

Title: Screening of prostate cancer patients by Detection of loss of heterozygosity (LOH) in Circulating Cell-Free DNA(cf-DNA) as a novel biomarker

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Abstract

Background: Several lines of evidence suggest that loss of heterozygosity (LOH) in specific chromosomal regions, a common mechanism for the inactivation of tumor suppressor genes that are implicated in pathogenesis of prostate cancer (PCa). Short tandem repeat (STR) sequences are extremely reliable genetic markers for the detection of LOH associated with cancers. Hence, in the current study we investigated whether detection of LOH at six STR markers (D8S360, D9S1748, D9S171, D8S137, D6S1631, and THRB) in blood circulating cell-free DNA (cf-DNA) could be used to distinguish PCa from benign prostate hypertrophy (BPH).

Material and methods: A total of 136 individuals were included in the current study, 76 males diagnosed with PCa (50 males with localized PCa (LPCa) and 26 males with metastatic PCa (MPCa)) as cases and 60 males with BPH as controls. Circulating Free DNA was extracted from plasma samples, also Genomic DNA from peripheral blood as a reference, and amplified with fluorescence-labeled primers specific for occurrence of LOH in studied STR markers. We compared the frequencies of homozygosity at all studied STR markers in genomic DNA in PCa and BPH subjects. We also evaluate serum prostate-specific antigen (PSA) and cfDNA levels in both groups.

Results: Our findings revealed that the frequency of LOH at D8S360, D9S1748, D9S171, D8S137 and D6S1631 markers was significantly higher in PCa subjects than in controls ($p < 0.05$). Of the six STR markers, LOH at D8S360 marker could be discriminate MPCa from LPCa. We also found that 71.05 % of patients with PCa and 1.66 % of BPH subjects had LOH at least in three markers in cf-DNA. We also showed correlation between occurrence of LOH in some STR with PSA-level.

Conclusion: Our findings provide additional evidence to support the hypothesis that analysis of LOH at D8S360, D9S1748, D9S171, D8S137 and D6S1631 STR markers in cf-DNA probably can be applied as non-invasive diagnostic approach for detection of PCa instead of unnecessary biopsies or other invasive method such as DRE or TRUS and can be a complementary test alongside PSA evaluation. However, further studies may be required on large scale of population and other STR markers to validate these data

Biography

Seyedeh-maryam seyedolmohadessin is a Ph.D student of molecular genetic in Science and Research Branch, Islamic Azad University in Iran.She is working on Prostate Cancer and Cell free DNA more than 3 years in Tehran Medical Genetic Center and cooperates with certified urologists in reference urology centers in Tehran for gathering cases and consulting about invasive and non-invasive methods for diagnosis of prostate cancer by working on a novel prognostic and diagnostic biomarker named circulating cell free DNA.

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