

# Vaccine escape: emergence of a multidrug resistant and virulent *Streptococcus pneumoniae* lineage GPSC10/CC230 post PCV-13 poses a global threat

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## Background:

Pneumococcal Conjugate Vaccine (PCV) which targets 13 serotypes of *S. pneumoniae* is very effective at reducing disease in young children, however, increases in replacement with non-PCV serotypes remains a concern. **Serotype 24F is one of the major invasive serotypes contributing to serotype replacement in France, Spain and multiple other countries.**

We aimed to

- 1) Investigate the global genetic diversity of serotype 24F
- 2) Identify and characterize the major pneumococcal lineage that drove the increase of serotype 24F in France and Spain
- 3) Elucidate the major lineage's spatiotemporal transmission dynamics at the national and international level.

## Methods

Whole-genome sequenced two collections:

- a) 419 isolates from asymptomatic colonization (n=229) and invasive disease cases (n=190) among individuals <18 years old in France, 2003-2018
- b) 68 invasive disease isolates from children <5 years old from Catalonia, 2003-2018

Extracted relevant genomes and metadata from the Global Pneumococcal Sequencing (GPS) project database (n~26,000) to provide a global context of serotype 24F and strain of interest.

*In silico* serotyping using SeroBA and cluster each isolate into Global Pneumococcal Sequence Clusters (GPSCs) using PopPUNK.

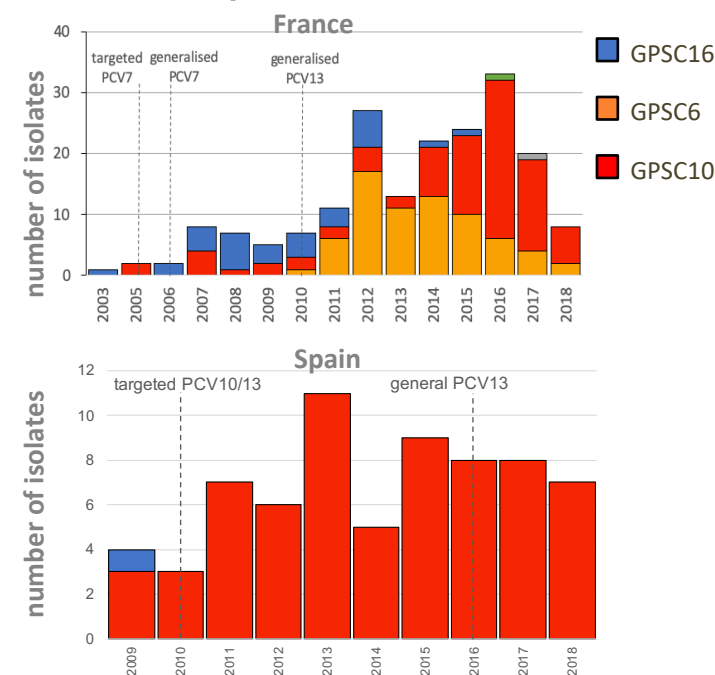
Phylogeny was built using GUBBINS. Evolutionary and spatiotemporal analysis were conducted using BEAST. We estimated the invasive disease potential by calculating the odds ratio of prevalence in invasive disease to carriage.

## Results

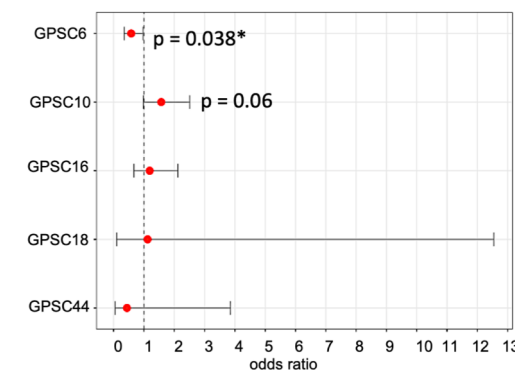
### 1) Global genetic diversity of serotype 24F

- Serotype 24F (n=671) is detected in **30 countries**
- **GPSC10, 16, 150 and 206** are main lineages
- GPSC10 is the only **multidrug-resistant lineage**, exhibiting resistance to penicillin, erythromycin, cotrimoxazole and tetracycline.

### 2a) GPSC10 is the main contributor to the rise of 24F in France and Spain

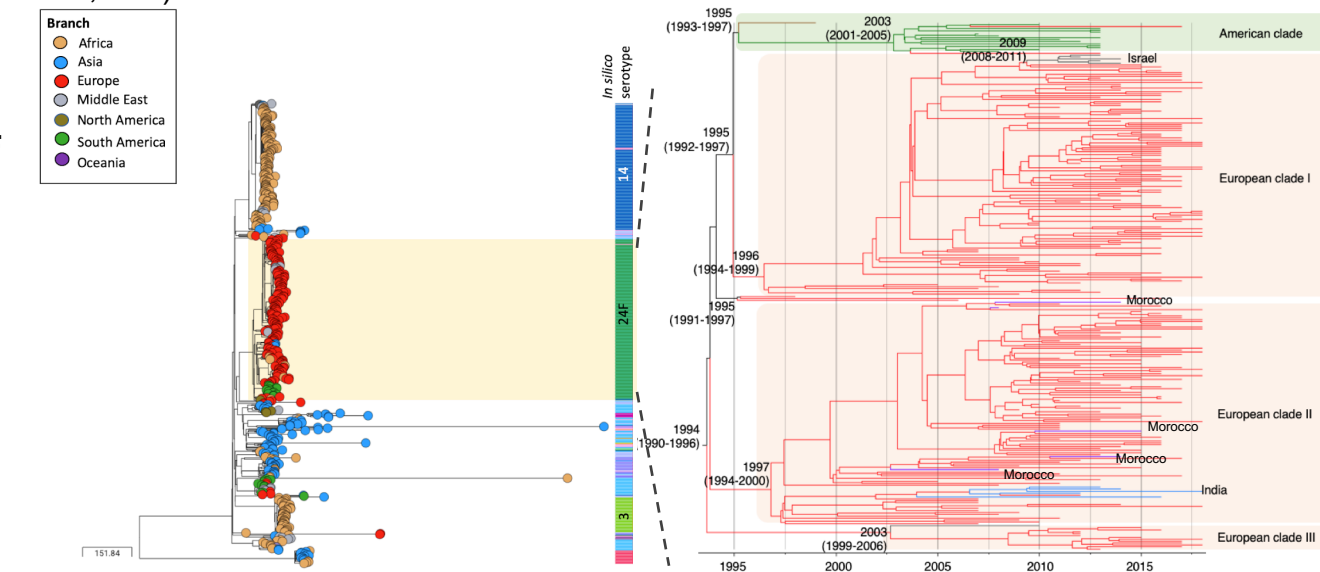


### 2b) GPSC10 shows a higher propensity to cause meningitis independent of 24F capsule



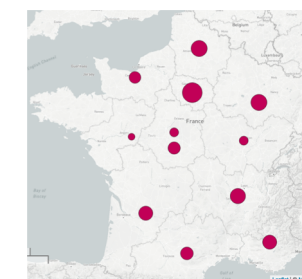
### 3a) Spatiotemporal transmission at international level

GPSC10 (n=888) expresses **17 serotypes**. Six PCV13 serotypes (3, 6A, 14, 19A, 19F, 23F) and eleven non-PCV13 serotypes (7B, 13, 10A, 11A, 15B, 15C, 17F, 22F, 23A, 23B, 24F)

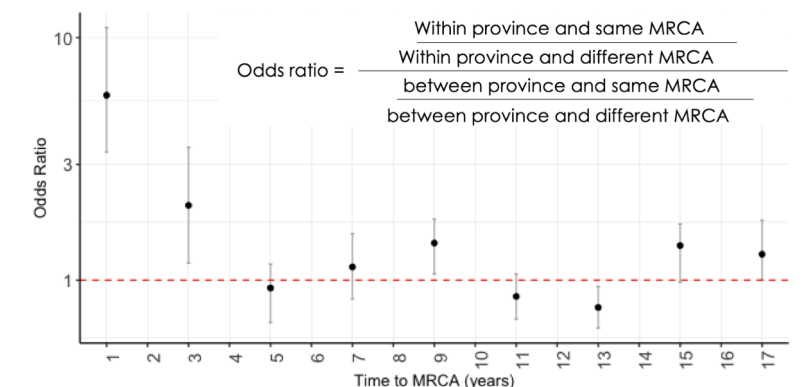


### 3b) Spatiotemporal transmission in France

(I) Geographical distribution



(II) Odds of being diverged from same most recent common ancestor (MRCA) and being recovered from the same province in France



## Conclusion

GPSC10 is the major pneumococcal strain that drove the increase in serotype 24F in France and Spain. The combination of high disease potential, multidrug resistance and expression of multiple serotypes suggests continued surveillance is needed to monitor this globally spreading lineage. Serotype 24F should be included for optimization of the next generation of vaccine formulations.

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