

Constantinou C, Hyatt JH, Vraka PS, Papas A, Papas KA, Neophytou C, Hadjivassiliou V, Constantinou AI. **Induction of Caspase-Independent Programmed Cell Death by Vitamin E Natural Homologs and Synthetic Derivatives.** Nutrition and Cancer 2009 61:864-874.

Abstract

Current observations in the literature suggest that vitamin E may be a suitable candidate for cancer chemotherapy. To investigate this further, we examined the ability of the vitamin E natural homologs [α -, β -, γ -, δ - tocopherols (α -TOC, β -TOC, γ -TOC, δ -TOC) and α -, β -, γ -, δ - tocotrienols (α -TT, β -TT, γ -TT, δ -TT)] and their corresponding succinate synthetic derivatives [α -, β -, γ -, δ - tocopheryl succinates and α -, β -, γ -, δ -tocotrienyl succinates (α -TS, β -TS, γ -TS, δ -TS)] to induce cell death in AR- (DU145 and PC3) and AR+ (LNCaP) prostate cancer cell lines. The most effective of all the natural homologs of vitamin E was determined to be δ -TT, whereas δ -TS was the most potent of all the natural and synthetic compounds of vitamin E examined. Both γ -TT and δ -TT induced caspase activity selectively in AR+ LNCaP cells, suggesting a possible role for AR for the activation of caspase-dependent programmed cell death (CD-PCD). More important, however, γ -TT, δ -TT, γ -TS, and δ -TS activated dominant caspase-independent programmed cell death (CI-PCD) in all prostate cancer cell lines examined. Thus, vitamin E homologs and synthetic derivatives may find applications in the treatment of prostate tumors that are resistant to caspase-activating therapeutic agents.