Molecular epidemiology of HIV-2 in Japan: identification of the first circulating recombinant form of HIV-2, CRF01_AB

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Major endemic areas for HIV-2

- West Africa.
- Several European and Asian countries.

Distribution map of HIV-2 sequences registered (Dec. 2008)
Molecular genetics of HIV-2

- 8 groups, A to H.
- Two AB recombinants.

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Demographic of HIV/AIDS cases in Nagoya Medical Center, 1994-2008

- **Number**: 843

- **Nationality**:
  - Japanese: 80.9% (n=682)
  - Non-Japanese: 19.1% (n=161)
    - African: 3.3% (n=28)

- **Gender**:
  - Male: 88.1% (n=743)
  - Female: 11.9% (n=100)

- **Risk factor for infection**:
  - Homosexual: 61.6% (n=519)
  - Heterosexual: 23.8% (n=201)
  - Others: 5.0% (n=42)
  - Unknown: 9.6% (n=81)

- **Age (years)**: Median 34, IQR 28 to 42
## Profiles of patients infected with HIV-2

<table>
<thead>
<tr>
<th>NMC ID #</th>
<th>Year</th>
<th>Sex</th>
<th>Age</th>
<th>Nationality</th>
<th>CD4⁺ cell count (cells/μl)</th>
<th>Western blottinga</th>
<th>Plasma viral load (copies/μl)</th>
<th>HIV-1</th>
<th>HIV-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>307</td>
<td>2004</td>
<td>M</td>
<td>28</td>
<td>Nigeria</td>
<td>241 ±</td>
<td>+</td>
<td>&lt;50 350,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>678</td>
<td>2007</td>
<td>F</td>
<td>28</td>
<td>Japan</td>
<td>883 ±</td>
<td>+</td>
<td>&lt;50 ND</td>
<td></td>
<td></td>
</tr>
<tr>
<td>716</td>
<td>2007</td>
<td>M</td>
<td>36</td>
<td>Nigeria</td>
<td>4 ±</td>
<td>+</td>
<td>&lt;50 680,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>786</td>
<td>2008</td>
<td>M</td>
<td>38</td>
<td>Ghana</td>
<td>1 -</td>
<td>±</td>
<td>&lt;40 60,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>842</td>
<td>2008</td>
<td>F</td>
<td>34</td>
<td>Japan</td>
<td>110 -</td>
<td>+</td>
<td>&lt;40 25,000</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ND, not detected.

• Their risk factors were **heterosexual contacts**, but **no direct relationship** was confirmed among them.

• All the cases were **infected by HIV-2 alone**.
Amplification of HIV-2 gene fragments

Gene map from the Los Alamos HIV Sequence Database


- DNA purified from PBMC sample was used as a template for PCR.

- Both PCR products were successfully obtained in 4 AIDS cases but not in an asymptomatic case.
Three isolates formed a cluster with an AB recombinant isolate, 7312A

Presented at the 5th International Workshop on HIV Transmission
Full-length genome sequencing

Gene map from the Los Alamos HIV Sequence Database

HIV-2 BEN

5’LTR, 915 bp

3’LTR, 791 bp

Circular 2LTR form, 597 bp

gag to nef, 9122 bp

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The four isolates have a common mosaic genome structure

AB.7312A

NMC307

NMC716

NMC842

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Identification of the first circulating recombinant form of HIV-2, CRF01_AB

First circulating recombinant form, HIV-2 CRF01_AB
HIV-2 CRF01_AB has a chimeric env gene

Presented at the 5th International Workshop on HIV Transmission
HIV-2 CRF01_AB emerged in the mid 20th century

<table>
<thead>
<tr>
<th>Data set</th>
<th>Group A region</th>
<th></th>
<th>Group B region</th>
<th></th>
<th>Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>95% HPD</td>
<td>Mean</td>
<td>95% HPD</td>
<td>Mean</td>
</tr>
<tr>
<td><strong>Clade</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV-2/SIV</td>
<td>1818</td>
<td>1670-1923</td>
<td>1821</td>
<td>1697-1930</td>
<td>1822</td>
</tr>
</tbody>
</table>

HPD, highest posterior density.

- Mean time of the most recent common ancestor (tMRCA) of CRF01_AB was estimated to be **1964 to 1973**, several decades after the emergence of HIV-2 groups A and B.
Conclusions and Suggestions

1. We identified 3 cases infected with the first CRF of HIV-2, CRF01_AB, in Japan.
   ➔ Ongoing global spread of HIV-2 CRF01_AB?

2. All the 3 cases were in AIDS.
   ➔ Higher pathogenicity of HIV-2 CRF01_AB?

HIV-2 CRF01_AB: First Circulating Recombinant Form of HIV-2

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