

Zinc and ageing (ZINCAGE Project)

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ZincAge (www.zincage.org) is a specific targeted research project (STREP) funded by the European Union in the 6th Framework Program (FP6). It involves epidemiological studies on the influence of diet and lifestyle on healthy ageing, aimed at preventing adult degenerative disease, particularly focusing on atherosclerosis and also addressing malnutrition of the elderly. The 3rd ZincAge meeting, held in Madrid (February 11–13, 2006) at CNIO Institute, brought together biochemical, genetic and lifestyle implications for healthy ageing in the context of nutritional impact of zinc.

It is quite clear that antioxidant and micronutrients in the diet, such as zinc, influence the development and function of immune cells, the

activity of stress-related proteins and antioxidant enzymes and help to maintain genomic integrity and stability. All these functions occur through the action of proteins involved in the regulation of zinc homeostasis, such as Metallothioneins (MT), which bind zinc with high affinity but, at the same time, release free zinc ions in response to oxidative/nitrosative stress to modulate the expression of zinc-dependent genes and to activate antioxidant enzymes and impact immune response. Thus, the role of zinc is mainly to transduce oxidative stress and other signals converging at the production of nitric oxide into a specific intracellular response, suggesting an intriguing task of “signal transducer”, similar to that found for calcium in the past. However, many aspects of this model are still unexplored, because the intracellular mechanisms involved in the regulation zinc homeostasis have been poorly studied in ageing.

It is known that during ageing, the intake of zinc decreases, thus contributing to cause frailty, general disability and increased incidence of age-related degenerative diseases (cancer, infections and atherosclerosis). This situation may be better or worse in different European countries, taking into account the large differences in dietary habits between southern and northern areas. One of the aim of the ZincAge project is therefore to investigate how different dietary habits and intrinsic factors (genetic background) contribute to the

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risk of developing zinc deficiency in different European countries. In this volume the main results presented at 3rd conference of Zincage are reported with a special focus on the role played by zinc in counteracting stress in ageing through the activity of some zinc dependent enzymes and in modulating apoptosis. In this context, zinc has been found a relevant modulator of the apoptosis especially in preventing the cell death at physiological dose whereas higher doses of zinc seem to activate apoptosis especially in presence of strong inducer of stress, such as dRib, in peripheral blood mononuclear cells from old people. These aspects associated to the well known neurotoxic action of zinc in ischemia and other brain disturbance counteract the positive effect generally observed by a supplementation with physiological doses of zinc. However, these aspects might find an explanation in view of the fact that zinc may be considered an “hormetic factor”, upregulating the stress response induced gene expression thus

stimulating the related pathways of maintenance and repair. In other words, zinc might act by one side, as a possible factor in eliminating damaged cells that may become potentially harmful and, by the other side, might help to select immune cells resistant to stress. This role of zinc may be exerted in many systems, tissues and organs, including the brain with a role in strengthening the brain functions and cognitive performances. In this context, a relevant role is played by Metallothionein polymorphism in which old subjects with determinate alleles might have a major zinc ion bioavailability through a better zinc release by MT itself. Therefore, zinc may be useful in order to achieve health longevity escaping some age-related diseases, such as atherosclerosis, perhaps through an “hormetic effect”. The zinc supplementation in old people foreseen in Zincage project will get new light on this role of zinc as a relevant factor for health longevity.