How can genomics help us tackle typhoid?

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This presentation will focus on......

- How genomic data can be used to track S. Typhi/Paratyphi
- How we have the ultimate typing tool giving details of isolate origin, virulence traits, resistance in a single sample
- Replacing all other typing techniques including phage typing, VNTR, PFGE etc.
- Why we should set up a global database
- How we could track Typhi locally
- How it can help control measures
Salmonella enterica is a broad and variable species but harbours conserved host adapted pathotypes.

- 100,000 SNPs
  - Horizontal islands

10,000 SNPs

- Typhimurium

2,000 SNPs

- Paratyphi A
  - Typhi

Limited luminal replication

Shedding into lumen via bile

Stealth infection

Dissemination to bone marrow, spleen and systemic system
Evolutionary History of *Salmonella Typhi*


Natural pathogen variation discovery its exploitation in typhoid

S. Typhi reference genome

Whole genome sequence a
Global or local collection

2,000 SNPs

Variation Map

Typhi replicate over time

Typhi ancestor

Molecular Bar Code

Haplotype

One detected SNP
What do DNA-based population studies tell us?

- All S. Typhi isolates originate from the same bacteria that entered the human population once thousands of years ago.
- We have a fully parsimonious phylogenetic tree with limited recombination.
- ‘All’ isolates can be distinguished and placed in a evolutionary context on the tree.
- Lack of evidence of immune selection.
- Predicts small population size with carriers key to evolution?
High-throughput sequencing provides insights into genome variation and evolution in *Salmonella Typhi*

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Ancestral haplotype

~2000 SNPs

Nalidixic acid resistant

10 SNPs

H58 is expanding!
The global expansion of S. Typhi H58 with multiple antibiotic resistance potential

1993

2008
The spread of the H58 multidrug resistant, IncH1 plasmid super haplotype of S. Typhi around the world.

H58 displaces or out-competes resident old Typhi haplotypes.
H58s that loose their plasmid/MDR remain super fit.
S. Typhi H58 lineages in local regions around the globe
A snapshot of a typhoid epidemic in real time

Outbreak 1

Outbreak 2 (+1)

Outbreak 3

Endemic

H58 introduction!!!!
Incidence of typhoid and associated haplotypes in Kolkata, India
Typhi haplotypes mapped on Google Earth in Kathmandu
Evidence for H58b4 outbreak in Kathmandu
Proposal

• We form an international consortium to map and genotype S. Typhi/Paratyphi across the world

• We create a central web site based on free software to coordinate this

• We design simple SNP-based assays for field testing

• We use this to advocate typhoid control
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