Researchers uncover new clues to the development of blood and other cancers

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Scientists at Fox Chase Cancer Center have uncovered more details about how defects in components of the machinery that makes new proteins can lead to blood and other cancers. The findings, which will be presented at the AACR Annual Meeting 2012 on Monday, April 2, may one day lead to new targeted therapies that address those problems.

"These findings help explain how mutations in one class of proteins can trigger the development of cancer," says Shuyun Rao, Ph.D., a scientific associate in the lab of David L. Wiest, Ph.D., also a co-author on the study, at Fox Chase Cancer Center in Philadelphia. "If we find a way to block the pathway activated by these mutations, this may cause tumors to regress."

The research focused specifically on ribosomal proteins. Previous research has linked mutations in ribosomal proteins to cancers such as leukemia and lymphoma, as well as myelodysplastic syndromes (MDS), which can lead to acute myelogenous leukemia (AML). However, this study represents the first insights into how mutations in ribosomal proteins might increase cancer risk.

To investigate further how an individual ribosomal protein might trigger cancer, Rao, Wiest and their colleagues focused on one known as L22. To begin, they looked at blood samples from a small number of leukemia patients—approximately 50 —and found that in 9%, L22 was either mutated or deleted entirely. This suggested that problems in L22 may have played a role in the development of their cancers.

Next, they deleted L22 in mice that were bred to be prone to develop lymphomas, and saw that their tumors developed faster, and the mice died faster than those who had intact forms of L22 – further evidence of its important role in the disease.

Finally, in a sample of cells in the lab, the researchers inactivated L22 and saw that the cells experienced changes, signaling the early stages of lymphoma. Specifically, cells without L22 showed more activity in a pathway associated with inflammation known as NFkappaB, which other research has linked to cancer. "In theory, if we could find a way to block this pathway, we could add this to existing therapies to help treat the tumors it triggers," says Rao.

Although L22 is a ribosomal protein, and therefore helps build new proteins, previous research has found that eliminating L22 does not affect the rate with which cells make new proteins – suggesting L22 has additional functions, says Rao.

Previous research has found that L22 expression is strikingly reduced in a number of liquid and solid tumors including breast cancer, lung adenocarcinoma and ovarian carcinoma. "These findings don't just have implications for people with leukemia," Wiest says. "It is likely that L22 repression or inactivation will play a role in other cancer types as well"

Provided by Fox Chase Cancer Center