General overview of bacterial population structures

Hajo Grundmann

National Institute for Public Health and the Environment, Bilthoven
Rijksuniversiteit Groningen, NL
Topics

- Objectives for molecular typing of pathogens
- Diversity
- Confounding in molecular epidemiology
- The genetic population structure of nosocomial pathogens
Objectives for molecular typing of pathogens

To identify:

- transmissions
- major clones (genetic population structure)
- geographical dissemination
- secular trends
- evolutionary trajectories
- epidemiological success (coalescence)
Why networking typing information?

To describe the dissemination of certain pathogens at different geo-administrative levels:

- hospital
- communal
- regional
- national
- continental
- global
How to determine the ideal network approach?

Depending on the objectives, the reference level and the pathogens under study

- technical aspects
- mode of genomic evolution
- population structure
Test characteristics of molecular typing techniques for *Staphylococcus aureus*

<table>
<thead>
<tr>
<th>Technique</th>
<th>Time</th>
<th>Skill</th>
<th>Cost/Strain (€)</th>
<th>Lab. Invest (k€)</th>
<th>Comparative Fingerprint</th>
<th>ID</th>
<th>GV</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFGE</td>
<td>3-5 d</td>
<td>++</td>
<td>12</td>
<td>25</td>
<td>Comparative fingerprint</td>
<td>97.6</td>
<td>25.5</td>
</tr>
<tr>
<td>RAPD</td>
<td>1 d</td>
<td>+</td>
<td>3</td>
<td>15</td>
<td>Comparative fingerprint</td>
<td>86.3</td>
<td>47.4</td>
</tr>
<tr>
<td>AFLP</td>
<td>3 d</td>
<td>++</td>
<td>12</td>
<td>15</td>
<td>Comparative fingerprint</td>
<td>-</td>
<td>18.4</td>
</tr>
<tr>
<td>MLVA</td>
<td>1 d</td>
<td>++</td>
<td>3</td>
<td>15</td>
<td>Comparative fingerprint</td>
<td>99.3</td>
<td>59.3</td>
</tr>
<tr>
<td>MLST</td>
<td>5-7 d</td>
<td>+(+)+</td>
<td>60-80</td>
<td>50</td>
<td>Library</td>
<td>95.5</td>
<td>0.6</td>
</tr>
<tr>
<td>spa</td>
<td>1-2 d</td>
<td>++</td>
<td>24</td>
<td>50</td>
<td>Library</td>
<td>98.0</td>
<td>?</td>
</tr>
<tr>
<td>WGS</td>
<td>2 d</td>
<td>+++</td>
<td>60-100</td>
<td>100</td>
<td>Library</td>
<td>99.9</td>
<td>-</td>
</tr>
</tbody>
</table>
Discriminatory ability of molecular typing techniques for *S. aureus*
Constraints when identifying episodes of transmissions for hospital infection control

- Genetic diversity in catchment population (biological)
- Discriminatory ability (methodological)
- Hospital/ward admission rate (institutional)
Average waiting times until isolation of identical S. aureus strain under different assumptions
Observed waiting times: *S. aureus*
Waiting times under different ecological assumptions

- \( H_0 = \) no transmission, low ID
- \( H_a = \) only transmission, high ID
Observed waiting times: *P. aeruginosa*
Diversity of *Staphylococcus aureus* carriage strains in the UK

Expected average waiting times depend strongly on catchment population

<table>
<thead>
<tr>
<th>Area</th>
<th>Average Waiting Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community</td>
<td>245 days</td>
</tr>
<tr>
<td>Hospital</td>
<td>21 days</td>
</tr>
<tr>
<td>Intensive Care Unit</td>
<td>9 days</td>
</tr>
<tr>
<td>Observed</td>
<td>165 days</td>
</tr>
</tbody>
</table>
Diversity of *Staphylococcus aureus* carriage strains and *P. aeruginosa* from CF patients in the UK

![Genetic diversity of S. aureus in various environments](image)

- Community
- Hospital
- ICU
- *P. aeruginosa* (CF patients)
Genetic diversity of 950 strains of *P. aeruginosa* from the cystic fibrosis community in the UK

(Spe I macrorestriction analysis)
Different tree topologies

geneA

no recombination

geneB

frequent recombination
Multilocus sequence typing (MLST)

EMRSA 16
2,902,619 bp
Pairwise comparison of tree topologies:
Congruence test

Determining the genetic structure of the natural population of Staphylococcus aureus.

Pairwise comparison of tree topologies: Congruence test

Curran B, Jonas D, Grundmann H, Pitt T, Dowson C.
Clonal versus panmictic evolution


Split decomposition tree for *P. aeruginosa*
CIP resistance

Nuebel et al. 2013
ST22 tree rooted with ST1 and ST5
Sharing of mobile genetic elements in *S. aureus*
Dynamics of different mobile genetic elements in S. aureus

- phage (very frequent)
- genomic islands (frequent)
- SCCmec (rare)
- large chromosomal replacements (very rare)
Resumée

- Epidemiological inference drawn from molecular typing results requires careful consideration of methodological, biological and institutional parameters.
- Not all nosocomial pathogens are equal.
- Genetic population structures differ widely and analysis tools need to take them into account.
- Recombination and mobile genetic elements are the driving forces behind niche specialisation and evolution in bacterial pathogens.
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