

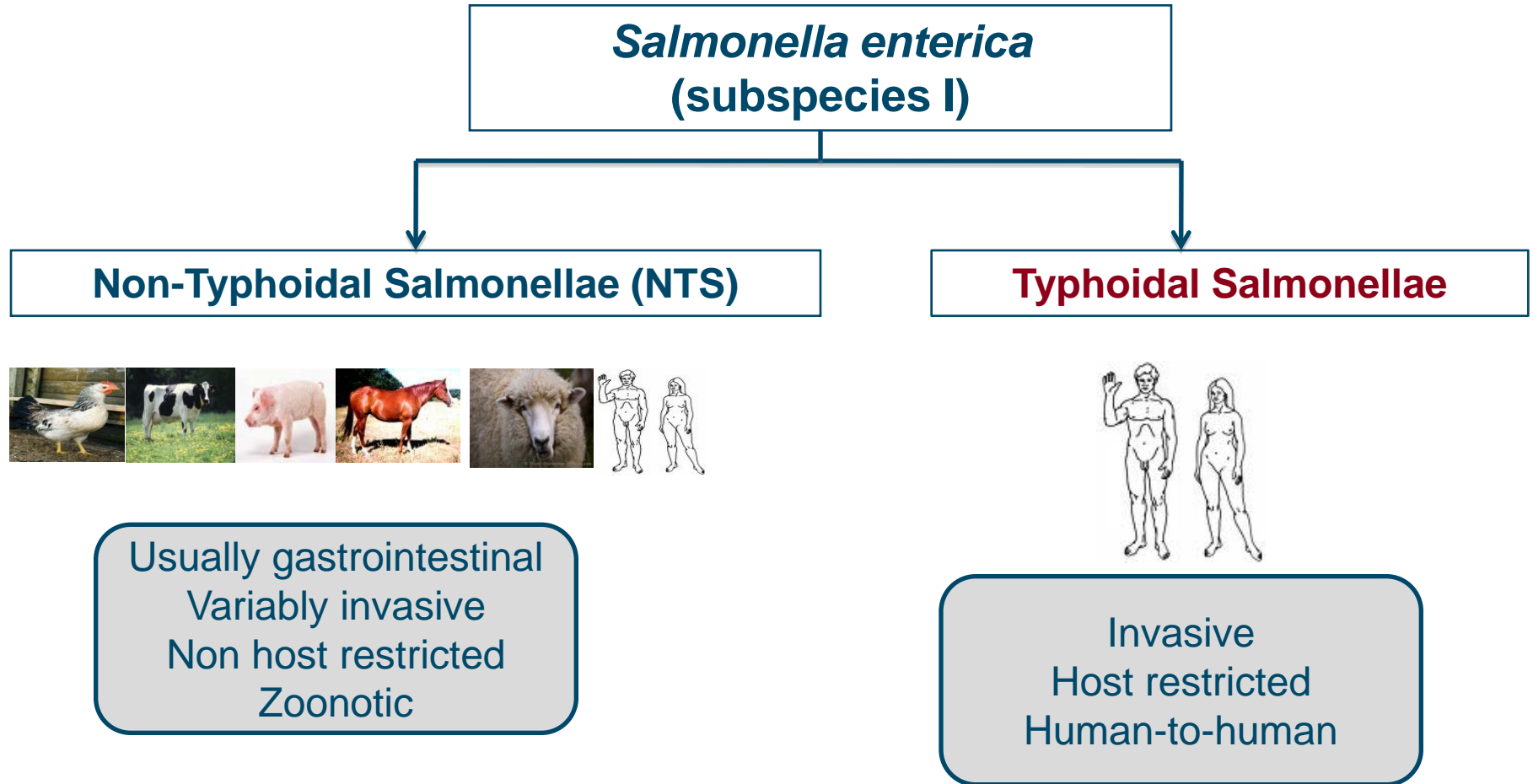
Intra-continental transmission of human invasive *Salmonella* Typhimurium variants

Chinyere Okoro

Wellcome Trust Sanger Institute
Cambridge

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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*

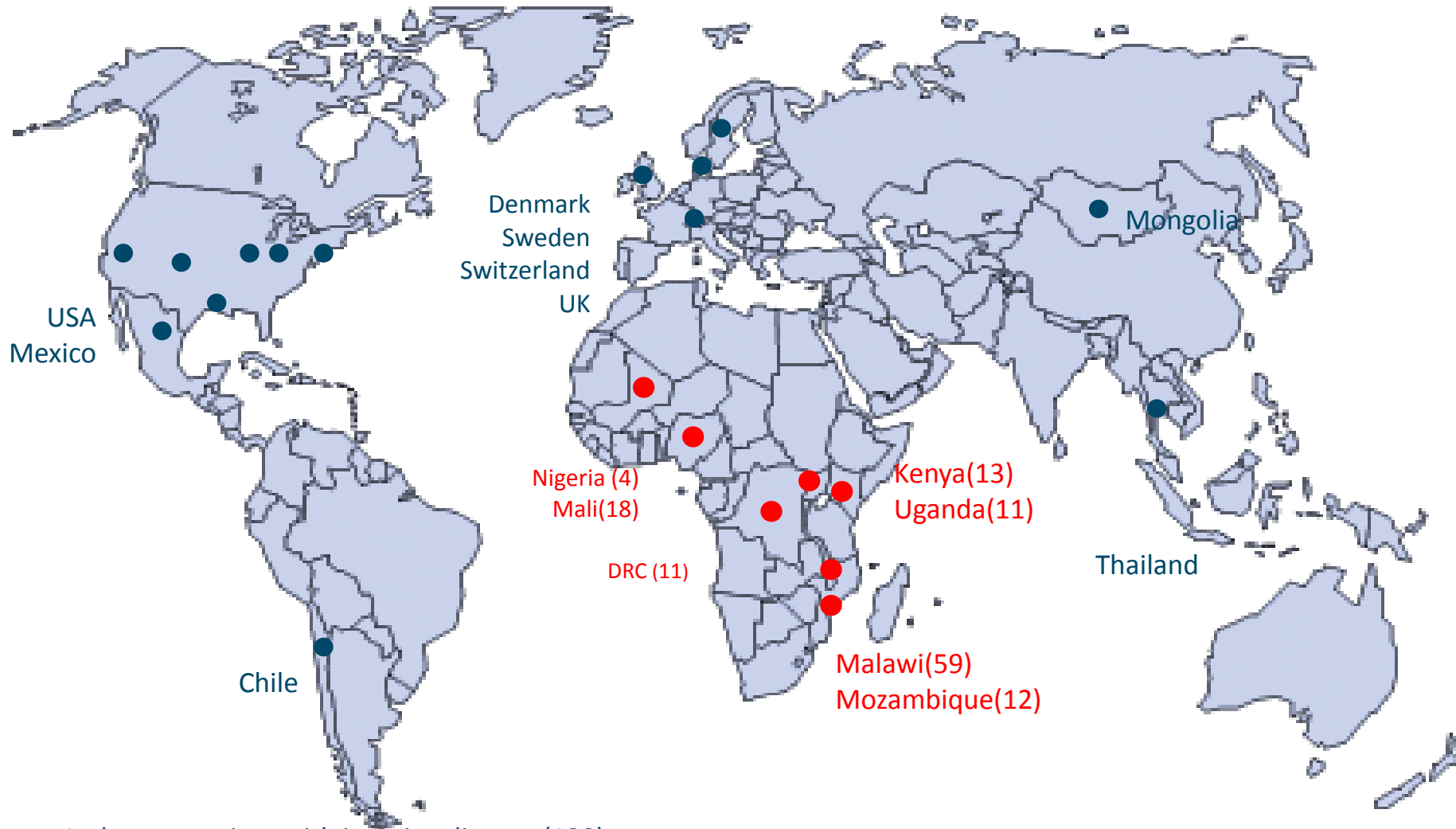
Bacteraemia - Distinct syndrome

- 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



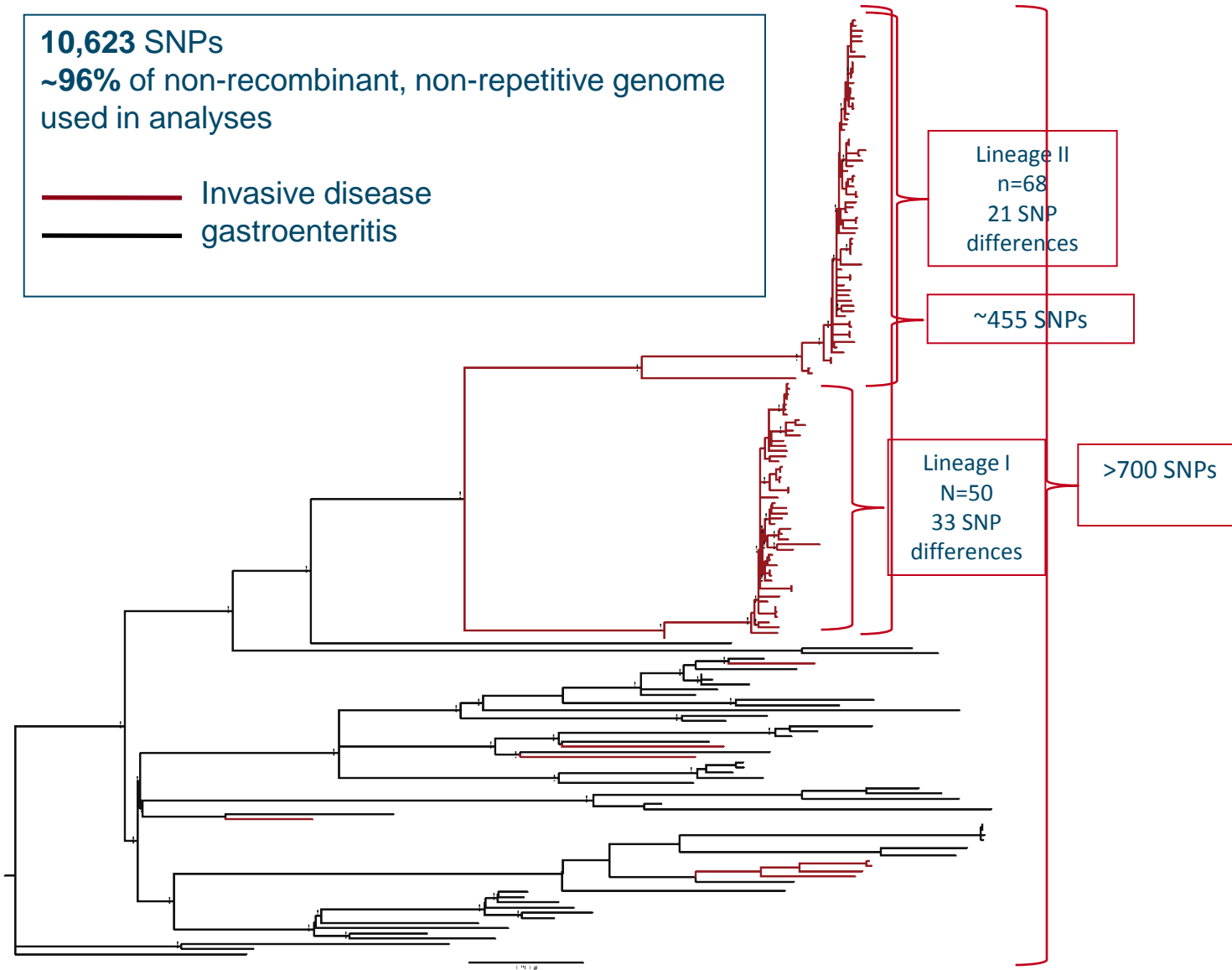
- Isolates associate with invasive disease (129)
- Gastroenteritis-associated isolates(50)

Sub-Saharan isolates fall into two epidemic lineages that emerged independently

10,623 SNPs

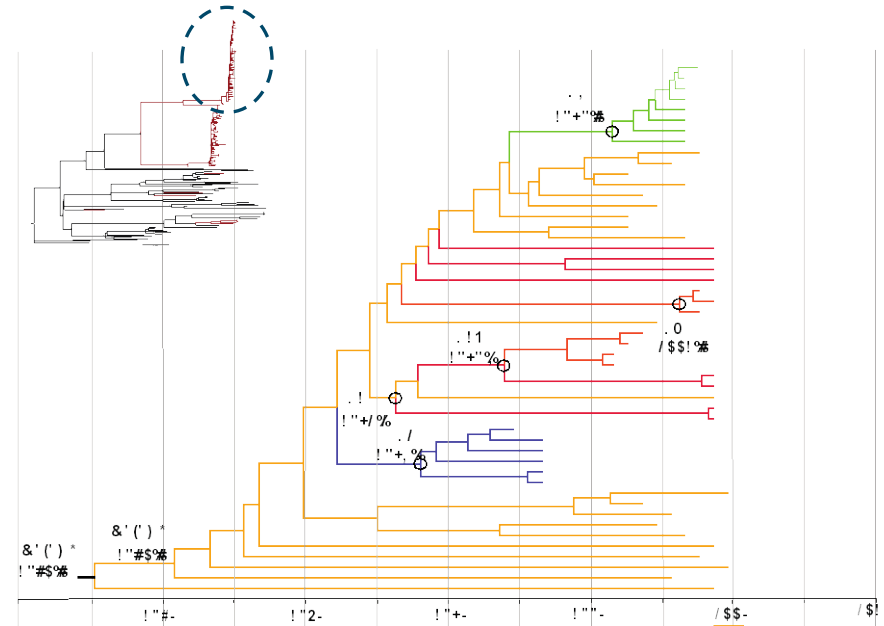
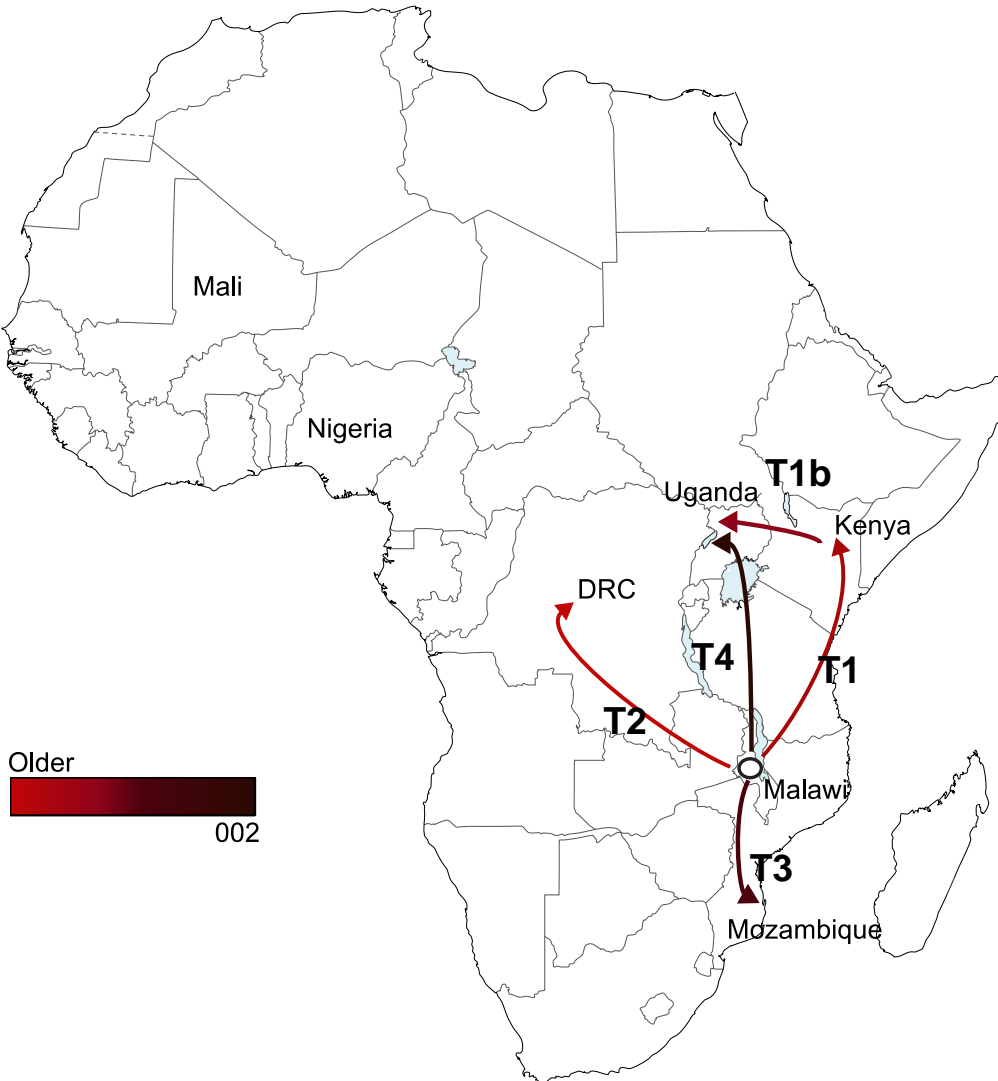
~96% of non-recombinant, non-repetitive genome used in analyses

— Invasive disease
— gastroenteritis



Multiple international transmission events occurred across SSA within each lineage

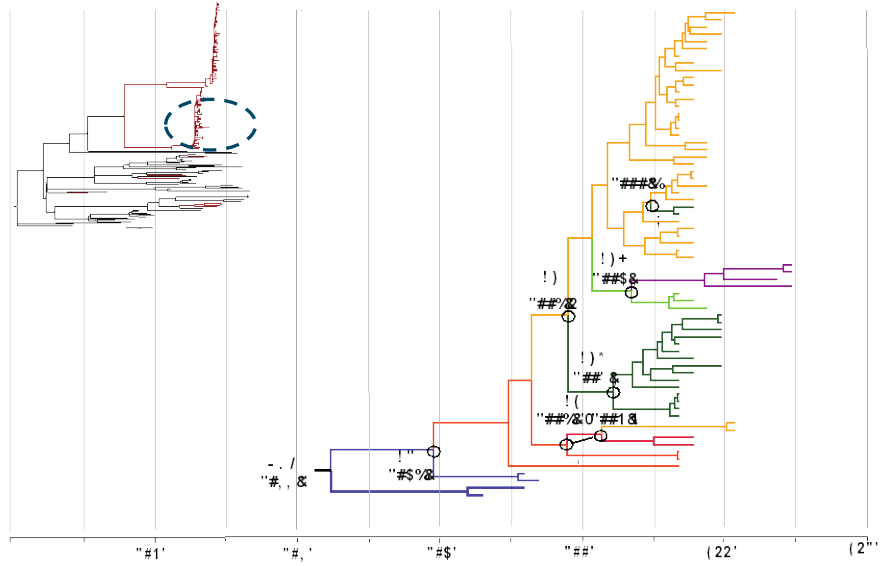
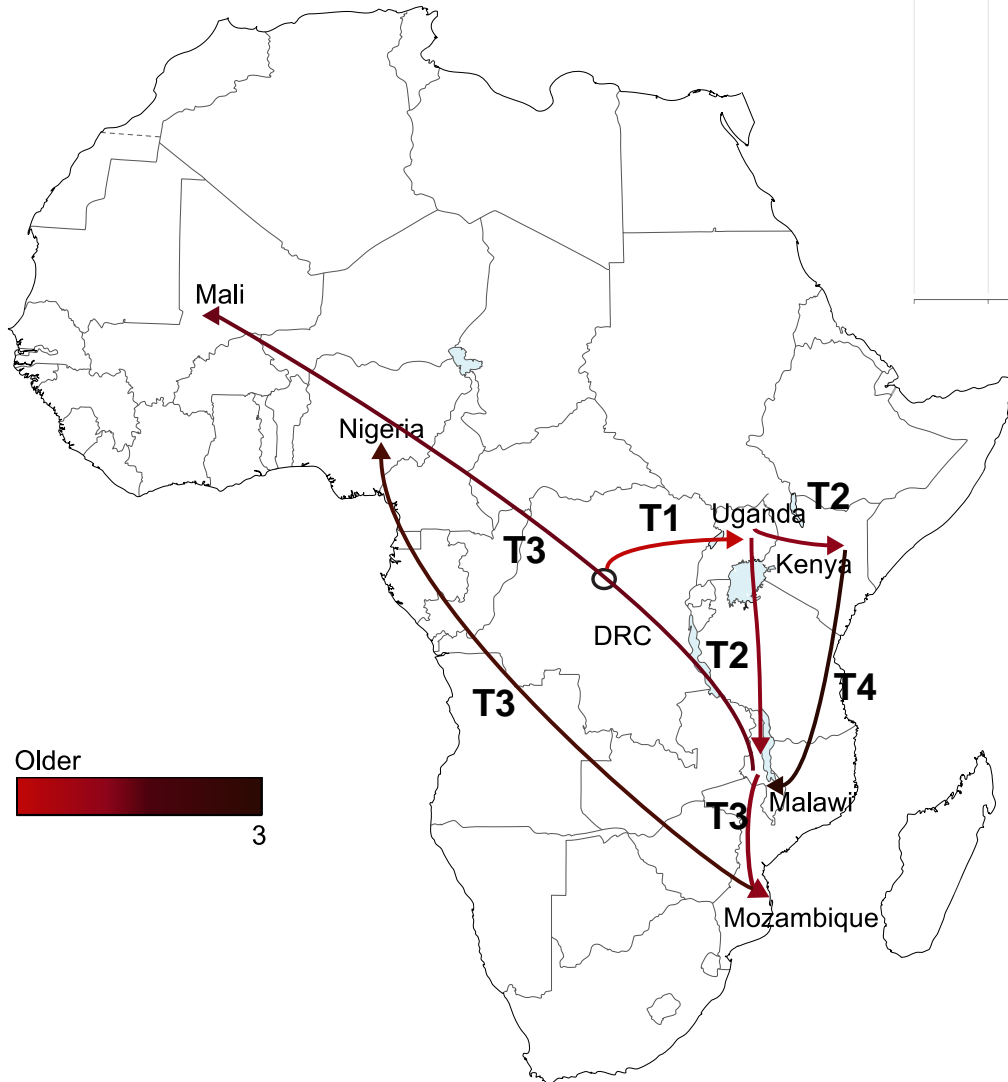
Spread of lineage I clones



○ Nodes where transmissions occur

- ! "# \$%& ()%*+ , - . /)%\$0' \$23\$*4 + 15
- 6"27'
- 8' /' 9)
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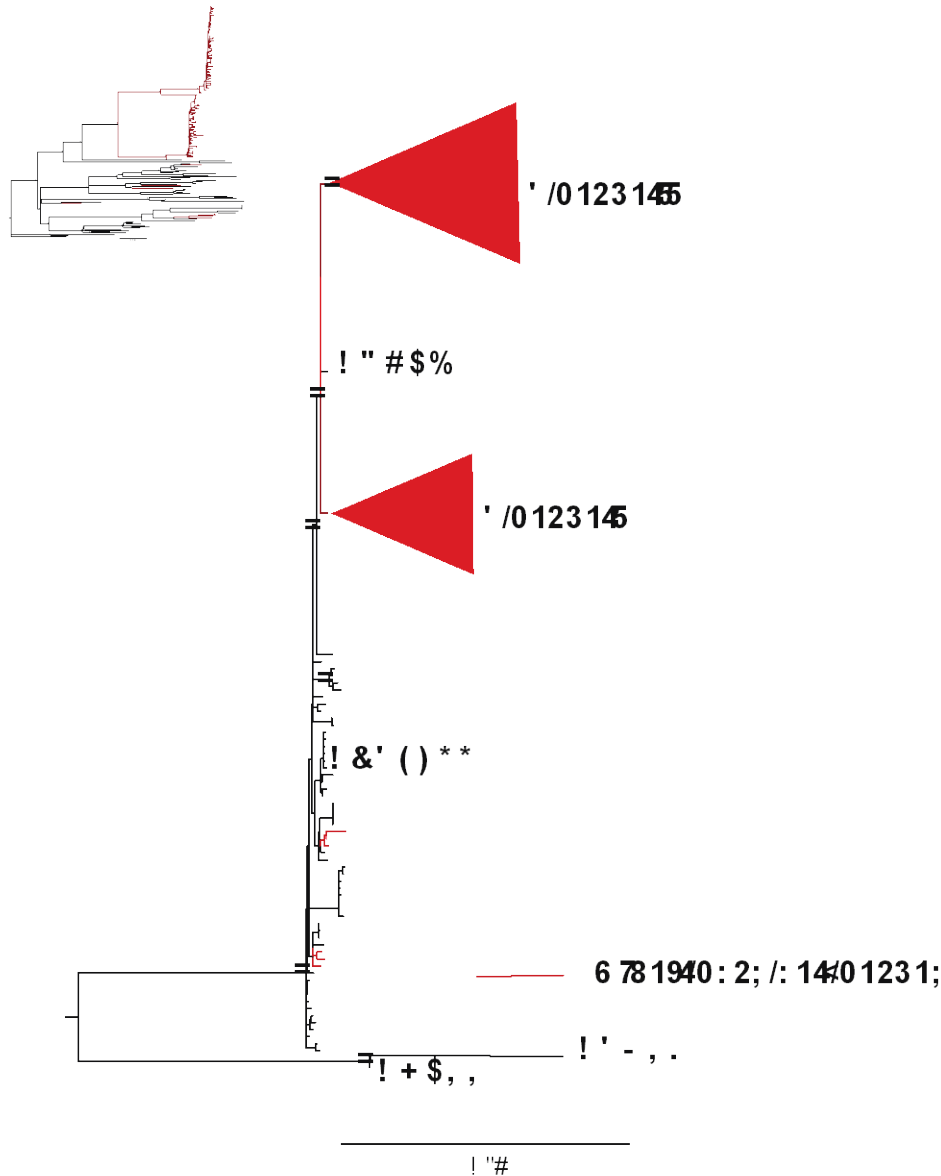
Spread of lineage II clones



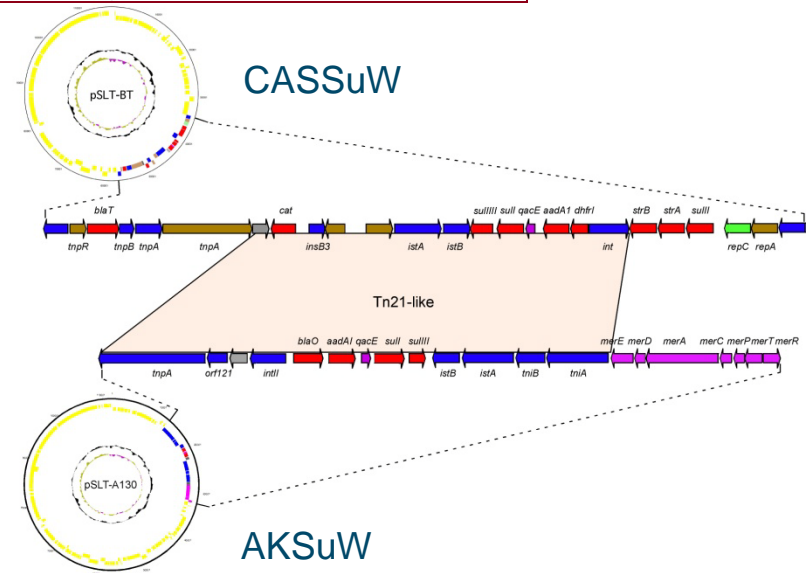
○ Nodes where transmissions occur

- ! "# \$%& ()/*+, - ./)%\$01 \$23\$*4 + 15
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- 8 ' /' 9)
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- 8 \$: ' # . .); - "
- > }3" &'
- < 3' 2='

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



D23580 - pSLT-BT (from Lineage II)



Kingsley *et al*, Genome Research, 2009

A130 - pSLT-A130 (from Lineage I)

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

Orthologous genes in Tn21 variants

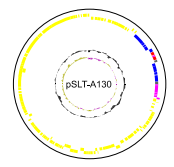
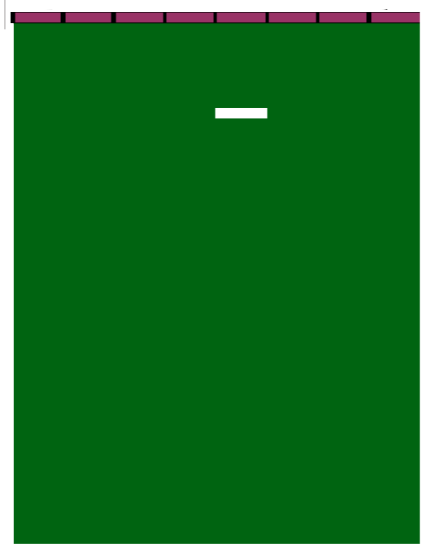
■ 100% ■ <100% □ absent

I

Tn21
Malawi
~1960 -1965



1955 1965 1975 1985 1995 2005 2015

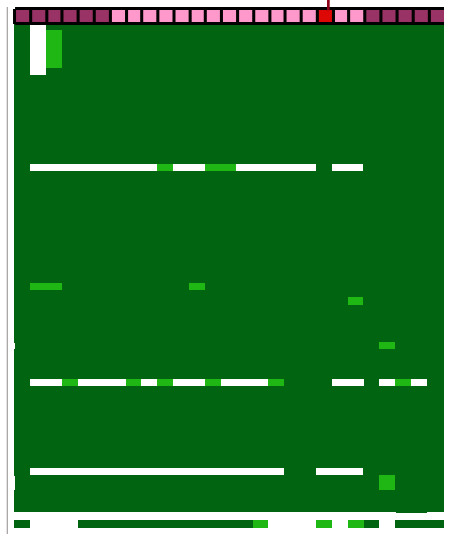


II

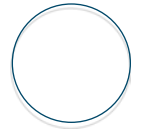
Tn21+*cat*
DRC
~1984 - 1987



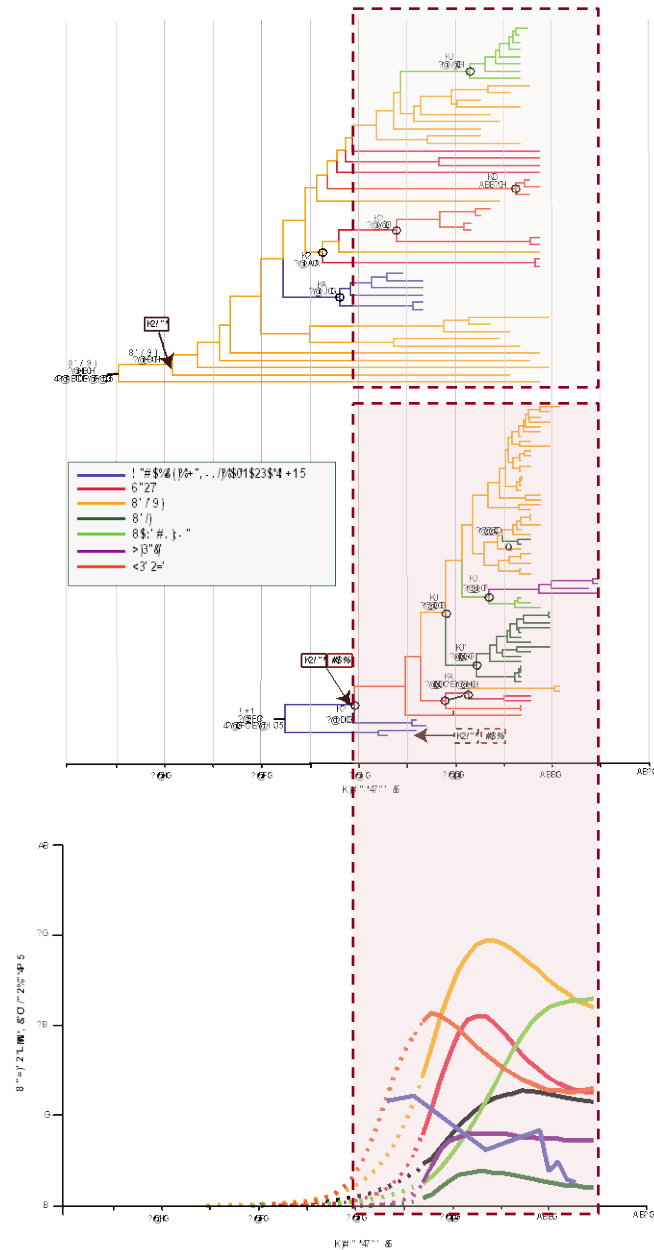
1955 1965 1975 1985 1995 2005 2015



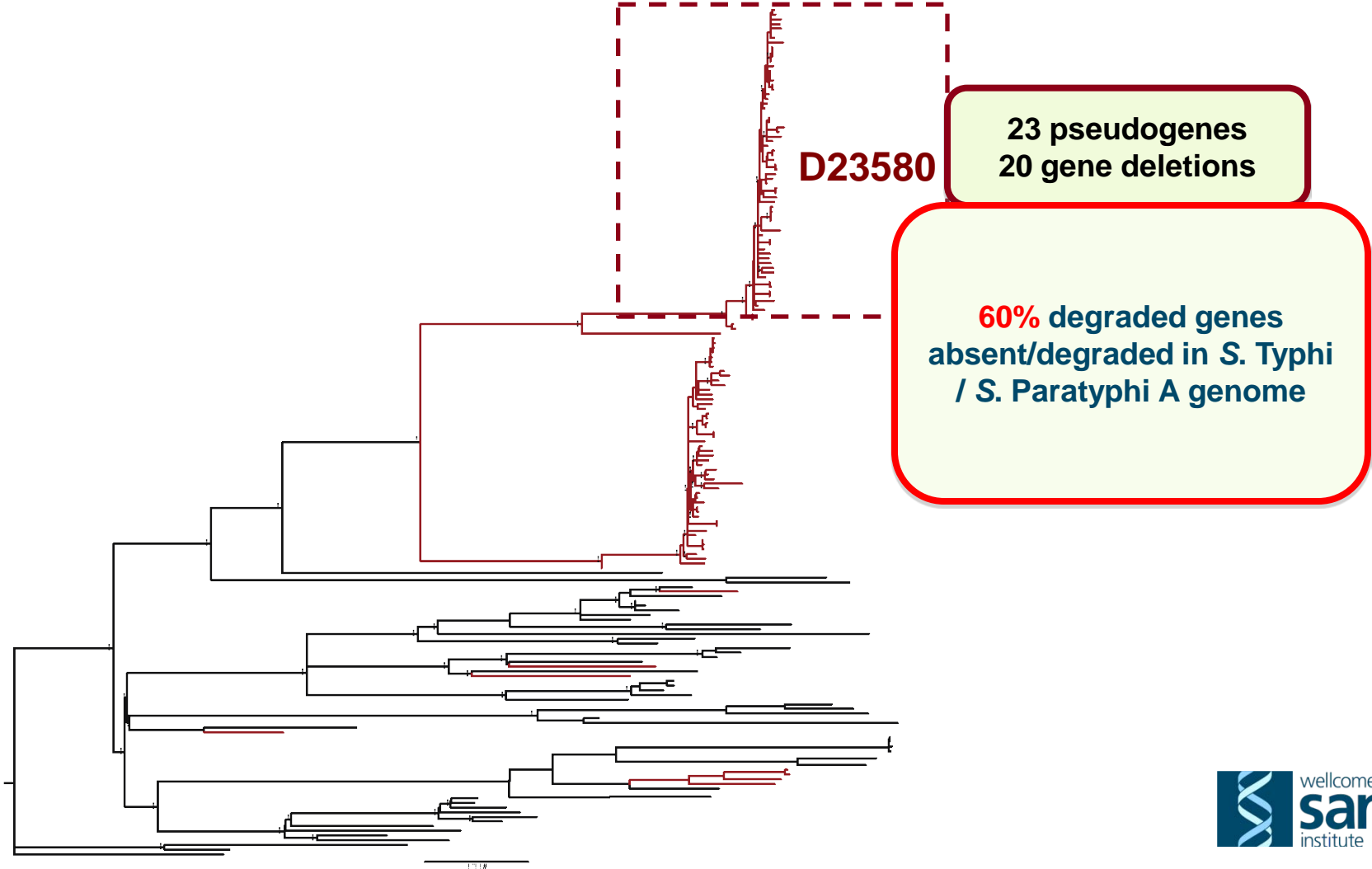
→ *cat*



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*



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

Kariuki *et al*, 2006; Fashae *et al*, 2010.

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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