methionine residues. **Bertrand Friguet (University Denis-Diderot, Paris, France)** [12,13] has developed enzymatic and immunochemical assay using cellular extracts from cells isolated from young and middle-aged individuals to monitor proteasome and methionine sulfoxide reductase activity and/or expression. The goal is to establish, within the ZincAge project, whether there is evidence for a correlation of the monitored parameters with age, gender and other factors relevant to zinc and oxidative stress.

Preliminary results, shown by **Filipe Cabreiro (University Denis-Diderot, Paris, France**), during the "young scientists session", on the effect of zinc on MOLT-4 cells overexpressing MsrA or MsrB demonstrate that increasing zinc concentration up to 50–75 μM lead to an increase in cells viability. Surprisingly, the addition of zinc seems also to decrease MsrA and MsrB activity, whereas chelating reagents have no effect on the metal content and on the activity of MsrB, thus suggesting a tight binding of the metal on the active site of this protein.

Molecular chaperones or stress proteins maintain the correct conformational homeostasis of proteins, protecting them against a number of stresses [14]. Proper function of these stress proteins is required for longevity [15]. Indeed, a hallmark of ageing is represented by an increase of aggregated and oxidized proteins. However, little is known about the causal relationship between protein misfolding, oxidative stress and chaperone induction. Moreover, the role of zinc as an immunomodulator and as an inducer of the stress response is not clear in this process. **Csaba Sőti (Semmelweis University, Budapest, Hungary**) [14] used the T-lymphocytic Jurkart cell line to analyze the relationship between protein misfolding, aggregation and chaperone induction. He found that, in contrast to the already known non-specific induction of heat shock proteins (Hsp70, Hsp90) caused by heat shock, oxidative stress increased expression of only certain Hsp proteins (Hsp90). Moreover, mild oxidative stress did not induce bulk protein denaturation and stress responses raising the question of how oxidative modification is able to induce chaperone expression. The mobilization of free zinc ions in response to oxidative stress might be involved in this phenomenon. Regarding the role of *in vitro* zinc on the modulation of chaperone expression in Jurkat cells, **Soti** showed that 12 μM was the optimal doses to induce chaperone expression and that higher zinc concentrations counteracted the heath shock and oxidative stress mediated induction of chaperones. Therefore, inhibition of chaperone expression might be one of the mechanisms involved in the toxicity of excessive amount of zinc.

Together with intracellular antioxidant and stress response proteins, an important role during ageing is assigned to the proteins involved in the extracellular antioxidant response. **Patrizia Mecocci (University of Perugia, Italy**) [16] measured the activities of a large spectrum of enzymatic antioxidants, such as plasma glutathione peroxidase (GPx), plasma catalase (Cat), plasma and erythrocyte superoxide dismutase (pSOD and eSOD) in subjects enrolled from different European geographical areas, including old subjects, atherosclerotic patients, nonagenarians, patients with infection and patients with cancer. Higher activity of GPx and pSOD was found in old subjects with atherosclerosis compared to old subjects with infection and to nonagenarians. The activity of GPx, Cat and pSOD did not differed with respect to gender, whereas eSOD was present higher values in women. The same enzyme displayed an age-associated increased activity, but the addition of zinc to erythrocytes from old donors *in vitro* was able to influence eSOD activity only slightly. Therefore, factors other than zinc, could be involved in the age-related up-regulation of eSOD activity. One of these factors may be the trace element copper which, in addition to zinc, is necessary for the catalytic activity of the enzyme. Therefore, further studies will be also undertaken to clarify the influence of the zinc/copper ratio on eSOD activity in elderly and nonagenarian subjects.

Session 3) Zinc and genome stability

Dysfunctional telomeres trigger a stress response and provide molecular clues to the mechanisms linking growth suppression, zinc homeostasis and dysfunctional telomeres in mammalian cells.

Maria Blasco (CNIO, Madrid, Spain) [17], studying the effect of telomerase expression and telomere length on stem cell behaviour, demonstrated that critical telomere shortening has a negative impact on the proliferative capacity of bone marrow and neural stem cell and that telomere shortening in the absence of telomerase negatively impacts on the mobilization of epidermal stem cells. Using a microarray approach, **Blasco** showed also that overexpression of the catalytic subunit of telomerase (mTert), in primary murine cells, abrogates expression of the growth-inhibiting genes of the TGF-beta pathway and down-regulates some zinc-dependent transcription factors, such as Egr2, Klf4 and Zfp36. In contrast, the gene Txnip, involved in the redox-recycling of MT sulphur ligands, was found to be up-regulated by mTert overexpression. These results suggest that MT might also be involved in the stress response mediated by dysfunctional telomeres.

Gene array technology was also applied by **Dawn Mazzatti** and **Jonathan Powell (Unilever, Colworth, United**