**Objectives**

Determine whether polymorphic genes associated with lower loads of HIV-1 in blood plasma exhibit a similar association with the load of HIV-1 in cerebrospinal fluid (CSF) samples obtained from the Central Nervous System (CNS).

**Background & Significance**

Certain polymorphic genes in the human histocompatibility locus (HLA) are associated with heightened control of HIV replication in the blood plasma of patients not taking combinatorial antiretroviral therapy (cART) during acute infection (see Carrington, M, Walker BD, Ann Rev Med 63:131-145, 2012). Several aspects of these genetic associations remain to be elucidated: 1) It is not clear whether these genotypes are associated with the control of HIV replication in the CNS, a body compartment that is associated with brain dysfunction. 2) Associations between HLA genotype and HIV control vary markedly between different ancestries, and implications for gene based therapies in various kinds of patients need to be explored further. 3) Whether the genes influence HIV replication in patients with good viral suppression on cART is not established. We compared key HLA genotypes with the level of HIV RNA in cerebrospinal fluid and blood plasma of 567 infected subjects in the CHARTER cohort, which contains patients with varied racial and treatment backgrounds.

**Hypotheses**

**Hypothesis 1:** White subjects who are treatment naïve and have the protective HLA alleles HLA-C*03:55/C (n9264942) or HLA-B*5701/n2395029 will exhibit better control of HIV-1 in cerebrospinal fluid (CSF) and blood plasma.

**Hypothesis 2:** White subjects who are treated with cART will not exhibit an association between the HLA gene loci and control of HIV RNA in blood and CSF.

**Hypothesis 3:** No associations with the gene will be present in treated or untreated African Americans (in accord with prior reports).

**Method**

**Subjects.** 567 subjects were followed longitudinally in the CHARTER cohort, which is composed of HIV infected patients from a variety of ancestries and cART treatment histories.

**Specimens.** Blood and CSF were collected at entry and regularly thereafter. HIV loads: The HIV RNA concentration in blood plasma and CSF was assayed using Roche Amplicor, Genotyping: Genomic DNA was isolated from blood and HLA alleles HLA-C*03:55/C (n9264942) or HLA-B*5701/n2395029 were measured using polymerase chain reaction.

**Statistics.** The statistical tests that were used are as shown in the tables.

**Results**

<table>
<thead>
<tr>
<th>Subjects on cART</th>
<th>Viral Load Type</th>
<th>Mean VL (TT)</th>
<th>Mean VL (CT)</th>
<th>Mean VL (CC)</th>
<th>P-value (CC vs. CT &amp; TT)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overall</strong></td>
<td></td>
<td></td>
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<tr>
<td>N (CSF) = 342</td>
<td>CSF = LLQ</td>
<td>118</td>
<td>145</td>
<td>30</td>
<td>0.45</td>
</tr>
<tr>
<td>N (Plasma) = 383</td>
<td>Plasma &lt; LLQ</td>
<td>99</td>
<td>114</td>
<td>22</td>
<td>0.40</td>
</tr>
<tr>
<td>N (Plasma) = 205</td>
<td>Plasma ≥ LLQ</td>
<td>57</td>
<td>73</td>
<td>18</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusions**

1. Results from the CHARTER cohort confirm that ancestry and cART both influence whether the protective HLA alleles were associated with control of HIV-1 replication.

2. Whites not treated with cART: The protective HLA alleles were associated with stronger control of HIV-1 replication in blood plasma, but not in CSF of these subjects.

3. Whites treated with cART: The protective HLA alleles were not associated with stronger control of HIV-1 in plasma or CSF because the genetic influence was weaker than cART.

4. African Americans not treated with cART: Unlike treatment naive whites, the HLA alleles were not associated with stronger control of HIV-1 in plasma or CSF. That agrees with prior observations of plasma HIV-1 set point.

5. African Americans treated with cART: Unexpectedly, a "protective" HLA allele in Africans on cART was linked with higher-than-expected viral loads only in Africans. Wilcoxon Rank Sum Test above. Fisher’s exact test below.

**References**


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