

# Scientists document the development of cancer stem cells

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Xi He, M.D., Research Specialist II, and Linheng Li, Ph.D., Associate Investigator, are the first and last authors, respectively, on a new publication that clarifies how normal stem cells become cancer stem cells and how cancer stem cells can cause the formation of tumors.

The paper, "PTEN-deficient intestinal stem cells initiate intestinal polyposis" was posted to the *Nature Genetics* Web site on January 21.

The theory that cancer stem cells initiate and drive cancer cell growth has been gaining popularity in both clinical and basic research. Recent studies have identified cancer stem cells and shown that they may cause tumors when transplanted into a secondary host. Until now, however, little was known about the process by which mutations in a stem cell result in primary tumor initiation.

The Li Lab team studied the intestinal system in mice in which one of the human tumor suppressor genes, PTEN, had been deleted. They found that the PTEN/Akt pathway likely regulates stem cell activation by helping control nuclear localization of beta-catenin, the Wnt pathway effector, through phosphorylation of beta-catenin -- including Serine552.

"We found that a loss of PTEN in intestinal epithelial cells accompanied by a loss of PTEN in stromal cells can lead to changes that may increase the number of stem cells and change their position or location," said Dr. Li. "These changes result in crypt fission and budding and can lead to intestinal polyposis and uncontrolled tumor growth."

"All of us were very excited to be part of these efforts to reveal basic features of cancer stem cells," said Dr. He. "What we learned -- that cancer stem cells are a rare population in the tumor mass; that they are slow cycling but more active than normal stem cells; and that cancer stem cells and

stromal insertions initiate the process of primary tumorigenesis -- will be influential in our future work."

"Findings from the Li Lab create opportunities to further characterize cancer stem cells and to obtain their molecular signature -- providing important insight into targeting these cells," said Robb Krumlauf, Ph.D., Scientific Director. "This is a fascinating new area of cancer research, and Linheng Li and his colleagues will continue to make important contributions."

Source: Stowers Institute for Medical Research

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