Effect of interleukin 6 on T cell subsets in old age: A search for new markers of immunological competence and frailty

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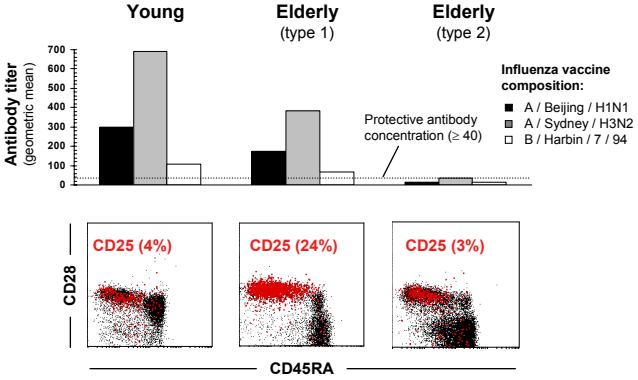
INTRODUCTION

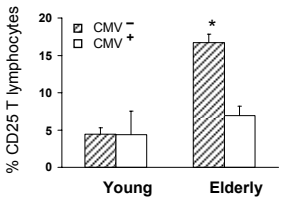
Infectious diseases are frequent and severe in elderly persons and the efficacy of vaccinations is low (1). This is due to age-related changes within the immune system - with the involution of the thymus being the most prominent event during aging. We discovered a new T lymphocyte subset which occurs in healthy elderly persons who still have an intact humoral immune response following influenza vaccination (2). These CD25 T cells compensate for the loss of naive T cells and therefore represent a biomarker of immunological competence in old age (3, 4). Our aim is to understand how CD25 T cells develop and how their function is conserved. We believe that the cytokine interleukin (IL)-6, a key player involved in the regulation of inflammatory and immunologic responses, contributes to the survival of CD25 T cells. We will therefore study the effects of IL-6 and aim to identify new molecules that can be tested in geriatric patients under stress situation (e.g. hip fracture) in whom they should predict quick recovery or complications. The clinical part will be performed in collaboration with Prof. Janet Lord (Univ. of Birmingham, Medical School).

RESULTS

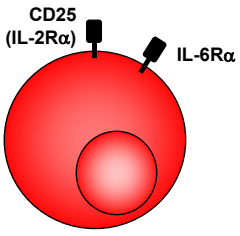
1. Effectiveness of influenza vaccination depends on T lymphocyte composition



2. CD25 T lymphocytes accumulate in a subgroup of healthy elderly persons and represent a biomarker of immunological competence in old age

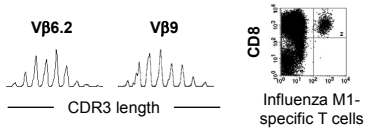


Frequency of CD25 T lymphocytes in young (24-34 years) **and elderly persons** (64-85 years). Bars represent mean ± SEM. Serum Cytomegalovirus (CMV) IgG titers were determined by ELISA. *, p<0.05 to all other groups.



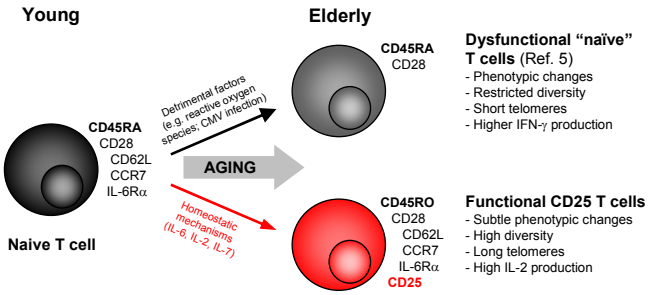
Functional characteristics of CD25 T lymphocytes:

- High interleukin 2 production
- Long telomeres
- Highly diverse T cell pool



Influenza M1-specific T cells

3. Working model on the development of CD25 T lymphocytes

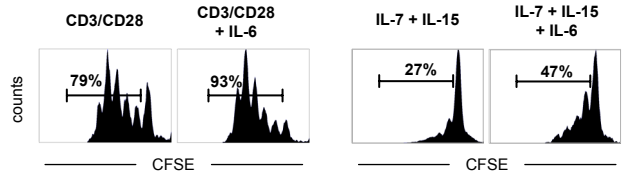


Dysfunctional "naïve" T cells (Ref. 5)
- Phenotypic changes
- Restricted diversity
- Short telomeres
- Higher IFN-γ production

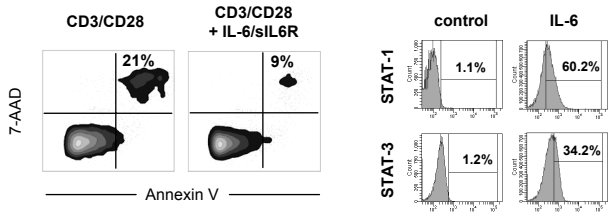
Functional CD25 T cells
- Subtle phenotypic changes
- High diversity
- Long telomeres
- High IL-2 production

4. Effects of interleukin 6 on T lymphocytes

IL-6 stimulates antigen-dependent and -independent proliferation of T cells



IL-6 contributes to the survival of T cells and signals via STAT1 and STAT3



5. Future perspectives

Further experiments aim to elucidate the effect of IL-6, together with other cytokines, on the differentiation and function of T cell subsets and to uncover the underlying molecular mechanisms. Candidate molecules will then be tested in geriatric patients under stress situation (e.g. hip fracture) to evaluate their diagnostic potential.

SUMMARY

We have recently discovered a new T lymphocyte population which accumulates in a subgroup of healthy elderly persons who still have an intact humoral immune response following vaccination. CD25 T cells therefore represent a biomarker of immunological competence in old age. Our goal is to understand how CD25 T cell develop and how their function is conserved. The pleiotropic cytokine interleukin 6 seems to play a key role and its effects will be investigated.

ACKNOWLEDGEMENTS & REFERENCES

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