

Segregating out UbcH10's role in tumor formation

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A single chromosome lags behind the others in a dividing cell overexpressing UbcH10. Credit: van Ree, J.H., et al. 2010. J. Cell Biol. doi:10.1083/jcb.200906147

A ubiquitin-conjugating enzyme that regulates the cell cycle promotes chromosome missegregation and tumor formation, according to van Ree et al. in the January 11 issue of the *Journal of Cell Biology*.

The mitotic E2 enzyme UbcH10 partners with the anaphase-promoting complex/cyclosome (APC/C) to ubiquitinate cell cycle regulators, targeting them for proteasomal destruction, and ensuring progression through mitosis. UbcH10 is overexpressed in a variety of human cancers, but whether it causes tumors or is simply up-regulated due to the increased number of proliferating cancer cells is unknown.



van Ree et al. generated mice expressing high levels of UbcH10 and found that they formed tumors in a broad range of tissues. Many of these tumors displayed aneuploidy—abnormal numbers of <u>chromosomes</u> resulting from errors in cell division. Live microscopy showed that cells expressing high amounts of UbcH10 had problems segregating sister chromatids correctly, possibly because the cells contained extra numbers of centrosomes that might complicate formation of a normal mitotic spindle. UbcH10 overexpression also reduced levels of the mitotic regulator cyclinB—a substrate of the APC/C—though it remains to be seen if this contributes directly to centrosome amplification and aneuploidy.

The same research group recently demonstrated that chromosome segregation defects drive tumorigenesis by promoting the loss of tumor suppressor genes like <u>p53</u>. Senior author Jan van Deursen now wants to investigate whether UbcH10 synergizes with other factors to promote chromosome instability in human cancers.

More information: van Ree, J.H., et al. 2010. J. Cell Biol. <u>doi:10.1083/jcb.200906147</u>

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