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Titel des Beitrags: Genome-wide linkage analysis of TMPRSS2-ERG fusion in familial prostate cancer.

Abstract: Fusion of the 5'-untranslated region of androgen-regulated TMPRSS2 promoter with ETS transcription factor family members is found frequently in prostate cancers, and recent work suggests that the most common TMPRSS2-ERG fusion is associated with an aggressive clinical phenotype compared with fusion-negative prostate cancer. Thus far, analysis of the fusion has been limited to sporadic cases of prostate cancer. In the current study, we explore for an enrichment of TMPRSS2-ERG fusion in familial prostate cancer. TMPRSS2-ERG fusion was identified using a break-apart fluorescence in situ hybridization assay on tissue microarrays. Presence of TMPRSS2-ERG fusion was associated with higher Gleason scores ($P = 0.027$). Of 75 patients with established history of prostate cancer, we detected the TMPRSS2-ERG fusion in 44 (59%) patients. Almost three quarters (73%) of fusion-positive patients accumulated within 16 specific families whereas only 27% were single fusion-positive cases within one family. Based on reported prevalence rates, we calculated a sibling recurrence risk ratio of up to 18.9. A subset (63%) of families with uniformly TMPRSS2-ERG-positive prostate cancer underwent a genome-wide linkage scan at 500 markers. This revealed several loci located on chromosomes #9, #18, and X that were suggestive of linkage to
the TMPRSS2-ERG fusion-positive prostate cancer phenotype with linkage-of-disease scores up to 2.16 and nonparametric linkage scores up to 2.77. This suggests the presence of an inherited susceptibility to developing the TMPRSS2-ERG fusion. Given the association of TMPRSS2-ERG fusion and aggressive prostate cancer, close surveillance of relatives of patients with established fusion-positive prostate cancer or a family history of prostate cancer in general would be warranted.