α-Tocopherol decreases the somatostatin receptor-effector system and increases the cyclic AMP/cyclic AMP response element binding protein pathway in the rat dentate gyrus. A.M. Hernández-Pinto, L. Puebla-Jiménez, and E. Arilla-Ferreiro, *Neurosci.*, **162**, 106-117 (2009).

Neuronal survival has been shown to be enhanced by α-tocopherol and modulated by cyclic AMP (cAMP). Somatostatin (SST) receptors couple negatively to adenylyl cyclase (AC), thus leading to decreased cAMP levels. Whether α-tocopherol can stimulate neuronal survival via regulation of the somatostatinergic system, however, is unknown. The aim of this study was to investigate the effects of α-tocopherol on the SST signaling pathway in the rat dentate gyrus. To that end, 15-week-old male Sprague–Dawley rats were treated daily for 1 week with (+)-α-tocopherol or vehicle and sacrificed on the day following the last administration. No changes in either SST-like immunoreactivity (SST-LI) content or SST mRNA levels were detected in the dentate gyrus as a result of α-tocopherol treatment. A significant decrease in the density of the SST binding sites and an increase in the dissociation constant, however, were detected. The lower SST receptor density in the α-tocopherol-treated rats correlated with a significant decrease in the protein levels of the SST receptor subtypes SSTR1-SSTR4, whereas the corresponding mRNA levels were unaltered. G-protein-coupled-receptor kinase 2 expression was decreased by α-tocopherol treatment. This vitamin induced a significant increase in both basal and forskolin-stimulated AC activity, as well as a decrease in the inhibitory effect of SST on AC. Whereas the protein levels of AC type V/VI were not modified by α-tocopherol administration, ACVIII expression was significantly enhanced, suggesting it might account for the increase in AC activity. In addition, this treatment led to a reduction in Giα1-3 protein levels and in Gi functionality. α-Tocopherol did not affect the expression of the regulator of G-protein signaling 6/7 (RGS6/7). Finally, α-tocopherol induced an increase in the levels of phosphorylated cAMP response element binding protein (p-CREB) and total CREB in the dentate gyrus. Since CREB synthesis and phosphorylation promote the survival of many cells, including neurons, whereas SST inhibits the cAMP-PKA pathway, which is known to be involved in CREB phosphorylation, the α-tocopherol-induced reduction of SSTR observed here might possibly contribute, via increased cAMP levels and CREB activity, to the mechanism by which this vitamin promotes the survival of newborn neurons in the dentate gyrus.