Pepper and Halt: Spicy Chemical May Inhibit Gut Tumors

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Researchers at the University of California, San Diego School of Medicine report that dietary capsaicin – the active ingredient in chili peppers – produces chronic activation of a receptor on cells lining the intestines of mice, triggering a reaction that ultimately reduces the risk of colorectal tumors.

The findings are published in the August 1, 2014 issue of *The Journal of Clinical Investigation*.

The receptor or ion channel, called TRPV1, was originally discovered in sensory neurons, where it acts as a sentinel for heat, acidity and spicy chemicals in the environment. "These are all potentially harmful stimuli to cells," said Eyal Raz, MD, professor of Medicine and senior author of the study. "Thus, TRPV1 was quickly described as a molecular 'pain receptor.' This can be considered to be its conventional function, which all takes place in the nervous system."

But Raz and colleagues have found that TPRV1 is also expressed by epithelial cells of the intestines, where it is activated by epidermal growth factor receptor or EGFR. EGFR is an important driver of cell proliferation in the intestines, whose epithelial lining is replaced approximately every four to six days.

"A basic level of EGFR activity is required to maintain the normal cell turnover in the gut," said Petrus de Jong, MD, first author of the study. "However, if EGFR signaling is left unrestrained, the risk of sporadic tumor development increases."

The scientists discovered that TRPV1, once activated by the EGFR, initiates a direct negative feedback on the EGFR, dampening the latter to reduce the risk of unwanted growth and intestinal tumor development. They found that mice genetically modified to be TRPV1-deficient suffered higher-than-normal rates of intestinal tumor growths.

"These results showed us that epithelial TRPV1 normally works as a tumor suppressor in the intestines," said de Jong. In addition, molecular studies of human colorectal cancer samples recently uncovered multiple mutations in the TRPV1 gene, though Raz noted that currently there is no direct evidence that TRPV1 deficiency is a risk factor for colorectal cancer in humans.

"A direct association between TRPV1 function and human colorectal cancer should be addressed in future clinical studies," he said.

But if such proves to be the case, the current study suggests one potential remedy might be spicy capsaicin, which acts as an irritant in mammals, generating a burning sensation in contact with tissue. Capsaicin is already broadly used as an analgesic in topical ointments, where its properties as an irritant overwhelm nerves, rendering them unable to report pain for extended periods of time. It's also the active ingredient in pepper spray.

The researchers fed capsaicin to mice genetically prone to developing multiple tumors in the gastrointestinal tract. The treatment resulted in a reduced tumor burden and extended the lifespans of the mice by more than 30 percent. The treatment was even more effective when combined with celecoxib, a COX-2 non-steroidal anti-inflammatory drug already approved for treating some forms of arthritis and pain.

"Our data suggest that individuals at high risk of developing recurrent intestinal tumors may benefit from chronic TRPV1 activation," said Raz. "We have provided proof-of-principle."

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