

VITAMIN A, VITAMIN E AND CAROTENOID STATUS AND METABOLISM DURING AGEING: FUNCTIONAL AND NUTRITIONAL CONSEQUENCES (PROJECT PROPOSAL)

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The overall objective of the project is to provide scientific evidence about the changes in the status, the metabolism and the functions of vitamin A, vitamin E and carotenoids (FSV), that may occur during non pathological ageing in humans. According to their nature, to their extent, and to their frequency, these age-related changes may or may not result in modifications of the vitamin needs.

This objective will be achieved through a series of cross-sectional studies (baseline measurements), single dose and long-term intervention studies with measurements before and after dosing, and performed on healthy male volunteers, between 20 and 75 years of age. Three study groups, 100 subjects each, will be recruited in Austria, France and Spain. All the subject characteristics but age will be as close as possible, in order to minimise the impact of confounding factors such as disease status. A large part of the assays will be done on all 3 populations, thus allowing for geographical comparisons, which are of particular interest, since the dietary and life habits are different in these countries.

The vitamin status will be assessed using dietary surveys and measures of the circulating and tissue concentrations of FSV (buccal mucosa cells, adipose tissue). The overall status assessed by these biomarkers of exposure will be evaluated against the dietary intakes to estimate the "storage" efficiency in

each age group. The variations in the vitamin status that will not be explained by the dietary intake will then give a first insight into variations in the metabolism or the utilisation of the FSV.

Metabolism will be investigated further through experiments designed to assess some specific metabolic steps of FSV (intestinal absorption, mobilisation of storage compartments, etc.). More comprehensive information will be obtained through pharmacokinetic studies for each of the FSV, using stable isotope dilution methodology. These studies will demonstrate whether the utilisation rate of the FSV varies between young and elderly subjects, which is a key point to determine if their needs are different or not. Status and metabolism will be studied both at baseline, and during periods of depletion and repletion of a specific FSV. Such an approach allows to examine how a subject reacts when he has to mobilise his body stores, then how he recovers.

A critical aspect deals with the extent to which elderly subjects can fulfill the FSV dependent functions. The immune system, known to be impaired in the elderly and modulated by FSV, will be studied using different variables related to humoral or cell mediated immunity. A major focus will also be given to the balance of the oxidant/antioxidant system of which vitamin E is a major part and the role of carotenoids is still a matter of discussion. Since there

is no single “best” index for identifying subjects susceptible to or exhibiting increased oxidative stress, a well selected combination of indexes will be applied. Besides the assessment of the immune status, vitamin A dependent functions will be investigated at the molecular level, through determination of the expression and functionality of retinoic acid receptors (RAR) in tissues.

It is expected that, following adequate statistical analysis treatment of the data obtained, these comprehensive investigations will provide clear evidence about the specificity of FSV nutrition in healthy elderly subjects. It will thus help in substantiating any discussion on the opportunity to recommend a particular level of FSV intake for the elderly and the

possible development of specifically-designed food products.

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