Immunosenescence in HIV infection

Dr Julià Blanco
HIV infection: a double attack to the immune system
THE IMMUNE SYSTEM: EVERYTHING IS LINKED
Immunosenescence. A natural process

![Graph showing the progression of immunosenescence over age]

- **Memory generation**
- **Memory homeostasis**
- **Immunosenescence**

- **Total T cells (%):**
  - Memory T cell
  - Circulating memory T cell
  - Pathogen susceptibility

- **Age (years):**
  - 0
  - 5
  - 10
  - 15
  - 20
  - 25
  - 30
  - 35
  - 40
  - 45
  - 50
  - 55
  - 60
  - 65
  - 70
  - 75
  - 80

- **Infectious disease hospitalization rate (per 10,000 individuals):**
  - 0
  - 200
  - 400
  - 600
  - 800

Source: Nature Reviews | Immunology
The life and death of a T cell

Inflammation (inflam-aging)
Pathogens: Viruses (CHRONIC CMV), bacteria (MICROBIOTA?)
Immunosenescence. A natural process

Cells undergo a limited number of divisions. This number is controlled by the quality of the chromosome ends (TELOMERS)

Cells with damaged (short) telomers undergo apoptosis or become refractory to division signals (senescence)
### The life and death of a T cell

<table>
<thead>
<tr>
<th>NAIVE</th>
<th>CM</th>
<th>TM</th>
<th>EM</th>
<th>TD</th>
<th>CCR7</th>
<th>CD27</th>
<th>CD28</th>
<th>PD1</th>
<th>CD57</th>
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![Diagram showing the life cycle of a T cell](image)
HIV infection

Viral spread
- Massive replication
- GALT destruction

VIRAL DISEASE

Partial Immune control
- Partial control of viral replication
- Tissue damage
- Persistent inflammation

VIRO-IMMUNO DISEASE

Pharmacological control
- Viral persistence
- Incomplete tissue repair

INFLAMMATORY DISEASE?

HIV PERSISTENCE
APOP VI II STUDY

CROSS SECTIONAL STUDY TO ASSESS:

- IMMUNOSENESCENCE AND MATURATION MARKERS IN ART TREATED HIV INFECTED INDIVIDUALS.
- THE IMPACT OF CD4 T CELL RECOVERY

Massanella et al, JTM, 2015, 13:230
DEFINITION OF IMMUNE RECOVERY

![Graph showing CD4 T Cell counts over time for different groups: Concordant High Nadir, Concordant Low Nadir, and Discordant.](image-url)
<table>
<thead>
<tr>
<th></th>
<th>Discordant (n = 23)</th>
<th>Concordant All (n = 33)</th>
<th>Concordant Low Nadir (n = 17)</th>
<th>Concordant High Nadir (n = 16)</th>
<th>Uninfected (n = 11)</th>
</tr>
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<tr>
<td></td>
<td>a</td>
<td></td>
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<tr>
<td>Gender (% of male)</td>
<td>91</td>
<td>ns</td>
<td>85</td>
<td>76</td>
<td>94</td>
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<tr>
<td></td>
<td>ns</td>
<td>y</td>
<td>42</td>
<td>ns</td>
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<td>Current HAART (% PI-based)</td>
<td>70</td>
<td>*</td>
<td>33</td>
<td>41</td>
<td>25</td>
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<td>HCV coinfection (%)</td>
<td>35</td>
<td>ns</td>
<td>21</td>
<td>36</td>
<td>15</td>
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<tr>
<td></td>
<td>ns</td>
<td>*</td>
<td>0</td>
<td>ns</td>
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<tr>
<td>Ratio CD4/CD8, Median [IQR]</td>
<td>0.23 [0.17–0.33]</td>
<td>*</td>
<td>0.87 [0.60–1.11]</td>
<td>0.76 [0.54–0.87]</td>
<td>1.06 [0.86–1.1]</td>
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<tr>
<td>HLA-DR⁺CD95⁺ (% of CD4 T cells), Median [IQR]</td>
<td>16 [7.7–21.6]</td>
<td>*</td>
<td>4.5 [3.7–6.7]</td>
<td>4.7 [4.2–6.3]</td>
<td>4.4 [3.2–7.1]</td>
</tr>
<tr>
<td>CD8 T cell counts (cells/μL), Median [IQR]</td>
<td>940 [754–1,146]</td>
<td>ns</td>
<td>908 [771–1,239]</td>
<td>1,118 [855–1,380]</td>
<td>811 [637–1,121]</td>
</tr>
</tbody>
</table>

*a* Comparison of concordant and discordant subjects. * denotes *p* < 0.05; ns non significant (Mann–Whitney U or Fisher exact test).

*b* Comparison of concordant subjects with low and high nadir. * denotes *p* < 0.05; ns non significant (Mann–Whitney U or Fisher exact test).
MATURATION OF CD4 T cells

% of CD4 T cells

$T_N$  $T_{CM}$  $T_{TM}$  $T_{EM}$  $T_{TD}$
SENESCENCE (CD57 EXP) IN CD4 T CELLS
MATURATION IN CD8 T CELLS
SENEGENCE (CD57 EXP) IN CD8 T CELLS

CD57+ cells (% of CD8 T cells)

- $T_N$
- $T_{CM}$
- $T_{TM}$
- $T_{EM}$
- $T_{TD}$

Statistical significance:
- * $p<0.05$
- ** $p<0.01$
- *** $p<0.001$
CONCLUSIONS

- CD4 T CELL MATURATION MARKERS ARE STRONGLY ALTERED IN IMMUNODISCORDANT INDIVIDUALS. AN APPARENT FULL RECOVERY OCCURS IN IMMUNOCONCORDANT INDIVIDUALS

- CD4 T CELL IMMUNOSENESCENCE IS HIGHER IN LONG TERM SUPPRESSED HIV INFECTED INDIVIDUALS COMPARED TO CONTROLS

- CD4 T CELL IMMUNOSENESCENCE IS ASSOCIATED WITH THE LEVEL OF CD4 T CELL RECOVERY
CONCLUSIONS

- CD8 T CELL MATURATION MARKERS SHOW SLIGHT DIFFERENCES IN ART TREATED HIV INFECTED INDIVIDUALS COMPARED TO CONTROL INDIVIDUALS.

- CD8 T CELL IMMUNOSENESCENCE IS HIGHER IN LONG TERM SUPPRESSED HIV INFECTED INDIVIDUALS COMPARED TO CONTROLS.

- CD8 T CELL IMMUNOSENESCENCE IS LARGELY INDEPENDENT OF THE LEVEL OF CD4 T CELL RECOVERY.
CONCLUSIONS

- Despite full recovery of CD4 T cell numbers, immunocompromised treated HIV infected individuals maintain immunological alterations in all CD4 and CD8 T cell compartments.

- Senescence accumulated during untreated infection leaves a irreversible imprint in the immune system.
THANKS

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