

Researchers report new understanding of role of telomeres in tumor growth

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The first report of the presence of alternative lengthening of telomeres (ALT) in cancers arising from the bladder, cervix, endometrium, esophagus, gallbladder, liver, and lung was published today in *The American Journal of Pathology*. The presence of ALT in carcinomas can be used as a diagnostic marker and has implications for the development of anti-cancer drug therapies.

Telomeres are nucleoprotein complexes located at the ends of chromosomes. During normal cell division, these telomeres become shorter with each division, potentially resulting in cell death. In some cancers, however, this shortening is counteracted by the ALT mechanism, thus allowing the unlimited growth of the [cancer cells](#).

"The present study offers a springboard to guide future investigations in larger cohorts that specifically focus on the tumor types exhibiting ALT to more precisely determine the prevalence and potential prognostic value of this phenotype," commented lead investigator Christopher Heaphy, PhD, a postdoctoral research fellow at The Johns Hopkins School of Medicine.

"These results may have therapeutic consequences, given that cancers using the ALT pathway are predicted to be resistant to anti-telomerase therapies, some of which have entered phase I/II clinical trials. Further understanding of the [molecular mechanisms](#) of ALT will be paramount in designing novel anti-cancer therapeutics targeting cancers utilizing the ALT pathway," observed corresponding author Alan K. Meeker, PhD, Assistant Professor of Pathology at Johns Hopkins.

Meeker and co-investigators have assessed the prevalence of the ALT mechanism in a wide range of [human cancer](#) subtypes. Analyzing 6,110 tumor samples from 94 different cancer subtypes, 541 benign neoplasms, and 264 normal tissue samples, researchers found that the overall

prevalence of the ALT phenotype was 3.73%. It was not observed in benign neoplasms or normal tissues.

Additionally, this is the first report of ALT in medulloblastomas, [oligodendrogliomas](#), meningiomas, schwannomas, and pediatric glioblastoma multiformes.

The authors also note that they were able to identify many tumor types that apparently may not use the ALT pathway for telomere maintenance. In particular, they assessed hundreds of cases of adenocarcinomas arising from the prostate, colon, pancreas, or small intestine and did not observe a single ALT-positive tumor.

Previous studies have shown associations between ALT status and prognosis in some tumor types. The authors suggest that further studies are warranted to assess the potential prognostic significance and unique biology of ALT-positive tumors.

More information: The article is "Prevalence of the Alternative Lengthening of Telomeres Telomere Maintenance Mechanism in Human Cancer Subtypes" by Christopher M. Heaphy, Andrea P. Subhawong, Seung-Mo Hong, Michael G. Goggins, Elizabeth A. Montgomery, Edward Gabrielson, George J. Netto, Jonathan I. Epstein, Tamara L. Lotan, William H. Westra, Ie-Ming Shih, Christine A. Iacobuzio-Donahue, Anirban Maitra, Qing K. Li, Charles G. Eberhart, Janis M. Taube, Dinesh Rakheja, Robert J. Kurman, T.C. Wu, Richard B. Roden, Pedram Argani, Angelo M. De Marzo, Luigi Terracciano, Michael Torbenson, and Alan K. Meeker. ([doi:10.1016/j.ajpath.2011.06.018](https://doi.org/10.1016/j.ajpath.2011.06.018)). It will appear in *The American Journal of Pathology*, Volume 179, Issue 4 (October 2011).

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