Comment Re: Vitamin E Transport Gene Variants and Prostate Cancer

To the Editor:

In the February 15, 2009 issue of Cancer Research, Wright and colleagues (1) investigated whether polymorphisms in two vitamin E transport genes are associated with elevated prostate cancer risk resulting from altered plasma vitamin E concentrations. However, the circulating vitamin E level is influenced by many genes (2), and thus the observed associations may not necessarily reflect the function of the two analyzed genes. As discussed here, the expression level and activity of these genes in peripheral tissues, and the consequent local levels and molecular actions of vitamin E, may be more relevant for influencing the prostate cancer risk.

So far, a role in determining the plasma vitamin E concentration has been firmly established only for α-tocopherol transfer protein (α-TTP). A role of tocopherol associated protein 1 (hTAP1) in tissue vitamin E transport is likely but so far only supported in vitro (3–5).

For hTAP1, the described associations may be compatible with linkage with neighboring genes and regulatory sequences. Two related genes (hTAP2/SEC14L3 and hTAP3/SEC14L4) are located close to hTAP1/SEC14L2/SPF, and their predominant expression in epithelial duct cells of several glands as well as possible secretion into prostate lumen anticipates their regulatory role in prostate cells (5).

The hTAP proteins may transport other lipids and regulate lipid-dependent events, e.g., by modulating the activity of enzymes involved in cholesterol biosynthesis (squalene epoxidase, HMG-CoA reductase) or in signaling, secretion, and gene expression (phosphatidylinositol-kinases). In particular, their role in cholesterol and possibly steroid biosynthesis may influence the risk for androgen-sensitive prostate cancer (5).

The described polymorphisms in hTAPs may also affect their expression level. Proliferation of prostate cancer cells is associated with reduced expression of hTAP1 that can be activated by the demethylating agent 5-azadeoxycytidine suggesting epigenetic regulation (3). We observed a similar reactivation of hTAP3 expression, which is silenced in most tested cell lines (5).

Whereas α-TTP maintains mainly plasma levels of α-tocopherol, the three hTAPs may also respond to other tocopherol analogs (α-, β-, γ-, δ-tocopherols, and tocotrienols) and derivatives (e.g., α-tocopheryl succinate), and increase their anticancer activity (3, 4).

In conclusion, the observed association of gene polymorphisms of vitamin E transport genes and prostate cancer risk is interesting, but without further basic research into the function of these genes a link to circulating vitamin E levels remains elusive.

Jean-Marc Zingg
Angelo Azzi
Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, Boston, Massachusetts

Disclosure of Potential Conflicts of Interest

J.-M. Zingg: Research fellowship, Phosphagenics, Ltd. A. Azzi: Consultant/advisory board, Phosphagenics, Ltd.

References


Published OnlineFirst August 4, 2009; DOI: 10.1158/0008-5472.CAN-09-0535
Comment Re: Vitamin E Transport Gene Variants and Prostate Cancer

Jean-Marc Zingg and Angelo Azzi


Updated version
Access the most recent version of this article at:
doi:10.1158/0008-5472.CAN-09-0535

Cited articles
This article cites 5 articles, 3 of which you can access for free at:
http://cancerres.aacrjournals.org/content/69/16/6756.1.full.html#ref-list-1

E-mail alerts
Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions
To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions
To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.