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Regulation of vitamin E status by the α-tocopherol Transfer Protein



Dr Danny Manor

Associate Professor of Nutrition and Pharmacology at the School of Medicine
Case Western Reserve University
(Cleveland, OH, USA)

Alpha-tocopherol (Vitamin E) is plant-derived neutral lipid that is vital for human health. The vitamin's protective properties are thought to stem from its ability to terminate lipid peroxidation in biological membranes, i.e. to function as a lipophilic antioxidant. The major regulator of vitamin E status is the α-tocopherol Transfer Protein (αTTP). In its primary site of expression, the liver, αTTP regulates secretion of the vitamin into circulating lipoproteins that deliver the antioxidant to extra-hepatic cells. Alpha-TTP is also expressed in two other tissues that are uniquely sensitive to oxidative insults: the central nervous system, and the placenta. Heritable mutations in αTTP cause familial vitamin E deficiency, accompanied by neurological deficits such as spinocerebellar ataxia.

Our research aims to understand the molecular mechanisms that underlie αTTP's action, and the physiological events that regulate the protein's levels and activity. We have found that the gene encoding αTTP is transcriptionally regulated by hormones, oxidative stress, and by α-tocopherol. On the post-translational level, activity of hepatic αTTP is modulated by ubiquitination and degradation, and by reversible tyrosine phosphorylation. Recent findings on the role of αTTP in vitamin E transport in the cerebellum will also be discussed.

Biography

Dr. Manor earned his BSc in Biochemistry in Tel Aviv University (Israel), and his PhD in Biophysics at the Albert Einstein College of Medicine (NY, USA). During his post-doctoral studies, he studied the mechanisms of actions of small GTPases and their roles in cell proliferation and carcinogenesis. He was appointed Assistant Professor at Cornell University (Ithaca, NY, USA), where he began to study the molecular mechanisms of vitamin E transport. He is currently an Associate Professor of Nutrition and Pharmacology at the School of Medicine, Case Western Reserve University (Cleveland, OH, USA).

Date: **26 August 2013**
Time: **4-5 pm**
Venue: **NUS Centre for Life Sciences Seminar Room 1**
Host: **Prof Barry Halliwell**