Newly discovered genetic markers could signal colon cancer development

August 24 2012

University of Minnesota Medical School and Masonic Cancer Center researchers have partnered with geneticists from Genentech, Inc., to discover how some proteins may cause the development of some forms of colon cancers.

The proteins – part of R-spondin family – normally help activate cell proliferation during embryonic development. Now, University of Minnesota researchers have discovered that when two types of R-spondins – RSPO2 and RSPO 3 – are reactivated in adults through certain gene mutations, they can signal cells to restart the cell proliferation process, which can lead to tumor growth in the colon.

The discovery, which involved multiple researchers from the University's Masonic Cancer Center, could lead the way to more personalized colon cancer therapy designed around the genetics of a patient's specific cancer. The results are available online now, in the journal *Nature*.

"These results suggest there is a potential for personalized therapies based on knowing a tumor's specific genetics," said David Largaespada, Ph.D., associate director of Basic Sciences and professor in the Department of Genetics, Cell Biology and Development. "And because these R-spondins are related to embryonic growth, and seem to not have major roles in the adult, targeting them would likely be low in side effects."

To arrive at the results, researchers analyzed more than 70 pairs of human colon tumors and a mouse model engineered using the Sleeping Beauty transposon by Largaespada. Through a series of investigations, researchers identified 36 rearrangements that result in gene fusions, including two recurrent ones involving R-spondin family members RSPO2 and RSPO3.

While the results could generate more personalized approaches to the treatment of colon cancer, researchers stress more research is needed before these results can be applied to actual patient care.

Caitlin Conboy, an M.D./Ph.D. student studying at the University of Minnesota, worked closely on this project and is nowworking to advance the science of this paper to the next stage.

"What we're finding is that tumors may look the same, but they're fundamentally different," said Conboy. "Diagnosis may be less about the tissue where the tumor is found, like the breast or colon, but the drivers of the tumor's growth."

Conboy is beginning work on a study that will help determine if a blocking agent could be useful in treating tumors driven by R-spondin production. If this project is successful, it could help create new therapeutic approaches useful in certain patients after a tumor genetic test is done.

Provided by University of Minnesota