'Two-faced' cells discovered in colon cancer: Immune cells can suppress or promote tumor growth

December 13 2012

Northwestern Medicine researchers have discovered a "two-faced" group of cells at work in human colon cancer, with opposing functions that can suppress or promote tumor growth. These cells are a subset of T-regulatory (Treg) cells, known to suppress immune responses in healthy individuals

In this previously unknown Treg subset, the presence of the protein RORγt has been shown to differentiate between cancer-protecting and cancer-promoting properties.

The Northwestern team, led by Khashayarsha Khazaie, research associate professor at the Robert H. Lurie Comprehensive Cancer Center of Northwestern University, recently reported their findings in the journal *Science Translational Medicine*.

"The subset of Tregs that expand in human colon cancer is different from the Tregs that abound in healthy individuals in their ability to suppress inflammation," said Khazaie. "Since their discovery, Tregs have been assumed to be harmful in cancer based on the knowledge that they suppress immunity. More recent clinical studies have challenged this notion. Our work shows that Tregs, by suppressing inflammation, are normally very protective in cancer; it is rather their switch to the expression of RORγt that is detrimental."

The Northwestern team's work builds on observations, which demonstrated that the transfer of Tregs from healthy mice to mice with colitis or colitis-induced cancer actually protected the mice from colitis and colitis-induced cancer.

After identifying the abnormal Treg subset in mice with hereditary colon cancer, Khazaie and lead author Nichole Blatner, research assistant professor at Lurie Cancer Center, worked with Mary Mulcahy, MD, associate professor of hematology and oncology, radiology, and organ transplantation, and David Bentrem, MD, Harold L. and Margaret N. Method Research Professor in Surgery, of Northwestern University Feinberg School of Medicine, to look for the same cells in colon cancer patients.

"To our delight, we found the same Treg alterations in cancer patients," said Khazaie.

Of cancers affecting both men and women, colorectal cancer (cancer of the colon and rectum) is the second leading cancer killer in the United States. In 2012, approximately 140,000 Americans were diagnosed with colon or rectal cancer, while more than 50,000 deaths occurred from either cancer, according to the Centers for Disease Control.

"The significance of our discovery became apparent when by inhibiting RORgt in Tregs we were able to protect mice against hereditary colon cancer," Khazaie said.

He notes that several ongoing clinical trials exist based on targeted elimination of all Tregs in cancer patients. However, the discovery of Treg diversity in cancer, and its central role in control of cancer inflammation, may lead to new approaches for therapeutics.

"Tregs are actually very useful in the fight against cancer," he says. "We

can do better by targeting RORγt or other molecules that are responsible for the expansion of this Treg subset, instead of indiscriminately eliminating all Tregs. We are very excited about the therapeutic options that targeting specific subsets of Tregs could provide in human solid tumor cancers, and that is our next immediate goal."

Khazaie's team is moving forward with plans to test novel drugs that inhibit RORγt.

Provided by Northwestern University