Modulation of gene expression by α-tocopherol and α-tocopheryl phosphate in THP-1 monocytes. J. Zingg, R. Libinaki, C. Lai, M. Meydani, R. Gianello, E. Ogru, A. Azzi, *Free Radic. Biol. Med.*, **49,** 1989-2000 (2010).

The natural vitamin E analog α-tocopheryl phosphate (αTP) modulates atherosclerotic and inflammatory events more efficiently than the unphosphorylated α-tocopherol (αT). To investigate the molecular mechanisms involved, we have measured plasma levels of αTP and compared the cellular effects of αT and αTP in THP-1 monocytes. THP-1 cell proliferation is slightly increased by αT, whereas it is inhibited by αTP. CD36 surface expression is inhibited by αTP within hours without requiring transport of αTP into cells, suggesting that αTP may bind to CD36 and/or trigger its internalization. As assessed by gene expression microarrays, more genes are regulated by αTP than by αT. Among a set of confirmed genes, the expression of vascular endothelial growth factor is induced by αTP as a result of activating protein kinase B (PKB/Akt) and is associated with increased levels of reactive oxygen species (ROS). Increased Akt (Ser473) phosphorylation and induction of ROS by αTP occur in a wortmannin-sensitive manner, indicating the involvement of phosphatidylinositol kinases. The induction of Akt (Ser473) phosphorylation and ROS production by αTP can be attenuated by αT. It is concluded that αTP and αT influence cell proliferation, ROS production, and Akt (Ser473) phosphorylation in an antagonistic manner, most probably by modulating phosphatidylinositol kinases.