α-Tocopherol is an effective Phase II enzyme inducer: protective effects on acrolein-induced oxidative stress and mitochondrial dysfunction in human retinal pigment epithelial cells. Z. Feng, Z. Liu, X. Li, H. Jia, L. Sun, C. Tian, L. Jia, J. Liu, *J. Nutr. Biochem.*, **21**, 1222-1231 (2010).

Vitamin E has long been identified as a major lipid-soluble chain-breaking antioxidant in mammals. α-Tocopherol is a vitamin E component and the major form in the human body. We propose that, besides its direct chain-breaking antioxidant activity, α-tocopherol may exert an indirect antioxidant activity by enhancing the cell's antioxidant system as a Phase II enzyme inducer. We investigated α-tocopherol's inducing effect on Phase II enzymes and its protective effect on acrolein-induced toxicity in a human retinal pigment epithelial (RPE) cell line, ARPE-19. Acrolein, a major component of cigarette smoke and also a product of lipid peroxidation, at 75 μmol/L over 24 h, caused significant loss of ARPE-19 cell viability, increased oxidative damage, decreased antioxidant defense, inactivation of the Keap1/Nrf2 pathway, and mitochondrial dysfunction. ARPE-19 cells have been used as a model of smoking- and age-related macular degeneration. Pretreatment with α-tocopherol activated the Keap1/Nrf2 pathway by increasing Nrf2 expression and inducing its translocation to the nucleus. Consequently, the expression and/or activity of the following Phase II enzymes increased: glutamate cysteine ligase, NAD(P)H:quinone oxidoreductase 1, hemeoxygenase 1, glutathione S-transferase and superoxide dismutase; total antioxidant capacity and glutathione also increased. This antioxidant defense enhancement protected ARPE-19 cells from an acrolein-induced decrease in cell viability, lowered reactive oxygen species and protein oxidation levels, and improved mitochondrial function. These results suggest that α-tocopherol protects ARPE-19 cells from acrolein-induced cellular toxicity, not only as a chainbreaking antioxidant, but also as a Phase II enzyme inducer.