

A high-throughput approach to measure cell type-specific telomere lengths in archival prostate tissues

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Telomeres, the repetitive DNA elements at chromosome ends, are pivotal for maintenance of genome integrity. The function of the telomeres is to inhibit exonucleolytic degradation, prohibit inappropriate homologous recombination, and prevent chromosomal fusions by suppressing double-strand break signals. We have previously shown that tissue-based measurement of telomeres is useful in predicting prostate cancer death in men surgically treated for their clinically localized prostate cancer. Here, we describe a robust and high-throughput method to quantitate cell type-specific telomere lengths at a single cell level in archival prostate tissues. This approach is based on telomere-specific FISH combined with immunostaining for basal cells (basal specific-specific cytokeratin), epithelial cells (NKX3.1 and FOXA1), and T-cell and B-cell (CD3 and CD20). Next, semi-automated slide scanning and multi-channel acquisition of fluorescent images (DAPI, FITC, Cy3, and Cy5) is accomplished using the TissueFAXS Plus microscopy workstation and TissueQuest software (Tissue Gnostics). Using this system, we have documented reliable within- and between-operator measurements of telomere lengths in prostate cancer and cancer-associated stromal cells. Thus, this new method is sufficiently robust and reproducible to detect biologically significant differences in telomere lengths in the prostate using biopsy or prostatectomy specimens, either on whole slide or on tissue microarray format, and should be readily translated into other tissue types. We are currently validating the translational potential of cell type-specific telomere lengths for prognostication and risk stratification for individualized therapeutic and surveillance strategies.

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