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Vitamin E metabolite 13'-carboxychromanols inhibit pro-inflammatory enzymes, induce apoptosis and autophagy in human cancer cells by modulating sphingolipids and suppress colon tumor development in mice

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Vitamin E forms are substantially metabolized to various carboxychromanols including 13'-carboxychromanols (13'-COOHs) that are found at high levels in feces. However, there is limited knowledge about functions of these metabolites. Here we studied δT-13'-COOH and δTE-13'-COOH, which are metabolites of δ-tocopherol and δ-tocotrienol, respectively. Both 13'-COOHs are much stronger than tocopherols in inhibition of pro-inflammatory and cancer promoting cyclooxygenase-2 (COX-2) and 5-lipoxygnease (5-LOX) and in induction of apoptosis and autophagy in colon cancer cells. The anti-cancer effects by 13'-COOHs appeared to be partially independent of inhibition of COX-2/5-LOX. Using liquid chromatography tandem mass spectrometry, we found that 13'-COOHs increased intracellular dihydrosphingosin and dihydroceramides after short-time incubation in HCT-116 cells and enhanced ceramides while decreased sphingomyelins during prolonged treatment. Modulation of sphingolipids by 13'-COOHs was observed prior to or coinciding with biochemical manifestation of cell death. Pharmaceutically blocking the increase of these sphingolipids partially counteracted 13'-COOH-induced cell death. Further, 13'-COOH inhibited dihydroceramide desaturase without affecting the protein expression. In agreement with these mechanistic findings, δTE-13'-COOH significantly suppressed the growth and multiplicity of colon tumor in mice. Our study demonstrates that 13'-COOHs have anti-inflammatory and anticancer activities may contribute to *in vivo* anticancer effect of vitamin E forms and are promising novel cancer prevention agents.

Biography

Qing Jiang is a Professor in Nutrition Science at Purdue. She has focused on different forms of vitamin E and novel vitamin E metabolite long-chain carboxychromanols with respect to their anti-inflammatory and anticancer activities in cell-based and preclinical studies. Her lab has developed various analytical methods for quantifying vitamin E metabolites. Dr. Jiang has 45 publications and obtained three patents. She is a member of the editorial board of Journal of Nutritional Biochemistry. She has served as a reviewer in study sections of NIH and USDA. She is a recipient of E.L.R. Stokstad Award for outstanding fundamental research in nutrition from American Society for Nutrition and University Faculty Scholar Award from Purdue.

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