

Detection of Streptococcus pneumoniae non vaccine serotype 12F clone 989 with acquired antibiotic resistance, circulating globally

Rebecca A. Gladstone, Brenda Kwambana-Adams, Mignon Du Plessis, Paulina Hawkins, Maaike Alaerts[,], Sarah E. Burr, Elita Jauneikaite, Martin L. Hibberd, Berthe-Marie Njanpop-Lafourcade, Jennifer C. Moisi, Stuart C. Clarke, Somporn Srifuengfung, Abdullah W. Brooks, Veeraraghavan Balaji, Fredrick M. Mobegi, Amelieke J. Cremers, Marien I. de Jonge, Aldert Zomer, Diederik van de Beek, Arie van der Ende, Ben J. Metcalf, Bernard Beall, Rama Kandasamy, Andrew J. Pollard, Paul Turner, Susan A. Nzenze, Shabir A. Madhi, Keith P. Klugman, Dean B. Everett, Martin Antonio, Anne Von Gottberg, Lesley McGee, Robert F. Breiman, Stephen D. Bentley

On behalf of all Global Pneumococcal Sequencing project partners. www.pneumogen.net/gps

The Global Pneumococcal Sequencing project (GPS) aims to capture changes in the pneumococcal population through the introduction of pneumococcal conjugate vaccines (PCV).

Background

- Clonal complex (CC)989 is the largest 12F clone in GPS and represents a lineage distinct from the 12F PMEN clone Denmark12F-34.
- CC989 12F has previously been observed in small numbers; the MLST database includes 55 sporadic isolates, the oldest from 1998 (Kenya).
- Serotype 12F has been reported to be more frequently found in disease than carriage and has been increasing in the PCV era.

Methods

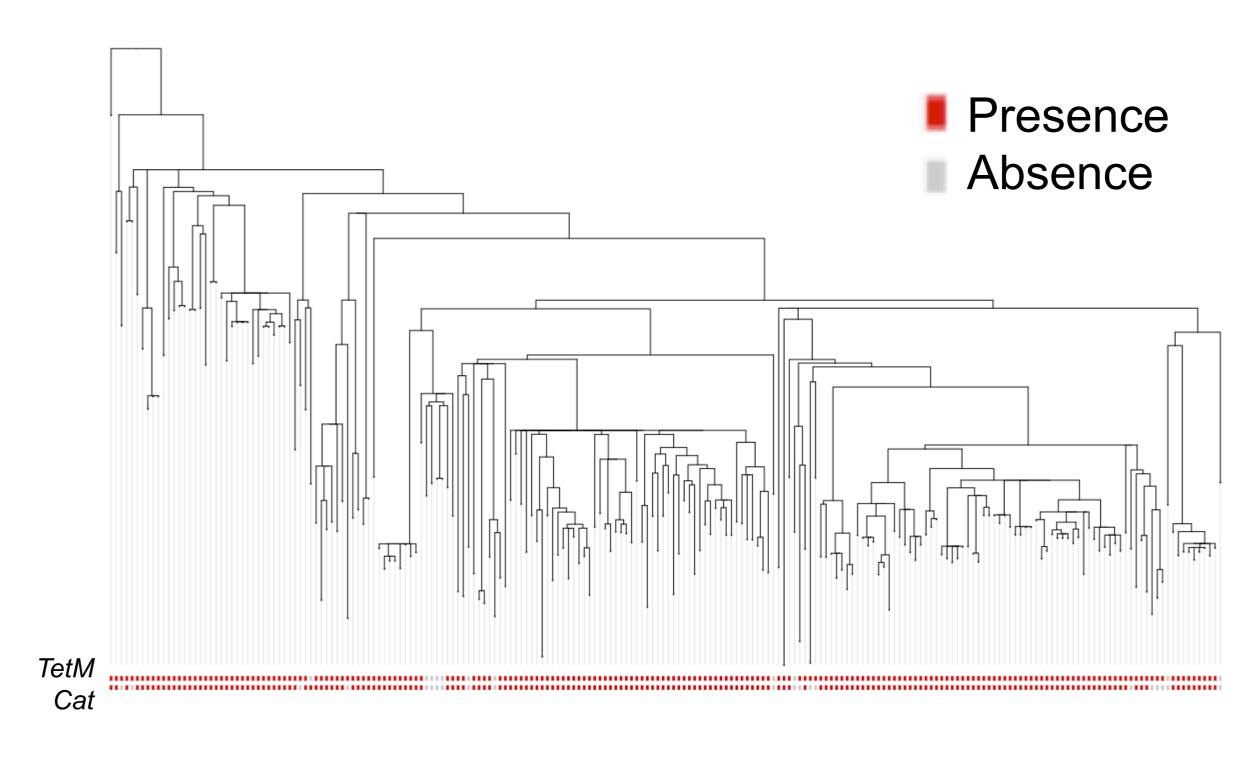
ARIBA detected acquired antibiotic resistance genes. Reads were mapped to CC989 reference, Gubbins removed recombination and phylogeny produced using RAxML with Path-O-Gen for lineage dating. Visualisations with Phylocanvas.org and Microreact.org

Results

212 CC989 genomes were available with Isolation dates ranging from 2005 -2015. The phylogenetic temporal signal estimates that the clone arose around 1971.

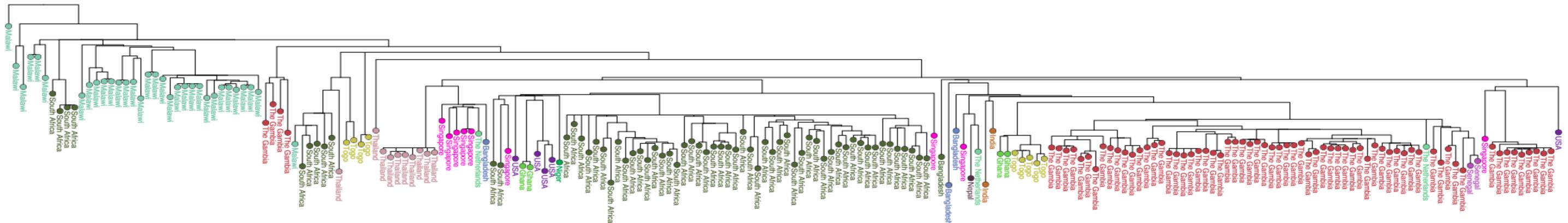
Antibiotic resistance

Tet(M) and chloramphenicol acetyltransferase (cat) were detected in >85% of isolates. 29% had a resistant cotrimoxazole MIC of ≥2 µg/ml correlating with a *folA* recombination hotspot. All isolates were penicillin susceptible from phenotype or inferred from pbp allele profile.



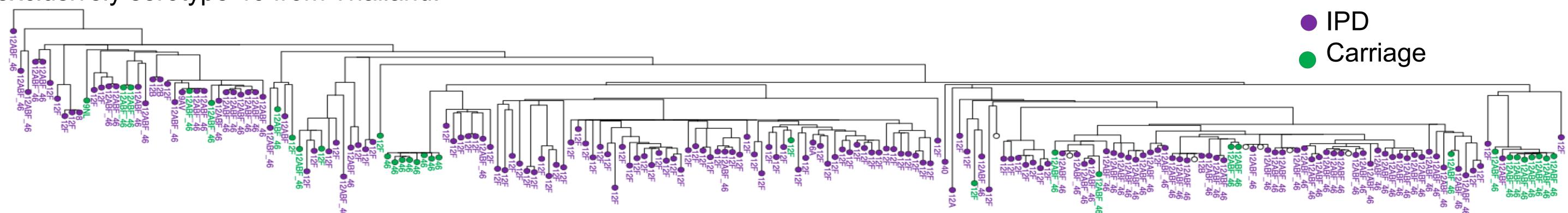
Phylogeography

Isolates were from The Gambia (69), South Africa (61), Malawi (33) and 11 additional countries with clear geographical clustering.



Phylogeny in context of clinical manifestation

80% of the CC989 isolates were from disease, with two small phylogenetic clusters accounting for 48% of the carriage isolates; one exclusively serotype 46 from Thailand.



Conclusions

- CC989 is a intercontinentally disseminated NVT clone with multidrug resistance which expresses disease associated serotype 12F.
- Global genomic surveillance allows detection and high resolution description of NVT lineages which pose potential threats in vaccine replacement.

