Reviewer's report

Title: Immunosenescence in the Nursing Home Elderly

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Reviewer: Rafael Solana

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In this work the authors analyse T-cell and NK cell phenotypes within nursing home elderly in comparison with healthy adults and how individual immune phenotypes could be influenced by age, sex, frailty and nutritional status in the nursing home elderly.

The results presented show lower naïve CD8+ T-cells and higher terminally differentiated and senescent CD8+ T-cells; higher CD4+ T-cells with central and effector memory phenotypes; higher CD4+/CD8+ T-cell ratio; higher percentage of T-regs; and higher mature percentages of NK cells when compared to healthy adults. Age, sex, frailty and nutrition did not appear to have a significant association with these parameters (only with senescent NK cells).

Comments

Most results presented confirm previous data on the differences in naïve CD8+ T-cells, terminally differentiated and senescent CD8+ T-cells, Tregs and NK cells in other studies using community dwelling elderly or healthy ageing. However considering the high number of subjects and the fact that they are nursing home individuals with different degrees of frailty makes this study of interest in Geriatrics.

The paper is well written, the methods are adequate and the results support the discussion and the conclusions obtained.

Minor Essential Revisions

The authors indicate that “CD4+ and CD8+ immune phenotypes and T-regs were expressed as a percentage of CD3+ and NK cell subsets were expressed as a percentage of CD3- cells”. Whereas these values might be correct for the T cell subsets, it is very unlikely that the median of mature NK cells are 12.1 (IQR 7.9 – 16.6) within the CD3- populations. On the contrary the values presented are more likely referred to the total gate of PBLs. Please check and revise the calculations of these percentages.

Discretionary Revisions

Please indicate the statistical analysis used in the different tables.

The authors discuss the low frequency of old individuals with ratios CD4/CD8 <1 (6.5%) compared with the frequency of IRP in the OCTO study (14%). Please consider the possibility to include studies of other groups (Ferrando-Martinez et
al., 2013) that have also found frequency of CD4/CD8 <1 in approximately 7% of old individuals. The age range can also be an important factor as the frequency of donors with CD4/CD8 <1 is lower in the NONA cohort and disappears in centenarians.

The authors should consider including in the discussion the possibility that the changes observed in T and NK cells are the consequence of a remodelling of these subpopulations due decreased output of new (naïve T or immature NK cells) and the expansion of effector or senescent cells associated with chronic antigenic stress (e.g. CMV).

The authors define senescent NK cells as CD56dimCD16negative (18). However other authors have recently shown that the expression of CD57 is a marker of highly differentiated NK cells. Are there evidences of a relationship between these 2 parameters?

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests