Hepatic α-tocopherol transfer protein: ligand-induced protection from proteasomal degradation. V. Thakur, S. Morley, and D. Manor, *Biochemistry*, **49**, 9339-9244 (2010).

There are eight naturally occurring forms of the dietary antioxidant vitamin E. Of these, only α-tocopherol is retained at high levels in vertebrate plasma and tissues. This selectivity is achieved in part by the action of the hepatic α-tocopherol transfer protein (TTP), which facilitates the selective incorporation of dietary α-tocopherol into circulating lipoproteins. We examined the effects of vitamin E on TTP expression in cultured hepatocytes. Treatment with vitamin E precipitated a time- and dose-dependent increase in the steady-state levels of TTP. This stabilization was caused by α-tocopherol-induced attenuation of the ubiquitination of TTP and its subsequent degradation by the proteasome. In vitro, vitamin E protected TTP from proteolytic degradation by trypsin, suggesting ligand-induced changes in protein conformation. Cell fractionation studies showed that TTP is distributed between the cytosolic and membranous organelle fraction, and that tocopherol induced the translocation of some TTP from the cytosol to the organelle fraction. Furthermore, vitamin E markedly attenuated the degradation of organelle-bound TTP. These findings suggest that vitamin E imparts a distinct conformation on TTP that is associated with localization to a specific cellular compartment, where the protein is less susceptible to proteasomal degradation.