Zoonotic leprosy in the Americas

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Armadillo Reservoir

- Only non-human reservoir
  - Discovered 1975
  - Across the Southern US

- Retrospective survey confirmed natural origins
  - Large natural reservoir
  - 0-24% Ab prevalence

- Attributable risk uncertain
  - Armadillo handlers

- Animal model for leprosy

- Armadillo as Food
Human interaction with Armadillos
Distribution of US cases and armadillo range
# M. leprae Genomes in the United States

## Table 1. Single-Nucleotide Polymorphisms (SNPs) and Indels in 3I-Type Mycobacterium leprae Genomes Found in the United States.*

<table>
<thead>
<tr>
<th>M. leprae Strain</th>
<th>Average Coverage†</th>
<th>Markers Specific to 3I Type</th>
<th>Markers Differing within 3I Type</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>SNP</td>
<td>Indel</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 bp</td>
<td>11 bp</td>
</tr>
<tr>
<td>NHDP-63</td>
<td>46</td>
<td>49</td>
<td>2</td>
</tr>
<tr>
<td>NHDP-55</td>
<td>57</td>
<td>49</td>
<td>2</td>
</tr>
<tr>
<td>NHDP-98</td>
<td>78</td>
<td>49</td>
<td>2</td>
</tr>
<tr>
<td>I-30</td>
<td>22</td>
<td>49</td>
<td>2</td>
</tr>
</tbody>
</table>

* The SNPs were identified by means of comparative genomic methods based on M. leprae reference standards (strains TN, Br4923, and Thai53). NHDP denotes National Hansen’s Disease Program.

† Average coverage is defined as the average number of consensus sequence reads obtained from the strain; there were no gaps except for the dispersed repeats that could not be distinguished owing to the short read length from Illumina sequencing.

- Brazil, India, Thailand
- Highly monomorphic 99.995% identical

Next Generation Sequencing

- 3 US cases

Wild Armadillo Strain

- 52 Global Markers
- 12 SNP and 4 InDel

US region

Higher discrimination by 10 Highly polymorphic VNTRs
Range of Armadillos

Probable Zoonotic Leprosy in the Southern United States

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http://www.hrsa.gov/hansens
Emerging infection in Armadillos

No evidence of infection were found in surveys in 1987-94 Among 179 Armadillos from St. Marks NWR and N. Florida

Prevalence = 16.43% (106/645)
Second zoonotic strain of *M. leprae*

Patient Samples
N = 26

- 3I-2 31%
- 3I-2-v1 15%
- 3I-2-v15 39%
- not 3I 15%
# Genome sequencing of Zoonotic strains of *M. leprae*

<table>
<thead>
<tr>
<th>Strain</th>
<th>Source</th>
<th>SNP - VNTR type</th>
<th>Average Coverage</th>
<th>Genome Coverage</th>
<th>Variants</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI 17</td>
<td>Wild infected Armadillo</td>
<td>3I-2 - v15</td>
<td>49.03 X</td>
<td>98.33%</td>
<td>4</td>
</tr>
<tr>
<td>MRI 57</td>
<td>Wild infected Armadillo</td>
<td>3I-2 - v15</td>
<td>53.72 X</td>
<td>98.70%</td>
<td>5</td>
</tr>
<tr>
<td>NHDP 63</td>
<td>Mouse Foot Pad</td>
<td>3I-2 - v1</td>
<td>78.3 X</td>
<td>99.91%</td>
<td>2</td>
</tr>
<tr>
<td>Thai 53</td>
<td>Mouse Foot Pad (Control)</td>
<td>1A</td>
<td>2275 X</td>
<td>99.98%</td>
<td>10</td>
</tr>
</tbody>
</table>

**Emerging Zoonotic strain of *M. leprae* in Central Florida**

<table>
<thead>
<tr>
<th>MRI 17 &amp; 57 Common</th>
<th>MRI 17 &amp; 57 Conflict</th>
</tr>
</thead>
<tbody>
<tr>
<td>InDel</td>
<td>SNP</td>
</tr>
<tr>
<td>3</td>
<td>94</td>
</tr>
</tbody>
</table>

- All the variants were identified by comparing the next generation sequencing data to the standard genome (TN)
- Variant frequency >90%
- Coverage > 10 X
Molecular ecology of leprosy in The United States

**Figure.** Minimum spanning tree based on SNPs and VNTRs

- Find ¾ Major SNP Subtypes
- Discriminate Different Strain
- 88% of Armadillos 64% of US Human cases
- With endemic exposure Share the Zoonotic strain
- Both zoonotic strains are Unique Not reported elsewhere

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