

Mayo Clinic uncovers how one gene, protein suppresses tumor formation

June 2 2016

Pten (short for phosphatase and tensin homolog) is a tumor suppressor that is defective in about 20-25 percent of all patients with cancers. Mayo Clinic researchers now have discovered that Pten safeguards against tumor formation by keeping chromosome numbers intact when a cell splits into two daughter cells. In this study, the last three amino acids of the Pten protein, which are often missing in human cancers, were found to be critical for forming an intact mitotic spindle, a structure required for accurate chromosome segregation. The findings appear in the online issue of *Nature Cell Biology*.

Pten is the most prominent human [tumor suppressor](#) after p53. The current thinking is that Pten's phosphatase activity counteracts PI3 kinase activity. Loss of this function causes [tumor formation](#) through uncontrolled stimulation of AKT, an enzyme that stimulates cell proliferation and survival and is often hyperactive in human tumors. For years, there has been speculation that Pten defects found in cancer patients also lead to the reshuffling of the cell's chromosomes, but it was unknown how that would happen and how it propels cancer growth. The Mayo study now provides definitive answers to these long-standing questions.

"We found that Pten localizes to mitotic spindle poles to recruit the 'motor' protein EG5, which moves the poles apart to form a perfectly symmetrical bipolar spindle that accurately separates duplicated chromosomes," says senior author Jan van Deursen, Ph.D., a molecular biologist and cancer researcher at Mayo Clinic. The research team

further found that the recruitment process involves Dlg1, an Eg5-binding protein that docks to the last three Pten amino acids at spindles poles. Importantly, mutant mice lacking these amino acids have abnormal chromosome numbers and form tumors at high frequency. The researchers say these new findings predict that a large proportion of Pten tumors will be hypersensitive to Eg5-inhibiting drugs, providing new opportunities for targeted cancer therapy.

More information: Janine H. van Ree et al, Pten regulates spindle pole movement through Dlg1-mediated recruitment of Eg5 to centrosomes, *Nature Cell Biology* (2016). [DOI: 10.1038/ncb3369](https://doi.org/10.1038/ncb3369)

Provided by Mayo Clinic

Citation: Mayo Clinic uncovers how one gene, protein suppresses tumor formation (2016, June 2) retrieved 20 September 2024 from <https://phys.org/news/2016-06-mayo-clinic-uncovers-gene-protein.html>

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