Genomic Epidemiology of TB in the Northern Territory

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Outline

• TB in the NT
• Whole genome sequencing for TB
• Research plans
Figure 3: Notification rate for tuberculosis, Australia, 2003 to 2013, by state or territory

### Table 2: Demographics of multidrug-resistant tuberculosis cases undergoing treatment in the Northern Territory, 2004 to 2013

<table>
<thead>
<tr>
<th>Case</th>
<th>Year of diagnosis</th>
<th>State or territory of notification</th>
<th>Sex</th>
<th>Age</th>
<th>Country of birth</th>
<th>Visa status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2004</td>
<td>NT</td>
<td>Female</td>
<td>36</td>
<td>South Africa</td>
<td>Working visa</td>
</tr>
<tr>
<td>2</td>
<td>2006</td>
<td>NT</td>
<td>Male</td>
<td>50</td>
<td>Indonesia</td>
<td>Illegal fisherman</td>
</tr>
<tr>
<td>3</td>
<td>2009</td>
<td>NT</td>
<td>Female</td>
<td>33</td>
<td>Vietnam</td>
<td>Permanent resident</td>
</tr>
<tr>
<td>4</td>
<td>2010</td>
<td>NT</td>
<td>Male</td>
<td>26</td>
<td>Bulgaria</td>
<td>Permanent resident</td>
</tr>
<tr>
<td>5</td>
<td>2010</td>
<td>Victoria</td>
<td>Female</td>
<td>29</td>
<td>Burma</td>
<td>Working visa</td>
</tr>
<tr>
<td>6</td>
<td>2012</td>
<td>NT</td>
<td>Male</td>
<td>21</td>
<td>Afghanistan</td>
<td>Illegal arrival</td>
</tr>
</tbody>
</table>

### Table 3: Risk factors for multidrug-resistant tuberculosis cases, Northern Territory, 2004 to 2013

<table>
<thead>
<tr>
<th>Case</th>
<th>Country of birth in a high-burden MDR-TB country</th>
<th>Previous diagnosis of tuberculosis +/- exposure to treatment</th>
<th>Suspected non-adherence or inappropriate tuberculosis therapy</th>
<th>Exposure to a known MDR-TB case</th>
<th>Residence in areas of high MDR-TB prevalence (other than country of birth)</th>
<th>HIV status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Negative</td>
</tr>
<tr>
<td>2</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Negative</td>
</tr>
<tr>
<td>3</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Negative</td>
</tr>
<tr>
<td>4</td>
<td>Yes</td>
<td>Yes*</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Negative</td>
</tr>
<tr>
<td>5</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Negative</td>
</tr>
<tr>
<td>6</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Negative</td>
</tr>
</tbody>
</table>

* Empiric treatment in Australia for possible fully susceptible tuberculosis as no culture/susceptibility testing was available.

Adapted from the World Health Organization 2008 guidelines

NT CDC: TB services and clinics in the NT

- DOTs
- Contact tracing
- Mantoux testing & LTBI treatment
- BCG vaccination
Whole genome sequencing for TB

• Typing: greater resolution between strains than previous techniques
  – Surveillance and outbreak detection
• Detection of resistance mutations
  – Faster turnaround time than culture
  – Knowledge on genotype-phenotype relationships increasing, but remains a limitation
• Sequenced all *M. tb* isolates over 8 month period
• Predicted drug susceptibilities
• Calculated genetic distance to previously sequenced UK isolates
• Drug susceptibility info 93% accurate for 1st-line drugs compared to culture
• Linked 15 of 91 UK patients to an outbreak
• Report generated a median of 21 days earlier than final reference lab report

Research questions

• Whole genome sequencing to assist with identification of clusters of TB cases?
• Relationship between NT and international *M. tuberculosis* strains?
• Whole genome sequencing to determine drug susceptibilities in the NT?
Methods

• NT CDC
  – Clinical & public health aspects of TB in the NT
  – National Notifiable Diseases Surveillance System

• Victorian Infectious Diseases Reference Laboratory
  – Antimicrobial susceptibility testing
  – MIRU-VNTR typing
Analysis

• Clusters
  – Examine phylogeny & distribution of SNP distances
  – Review with NT CDC with epidemiologic information

• Global phylogeny
  – Utilise publicly available sequences from diverse locations
  – Evolutionary relationships

• Antimicrobial susceptibilities
  – Examine genomes for mutations associated with drug resistance
  – Compare with phenotypic susceptibility results
Acknowledgements

• NT CDC
  – Vicki Krause
  – Belinda Farmer

• Doherty Institute
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  – Deb Williamson
  – Tim Stinear

• Menzies
  – Anna Ralph
  – Bart Currie