

# Abstract

Cancer Res. 2009 Feb 15;69(4):1429-38.

## Association of variants in two vitamin e transport genes with circulating vitamin e concentrations and prostate cancer risk.

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**OBJECTIVE:** Significant reductions in prostate cancer incidence and mortality were observed in men randomized to receive 50 mg supplemental vitamin E (alpha-tocopherol) per day in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study. We hypothesized that variation in key vitamin E transport genes might directly affect prostate cancer risk or modify the effects of vitamin E supplementation.

**METHODS:** Associations between prostate cancer risk and 13 polymorphisms in two genes, TTPA and SEC14L2, were examined in 982 incident prostate cancer cases and 851 controls drawn from the ATBC Study.

**RESULTS:** There was no association between the genetic variants and prostate cancer risk. Significant interactions were observed, however, between two variants in SEC14L2 (IVS11+931A>G and IVS11-896A>T) and the trial alpha-tocopherol supplement such that vitamin E supplementation reduced prostate cancer risk among men who were homozygous for either common allele [odds ratios (OR) and 95% confidence intervals (95% CI), 0.52 (0.30-0.90) and 0.64 (0.46-0.88), respectively] and nonsignificantly increased risk among those who carried one or two copies of either variant allele [ORs and 95% CIs, 1.27 (0.90-1.79) and 1.21 (0.96-1.52), respectively; both P for interaction < 0.05]. Genotype-phenotype analyses revealed significant but modest differences in baseline circulating concentrations of alpha-tocopherol and serum responses to the vitamin E supplementation for several polymorphisms.

**CONCLUSION:** This study shows that genetic variation in TTPA and SEC14L2 is associated with serum alpha-tocopherol but does not have a direct effect on prostate cancer. Our results do, however, suggest that polymorphisms in SEC14L2 may modify the effect of vitamin supplementation regimens on prostate cancer risk.

PMID: 19190344

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