Kingdom) [18] to investigate the regulation of gene expression by zinc *in vitro*. Preliminary data indicate that several zinc-dependent genes (mainly specific MT isoforms and zinc transporters) and functional pathways are conserved between models, indicating their importance in zinc-mediated regulation of gene expression. The translation of these data to *in vivo* zinc supplementation is currently in progress.

Genome stability is controlled by a complicated network which involves many regulators. Zinc has been generally reported as a positive regulator of genome stability because it contributes to preventing DNA damage via modulation of the zinc dependent stress-response genes.

Jolanta Jajte and **Janusz Blasiak** (**Medical University of Lodz, Poland**) [9] found a significant correlation between DNA damage and DNA repair activity in lymphocytes of healthy elderly subjects and ill old atherosclerotic patients. Considering that increased levels of DNA damage is associated with the ageing process and that zinc status decreases with age, the capability of *in vitro* zinc to protect human PBMC from oxidative stress and DNA damage was tested. In contrast to the general protective effects shown in PBMC taken from young subjects, zinc was found to differently affect DNA damage induced by hydrogen peroxide in PBMC taken from old subjects. Thus, not all elderly subjects may respond in the same way to zinc supplementation perhaps due to a different genetic background. Therefore, genetic screening targeted to pro-inflammatory cytokines and MT genes might be the key to understanding the different behaviour of cells taken from elderly and identify old subjects who really need to be supplemented with zinc.

Session 4) Zinc and signal triggering

Zinc plays an important role in cellular signalling and the zinc finger motifs which characterize several transcription factors are extraordinarily conserved among eukaryotic cells.

Tamas Fulop (**University of Sherbrooke, Canada**) [19] reviewed the multiple functions of zinc in biological systems, with an emphasis on the modulation of cytokine signal transduction in immune cells. Zinc can also influence other transcription factors by affecting DNA binding domain as well as their activation. Furthermore, zinc itself can also activate signalling molecules like calcium, by stimulating various pathways. Altogether these functions can modulate T cells response, proliferation and survival in response to pro-apoptotic signals. Thus, zinc deficiency observed with ageing can play a significant role in T cell activation changes and consequently in immunosenescence.

Since it is very well known that immune responses decline with ageing, **Audrey Varin** and **Georges Herbein** (**University of Franche-Comté, Besancon, France**) [20] studied the signal transduction, focusing on the activation of STAT pathway in T cells of elderly healthy subjects on exposure to cytokines (IL-2 and IL-6) and zinc stimulation. They found that with ageing there is an alteration in the Jak/STAT activation in response to IL-2 and IL-6 activation. Zinc supplementation *in vitro* slightly improved the age-related decrease depending on the age groups tested and the basal level of the Jak/STAT pathway activation.

Daniela Monti and **Rita Ostan** (**University of Florence, Italy**) [21] analyzed the role of zinc in cell proliferation and apoptosis affecting the development and integrity of the immune system. They studied the impact of the substitution (Arg to Pro) in the p53 codon, which affects apoptosis and cell cycle in an age-dependent manner. They also investigated the relationship between apoptosis and zinc treatment. They found that in arginine/arginine carriers zinc is able to decrease early apoptosis and to increase late apoptosis/necrosis. In contrast, no effect was detected in proline/proline or proline/arginine carriers. Furthermore, zinc treatment induces decreased S phase commitment and concomitant increase of the cells in the G2/M phase in old subjects treated with different concentrations of zinc. These results suggest that functional polymorphisms other than MT and cytokine genes may be involved in the individual response to zinc supplementation. Thus, future efforts will also be directed towards the evaluation of apoptosis and cell-cycle control in old supplemented individuals in relationship to p53 polymorphisms.

Session 5) Zinc and immune mediators

Long term clonal cultures represent good models for studying the behaviour of T cells under chronic antigenic stress and facilitate the in vitro testing of interventions in a longitudinal ageing system. **Graham Pawelec** (**University of Tübingen, Germany**) [22] described the effect of zinc supplementation on growth characteristics surface molecule expression, cytokine production and heat shock protein expression of human CD4+ T cell clones (TCC) derived from young and old donors, including centenarians. The results suggested that at least for T cells, the impact of zinc over-supplementation may be limited to decreased cell growth rates, perhaps due to increased apoptosis, but that surviving cells are unlikely to be functionally compromised. Of particular interest, **Sven Koch** (**University of Tübingen, Germany**) [23] from the same **Pawelec** group has investigated the CMV repertorie in the elderly using MHC/peptide multimers in different European populations, including Zincage donors (62–90 yrs. old). He found that T cells specific for CMV specific, such as $CD8^+CD45RA^-CCR7^-CD28^-CD57^+$ terminally differenti-