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Functionality of CD57 expressing T cells

Paulina Dominika Rymkiewicz, SY Lim, F Malinarich Gonzales, B Lee and A Larbi

SIgN (Singapore Immunology Network), A*STAR BMSI (Agency for Science, Technology and Research, Biomedical Sciences Institutes) Singapore

Abstract

Meeting the medical needs of the growing elderly population is a huge challenge while, finding strategies to improve the health of the aged would have enormous beneficial effects. The aging of the immune system is one theory to explain age-related increased susceptibility to diseases. Senescent T cells are characterized with impaired functionality. These cells can be phenotypically recognized by the lack of CD27 and CD28 on their surface. In this study, we compared the phenotype of $CD27^-CD28^-CD57^+$ T cells in the elderly (≥65 years) and young (≤35 years) Chinese Singaporeans. We also investigated the functionality of $CD27^-CD28^-$ CD57 expressing $CD4^+$ and $CD8^+$ cells. CD57 is a marker for senescence, as most of terminally differentiated $CD8^+$ cells, but also $CD4^+$ cells will express it. As CD8 cells are more sensitive to immune aging high levels of CD57 expression are detected on the CD8+ population in both young and old donors, while the $CD4^+$ population shows lower levels of CD57 expression especially in the young donors. Flow-sorted $CD4^+CD57^+$ and $CD8^+CD57^+$ population showed that the CD57 molecule is being down regulated following consecutive proliferation, whereas the more the cells divide the higher is the expression of the co-stimulatory molecule CD28. Also other cell surface molecules like CD27 used to characterize the phenotypically “aged” cells, change expression profile in vitro. CFSE-based proliferation assay revealed that the $CD4^+$ $CD57^+$ and the $CD8^+$ $CD57^+$ populations hardly proliferate following CD3/CD28 or PHA stimulation while $CD57^-$ T cells are very responsive. Similar results have been obtained in the allogeneic reaction of $CD57^+$ cells with the mDCs and imDCs. $CD4^+CD57^+$ cells show higher susceptibility to apoptosis (H2O2 or Etoposide) than the $CD8^+CD57^+$ population. Gene expression profiles were tested in order to understand the mechanisms for poor responses to stimulation. The impact of CD57 expression on susceptibility to immunosenescence will be discussed.