Low genetic diversity of *Treponema pallidum* ssp. *pertenue* (TPE) isolated from patients' ulcers in Namatanai District of Papua New Guinea

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INTRODUCTION

- Yaws is an endemic disease caused by *Treponema pallidum* subsp. *pertenue* (TPE) that primarily affects children in rural regions of the tropics.
- Clinical manifestations in the primary stage include chronic skin ulcers and other skin lesions, potentially affecting bones and cartilage in the later stages.
- A newly developed multilocus sequence typing (MLST) scheme for TPE isolates was used to characterize the bacterium causing yaws in the Namatanai District, New Ireland province of Papua New Guinea during the Yaws 3 Trial.
- This multi-locus sequence typing (MLST) scheme was applied to TPE-containing clinical isolates obtained during a mass drug administration study conducted in the Namatanai District of Papua New Guinea between June 2018 and December 2019 (John et al. 2022).
- Out of the 1081 samples collected, 302 (28.5%) tested positive for TPE DNA, and 255 (84.4%) of these samples were fully typed.

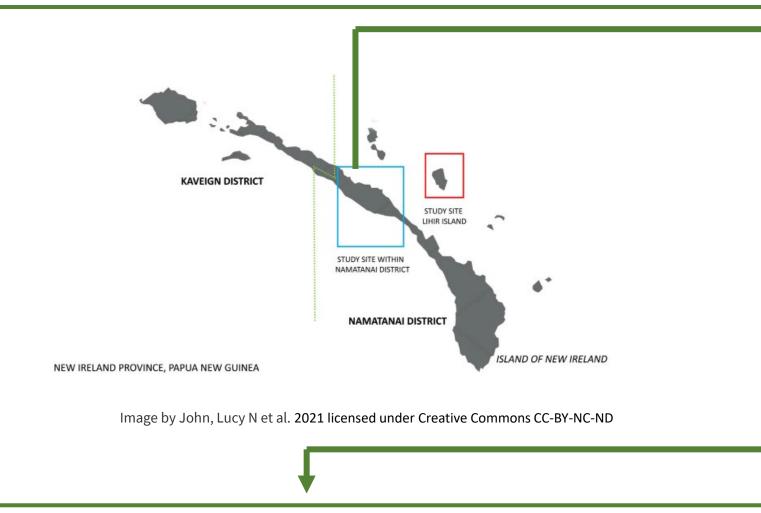


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METHODS

The Yaws 3 trial was held from April 2018 to October 2019 in the Namatanai District of Papua New Guinea, focusing on three selected local-level government (LLG) areas:

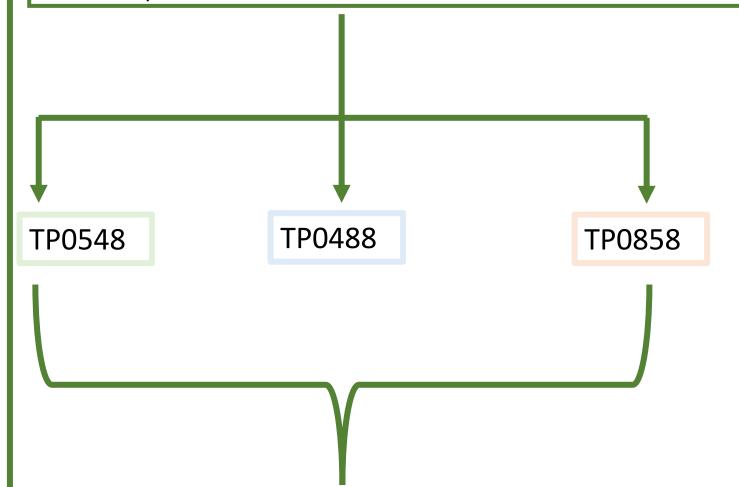
Matalai Rural (MAT), Namatanai Rural (NTI) and Sentral Niu Ailan Rural (SNA)



Collection of swab samples from suspected yaws lesion

Swab samples shipped to Masaryk University, Czech Republic

DNA isolation and MLST of three typing targets namely, TP0548, TP0488 and TP0858



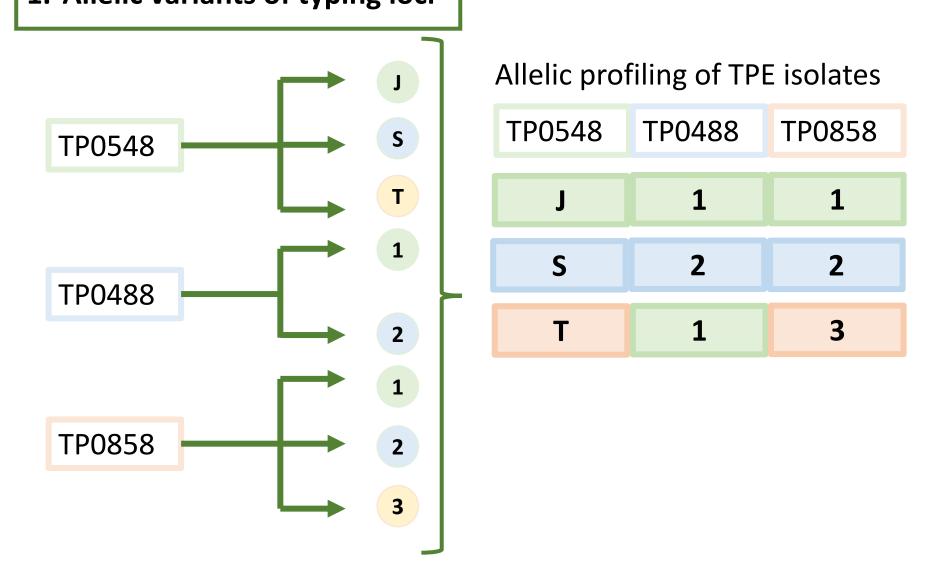
MLST amplified PCR products were Sanger sequenced by Eurofins Genomics (Constance, Germany; Eurofins Genomics Company).

The sequencing reads were edited using Lasergene's EditSeq sequence editor program (DNASTAR Lasergene EditSeq v.7.1.0; DNASTAR, Madison, WI, USA), consensus sequences were generated using the Seqman sequence assembling program (Lasergene, DNASTAR v.7.1.0)

Determination of allelic variants of typing targets and profiling yaws clinical isolates

RESULTS

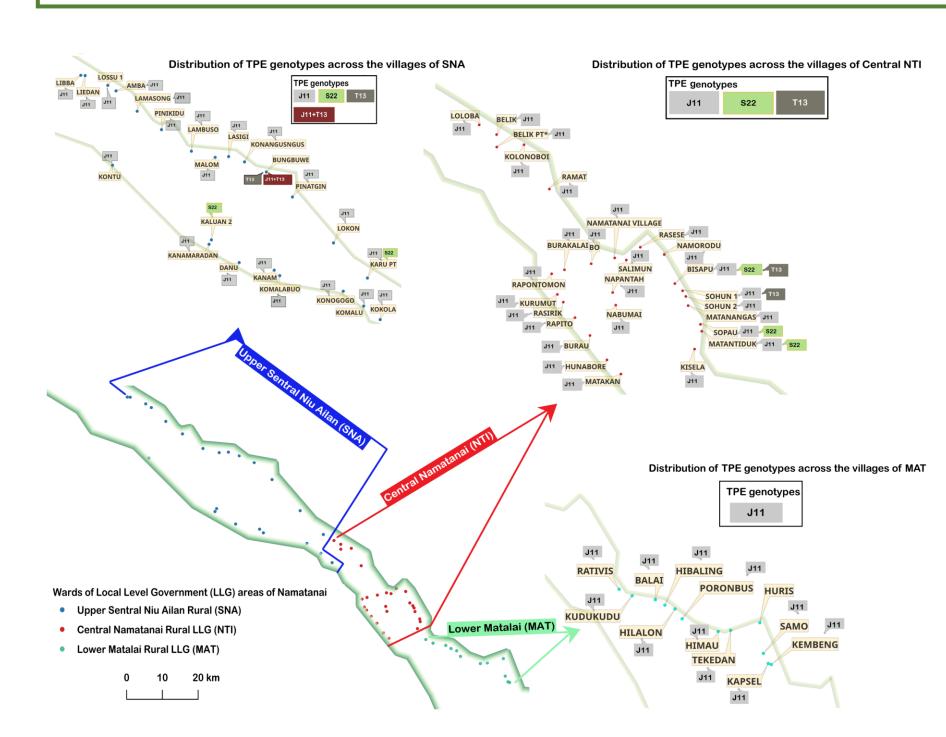
1. Allelic variants of typing loci



2. MLST typing of TPE-containing isolates from Namatanai, Papua New Guinea.

Genotype	TP0548 allele	TP0488	TP0858	Percentage of genotypes from all typeable
				samples (n = 255)
J11	J	1	1	93.3 % (n = 238)
S22	S	2	2	4.3 % (n = 11)
T13	Т	1	3	2.0 % (n = 5)
J11/T13	J/T	1	1/3	0.4 % (n = 1)

3. Geographical locations of detected genotypes in sampled wards of LLG areas in Namatanai, Papua New Guinea



The map is based on information from 164 participants from first round of the Yaws 3 trial. This map was constructed using QGIS 32.8.0.

4. Namatanai Yaws 3 study design

CONTROL ARM: Morges strategy (One round of MDA at baseline)

EXPERIMENTAL ARM: Three rounds (Round 1, Round2 and Round 3) of MDA

Three rounds of azithromycin significantly decreases yaws cases in the experimental arm at Round 4 (follow-up).

Control arm
47 yaws cases/
29,954 persons

p <0.0001

Experimental arm 10 yaws cases/ 29,987 persons

CONCLUSIONS

- The newly developed MLST scheme revealed low level of genetic diversity among TPE isolates consistent with the endemic nature of yaws.
- The most predominant strain in Namatanai was J11 and the two minor genotypes were S22 and T13.
- TPE PCR positivity was higher in younger patients (> 15 years of age)
 with single ulcers during the first ulcer episode and with ulcer
 duration less than six months.
- While the predominant J11 was detected in all wards of sampled areas, S22 and T13 were detected in specific areas suggesting local contacts are essential in yaws transmission.

ACKNOWLEDGEMENTS

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ABBREVIATIONS

- Papua New Guinea (PNG)
- Treponema pallidum subsp. pertenue (TPE)
- Multi-locus sequence typing (MLST)
- Mass drug administration (MDA)
- Local level government areas (LLG)
- Matalai Rural (MAT)
- Namatanai Rural (NTI) Sentral Niu Ailan Rural (SNA)

REFERENCES

- 1. John LN, Beiras CG, Houinei W, Medappa M, Sabok M, Kolmau R, et al. Trial of Three Rounds of Mass Azithromycin Administration for Yaws Eradication. New England Journal of Medicine. 2022;386: 47–56. doi:10.1056/NEJMoa2109449
- 2. John LN, Gonzalez-Beiras C, Vall-Mayans M, Kolmau R, Houinei W, Wangi J, et al. Safety of mass drug coadministration with ivermectin, diethylcarbamazine, albendazole, and azithromycin for the integrated treatment of neglected tropical diseases: a cluster randomized community trial. Lancet Reg Health West Pac. 2021 Nov 2;18:100293.
- 3. Mitjà O, Šmajs D, Bassat Q. Advances in the Diagnosis of Endemic Treponematoses: Yaws, Bejel, and Pinta. PLOS Neglected Tropical Diseases. 2013;7: e2283. doi: 10.1371/journal.pntd.0002283



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