

Science Health

Food Innovation

# Characterising Genomic Variation within Salmonella Paratyphi A Isolates Associated with the Bacterial Carrier State



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Objective

To explore the genomics and genealogy of S. Paratyphi A isolates, primarily those associated with bacterial carriage in UK patients, utilising both short and long read sequencing technologies, in comparison to S. Typhi.



## Background



Enteric fever is the inclusive term for infections caused by *Salmonella enterica* serovar Typhi and serovars Paratyphi A, B and C.



14.3 million cases of enteric fever are recorded per annum, causing 135,900 deaths<sup>3</sup>.



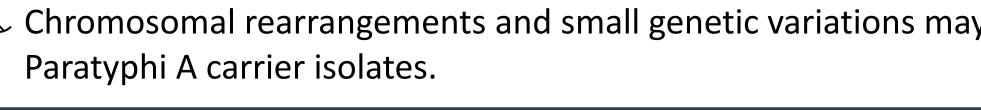
S. Paratyphi A is responsible for 36-50% of cases<sup>4,5</sup>.



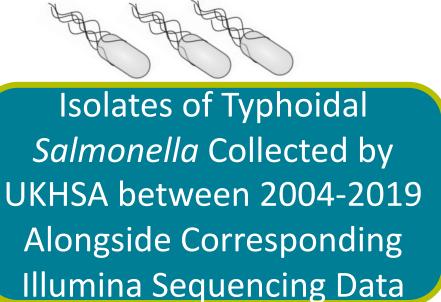
Humans can harbour typhoidal Salmonella asymptomatically and sporadically excrete the bacteria. This is known as the carrier state.

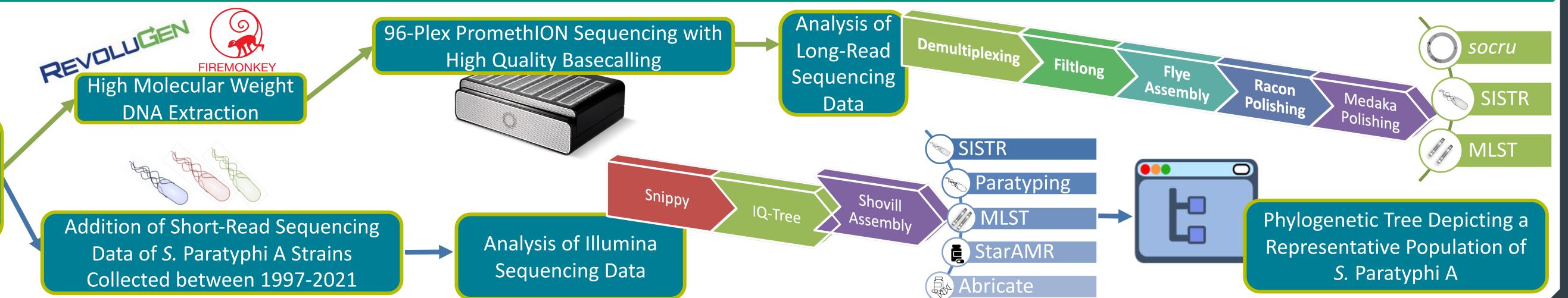


Chromosomal rearrangements and small genetic variations may affect gene expression in S.

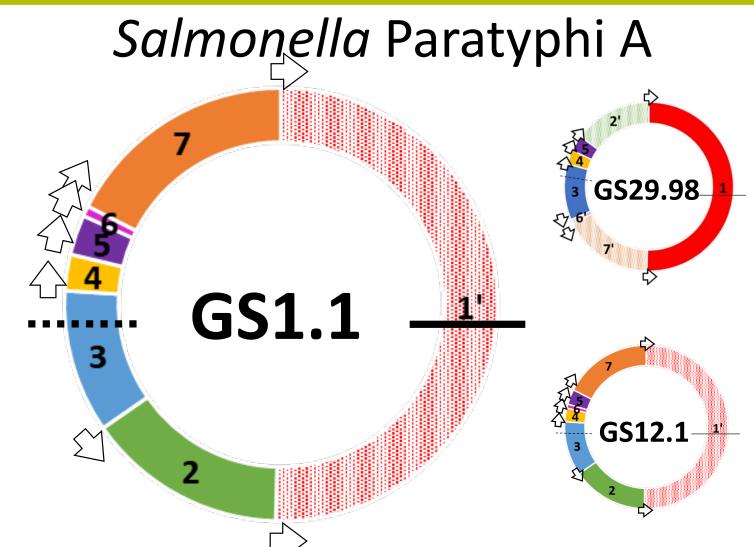


## Methodology





#### Genome Level Variation



Salmonella Typhi

GS11.0

**GS4.1** 

GS2.66-

Sequencing and complete assembly of 65 S. Paratyphi A and 3 S. Typhi isolates yielded numerous genome structures (GS). Every isolate of *S*. Typhi examined possessed a unique GS.



The majority of S. Paratyphi A were GS 1.1 (97%), where an inversion of fragment 1 may cause differential gene expression.



GS 1.1 is also highly prevalent in S. Infantis, a serovar associated with infection in both poultry and humans<sup>7</sup>.

The two S. Paratyphi A isolates identified as not having GS 1.1 were obtained from acute disease, suggesting that bacteria in this serovar may converge upon GS 1.1 during prolonged incubation in a host.

**Disease State** 

#### Nucleotide Level Variation

Combining short-read data from S. Paratyphi A infections in England with those isolated around the world allowed a tree, representative of the serovars population, to be built.

No specific SNP profile or epidemiological cluster was associated with carriage.



UK isolates with confirmed GS were distributed throughout the tree.



The ColRNAI and IncX1/IncX3 plasmid replicons were observed almost exclusively in paratypes 2.4 and 1.2 respectively but were not associated with a specific antibiotic resistance profile.



Fluoroquinolone resistance, via point mutations in gyrA, was present in ~70% of S. Paratyphi A isolates.



<2% of isolates exhibited multi-drug resistance (MDR), and no extensive drug resistance (XDR) was observed.



The Paratype scheme was used to type isolates. Results aligned with known epidemiological data regarding geographical location of sample isolation.

### Conclusions

**Medical** 

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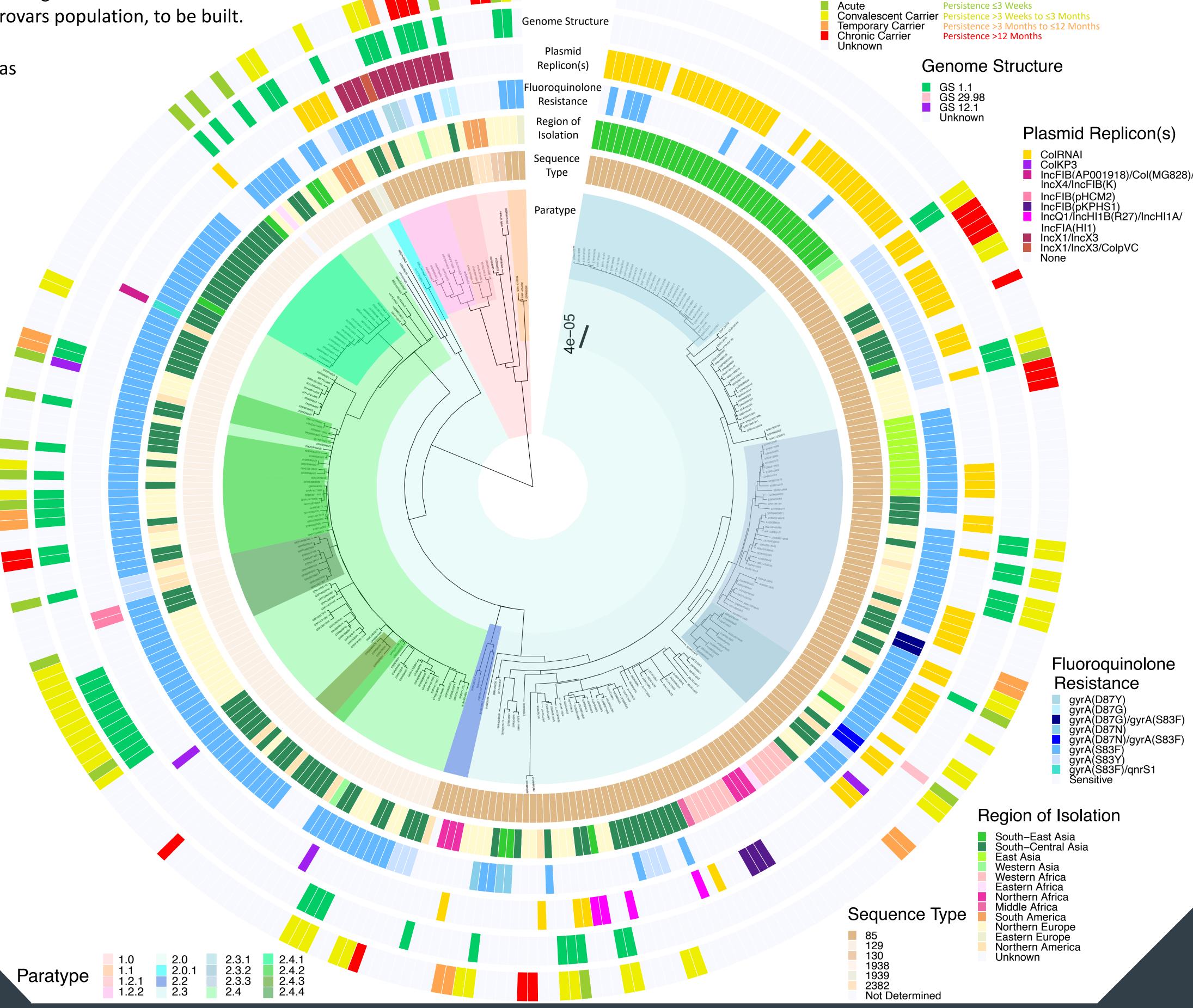


Variability of GS possession between S. Typhi and S. Paratyphi A, may highlight differences in their lifestyle and persistence mechanisms.



No specific SNP profile is associated with carriage, suggesting persistence capacity may depend on host and environmental factors.





Disease state

3. Stanaway, J.D., Reiner, R.C., Blacker, B.F., et al. (2019). The global burden of typhoid and paratyphoid fevers: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Infect. Dis. 19, 369-381. 4. Petersiel, N., Shresta, S., Tamrakar, R., et al. (2018). The epidemiology of typhoid fever in the Dhulikhel area, Nepal: A prospective cohort study. PLoS One 13, e0204479. 5. Woods, C.W., Murdoch, D.R., Zimmerman, M.D., et al. (2006). Emergence of Salmonella enterica serotype Paratyphi A as a major cause of enteric fever in Kathmandu, Nepal. Trans. R. Soc. Trop. Med. Hyg. 100, 1063-1067. **6.** Nath, G., Singh, Y.K., Kumar, K., et al. (2008). Association of carcinoma of the gallbladder with typhoid carriage in a typhoid endemic area using nested PCR. J Infect Dev Countr 2, 302-307. 7. Pardo-Este, C., Lorca, D., Castro-Severyn, J., et al. (2021). Genetic Characterization of Salmonella Infantis with Multiple Drug Resistance Profiles Isolated from a Poultry-Farm in Chile. Microorganisms 9. ARTN 2370.