ated phenotype cells, express high levels of the inhibitory killer lectin-like receptor KLRG1. However, high KLRG1 expression and CMV IgG titre did not correlate significantly with increasing ageing suggesting that KLRG1 may be a valuable biomarker of immunosenescence. Therefore, the deletion of CMV-specific KLRG1/CD57-double positive dysfunctional CMV-specific cells might be of benefit in at-risk elderly. The impact of zinc in this CD8+ cell populations will be assessed in old zinc supplemented individuals.

The role of the thymus is vital for orchestration of T cell development and maturation.**Richard Aspinal and Wayne Mitchell (Imperial College London, UK)** [24] evaluating the role played by zinc in maintaining thymic output in healthy elderly individuals used FACS analysis and real time PCR technology. They carried out experiments on thymic output in healthy individuals aged between 60–90 years, prior to supplementation with zinc. They analyzed 300 individuals for the total T cell numbers (CD3) and recent thymic emigrants (TRECs). The results indicate that TREC levels are stable between countries but females have slightly higher values compared to male. Further efforts will be addressed to understand the effects of zinc supplementation on thymic output in elderly.

Cellular components of both the adaptive and innate immune system produce different cytokines and chemokines which modulate effector function during the immune response. Accordingly, **Erminia Mariani (Istituti Ortopedici Rizzoli, Bologna, Italy**) [25,26] evaluated the concentration of three CC type chemokines (MCP-1, MIP-1alpha and RANTES), a CXC type chemokine (IL-8) and two pro-inflammatory cytokines (IL-6 and TNF-alpha) in human plasma samples obtained from subjects of various age and from the different European countries. The circulating levels of each soluble factor, analysed in pooled samples from old healthy subjects were significantly correlated with each other and with plasma zinc, suggesting that being high or low producers, at least for these factors, is a distinct intrinsic feature of each individual and may be related to the individual regulation of zinc homeostasis. There was also a general trend to increases in all these soluble factors under pathological conditions, including obesity, suggesting an inflammatory status in pathology independently of the age of the subjects.

Since experimental human zinc deficiency is known to decrease Th1 but not Th2 immune response, **Lothar Rink (Aachen University, Germany**) [27,28] investigated the effect of a preliminary supplementation trial with zinc in Germany on the Th1/Th2 balance and on T cell activation. Preliminary results showed that the number of CCR4 (TH2) and CCR5 (TH1)-positive T cells did not change significantly after zinc treatment, whereas the number of activated T cells (CD4+/CD25+) was significantly decreased. Additionally, a method to quantify zinc importer (hZIP), zinc exporter (ZnT) and intracellular free zinc by flow cytometry was established. The altered expression profile of these transporters and their homeostasis has a direct influence on the cells. Down regulation of hZIP seems to be a prerequisite for immortalisation, whereas up-regulation of hZIP favoured apoptosis in T cell. Despite the possibility that the effect of zinc in cells from elderly subjects might sometimes be to induce and sometimes to prevent apoptosis or DNA damage, depending on the doses and individual characteristics, there is a general agreement that zinc supplementation with physiological doses is generally beneficial for the individuals. One explanation for this potential paradox might be found in the hormetic theory. Hormesis in ageing, as discussed in details by **Suresh Rattan** (**University of Aarhus, Denmark**) [29], is characterized by the beneficial effect that results from the cellular response to mild stress. His studies have shown that repeated mild heat stress (RMHS) has anti-ageing effect on growth and various other cellular and biochemical characteristics of normal human skin fibroblasts undergoing ageing in vitro. RMHS has also been tested in combination with potential hormetic molecules, such as curcumin, on ageing and longevity of human cells in culture.

In contrast to mild stress, the life long antigenic burden leads to a condition of chronic inflammation with increased lymphocyte activation and pro-inflammatory cytokine production. In this context, **Calogero Caruso** (**University of Palermo, Italy**) [22,30] has studied zinc availability in old subjects with coronary artery disease, healthy controls and centenarians with respect to a pro-inflammatory or anti-inflammatory genotype. In age-related diseases zinc seems to influence, through biomolecular pathways, inflammatory mediators that, in turn, influence zinc availability. The results confirmed that the zinc sequestering proteins, such as MT, at least in ageing show a correlation with inflammation.

This last aspect may be also relevant in non-pathological conditions, taking into account that chronic antigenic load is the major driving force of immunosenescence

Finally, **Rafael Solana** (**University of Cordoba, Spain)** [22,31] showed that the T cell subpopulation CD8+CD28null, characterized by high NK associated receptor expression and effector memory (EM) phenotype, is expanded in elderly donors when compared to young and that this expansion is associated with CMV seropositivity and to increased risk of death. It has been described that CMV is major inducer of oligoclonal expansion in ageing. **Solana** found a significant expansion both in young controls and healthy elderly donors