APOL1 in the resistance/ susceptibility to infection to *Trypanosoma brucei gambiense*

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Animal Trypanosomes

APOA1
HPR
APOL1

TLF-1

T. b. gambiense
T. b. rhodesiense

APOL1 and African trypanosomiasis
Diversity of HAT outcome in endemic areas

- Stage 1: Parasite detectable in blood or lymph
  - Treatment
  - Seropositive subjects
  - Spontaneous cure
  - Asymptomatic or resistant individuals

- Stage 2: Parasite detectable in CSF
  - Treatment
  - Death
  - Susceptible individuals

➢ Mechanism?
Objective 1: test the relation between APOL1 expression levels in human populations and resistance/susceptibility to *T. b. gambiense* infection
Study area, inclusion and quantification of APOL1 expression

- Inclusion: 199 individuals
  - HAT patients: N= 110 (susceptible)
  - Seropositive (CATT and TL+ but P-): N= 37 (resistant)
  - Endemic controls: N= 52

- Quantification
  - RNA extraction
  - CDNA synthesis
  - Quantitative PCR:
    Target gene: APOL1
APOL1 expression: Highly variable trait

**Univariate analysis**

<table>
<thead>
<tr>
<th>Co-variates</th>
<th>n</th>
<th>APOL1</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25 ans</td>
<td>68</td>
<td>32.4 ± 1.7</td>
<td></td>
</tr>
<tr>
<td>25-39 ans</td>
<td>69</td>
<td>25.7 ± 1.2</td>
<td></td>
</tr>
<tr>
<td>≥45 ans</td>
<td>62</td>
<td>26.4 ± 1.1</td>
<td>0.002</td>
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<tr>
<td><strong>Foyer</strong></td>
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<td></td>
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<tr>
<td>Forecariah</td>
<td>58</td>
<td>22.5 ± 1.2</td>
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</tr>
<tr>
<td>Dubreka</td>
<td>111</td>
<td>30.5 ± 1.1</td>
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</tr>
<tr>
<td>Boffa</td>
<td>30</td>
<td>30.5 ± 2.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Infection status</strong></td>
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<tr>
<td>controls</td>
<td>52</td>
<td>24.5 ± 1.6</td>
<td></td>
</tr>
<tr>
<td>SERO TL+</td>
<td>37</td>
<td>28.1 ± 1.3</td>
<td></td>
</tr>
<tr>
<td>HAT patients</td>
<td>110</td>
<td>29.7 ± 1.2</td>
<td>0.0006</td>
</tr>
</tbody>
</table>

- APOL1 expression is induced by *T. b. gambiense*
- APOL1 expression levels are not related to resistance/susceptibility to infection: No significant difference between HAT patients and SERO TL+
Objective 2: investigate the role of APOL1 polymorphisms (G1 and G2) in resistance/susceptibility to *T. b gambiense* infection
inclusion and Genotyping

- Inclusion: 340 individuals
  - HAT patients: 173
  - Control: 106
  - SERO TL+: 61

- G1 genotyping: substitution polymorphism
  - PCR RFLP: enzyme used: HindIII
  - GGCCCTGTA[A/G]GCTTCTTTTCTTG

- G2 genotyping: indel of 6 pb
  - CAACAAATAA[-/TTATAA]GATTCTGCA
  - PCR LICOR
  - AG, GG, AA normal
  - 248-248, 254-254 normal, 248-254
Allelic frequency of G1 polymorphism

HAT vs Control

SERO TL+ vs Control

SERO TL+ vs HAT
Allelic frequency of G2 polymorphism

HAT vs Control

SERO TL+ vs control

SERO TL+ vs HAT
These primary results suggest that *APOL1* coding polymorphisms may provide a certain degree of resistance to *T.b. gambiense* infection.

To test others polymorphisms of APOL1.

To study the mechanisms implied in trypanotolerance.

To identify new targets for therapeutic or vaccine strategies.
A collaborative work:

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- IRD
- University of Glasgow

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