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Potent spice works to block growth of melanoma in lab test

HOUSTON - Curcumin, the pungent yellow spice found in both turmeric and curry powders, blocks a key biological pathway needed for development of melanoma and other cancers, say researchers from The University of Texas M. D. Anderson Cancer Center.

The study, to be published in the August 15, 2005 issue of the journal *Cancer*, but available on line at 12:01 a.m. (EDT) on Monday, July 11, demonstrates how curcumin stops laboratory strains of melanoma from proliferating and pushes the cancer cells to commit suicide.

It does this, researchers say, by shutting down nuclear factor-kappa B (NF-kB), a powerful protein known to promote an abnormal inflammatory response that leads to a variety of disorders, including arthritis and cancer.

The study is the latest to suggest that curcumin has potent anticancer powers, say the researchers.

"The antioxidant, anti-inflammatory and anti-carcinogenic properties of curcumin derived from turmeric are undergoing intense research here and at other places worldwide," says one of the study's authors, Bharat B. Aggarwal, Ph.D., professor of cancer medicine in the Department of Experimental Therapeutics.

At M. D. Anderson, for example, dramatic results from laboratory studies have led to two ongoing Phase I human clinical trials, testing the ability of daily capsules of curcumin powder to retard growth of pancreatic cancer and multiple myeloma. Another Phase I trial is planned for patients with breast cancer, and given this news of curcumin's activity in melanoma, animal studies will soon begin, Aggarwal says.

Ground from the root of the *Curcuma longa* plant, curcumin is a member of the ginger family. It has long been utilized in India and other Asian nations for multiple uses: as a food-preservative, a coloring agent, a folk medicine to cleanse the body, and as a spice to flavor food (two to five percent of turmeric is curcumin, for example).

While researchers had thought curcumin primarily has anti-inflammatory properties, the growing realization that cancer can result from inflammation has spurred mounting interest in the spice as an anti-cancer agent, Aggarwal says. He adds that another fact has generated further excitement: "The incidence of the top four cancers in the U.S. - colon, breast, prostate, and lung - is ten times lower in India," he says.

This work is just the latest by M. D. Anderson researchers to show how curcumin can inhibit cancer growth. "Curcumin affects virtually every tumor biomarker that we have tried," says Aggarwal. "It works through a variety of mechanisms related to cancer development. We, and others, previously found that curcumin down regulates EGFR activity that mediates tumor cell proliferation, and VEGF that is involved in angiogenesis. Besides inhibiting NF-kB, curcumin was also found to suppress STAT3 pathway that is also involved in tumorigenesis. Both these pathways play a central role in cell survival and proliferation."

He said that an ability to suppress numerous biological routes to cancer development is important if an agent is to be effective. "Cells look at everything in a global way, and inhibiting just one pathway will not be effective," says Aggarwal.

In this study, the researchers treated three different melanoma cell lines with curcumin and assessed the activity of NF-kB, as well the protein, known as "IKK" that switches NF-kB "on." The spice kept both proteins from being activated, so worked to stop growth of the melanoma, and it also induced "apoptosis," or programmed death, in the cells.

Surprisingly, it didn't matter how much curcumin was used, says the researchers. "The NF-kB machinery is suppressed by both short exposures to high concentrations of curcumin as well as by longer exposure to lower concentrations of curcumin," they say in their study. Given that other studies have shown curcumin is non-toxic, these results should be followed by a test of the spice in both animal models of melanoma and in human trials, they say.

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The study was funded by the National Cancer Institute and the Department of Defense. Co-authors included principle investigator Razelle Kurzrock, M.D.; first author Doris Siwak, Ph.D. and Shishir Shishodia.

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