Abstract


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


Department of Pathology, University of Illinois at Chicago, Chicago, Illinois 60612, USA.

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.

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