a novel mechanism

26 August 2014, by Darci Slaten

Curcumin is the pigment that gives turmeric its bright yellow color.

Novel research led by the UA Steele Children's Research Center has identified one of the mechanisms by which curcumin, a bioactive molecule derived from the spice turmeric, can prevent cancer cell metastasis in colon cancer.

A team of researchers led by the University of Arizona's Steele Children's Research Center discovered that curcumin – the bioactive molecule derived from the spice turmeric – blocks the protein cortactin in colon cancer.

Cortactin, a protein essential for cell movement, frequently is overexpressed in cancer, thus facilitating cancer cell metastasis to other organs in the body.

Colon cancer is the second leading cause of cancer-related deaths in the United States and the third most common cancer in men and women. When cancer metastasizes to other organs, a patient's chances of survival are greatly diminished. Thus, finding novel ways to prevent cancer metastasis remains an urgent need.

The National Institutes of Health-funded research recently was published in *PLOS One*.

The study was led by co-investigators Dr. Fayez K. Ghishan, professor and head of the UA Department of Pediatrics and director of the Steele Children's Research Center; Pawel Kiela, associate professor in the UA Department of Pediatrics; and Vijay Radhakrishnan, assistant scientist in the UA Department of Pediatrics. The study was conducted in collaboration with Jesse Martinez, a professor in the UA Cancer Center, and Eugene Mash, a professor in the UA Department of Chemistry and Biochemistry.

Turmeric gives curry its yellow color and flavor. It is part of the ginger family and has been used for thousands of years to treat colds, inflammation, arthritis and many other ailments, including cancer.

Curcumin is the active ingredient in turmeric and has been scientifically studied in many types of cancer. It has been shown to have a chemopreventative effect – the ability to reverse, suppress or prevent the development of cancer.

"What's novel about our research is that our study identified one of the mechanisms by which curcumin can prevent cancer cell metastasis in colon cancer," Ghishan said.

The research team discovered that the active part of the cortactin protein, known as Phopsho Tyrosine 421 (pTyr421), is hyper-activated in malignant tumors of the colon.

"We showed that the cortactin protein was hyper-activated due to a process called excessive phosphorylation," Kiela said.

Phosphorylation is the addition of a phosphate group to a protein, and is responsible for turning proteins on and off, altering the protein's function and activity. Too much cortactin, and its activation

by phosphorylation, has been linked with cancer aggressiveness.

The researchers treated human colon cancer tumor cells with curcumin.

"We discovered that curcumin turns off the active form of cortactin," said Radhakrishnan, who led the experiments in the lab. "Thus, when cortactin is turned off, cancer cells lose the ability to move and can't metastasize to other parts of the body."

More specifically, curcumin "turned off" cortactin by interacting with, and activating, an enzyme known as PTPN1. This enzyme acts as a phosphatase to remove phosphate groups from cortactin – a process known as "dephosphorylation."

"This effect, essentially known as 'dephosphorylating cortactin' correlated with reduced ability of colon cancer cells to migrate," Kiela said. "This suggests that curcumin reduces cancer cells' ability to migrate, meaning the cancer can't metastasize."

"By identifying the mechanism of action – that curcumin activates the enzyme PTPN1, which then 'turns off' the active component of cortactin pTyr421, we believe that chemopreventative drugs can be developed to target cortactin in cancer cells to prevent the cancer from metastasizing," Radhakrishnan said.

"Treatments aimed at the suppression of cancer metastasis remain an urgent therapeutic need," Ghishan said. "Our findings have laid the foundation for future research to develop treatments using curcumin to prevent cancer's deadly spread to other organs."

More information: Radhakrishnan VM, Kojs P, Young G, Ramalingam R, Jagadish B, et al. (2014) "pTyr421 Cortactin Is Overexpressed in Colon Cancer and Is Dephosphorylated by Curcumin: Involvement of Non-Receptor Type 1 Protein Tyrosine Phosphatase (PTPN1)." *PLoS ONE* 9(1): e85796. DOI: 10.1371/journal.pone.0085796

Provided by University of Arizona