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

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:
1. 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

- Culture of paired isolates
- Whole genome sequencing (HiSeq)
- In silico serotyping
- In silico MLST
- Core genome phylogeny
- Accessory genome 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.

<table>
<thead>
<tr>
<th>Site</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
</tr>
</thead>
<tbody>
<tr>
<td>NP swab</td>
<td>35B</td>
<td>ST5183</td>
<td>2</td>
<td>6B</td>
<td>ST4026</td>
<td>22A</td>
<td>ST10800</td>
<td>14</td>
<td>19F</td>
<td>ST915</td>
<td>ST925</td>
</tr>
<tr>
<td>Induced spum</td>
<td>35B</td>
<td>ST5183</td>
<td>2</td>
<td>5</td>
<td>ST289</td>
<td>6A</td>
<td>ST5527</td>
<td>12F</td>
<td>19A</td>
<td>ST989</td>
<td>35B</td>
</tr>
<tr>
<td>Blood</td>
<td>35B</td>
<td>ST5183</td>
<td>2</td>
<td>20</td>
<td>ST726</td>
<td>12F</td>
<td>ST989</td>
<td>12F</td>
<td>1</td>
<td>ST3081</td>
<td>12F</td>
</tr>
<tr>
<td>Lung</td>
<td>5</td>
<td>ST289</td>
<td>20</td>
<td>12F</td>
<td>ST989</td>
<td>ST989</td>
<td>ST989</td>
<td>ST5549</td>
<td>ST3081</td>
<td>6B</td>
<td>1</td>
</tr>
</tbody>
</table>

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)

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

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

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