

Can Diet and/or Sunlight Modify the Relationship Between Vitamin D Receptor Polymorphisms and Prostate Cancer Risk?

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Over the past 10 years, numerous studies have reported associations between genetic variation in the vitamin D receptor (VDR) gene and risk of prostate cancer. However, few studies have investigated whether these putative genetic risk factors can be modified by vitamin D from diet or from sunlight. Current evidence suggests that sunlight exposure or circulating levels of vitamin D metabolites might modify risk associated with polymorphisms in the VDR start codon (FokI) or promoter regions of the gene.

We present new data from the California Collaborative Study of Advanced Prostate Cancer, a population-based case control study. Cases of advanced prostate cancer were ascertained from the San Francisco Bay Area and Los Angeles County SEER cancer registries. Controls were frequency matched on age and ethnicity. Sunlight exposure was measured by reflectometry on the inner arm (constitutive pigmentation) and forehead (facultative pigmentation), and a sunlight exposure index (SEI) was calculated.

In white men, sun exposure, as measured by the SEI, was found to be protective against prostate cancer, especially for distant and high grade disease. After stratification on VDR start codon (FokI) genotype, sun exposure was seen to be protective only among men who carry a high activity (F) allele and who have lighter constitutive pigmentation. In contrast, among African American men, there was no evidence of a protective effect of sunlight.

To fine map additional risk loci in the VDR gene, we genotyped 632 African American subjects for 36 VDR tag SNPs. While there were no signals detected from block B (the 3'untranslated and coding regions) of the gene, 6 of 17 SNPs in block C (the promoter region) were statistically significantly associated with disease. Three SNPs remained significant after adjustment for multiple comparisons. These associations suggest that polymorphism in blocks C2 and C3 are related to prostate cancer risk. Significant interaction was detected between the block C3 SNP and sunlight exposure with respect to prostate cancer risk.