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Cancer-linked FAM190A gene found to regulate cell division

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Johns Hopkins cancer scientists have discovered that a little-described gene known as FAM190A plays a subtle but critical role in regulating the normal cell division process known as mitosis, and the scientists' research suggests that mutations in the gene may contribute to commonly found chromosomal instability in cancer.

In laboratory studies of cells, investigators found that knocking down expression of FAM190A disrupts mitosis. In three pancreatic cancer-cell lines and a standard human-cell line engineered to be deficient in FAM190A, researchers observed that cells often had difficulty separating at the end of mitosis, creating cells with two or more nuclei. The *American Journal of Pathology* published a description of the work online May 17, which comes nearly a century after German scientist Theodor Boveri linked abnormal mitosis to cancer. Until now, there had been no common gene alteration identified as the culprit for cancer-linked mitosis.

"These cells try to divide, and it looks like they succeed, except they wind up with a strand that connects them," explains Scott Kern, M.D., professor of oncology and pathology at Johns Hopkins University School of Medicine and its Kimmel Cancer Center. "The next time they try to divide, all the nuclei come together, and they try to make four cells instead of two. Subsequently, they try to make eight cells, and so on." Movies of the process taken by Kern's laboratory are available on the journal Web site.

Kern's group previously reported that deletions in the FAM190A gene could be found in nearly 40 percent of human cancers. That report, published in 2011 in the journal Oncotarget, and the current one are believed to be the only published papers focused solely on FAM190A, which is frequently altered in human cancers but whose function has been unknown. Alterations in FAM190A messages may be the third most common in human cancers after those for the more well-known genes p53 and p16, Kern says.

"We don't think that a species can exist without FAM190, but we don't think severe defects in FAM190A readily survive among cancers," Kern says. "The mutations seen here are very special – they don't take out the whole gene but instead remove an internal portion and leave what we call the reading frame. We think we're finding a more subtle defect in human cancers, in which mitosis defects can occur episodically, and we propose it may happen in about 40 percent of human cancers."

Abnormalities in FAM190A may cause chromosomal imbalances seen so commonly in cancers, Kern says. Multipolar mitosis is one of the most common functional defects reported in human cancers, and more than 90 percent of human cancers have abnormal numbers of chromosomes.

Kern says he plans to study FAM190A further by creating lab models of the subtle defects akin to what actually is tolerated by human cancer cells.

Provided by Johns Hopkins University School of Medicine