

## **Emergence of a multidrug resistant and virulent *Streptococcus pneumoniae* lineage GPSC10/CC230 mediates serotype replacement after PCV13**

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### **Background**

Serotype 24F is one of the emerging pneumococcal serotypes after the introduction of PCV. We aimed to identify lineages driving the increase of serotype 24F in France and Spain, and place these findings into a global context.

### **Methods**

Three collections of serotype 24F pneumococci: 1) asymptomatic colonization (n=229) and invasive disease (n=190) isolates from individuals <18 years old in France, 2003-2018; 2) 68 invasive disease isolates from children <5 years old from Catalonia, 2003-2018; 3) 155 genomes from the Global Pneumococcal Sequencing (GPS) project. Global Pneumococcal Sequence Cluster (GPSC) and clonal complex (CC) were assigned to each genome. Phylogenetic, evolutionary, and spatiotemporal analysis were conducted.

### **Results**

Serotype 24F was identified in numerous countries mainly due to clonal spread of three lineages: GPSC10/CC230 (27%), GPSC16/CC156 (18%) and GPSC206/CC7701 (21%). GPSC10 was the only multidrug-resistant lineage. It drove the increase in 24F in France and Catalonia and had high disease potential. The international dataset of GPSC10 (n=888) revealed that this lineage expressed 16 other serotypes (n=380), with only 6 included in PCV13 (n=508). All serotype 24F

isolates were clustered in a single clade within the GPSC10 phylogeny. Spatiotemporal analysis showed GPSC10-24F took 3-5 years to spread across France and long-range transmissions were detected from Europe to other continents.

### **Conclusions**

GPSC10 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. This study guided the inclusion of serotype 24F in the upcoming 25-valent vaccine.

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