

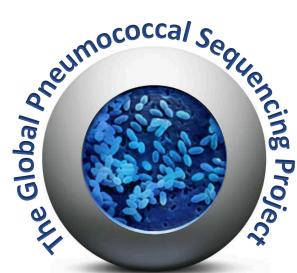
Emergence of a multidrug resistant and virulent pneumococcal lineage GPSC10/CC230 mediates serotype replacement after PCV13

Stephanie Lo, PhD

Senior Scientific Manager / Translational Science Lead

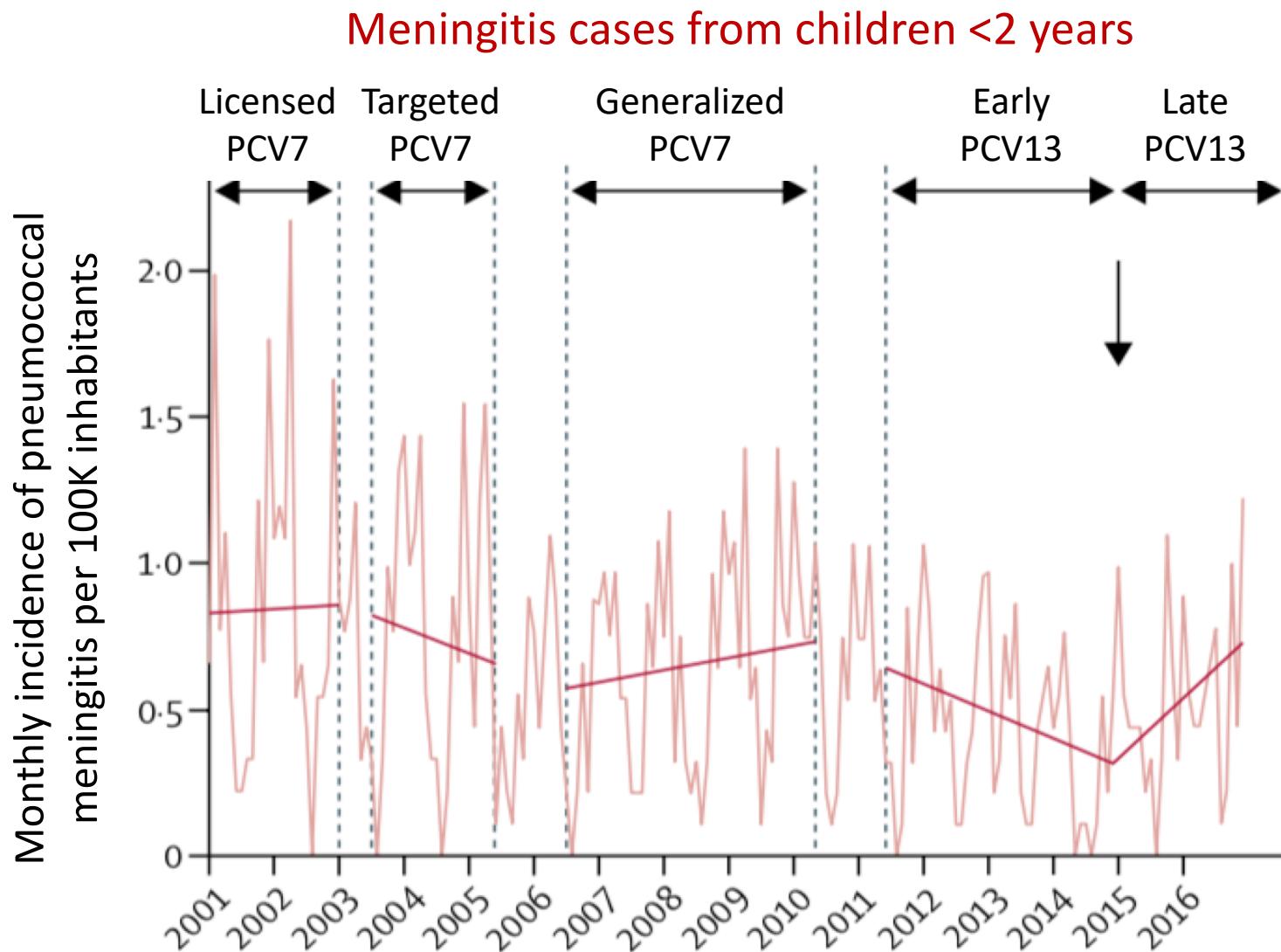
The Global Pneumococcal Sequencing Project

Wellcome Sanger Institute



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Emerging serotype 24F in France



What do we know about serotype 24F?

24F increased or became predominant

Belgium, Denmark, Germany, Israel, Italy, Japan,
Portugal, Lebanon, Norway, Spain, UK

High invasiveness

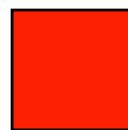
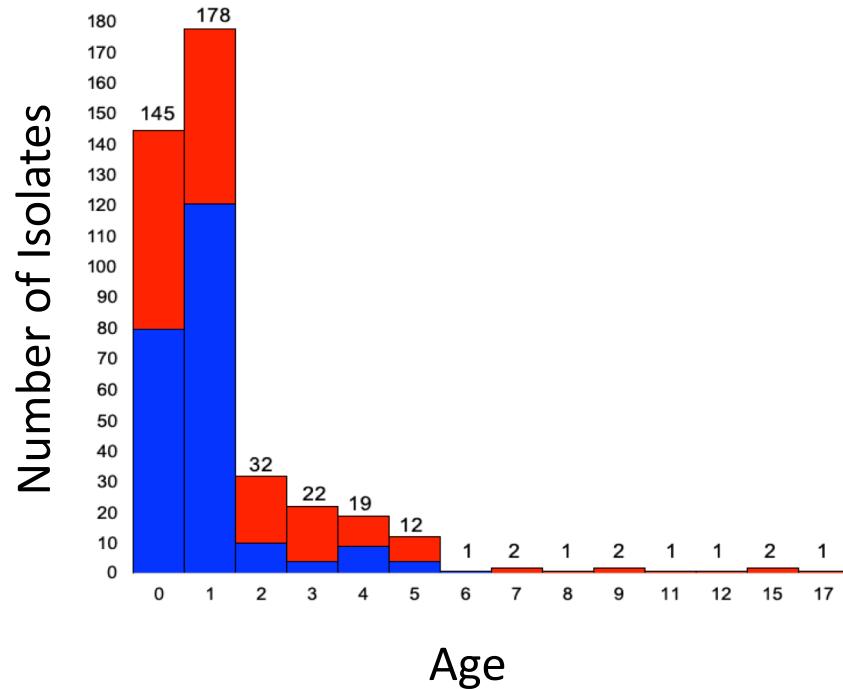
High invasive disease potential
Prone to cause meningitis
(Balsells et al 2018, meta-analysis)

Prevention

Not in current PCVs,
NOT in upcoming
PCV15, 20 and 24

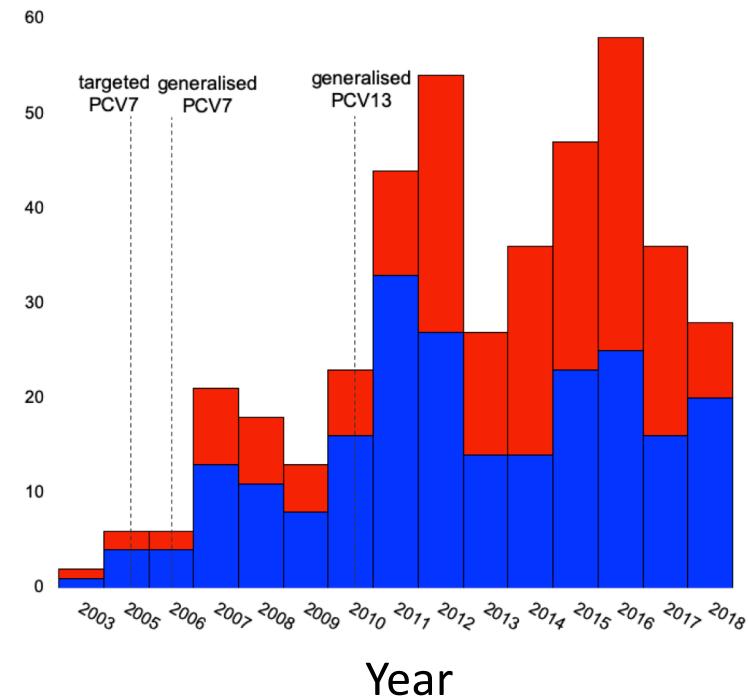
Nationwide French 24F collection for whole-genome sequencing

Most samples from <2 yr



Invasive Pneumococcal Disease
(IPD)

Matched carriage/disease over years



Carriage

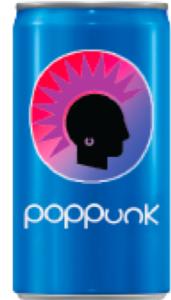
Total : n=419

IPD : n=190

Carriage : n=229

Robert Cohen

Emmanuelle Varon



PopPUNK

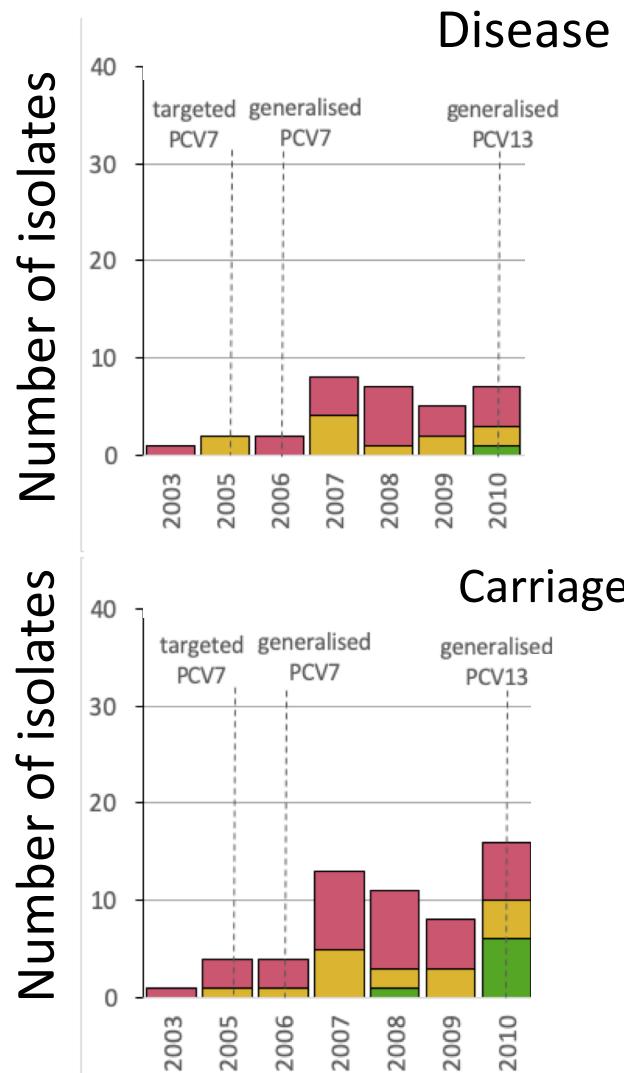
Global Pneumococcal Sequence Cluster (GPSC)

Genomic definition of lineage



John Lees

Clonal replacement in serotype 24F



GPSC16 (S)

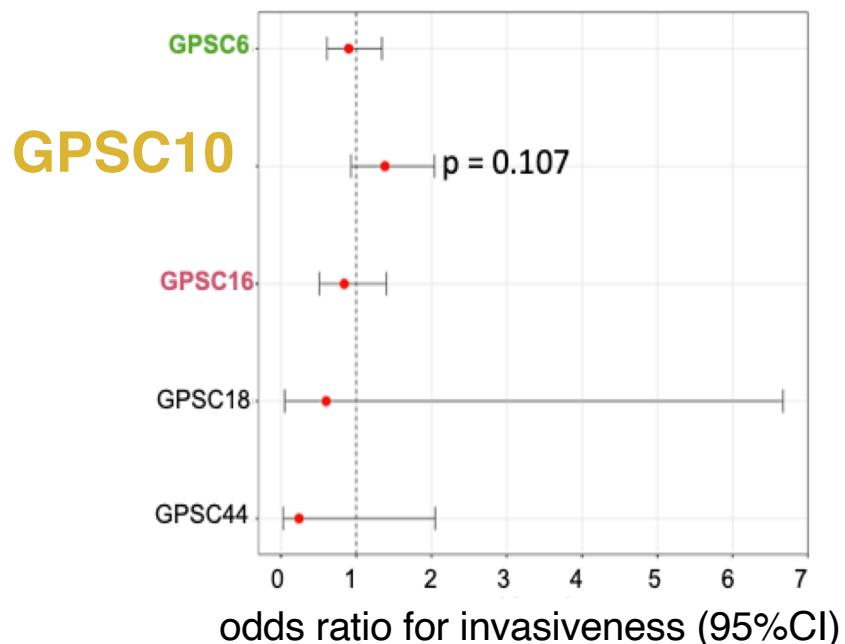


Antibiotic-selective
pressure

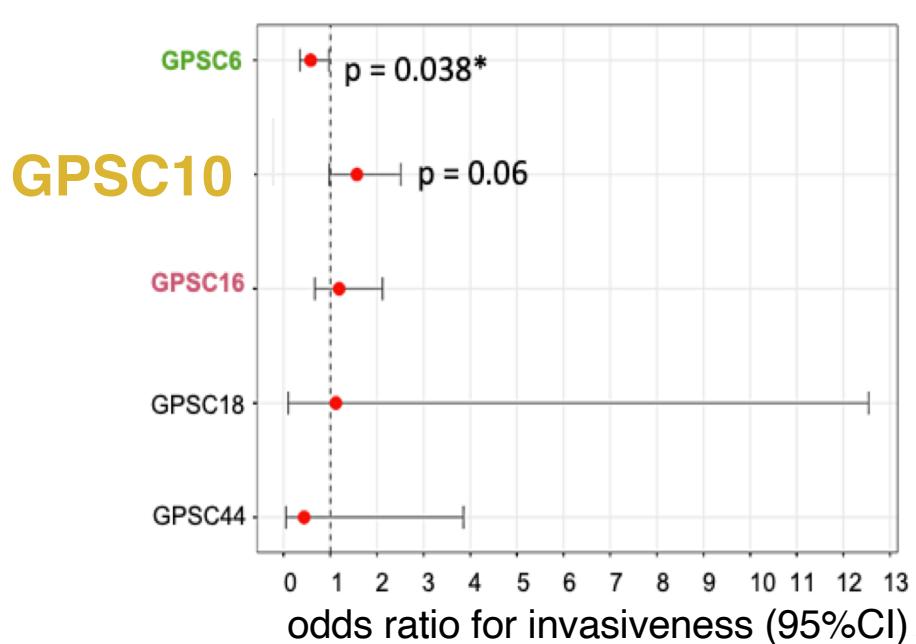


GPSC10 has high invasive disease potential independent of capsule

overall IPD vs carriage



meningitis vs carriage

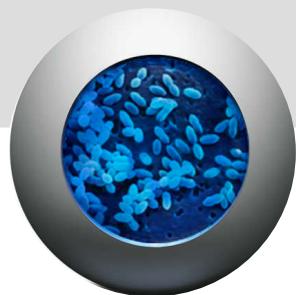
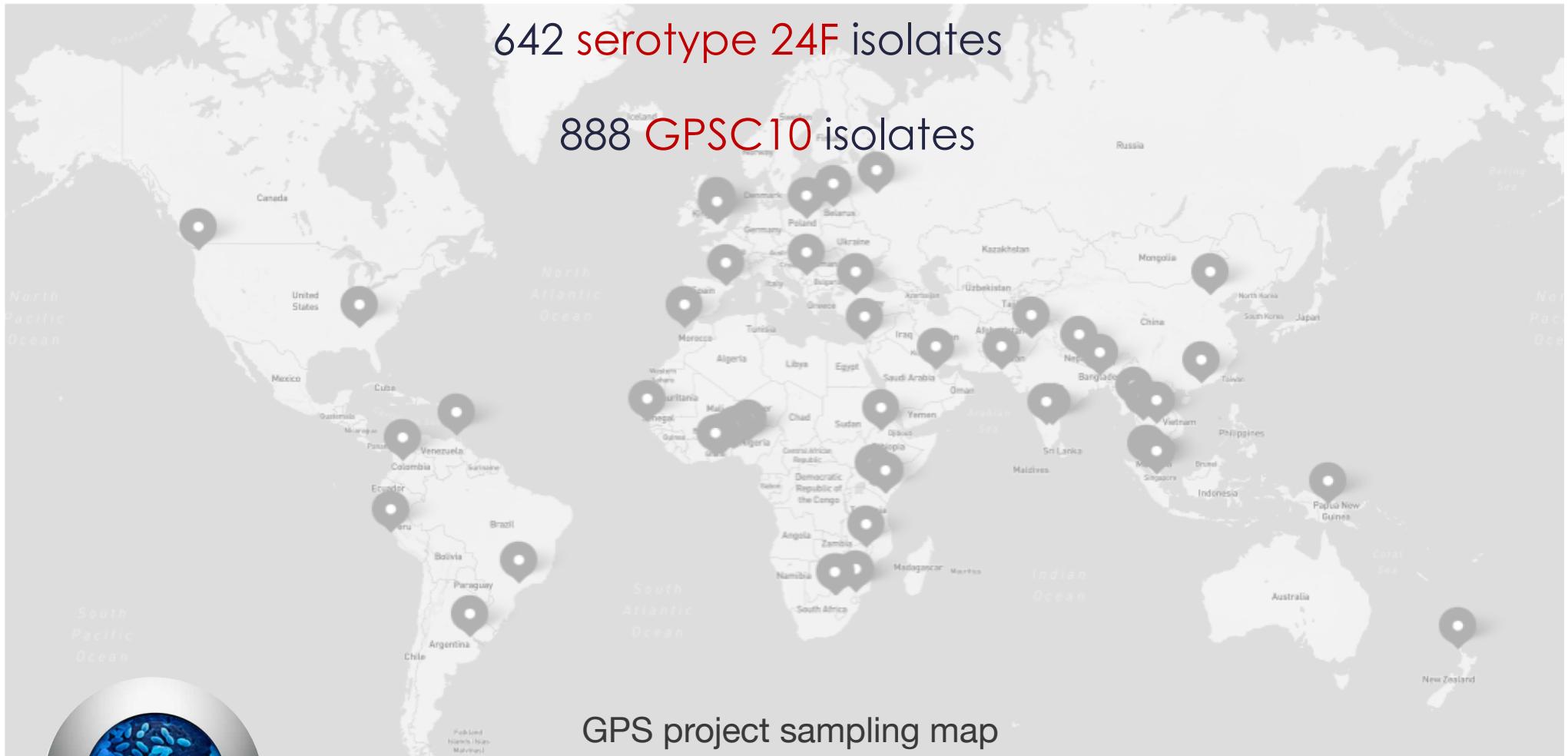


Global context

642 serotype 24F isolates

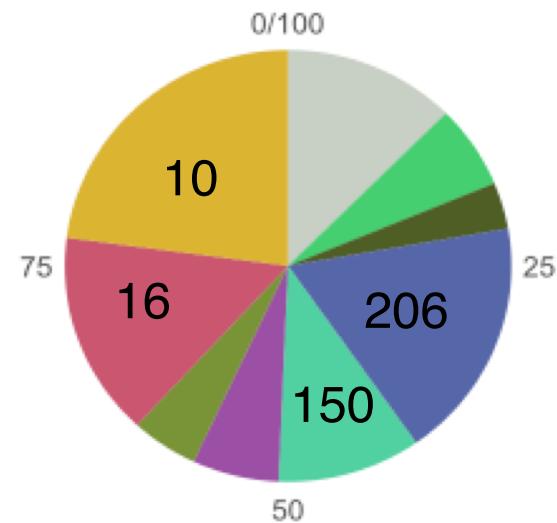
888 GPSC10 isolates

GPS project sampling map

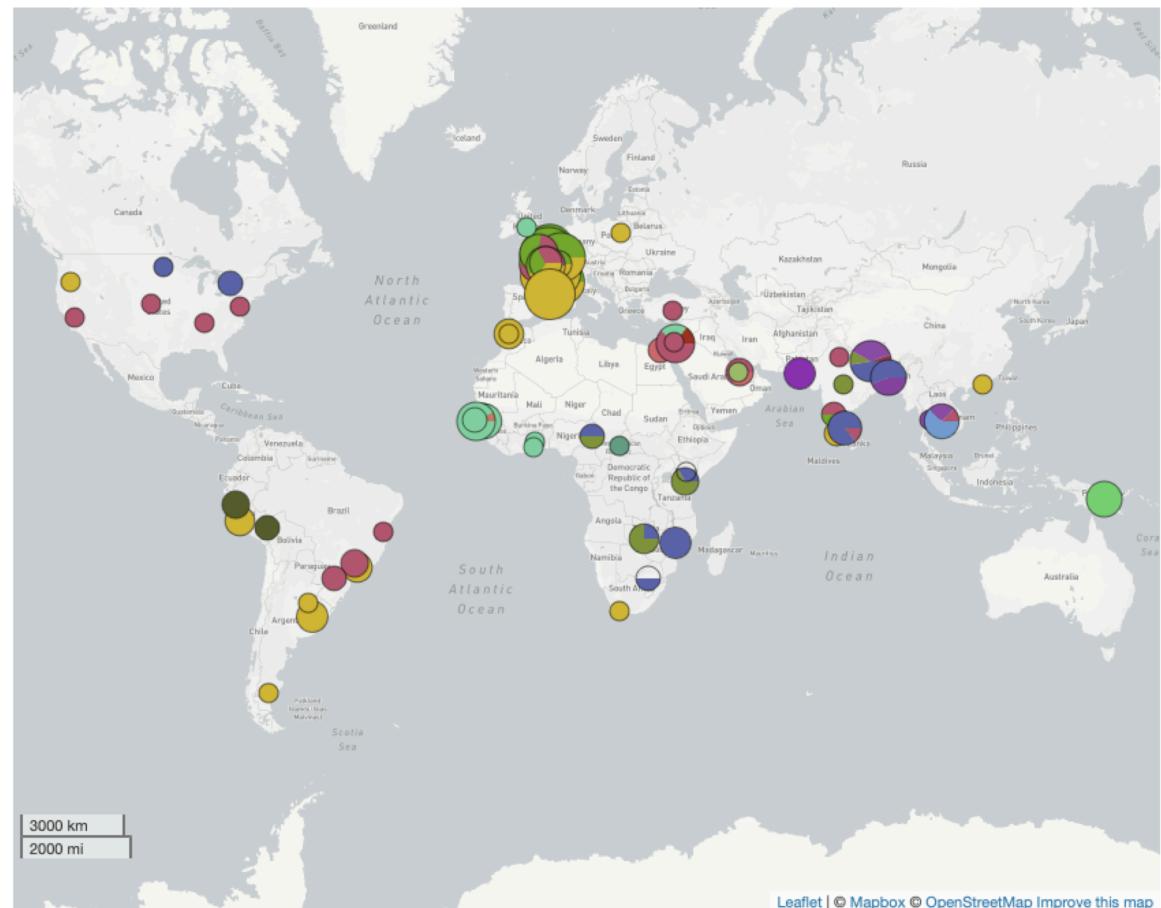


Global 24F lineages

Four major lineages



Geographical distribution

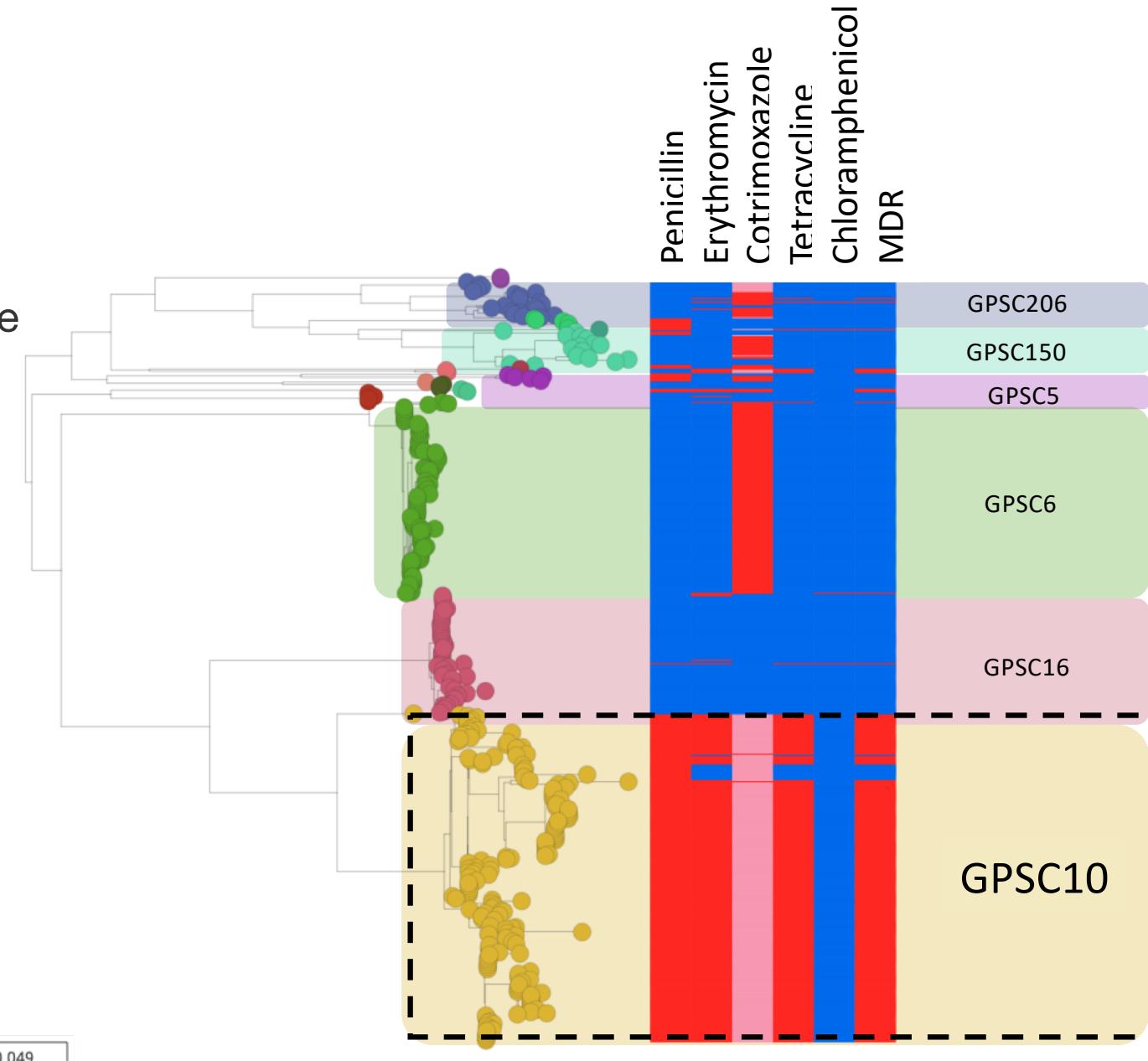


30 countries

- **GPSC10** – globally spread
- **GPSC16** – globally spread
- **GPSC206** – US, Africa, Asia
- **GPSC150** – West Africa

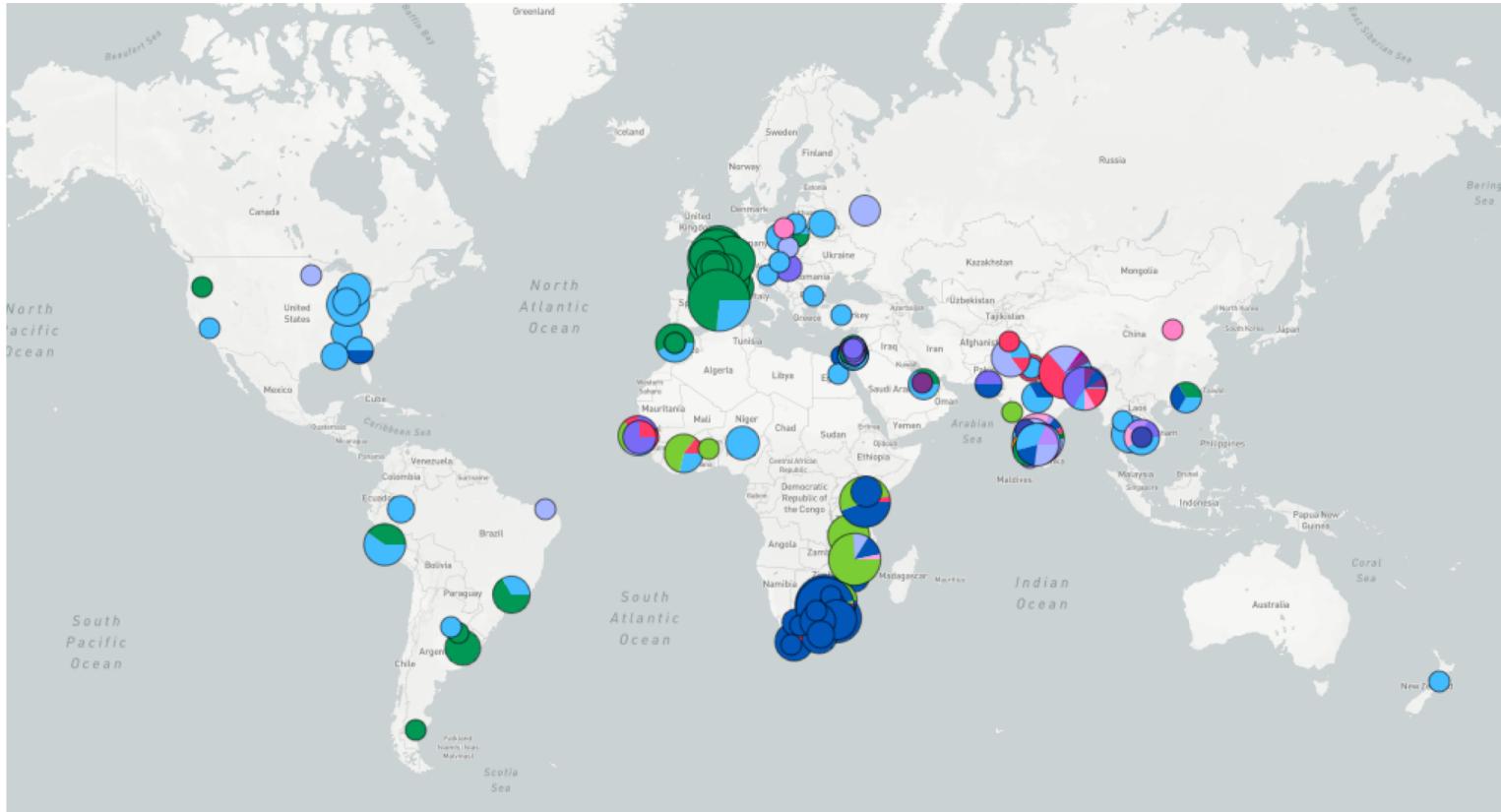
GPSC10 is the ONLY multidrug-resistant 24F lineage

GPSC10 is resistance to penicillin, macrolide, cotrimoxazole and tetracycline.



Globally-spreading GPSC10

33 countries



17 serotypes

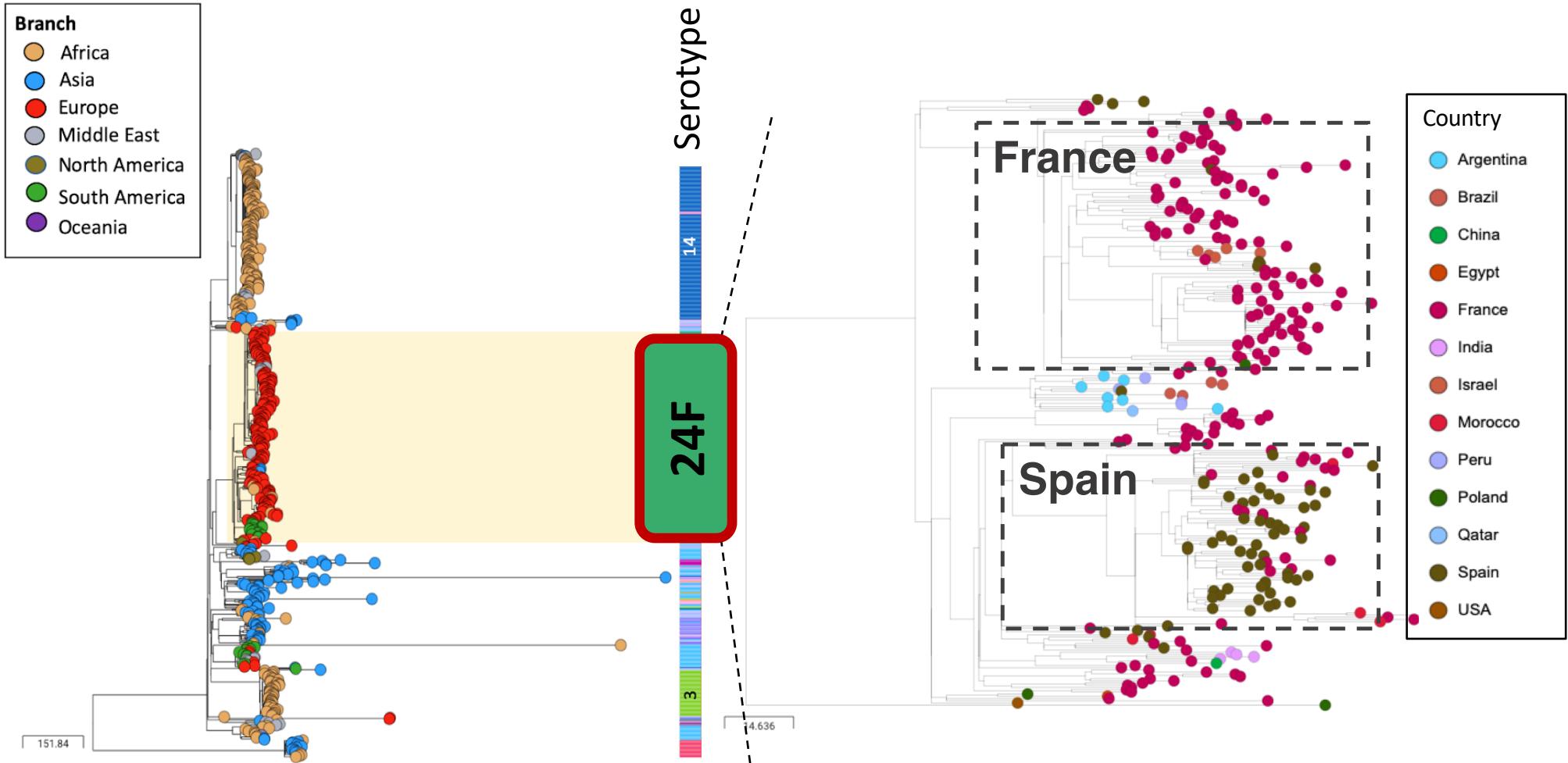
6 PCV13 serotypes

- | | | |
|-------|-------|-------|
| ● 3 | ● 6A | ● 14 |
| ● 19A | ● 19F | ● 23F |

11 non-PCV13 serotypes

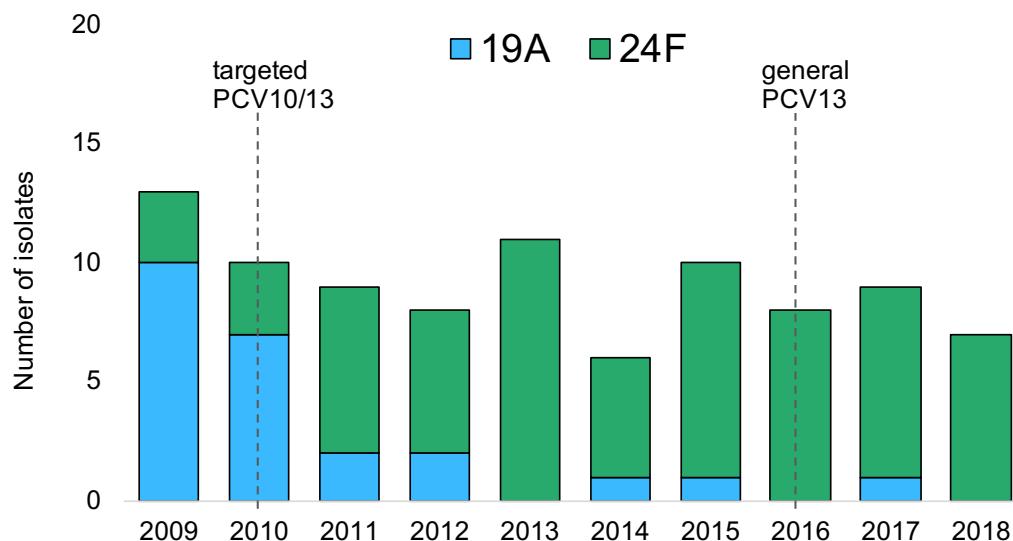
- | | | |
|-------|-------|-------|
| ○ 6C | ● 7B | ● 13 |
| ● 10A | ● 11A | ● 15B |
| ● 15C | ● 17F | ● 23A |
| ● 23B | ● 24F | |

Global GPSC10 phylogeny

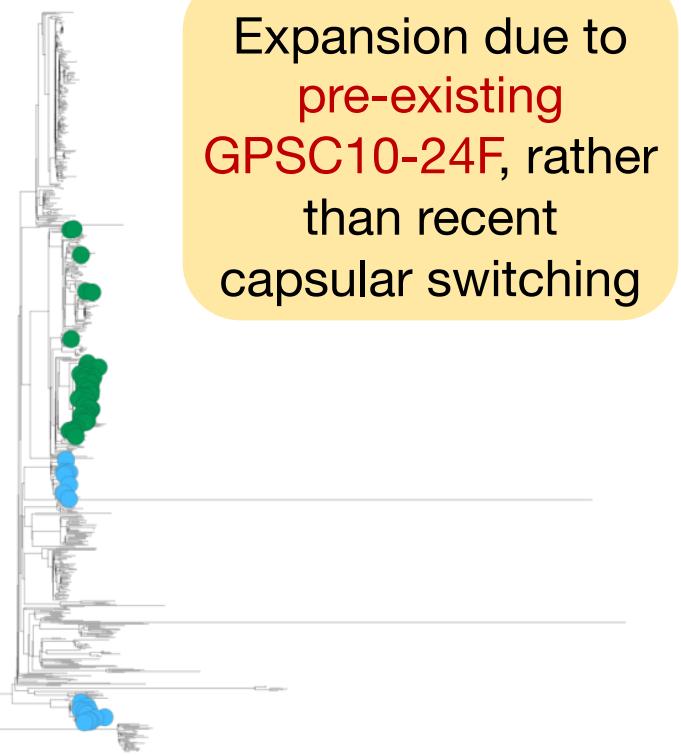


GPSC10's rapid adaptation in Spain

Rapid adaptation under vaccine-selective pressure



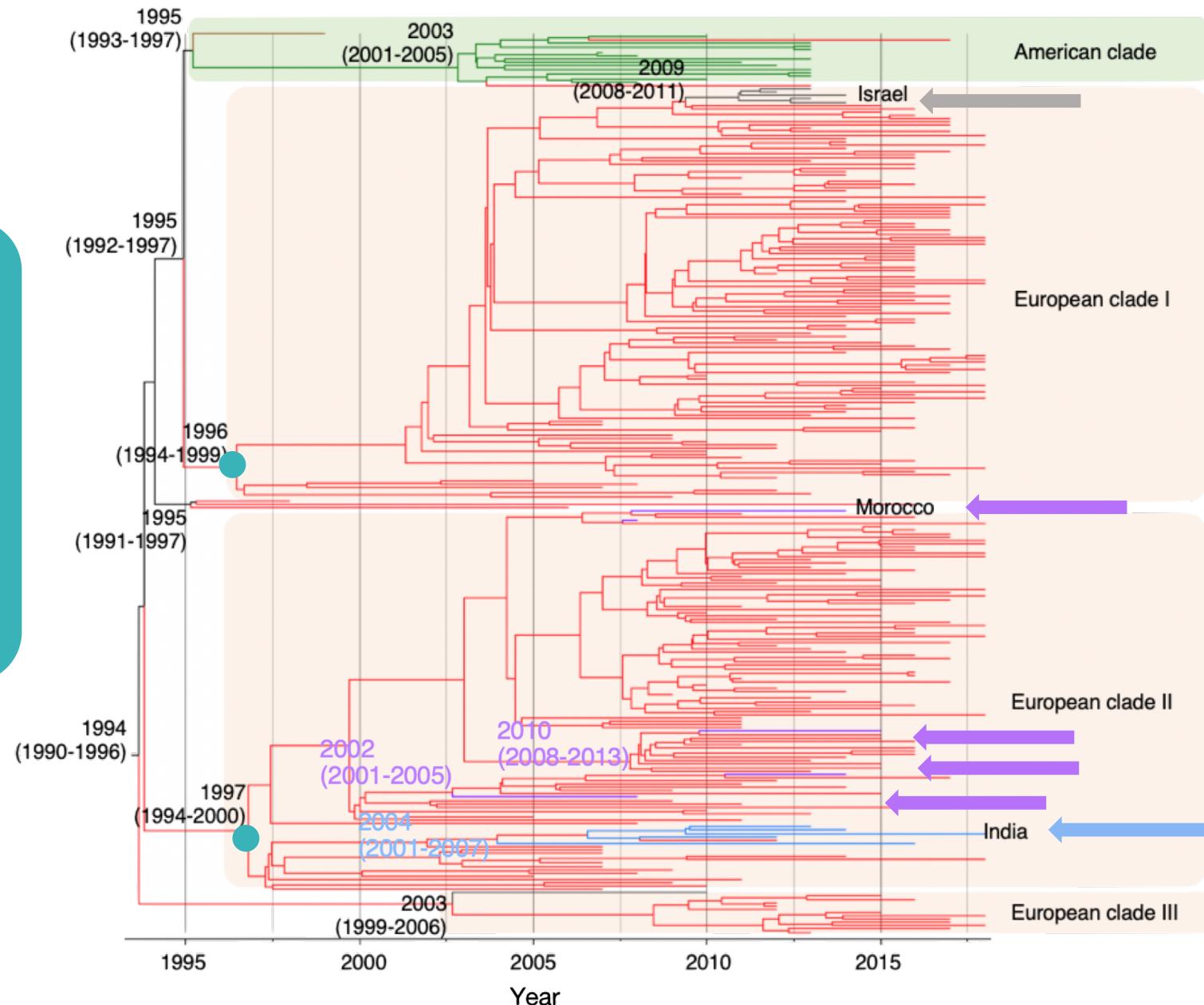
GPSC10 global phylogeny



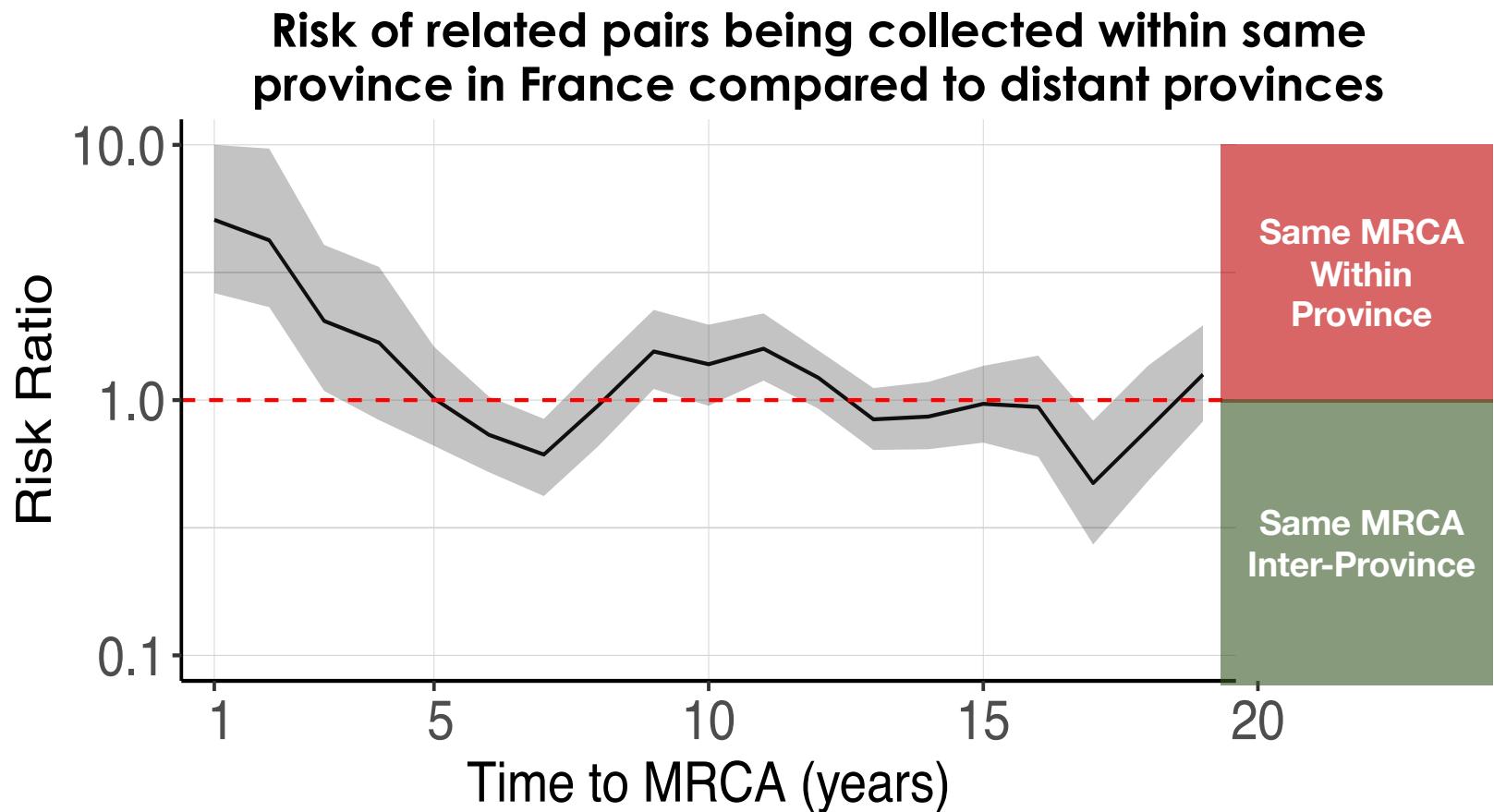
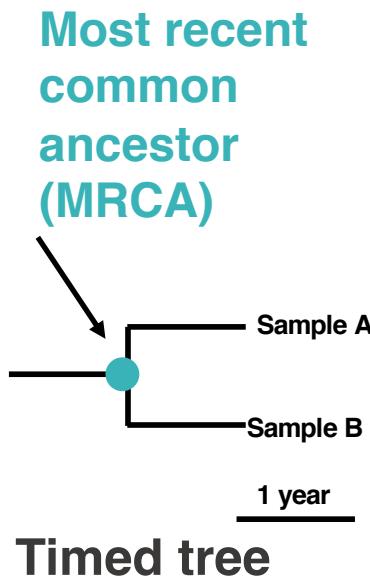
Carmen Muñoz Almagro

GPSC10-24F long-range transmissions

GPSC10-24F first found in three adult patients Naples Italy between 1997-1998



How long does it take for GPSC10-24F to spread across France?



Sophie Belman

<- Spatiotemporal dynamics talk on Friday morning!

Summary

THE LANCET
Microbe

GPSC10 **drove the serotype 24F increase in France** after PCV13 and is a **perfect storm** of invasiveness and MDR

GPSC10 is one of the major lineages responsible for the **global spread of an invasive serotype 24F**

Spatiotemporal analysis showed that GPSC10-24F spread across French provinces in **~4 years** and **cross-continental transmissions** were detected

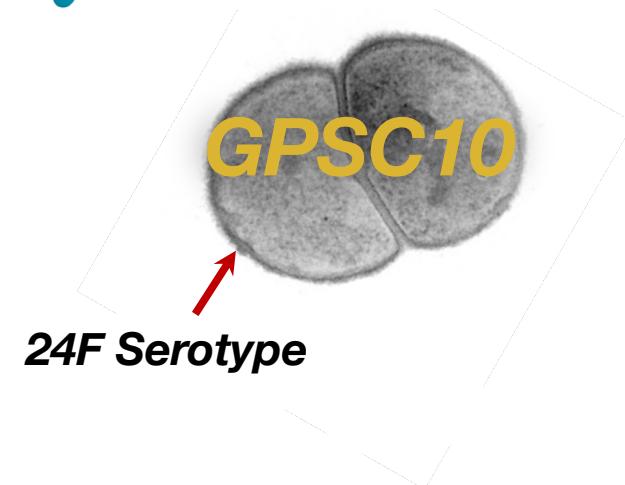
GPSC10 is capable of expressing a wide range of serotypes proves to be **a moving target** for current serotype-based vaccine strategy.

Additional knowledge from the GPS collection

GPSC10 also drove serotype 24F increase in **Argentina**

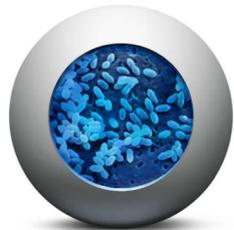
A top-5 lineage in **India, Pakistan, and Nepal**, where pneumococcal disease burden is high⁴

Globally, GPSC10 **consistently found to express multiple serotypes and MDR**



Gates Foundation:

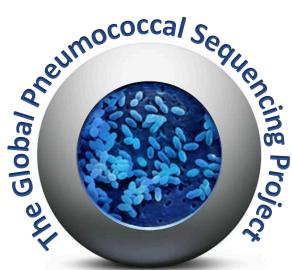
Serotype 24F is included in an upcoming vaccine formulation because of our concern about this lineage.



BILL & MELINDA
GATES foundation



Acknowledgement



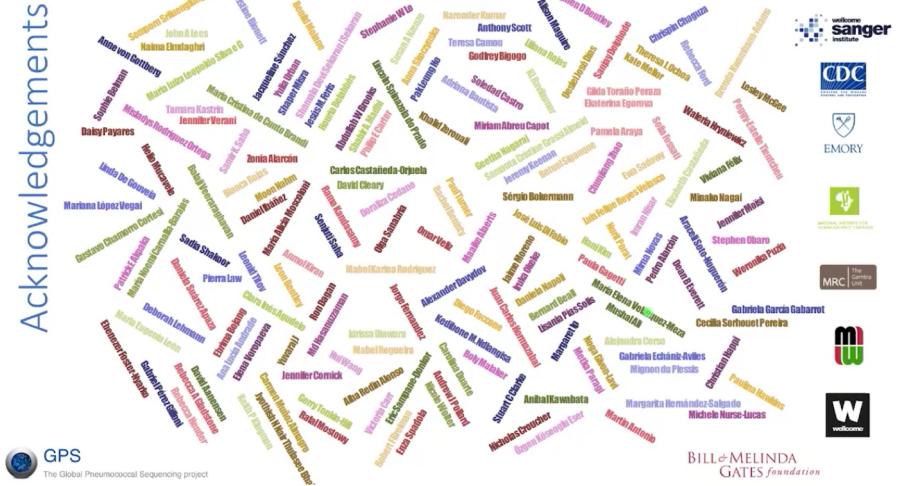
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GPS consortium



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Bentley team
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