Diversity and Antimicrobial Resistance of *Salmonella* Paratyphi A: A Global Typhoid Genomics Consortium initiative

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Kigali, Rwanda
Global Typhoid Genomics Consortium

2021-present
>200 members
>50 countries

Our Mission:
We aim to engage the global typhoid research community in order to aggregate *Salmonella* Typhi & Paratyphi A genomic data to monitor the emergence and spread of drug resistance and inform targeted public health action.

Consortium goals:
1. Encourage prompt sharing of typhoid genome data for public health benefit
2. Facilitate the extraction and reporting of key data of public health relevance
3. Promote and facilitate the dissemination and use of information derived from typhoid genomic data to monitor antimicrobial resistance and post-vaccination impact

Consortium coordinators:

Kathryn Holt
LSHTM

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Global diversity and antimicrobial resistance of typhoid fever pathogens: Insights from a meta-analysis of 13,000 Salmonella Typhi genomes


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Group author details: Global Typhoid Genomics Consortium Group Authorship
See page 32

Competing interests: See page 34

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Genetic diversity of Typhi from 13k genomes

Carey, Dyson, et al. 2023, eLife
Global Typhoid Genomics Consortium Resources

- **GenoTyphi genotyping software**
  - [github.com/typhoidgenomics/genotyphi](https://github.com/typhoidgenomics/genotyphi)

- **Typhi Pathogenwatch**: [http://pathogen.watch](http://pathogen.watch)

- **TyphiNET surveillance dashboard**: [http://typhi.net](http://typhi.net)

Global Typhoid Genomics Consortium Working Groups

1. Typhi transmission dynamics & phylodynamics
2. GenoTyphi Mykrobe software development
3. GenoTyphi genotyping scheme
4. Paratyphi A genetic epidemiology & software tools
Paratyphi A special interest group

Motivation
To curate a global collection of Paratyphi A whole genome sequences to better understand the global distribution of Paratyphi A pathogen variants, their transmission dynamics, and antimicrobial resistance for public health benefit.

Goals and aims
1. Extend the current GTGC standardised metadata template for use with Paratyphi A data and long-read nanopore data
2. To better understand the global genetic epidemiology of Paratyphi A, including spatio-temporal distribution of AMR pathogen variants, their emergence, and transmission dynamics
3. Increase the accessibility of the Paratyphi genotyping framework via Mykrobe and Pathogenwatch

Collaboration
• Contacted corresponding authors who have published at least a single Paratyphi A genome
• Responses from >90 consortium members in >40 countries

Working groups
1. Statistical analysis of AMR and pathogen genotypes
2. Phylodynamic analysis of pathogen transmission dynamics
3. Accessible software tools to facilitate the analysis of Paratyphi A genome data

Working group leads:
- Zoe Dyson, LSHTM
- Yogesh Hooda, CHRF
- Jaspreet Mahindroo, Imperial College
Public genome meta-analysis: samples available

Distribution of public Paratyphi A WGS data

Data from 41 countries

WGS data & metadata
- Data available
- No data available

n=2,561 genomes published prior to July 2023
Public genome meta-analysis: samples available

Data from 41 countries
9 countries with ≥10 genomes

Distribution of public Paratyphi A WGS data

WGS data & metadata
- Data available
- No data available

Number of WGS
- 200
- 400
- 600

n=2,561 genomes published prior to July 2023
Public genome meta-analysis: genotype & AMR prevalence

Minor genotypes present at <20%

Endemic countries with n≥20 non-targeted sequences post 2010

- MDR & ESBL rare
- High CipNS
Increased Ciprofloxacin MIC
Ciprofloxacin & Azithromycin co-resistance

Public genome meta-analysis: variants of concern

n=2,561 genomes published prior to July 2023
Travel-associated cases predict endemic populations

Pearson correlation 0.95
p = 2.2 x 10^{-16}

Pearson correlation 0.93
p = 7.1 x 10^{-12}

Post 2010; minor genotypes present at <20%
Future plans

• Inaugural special interest group meeting in January 2024

• Formal working group analyses
  • Integrate ~800 more genomes into the GTGC collection
  • Statistical analysis of genotype and AMR prevalence
  • Phylodynamic analysis of transmission dynamics
  • Develop accessible software solutions for Paratyphi A data analysis

• Inform Paratyphi A control and intervention strategies
  • Empirical therapy
  • Baseline data ahead of potential future vaccination programmes
How to get involved

Seeking:
• Paratyphi A genomes and metadata
• Contributors to working group analyses

How to contribute:
• Membership questionnaire: https://bit.ly/ParatyphiREG
• Come speak to us or email typhinetinfo@gmail.com
Acknowledgements & further information

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Global Typhoid Genomics Consortium
http://typhoidgenomics.org

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LSHTM, UK
Prof Kathryn Holt
Dr Megan Carey

Typhoid Genomics Consortium

Consortium membership

Paratyphi A working group membership

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Travel-associated paratyphoid cases

1. Healthy person
2. Travel abroad
3. S. Paratyphi A infection
4. Return travel
5. Paratyphoid patient
6. Consultation

DNA extraction
Illumina sequencing
Strain characterization from WGS data

Public Health Laboratory e.g. UKHSA

Travel questionnaire
Patient sample