Determinants of PD-1 Expression on CD4+ and CD8+ T Cells in Treated and Untreated HIV Disease

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Background

• There is intense interest in the role of inhibitory molecules, especially programmed death 1 (PD-1), in causing persistent T cell dysfunction in HIV infection.

• Expression of programmed death 1 (PD-1) is upregulated on CD4+ and CD8+ T cells in untreated HIV infection, resulting in decreased proliferation and function.

• However, the impact of HIV infection and antiretroviral therapy (ART) on the expression of PD-1 on T cells and the determinants of PD-1 expression is still poorly defined.

Methods

• PD-1 was measured longitudinally in a cohort of recently HIV-infected individuals (Options, n=121) who started ART early (< 6 months after infection) vs. later (≥ 2 years after infection).

• Mixed effects modeling was performed to assess the impact of ART on PD-1 expression, clinical factors and immunologic factors on PD-1 expression.

• PD-1 expression is still poorly defined.

Results

Baseline characteristics of Options cohort, recently infected

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Early ART (n=38)</th>
<th>Later ART (n=83)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (mos)</td>
<td>33 (29-40)</td>
<td>46 (36-56)</td>
<td>0.001</td>
</tr>
<tr>
<td>Male (%)</td>
<td>79 (21%)</td>
<td>72 (27%)</td>
<td>0.49</td>
</tr>
<tr>
<td>Baseline CD4 count, cells/μL</td>
<td>546 (397-748)</td>
<td>388 (302-489)</td>
<td>&lt;0.001</td>
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<tr>
<td>Baseline log VL, copies/mL</td>
<td>4.1 (3.3-5.7)</td>
<td>4.1 (3.3-5.7)</td>
<td>0.99</td>
</tr>
<tr>
<td>Baseline CD8+38+DR+, %</td>
<td>6.5 (5.2-8.6)</td>
<td>6.5 (5.2-8.6)</td>
<td>0.99</td>
</tr>
</tbody>
</table>

PD-1 expression increases over time without therapy and decreases rapidly during the first year of ART

Conclusions / Implications

• PD-1 expression increases without treatment and decreases rapidly after ART initiation in both CD8+ and CD4+ T cells. However, INRs still have persistent elevation in PD-1 expression despite effective ART.

• PD-1 expression on CD8+ T cells is strongly associated with peripheral CD4+ T cell count and frequency of activated CD4+ T cells.

• PD-1 expression appears to be driven by both direct antigen and homeostatic pathways. Prospective studies of anti-PD-1 antibody therapy will be needed to define whether PD-1 expression on CD4+ T cells is a cause or consequence of CD4+ T cell lymphopenia.