









Understanding the Links between Non-Invasive and Invasive Pneumococci in Children with Severe Pneumonia through Comparative Genomics

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Introduction

- > Pneumococcal carriage is a precursor for invasive pneumococcal disease (IPD)
- ➤ Mechanisms involved in progression of pneumococcal infection from carriage in non-invasive body sites to invasive sites are not understood
- ➤ We present comparative genomics of paired invasive and non-invasive isolates

Aims:

- Compare genotypes recovered from invasive and non invasive sites in the same patient at the same time.
- 2. Study mechanisms leading to progression to invasive disease

Study isolates & methods

- ➤ Paired invasive and/or non-invasive isolates from 11 pneumonia infants (0-2 years) were sequenced and comparative genomics was performed (Figure 1)
- > Invasive sites: blood and lung aspirate
- Non-invasive sites: nasopharyngeal swabs and induced sputum

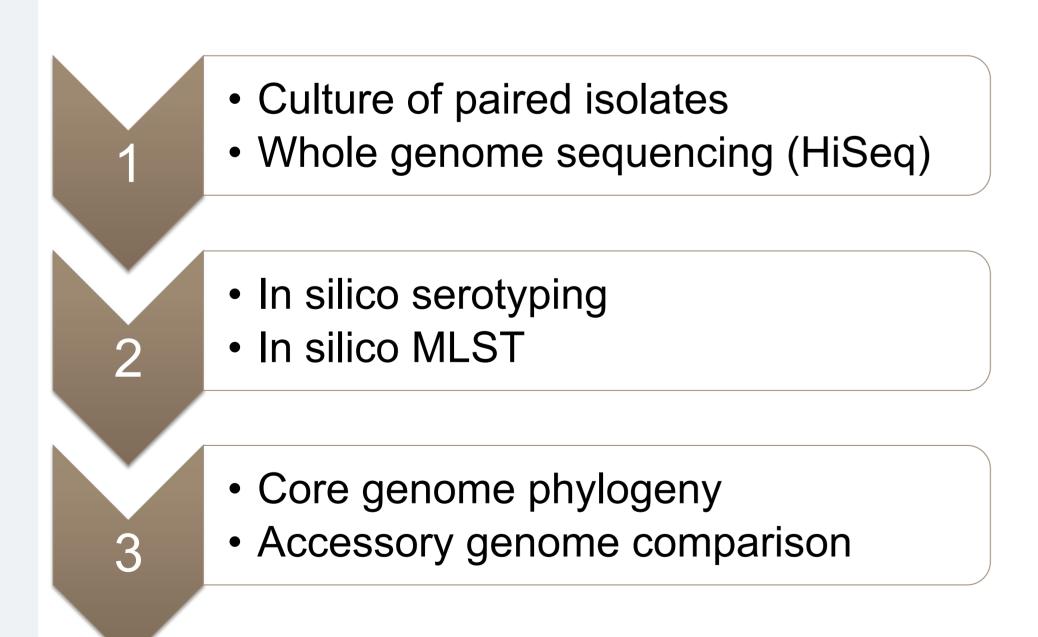


Figure 1. A flow diagram highlighting the methods employed in this study.

Results summary

- ➤ 6 patients had discordant genotypes at invasive and non-invasive sites
- ➤ 4 patients had shared genotype in invasive and non invasive isolates
- ➤ 2 patients had the same genotype in paired invasive isolates (Table 1)

Results: pairwise comparison

Table 1: Pairwise comparison of the genotypes recovered from multiple body sites in each patient. Each column represents one patient and shows (where available) the serotype (in blue above) and the ST (in black below) of the isolate recovered from a given site.

Site	1	2	6	7	8	9	3	4	5	10	11
NP swab	35B ST5183	2 ST74	6B ST4026				22A ST10600	14 ST915	19F ST925		
Induced	35B ST5183		2 ST74	5 ST289		6A ST5527			12F ST989	19A ST202	35B ST5183
Blood	35B ST5183	2 ST74	2 ST74		20 ST5726	12F ST989	12F ST989	1 ST3081			12F ST989
Lung Aspirate				5 ST289	20 ST5726	12F ST989			6B ST5549	1 ST3081	

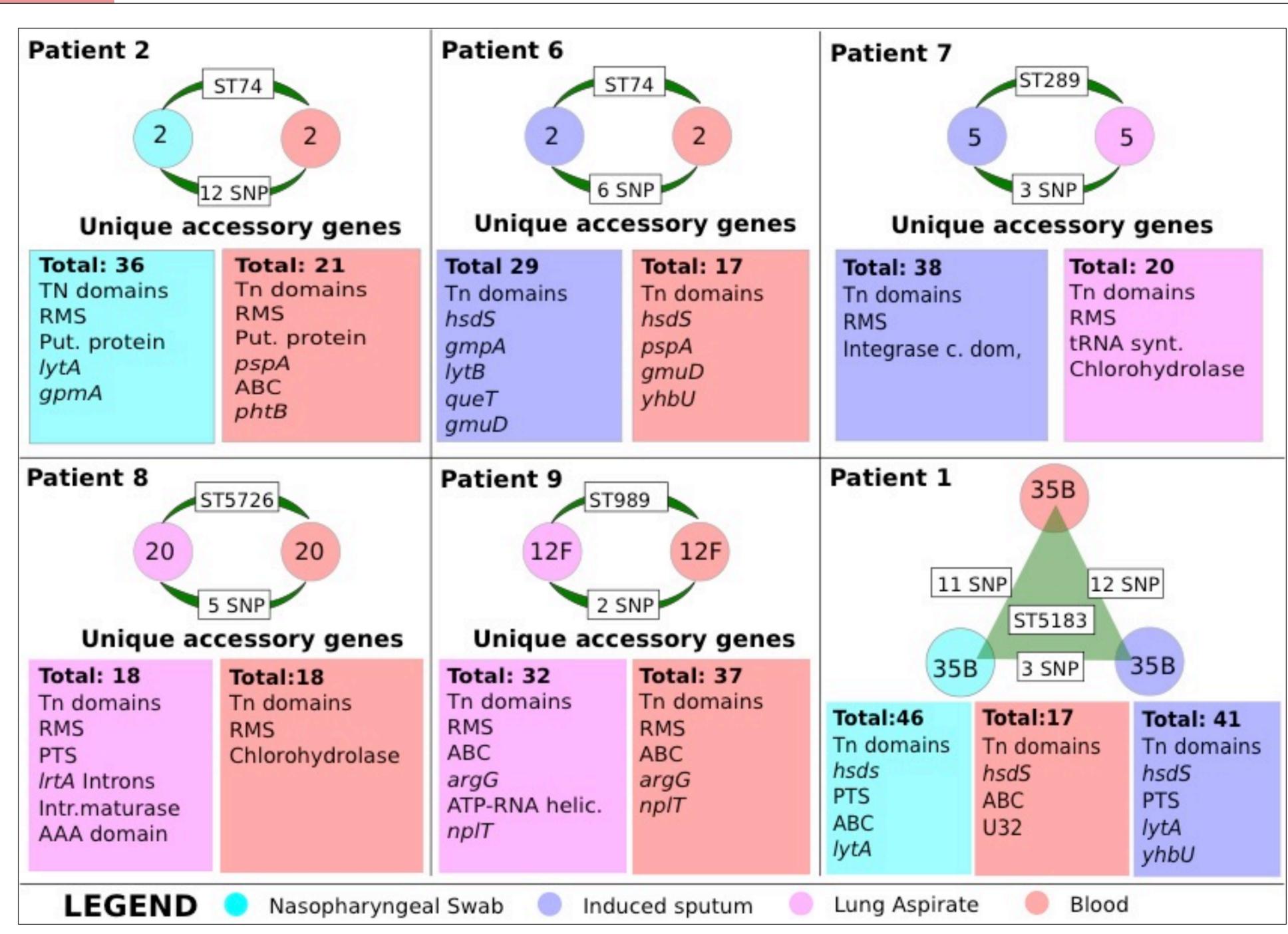


Figure 2. A pairwise comparison of the core and accessory genome for patients with shared genotype isolates from multiple body sites. Figure shows serotype (circle), ST (white box), core genome SNP difference (white box) and unique variants of key accessory genes found (coloured boxes).

Discussion

- ➤ Invasive strains isolated from the same patient tended to be more closely related than isolates from invasive and non-invasive specimens (Figure 2)
- ➤ Both the core genome and accessory genome were modified between paired invasive and non invasive isolates
- > Changes include important surface antigens and membrane proteins
- ➤ Invasive isolates had fewer unique accessory genes than non invasive isolates

Conclusion

Despite carriage diversity monoclonality is maintained in invasive disease. Genomic modifications may aid progression to cause severe pneumonia.

Acknowledgements

We thank all the children and families that participated in the Pneumonia Etiology Research for Children Health (PERCH) study in the Gambia and the Bill and Melinda Gates foundation for funding this project.