Salmonella Typhi in Thailand before and after a national immunization program

Zoe Anne Dyson, Duy Pham Thanh, Ladaporn Bodhidatta, Carl Mason, Apichai Srijan, Maia Rabaa, Phat Voong Vinh, Tuyen Ha Thanh, Guy Thwaites, Stephen Baker, and Kathryn Holt

Dr. Zoe Anne Dyson
University of Melbourne

10th International Conference on Typhoid and Other Invasive Salmonelloses
April 2017
Thai national immunization program

Outbreak start

Outbreak peak

Immunization program

Reproduced from Bodhidatta et al 1987
Thai national immunization program

Outbreak peak

Immunization program

Control of Typhoid Fever in Bangkok, Thailand, by Annual Immunization of Schoolchildren with Parenteral Typhoid Vaccine

Ladaporn Bodhidatta, David N. Taylor, Usa Thisyakorn, and Peter Echeverria

From the Department of Bacteriology, Armed Forces Research Institute of Medical Sciences; and the Department of Pediatric Infectious Diseases, Chulalongkorn University, Bangkok, Thailand

Reproduced from Bodhidatta et al 1987
S. Typhi isolates from 4 Thai hospitals

- 44 S. Typhi isolates
  - 1973-1992
  - 4 Thai hospitals
Analysis workflow


SRST2: [http://github.com/katholt/SRST2/](http://github.com/katholt/SRST2/)
Analysis workflow


SRST2: [http://github.com/katholt/SRST2/](http://github.com/katholt/SRST2/)
Analysis workflow


SRST2: http://github.com/katholt/SRST2/
Analysis workflow


SRST2: http://github.com/katholt/SRST2/

SRST2: http://github.com/katholt/SRST2/
Analysis workflow

S. Typhi (CT18) reference + AMR gene(s)

Thai Typhi reads


SRST2: http://github.com/katholt/SRST2/
Analysis workflow


SRST2: [http://github.com/katholt/SRST2/](http://github.com/katholt/SRST2/)
Analysis workflow


SRST2: [http://github.com/katholt/SRST2/](http://github.com/katholt/SRST2/)
Thai S. Typhi population structure

Genotyping framework: Wong et al 2016, Nat Comms 7
Genotyphi script: http://github.com/katholt/genotyphi/
Post-vaccine MDR isolates

- Resistance only observed in 4 post-vaccine 3.2.1

- Confirmed resistance genes for
  - Aminoglycosides (aadA1)
  - Chloramphenicol (catA1)
  - Tetracyclines (tet(B))
  - Sulphonamides (sul1)

- IncHI1 plasmid rep gene
  - Identical sequences
  - Inherited by common ancestor

---

**Typhi bacterial chromosome**

**IncHI1 Plasmid**

**sul2**
**aadA1**
**catA1**
**tet(B)**

---

Bandage: [https://github.com/rrwick/Bandage](https://github.com/rrwick/Bandage)
SRST2: [http://github.com/katholt/SRST2/](http://github.com/katholt/SRST2/)
Little persistence following vaccine

Genotyping framework: Wong et al 2016, Nat Comms 7
Genotyphi script: http://github.com/katholt/genotyphi/
Post-vaccine Typhi from neighboring countries

Genotyping framework: Wong et al 2016, Nat Comms 7
Genotyphi script: http://github.com/katholt/genotyphi/
### Post-vaccine Typhi from neighboring countries

#### SNP distance

<table>
<thead>
<tr>
<th>Post-vaccine isolate</th>
<th>SNP distance</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.4.0</td>
<td>0</td>
</tr>
<tr>
<td>3.2.1</td>
<td>100</td>
</tr>
<tr>
<td>3.1.2</td>
<td>200</td>
</tr>
<tr>
<td>3.0.0</td>
<td>300</td>
</tr>
<tr>
<td>2.4.0</td>
<td>0</td>
</tr>
<tr>
<td>2.3.4</td>
<td>100</td>
</tr>
<tr>
<td>2.2.0</td>
<td>200</td>
</tr>
<tr>
<td>2.1.7</td>
<td>300</td>
</tr>
</tbody>
</table>

#### Source Country

- Pre-vaccine Thailand
- Vietnam
- Laos
- China
- Other

Map indicating the source countries and the spread of Typhi strains.
Post-vaccine Typhi from neighboring countries

SNP distance

Post-vaccine isolate

Source Country
- Pre-vaccine Thailand
- Vietnam
- Laos
- China
- Other

Post-vaccine isolate
- 3.4.0
- 3.2.1
- 3.1.2
- 3.0.0
- 2.4.0
- 2.3.4
- 2.2.0
- 2.1.7

SNP distance range: 0 to 300

Map showing source countries with Typhi cases.
Conclusions and future work

- Vaccination program was highly effective
  - Elimination of endemic Typhi in Thailand
  - Later cases (post-vaccine) and resistance plasmid from sporadic introduction of common Typhi genotypes circulating in South East Asia

- Large-scale typhoid immunization programs in endemic areas could result in lasting local disease elimination

- Useful framework for using genetic epidemiology to monitor the impact of Typhoid fever control measures
Acknowledgements

Holt Research Group
Kathryn Holt

Oxford University Clinical Research Unit (Vietnam)
Steve Baker
Guy Thwaites
Duy Phan Thanh
Maia Rabba
Phat Voong Vinh
Tuyen Ha Thanh

Armed Forces Research Institute of Medical Science (Thailand)
Ladaporn Bodhidatta
Carl Mason
Apachai Srijan

Publication:
4 post-vaccine 3.2.1 have IncHI1 MDR Plasmid

- Resistance genes carried on plasmid – PST2
- Related to IncHI1 plasmid from Vietnam (1993)

Typhi bacterial chromosome
IncHI1 Plasmid

Resistance genes carried on plasmid:
- **aadA1**
- **sul2**
- **catA1**
- **tet(B)**

Bandage: [https://github.com/rrwick/Bandage](https://github.com/rrwick/Bandage)