# Working together for robust immune responses in the elderly

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For the majority of the elderly, the last part of their life is accompanied by physical and psychological degeneration, which decreases their quality of life and places significant financial burden on healthcare budgets. As the mean age of the population increases, it is important to focus research on alleviating age-associated disabilities. Imperfect immunity may be the main reason that infectious diseases are a significant cause of death in the elderly, and research on such "immunosenescence" may result in the development of treatments to alleviate suffering and reduce costs to health services towards the end of life.

Immunosenescence involves complex changes in many parameters, therefore expertise in different fields is required to advance understanding in this area. To this end, an interdisciplinary group of 30 researchers and clinicians have established a network entitled "ImAginE: Immunology and Aging in Europe", which is funded by the European Commission's Key Action on Aging program (http://www.medizin.uni-tuebingen.de/imagine/). The aim of the network is to study immunity in ageing at many different levels. The first meeting of the ImAginE group was recently held in Tübingen, Germany, and it focused on the identification and manipulation of immunological risk phenotypes *in vivo* and *in vitro*. The parameters to be studied included hematopoietic stem cells, thymic differentiation and involution, cytokine secretion and response, integrity of signal transduction, cell cycle and apoptosis control, telomerase and telomere length status and DNA damage, mutation and repair capacity.

Several major findings were reported at the meeting. A. Wikby (Jönköping, Sweden) presented the final follow-up of a longitudinal study of four cohorts of 100 individuals each, born in 1897, 1899, 1901 and 1903. These data led to a refinement of the "immunological risk phenotype", predictive of shorter survival times. This was defined by decreases in numbers of $CD4^+$ T cells and $CD28^+$ T cells together with increases in numbers of $CD57^+$ cells, low proliferative responses and poor IL-2 production. These changes were confirmed by *in vitro* aging models for $CD8^+$ cells (R. Effros, Los Angeles, USA) and $CD4^+$ cells (G. Pawelec, Tübingen, Germany).

In a pilot study of Alzheimer's disease patients, an increased IL-1β and IL-6 phenotype coupled with decreased IL-10 was prevalent in the patient group compared to nondemented controls. A cross-sectional analysis performed in the population-based "Leiden over-85s" program revealed that a pro-inflammatory phenotype, compared to a noninflammatory one, may be associated with an up to seven times greater occurrence of cognitive disability (E. Remarque, Leiden, Netherlands). In a study of more than a hundred centenarians, the genetic polymorphism in the *IL10* gene promoter region associated with high cytokine production was found to be more prevalent than the polymorphism associated with the low producer phenotype (C. Caruso, Palermo, Italy). These findings are consistent with the idea that a pro-inflammatory phenotype is detrimental to longevity.

Therapeutic intervention for compromised immune responses will require a multi-factorial approach. A reduction in the number of $CD34^+$ precursors in the elderly means that enhancement of stem cell production is a logical therapeutic goal (C. Franceschi, Bologna, Italy). The elderly show altered patterns of stem cell cycling that need to be corrected, in that their cells are more frequently in cycle, yet show reduced sequential replications (A. Globerson, Rehovot, Israel). Thymic involution may be combated by the use of cytokines such as IL-7 (R. Aspinall, London, UK), and proliferative senescence reduced by transfection of hTERT, the catalytic component of telomerase, into lymphoid cells (R. Effros). Different methods for immortalizing T cells were presented.

These and numerous other excellent presentations at the meeting resulted in a strategy for identifying critical parameters of immune dysfunction in the elderly, as well as raising the possibility of reconstituting immune function to protect the aged against the increased threat of morbidity and mortality due to infectious disease.

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