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Cancer researchers first to link intestinal inflammation with systemic chromosome damage

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(PhysOrg.com) -- UCLA scientists have linked for the first time intestinal inflammation with systemic chromosome damage in mice, a finding that may lead to the early identification and treatment of human inflammatory disorders, some of which increase risk for several types of cancer.

Researchers found that local intestinal inflammation induced DNA damage to lymphocytes of the peripheral blood circulating throughout the body. This means that chromosome damage was not limited to the intestine, but involved tissues of the body distant from the site of inflammation. The team found single- and double-strand DNA breaks in the blood, and chromosome damage in peripheral blood indicating systemic genetic damage.

Inflammatory diseases have been linked to some lymphomas and abdominal, liver and colorectal cancers, said Robert Schiestl, a professor of pathology, radiation oncology and environmental health sciences and a Jonsson Cancer Center scientist. If inflammation can be found early - before any symptoms arise - and the diseases treated immediately, it may prevent the damage that eventually leads to these cancers, he said.

The study appears in the June 1, 2009, edition of *Cancer Research*, the peer- reviewed journal for the American Association for Cancer Research.

"This was not known before, that intestinal inflammation causes damage that can be found throughout the body," said Schiestl, the study's senior author. "This may help explain how inflammation leads to these cancers."

Conditions that cause intestinal inflammation include Crohn's disease, inflammatory bowel disease, ulcerative colitis and Celiac disease. About 1.4 million people in the United States and 2.2 million Europeans currently suffer from inflammatory bowel diseases and incidence worldwide is increasing, Schiestl said.

The chromosome damage in the peripheral circulating blood could be used as a biomarker to identify those with intestinal inflammation before they show any symptoms or suffer any distress. In the study, the chromosome damage could be detected in the blood before the onset of colitis in the mouse models the team studied, which were engineered to develop the inflammatory disorder, said Aya Westbrook, a graduate student of the UCLA Molecular Toxicology Interdepartmental Program and first author of the paper. She also noted that the severity of the disease correlated with higher levels of chromosome damage in the blood.

Dr. Jonathan Braun, professor and chairman of the Department of Pathology and Laboratory Medicine at UCLA and a study author, said the chromosome damage may be the "earliest detectable indicator" of intestinal inflammatory diseases.

"Patients come to us with abdominal complaints and we can't tell if they are inflammatory, obstructive or a bacterial overgrowth," said Braun, who also is a researcher at UCLA's Jonsson Cancer Center. "At present, the only way to diagnose the patients is to do full endoscopic examinations, which are both invasive and expensive. "

In principle, Braun said, this biomarker blood test could replace the invasive endoscopic exam and allow physicians to identify smoldering inflammatory disease before it becomes full blown.

"This may give us the opportunity to ward off the disease early and avoid the subsequent organ damage," Braun said. "This could change the natural history of these diseases."

Treating these diseases early would not only bring patients relief, it could prevent the cancers that might have developed later, Braun said.

"We know that prolonged exposure to intestinal inflammatory disease leads to greatly increased risk of cancer," he said. "If we can reduce the inflammation, we may be able to prevent the cancer."

UCLA researchers have launched a clinical trial to confirm their findings in humans, Schiestl said. They're focusing on patients with Crohn's disease and ulcerative colitis.

"This discovery may give us an opportunity to test new strategies to treat smoldering disease, which we've never been able to identify before," Schiestl said. "We may be able to test new drugs to see which are best at treating early inflammatory disease."

The research also may uncover why some patients with inflammatory disease develop cancers, while others may have chronic inflammatory disorders for decades and never develop cancer. There may be molecular mechanisms at work that protect some patients and not others. If those mechanisms could be found, it could lead to tests that can predict which patients with intestinal inflammatory diseases are predisposed to cancer.

Source: University of California - Los Angeles