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NUTRIGENOMICS OF VITAMIN E AND FATTY ACID METABOLISM IN LIPOTOXICITY AND OXIDATIVE STRESS-RELATED DISEASES

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Vitamin E (alpha-tocopherol, VE) is a nutrient essential to prevent the severe neurological symptoms of a genetic form of ataxia associated with vitamin deficiency (AVED). Its essentiality is also proven in secondary deficiencies associated with malnutrition and/or malabsorption syndromes that besides to neurological abnormalities may induce metabolic, musculoskeletal, hematological and immune symptoms, especially in vulnerable subjects such as the elderly. Mechanistic aspects of such an essentiality are far from being understood. VE is the most abundant fat-soluble hydrogen atom donor of the plasmalemma and its relative concentrations with respect to phospholipid residues is sufficient to influencing the flux of lipoperoxyl radicals generated during both the enzymatic and non-enzymatic processes of lipid peroxidation. Consequently, VE affects membrane stability and the lipid signaling of inflammatory eicosanoids and ferroptosis mediators. Also, VE directly or indirectly interacts with different proteins with enzymatic, signal transduction and transcriptional function. All these VE biological roles might concur to some extent to the pathophysiology of deficiency symptoms or to explain the therapeutic potential of this vitamin, or may be none of them. New insights in the biological complexity of this vitamin came from a recent series of studies that supported the participation of the long-chain metabolites of this vitamin in at least some of its “non-antioxidant” functions. Omics technologies are now offering a great opportunity to deal with such a complexity, exploring with unprecedent efficacy the molecular properties of this vitamin and its effects in clinical trials on deficiency syndromes and other human diseases. Transcriptomics and lipidomics have been utilized in our laboratories, either separate or in multiomics protocols, to develop personalized and precision nutrition (i.e. nutrigenomics) platforms of investigation dedicated to this vitamin. Examples of their potential for innovation in VE research will be given in this presentation, including studies on the liver metabolism of free fatty acids and hepatocyte lipotoxicity, the key etiologic factor of non-alcoholic fatty liver disease, and studies in kidney disease patients that develop a characteristic form of VE deficiency, along with oxidative stress and lipid peroxidation symptoms.