HIV-DNA LEVELS, HLA-B*27 and HLA-DRB1*13 AMONG LTNPs, ECs and HIV controllers

Arianna Gabrielli1, Laura Galli2, Maciej Tarkowski3, Chiara De Giuli4, Annalisa Saracino4, Giulia Marchetti5, Stefano Bonora6, Emanuela Lattuada7, Maurizio Mené8, Antonella D’Arminio Montforte9, Anna Piccirillo10, Antonella Castagna2, Agostino Riva2, Stefano Rusconis1, on behalf of ICONA Foundation and ELVIS cohort.

1. University of Milan, Milan, Italy; 2. Ospedale San Raffaele, Milano, Italy; 3. IRCCS Lazzaro Spallanzani, Rome, Italy; 4. University of Bari, Bari, Italy; 5. University of Turin, Turin, Italy; 6. University of Verona, Verona, Italy; 7. Ospedale Civile di Legnano, Italy.

BACKGROUND

The composition and the development of the HIV-DNA reservoir either in treated or untreated patients is determined by integrated mechanism comprising virological factors, immune system and treatment strategies (1). HLA types have been associated with varying rate of disease progression and different effects have been reported between subtypes of HLA alleles (2). HIV-B*27 and HLA-B*57 are associated with a slower rate of HIV disease progression, and HLA Class II DRB1*13:03 is associated with a lower plasma viral load in chronic HIV infection.

AIMS

The aim of this study was to determine the association of HLA-B*27 and HLA-DRB1*13:03 with HIV-DNA in Elite Controllers, Long-term Non-progressors, HIV Controllers, ART-naive and ART treated patients.

STUDY DESIGN AND METHODS

We evaluated 231 HIV-1-infected patients from the ICONA and the Elvis Cohorts categorized in 5 distinct groups: 20 Elite Controllers (EC), 35 Long-term Non-progressors (LTNP), 17 HIV controllers, 122 ART-naive and 37 patients under suppressive ART.

Total HIV-DNA was extracted from PBMCs by droplet digital PCR (ddPCR) and assessed by real-time PCR. HLA typing was performed by TaqMan Assay.

STATISTICAL ANALYSIS

Statistical analysis was performed using SAS software. The correlations between clinical parameters and molecular data were performed by Spearman correlation test and linear regression analysis. Multivariable linear regression was performed to assess SNP association with HIV-DNA values.

RESULTS

The characteristics of the patients’ cohorts are described in Table 1:

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>CHARACTERISTIC</th>
<th>EC (n=20)</th>
<th>HIV-CONTROLLER (n=13)</th>
<th>LTNP (n=25)</th>
<th>NAIVE (n=122)</th>
<th>ART-TRATED (n=37)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>40.6 (24)</td>
<td>38.2 (24)</td>
<td>43.5 (28)</td>
<td>36.1 (24)</td>
<td>51.4 (24)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Male gender</td>
<td>12 (65%)</td>
<td>7 (54%)</td>
<td>26 (76%)</td>
<td>25 (65%)</td>
<td>15 (68%)</td>
<td>.153</td>
<td></td>
</tr>
<tr>
<td>Italian nationality</td>
<td>18 (90%)</td>
<td>11 (85%)</td>
<td>29 (90%)</td>
<td>38 (80%)</td>
<td>30 (81%)</td>
<td>.068</td>
<td></td>
</tr>
<tr>
<td>Years since HIV diagnosis</td>
<td>12.7 (5.4)</td>
<td>12.0 (5.4)</td>
<td>12.0 (5.4)</td>
<td>12.0 (5.4)</td>
<td>12.0 (5.4)</td>
<td>.778</td>
<td></td>
</tr>
<tr>
<td>CD4+ nadir (cells/µL)</td>
<td>712 (712)</td>
<td>566 (566)</td>
<td>566 (566)</td>
<td>566 (566)</td>
<td>566 (566)</td>
<td>&lt;.001</td>
<td></td>
</tr>
</tbody>
</table>

The analysis revealed that LTBPs, ECs and HIV controllers have fewer HIV-DNA copies than ART-naive and treated patients. The rs43498599 GG genotype was found in 16%, 6%, and 8% of EC, HIV-controllers, LTNP, ART-naive and ART-treated patients, respectively (p=0.778).

Conclusions

Significant differences among groups in regard to undetectable HIV-DNA levels were found in pts with rs43498599 AG genotype; lower values of HIV-DNA were found to be associated with HLA-B*27 rs43498599 GG genotype and with a higher nadir of CD4+ lymphocytes.

References


Contact Information: arianna.gabrielli@ist-fhf-sacco.it