

Telomere lengths differ significantly between small cell neuroendocrine carcinoma and adenocarcinoma of the prostate

Christopher M. Heaphy^{1,2,4}, Michael C. Haffner¹, Harrison K. Tsai¹, Jonathan I. Epstein^{1,2,3,4}, Angelo M. De Marzo^{1,2,3,4}, Alan K. Meeker^{1,2,3,4}, Tamara L. Lotan^{1,2,3,4}

Departments of Pathology¹, Oncology² and Urology³, Johns Hopkins University School of Medicine; ⁴Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

Background: Small cell neuroendocrine carcinoma (SCC) of the prostate is an aggressive subtype with frequent *TP53* mutation and *RB1* inactivation. However, the molecular phenotype remains an area of active investigation. Here, we compared telomere lengths in prostatic SCC and usual-type prostatic adenocarcinoma (AdCa).

Methods: We studied 32 cases of prostatic SCC (including 11 cases with concurrent AdCa) and 347 cases of usual-type AdCa on tissue microarrays (TMA). Telomere lengths in tumor cells were qualitatively compared to that in adjacent benign cells using a telomere-specific fluorescence *in situ* hybridization (FISH) assay. *ERG*, *PTEN* and *TP53* status were assessed in a proportion of cases using genetically validated immunohistochemistry protocols. Clinical-pathologic and molecular characteristics of cases with normal or long telomeres were compared to those with short telomeres using the chi-square test.

Results: A significantly higher proportion of prostatic SCC cases (50%, 16/32) displayed normal/long telomere lengths compared to AdCa cases (11%, 39/347; $p < 0.0001$). In 82% (9/11) of cases with concurrent SCC and AdCa, the components were concordant for telomere length status. Among AdCa cases, the proportion of cases with normal/long telomeres significantly increased with increasing tumor Grade Group ($p = 0.01$) and pathologic stage ($p = 0.02$). Cases with normal/long telomeres were more likely to be ERG positive ($p = 0.04$) and to have a *TP53* missense mutation ($p = 0.01$) compared to cases with short telomeres. Although, among a small cohort of 54 surgically-treated very high grade (Gleason 9 and 10) AdCa cases, there were no significant associations between cancer cell telomere length category and biochemical recurrence- or metastasis-free survival.

Conclusions: Normal or long telomere lengths are significantly more common in prostatic SCC compared to AdCa and are similar between concurrent SCC and AdCa tumors supporting a common origin. Among AdCa cases, longer telomere lengths are significantly associated with high risk pathologic and molecular features, although in a small high grade AdCa cohort, there were not significant associations with oncologic outcomes.

Conflicts of Interest: None.

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