Intra-continental transmission of human invasive *Salmonella Typhimurium* variants

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Salmonella enterica (subspecies I)

Non-Typhoidal Salmonellae (NTS)

- Usually gastrointestinal
- Variably invasive
- Non host restricted
- Zoonotic

Typhoidal Salmonellae

- Invasive
- Host restricted
- Human-to-human

3 billion human and animal infections/year
Invasive NTS (iNTS) disease in sub-Saharan Africa, emergence of a new disease?

Blood stream infections in SSA
- 58.4% NTS
- 51-80% S. Typhimurium
- 10-40% S. Enteritidis

Bacteraemia - Distinct syndrome
- Non-specific fever,
- infrequent diarrhoea
- Rapid progression
- 24-51% mortality
- 43% recurrence rate (without ART)

Host factors
- Malaria,
- Anaemia
- Sickle cell anaemia
- HIV (adults)
179 S. Typhimurium genomes sequenced

- Isolates associate with invasive disease (129)
- Gastroenteritis-associated isolates (50)
Sub-Saharan isolates fall into two epidemic lineages that emerged independently

10,623 SNPs
~96% of non-recombinant, non-repetitive genome used in analyses

**Lineage I**
- $N=50$
- 33 SNP differences

**Lineage II**
- $n=68$
- 21 SNP differences

~455 SNPs

>700 SNPs
Multiple international transmission events occurred across SSA within each lineage

Spread of lineage I clones
Spread of lineage II clones

Nodes where transmissions occur

- T1
- T2
- T3
- T4
- Uganda
- Kenya
- Malawi
- Mozambique
- Mali
- Nigeria
- DRC

Colors and symbols indicate:
- Older
- 3

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Successful transmission and clonal expansion is linked to acquisition of MDR genes

- Composite Tn21-like elements
- Borne on pSLT-like backbone with distinct phylogenetic history
- Different insertion sites on pSLT - virulence plasmid

Kingsley et al, Genome Research, 2009
Orthologous genes in Tn21 variants

Tn21
Malawi
~1960 - 1965

Tn21+cat
DRC
~1984 - 1987
Spread of epidemic invasive S. Typhimurium clones temporally coincides with the HIV epidemic
Genome degradation – Convergent evolution in human adapted serotypes e.g. S. Typhi

- 23 pseudogenes
- 20 gene deletions
- 60% degraded genes absent/degraded in S. Typhi / S. Paratyphi A genome
Summaries

• 2 lineages responsible for invasive S. Typhimurium disease epidemic in SSA

• Independent clonal expansion (beginning from the 1960’s)

• Successful transmission within a susceptible host population (MDR on Tn21-like elements)

• Clonal replacement 2002-2005 (acquisition chloramphenicol resistance in Lineage II)

• Rapid spread enhanced by the increase in susceptible host population (HIV in adults; malaria in children).

• Possible human-to-human transmission

Similar isolates to index cases not found in household animals, veterinary animals, environment etc

– genomic signatures of adaptation in invasive S. Typhimurium
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