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Researchers identify potential cancer target

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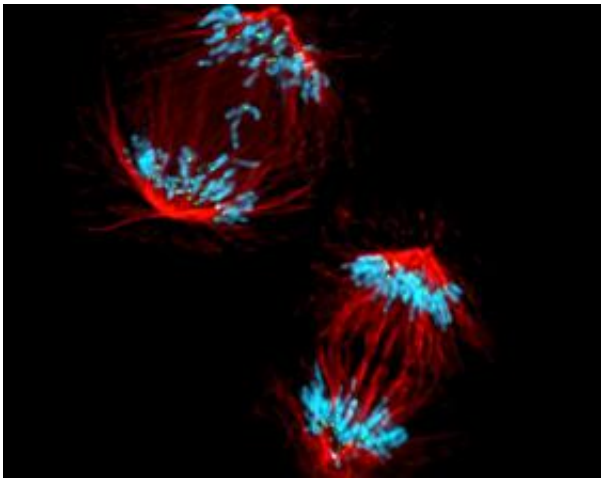

Two anaphase spindles from the control (lower) and Kif2b-depleted (upper) cells. See how the upper spindle contains two lagging chromosomes. Microtubules are shown in red, chromosomes in blue, and the kinetochore marker is in green. (image by Samuel Bakhoum)

(PhysOrg.com) -- Dartmouth Medical School researchers have found two proteins that work in concert to ensure proper chromosome segregation during cell division. Their study is in the January 2009 issue of the journal *Nature Cell Biology*.

This finding is relevant for treating solid cancerous tumors that lose the ability to accurately segregate their chromosomes. Tumors that shuffle chromosomes, a process called chromosomal instability, are known to have a poor prognosis.

"We show that the function of two proteins, called Kif2b and MCAK, is to correct improper attachments during cell division to prevent the mis-segregation of chromosomes" said Duane Compton, the senior author on the paper and a professor of biochemistry at Dartmouth Medical School. "The two proteins share the workload as Kif2b acts early in cell division and MCAK acts later. This cooperation underlines the importance of proper chromosome segregation for the healthy life of all cells." Compton is also director of the Cancer Mechanisms Research Program at Norris Cotton Cancer Center at Dartmouth-Hitchcock Medical Center.

Compton explained this finding follows a study his team published in the February 2008 issue of The Journal of Cell Biology that showed that the main cause of chromosomal instability is that chromosomes make improper attachments to the spindle apparatus during cell division. "These improper attachments occur normally during cell division in all cells, but in the tumor cells, the improper attachments fail to get corrected and cells attempt to divide with persistent improper attachments," said Compton.

The current study shows the two proteins complete their job by regulating the attachment between the chromosomes and the spindle apparatus. Based on these results, the team also determined that increasing quantities of either Kif2b or MCAK in tumor cells restored nearly normal accuracy of chromosome segregation.

"We discovered how to make the tumor cells faithfully segregate their chromosomes every time the cell divides," said Compton. "Chromosomal instability has been studied for over a decade in tumor cells; this is the first time anyone has suppressed it in tumor cells indicating a strong causal relationship between correction of improper attachments of chromosomes to the spindle apparatus and chromosomal instability. These results give us insight into the overall mechanisms of

cell division in tumor cells compared to normal cells, and we may be able to exploit that, leading to new therapeutic strategies or treatments that might prevent tumor progression."

Compton and his team will now work to directly test the contribution of CIN to tumor development.

Source: Dartmouth College

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