LS12-059 - Vitamin A metabolism in the regulation of energy balance

Abstract

Obesity and diabetes are the new epidemics of the 21st century. Obesity related diseases are mostly chronic, require life-long medical treatment, and are thus becoming a major social, economic, and medical burden for health care systems in industrial and developing countries. Despite enormous scientific, medical and public health efforts, the numbers of patients suffering from these diseases rise dramatically. This alarming development highlights the urgent need for identifying novel pathomechanistic pathways and targeted therapeutic strategies for obesity and related metabolic disorders. The role of bioactive food components in the regulation of energy balance and body weight has been underappreciated in the past.

However, recent reports by our own group suggest vitamin A as a nutrient of particular importance for the control of energy homeostasis and body weight through effects particularly in adipose tissue. Action of vitamin A and its metabolites (retinoids) is regulated by a complex network of binding proteins, converting enzymes, and signaling receptors. We are just beginning to understand how distinct components of the retinoid pathway regulate metabolic processes in animal models while relevance for human physiology and pathophysiology has remained largely unknown. Hence, the first aim of this project, the characterization of the vitamin A/retinoid axis in serum and adipose tissue of lean and obese humans and mice. This will inform us if all components of the pathway are expressed in human adipose tissue and if they are altered in obesity. We will then test a functional role of vitamin A in energy expenditure and thermogenic responses by combining unique in vivo models with molecular approaches. The goal is to uncover novel mechanisms by which vitamin A can impact energy balance and thus metabolic disease. Finally, these preclinical results will be translated into human physiology and pathophysiology. In a cross-sectional cohort study we will investigate a potential association between circulating retinoid levels and measures of energy expenditure in 1) lean subjects, 2) obese non-diabetics, and 3) obese diabetics. In sum, we believe that the results of the proposed project will add valuable new insight into the connection between retinoid biology and energy metabolism in humans and mice through a combination of unique and well-characterized in vivo models with cutting-edge techniques. Hence, these findings could stimulate the development of novel therapeutic concepts for obesity and related metabolic complications.

Keywords:
vitamin A, retinoids, obestiy, metabolic disease

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Further links to the persons involved and to the project can be found under
https://wwtf.at/funding/programmes/ls/LS12-059/