MDR TB Transmission and Reactivation / Reinfection Phenomenon

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MOLECULAR EPIDEMIOLOGY

• Tuberculosis (TB) is a major cause of mortality worldwide. India accounts for one fifth of the global incidence.

• To curtain this, molecular epidemiological studies are extremely important
  – Molecular biology
  – Clinical medicine
  – Statistics
  – Epidemiology
APPLICATION

– To analyse the transmission dynamics.

– To distinguish Recurrent TB (Exo and Endo).

– Detection of laboratory cross-contamination.

– Identification of hypervirulent strains in populations.

– Investigations of the evolution of *M. tuberculosis*.

– Evaluation of TB control programs.

– Monitoring of transmission of drug-resistant strains.
METHODS

- IS6110 RFLP
- Spoligotyping
- MIRU-VNTR
- PGRS
- Genomic deletion analysis
- Strain-specific markers for rapid diagnosis
- SNP
IS6110-RFLP

1335 bp repeat.

Genomic DNA

PvuII digestion and Agarose gel separation

Southern Blotting

Detection
SPOLIGOTYPING

Unique Spacer

Direct Variant Repeat DVR

DR : 36bp

Spacer: 35-41bp
MIRU-VNTR

- The *M. tb* genome contains 41 loci with direct tandem repeats of 50-70 bp
- The number of repeats per locus varies between strains
- **Variable Number of Tandem Repeats (VNTR)**
- **Mycobacterial Interspersed Repetitive Units (MIRU)**
Agarose Gel Method

Sequencer (Gene Scan)
Drug resistance among different genotypes of *Mycobacterium tuberculosis* isolated from patients from Tiruvallur, South India

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- Distribution of different genotypes of *M.tuberculosis*
- Association with drug resistance
IS6110 COPY NUMBER

% Single copy at 1.5kb = 39.8
% Single copy = 3.2
% 2 to 5 = 22.8
% 6 to 9 = 13.0
% >10 = 19.4
% No Copy = 1.8

IS6110
MDR Distribution Among Spoligotypes

Beijing: 12.8%
CAS: 11.4%
EAI 3: 3.6%
EAI 5: 2.9%
Other EAI: 3.6%
Harleem: 8.7%
T: 8.5%
Others: 3.8%
Spoligotypes and Treatment Regimen

Percentage

Cat I
Cat II
Cat III

CAS  Beijing  EAI 3  EAI 5  Other EAI  H  LAM  S  T  U  X  Orphan
MDR and Treatment Regimen

<table>
<thead>
<tr>
<th>Category</th>
<th>MDR</th>
<th>Any Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cat I</td>
<td>1.2</td>
<td>15.2</td>
</tr>
<tr>
<td>Cat II</td>
<td>12.0</td>
<td>39.8</td>
</tr>
<tr>
<td>Cat III</td>
<td>2.2</td>
<td>13.0</td>
</tr>
</tbody>
</table>
Type of tuberculosis recurrence among HIV–infected and HIV-uninfected patients.

44 HIV infected and 30 HIV-uninfected patients reoccurred.

Paired M.tb isolates from 25 HIV infected and 23 HIV-uninfected patients.

IS6110, Spoligotyping, and MIRU VNTR.
• **HIV-infected**
  - Exogenous reinfection  88 %
  - Endogenous reactivation  12 %
  - Primary resistance : 10 / 25

• **HIV-Uninfected**
  - Exogenous reinfection  9%
  - Endogenous reactivation 91%
  - Primary resistance : 5/23
  - Secondary resistance : 2/23
CONCLUSION

• Single and low copy IS6110 accounted for 66% M.tb.

• The majority of our strains belonged to the (84%) EAI

• MDR is more common in CAS, T and Beijing.

• MDR Is more common among Cat II patients.

• Recurrences after successful treatment of tuberculosis
  – Exogenous reinfection in HIV-infected persons
  – Endogenous reactivation in HIV-uninfected persons