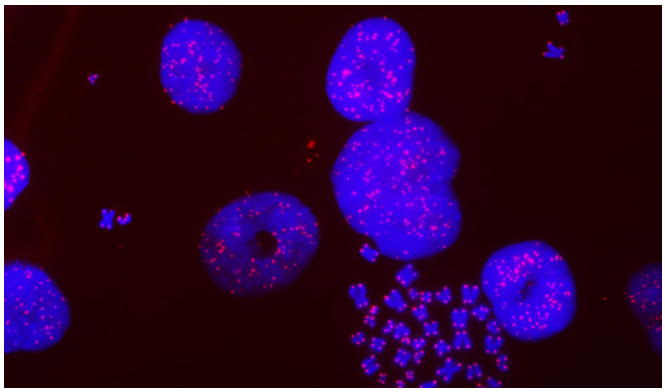
Researchers uncover new cancer cell vulnerability

18 July 2014



Chromosomes (in blue) and their telomores (in red). Credit: Lab of Narenda Wajepeyee, Yale School of Medicine

(Medical Xpress)—Yale School of Medicine and Yale Cancer Center researchers have uncovered a genetic vulnerability of cancer cells that express telomerase—an enzyme that drives their unchecked growth—and showed that telomerase-expressing cells depend upon a gene named p21 for their survival.

Authors found that simultaneous inhibition of both telomerase and p21 inhibited tumor growth in mice. The telomerase enzyme is overexpressed in over 90% of human cancers, but not in normal cells, and expression of telomerase is necessary to initiate and promote cancer growth. In this study, the Yale team, led by first author Romi Gupta and corresponding author Narendra Wajapeyee of the Department of Pathology, showed how new pharmacological drug combinations can be applied to simultaneously target both telomerase and p21 to induce cell death in telomerase-expressing cancer cells.

Finally, the authors also showed that their approach is also applicable for p53 mutant cancers if telomerase and p21 inhibition is combined with pharmacological restoration of p53 tumor suppressor activity. The study, which could open doors to novel therapies for telomerase inhibition, appears in the *Proceedings of the National Academy of Sciences*.

More information: Romi Gupta, Yuying Dong, Peter D. Solomon, Hiromi I. Wettersten, Christopher J. Cheng, JIn-Na Min, Jeremy Henson, Shaillay Kumar Dogra, Sung H. Hwang, Bruce D. Hammock, Lihua J. Zhu, Roger R. Reddel, W. Mark Saltzman, Robert H. Weiss, Sandy Chang, Michael R. Green, and Narendra Wajapeyee. "Synergistic tumor suppression by combined inhibition of telomerase and CDKN1A." *PNAS* 2014 ; published ahead of print July 14, 2014, DOI: 10.1073/pnas.1411370111

Provided by Yale University