Exploring the unseen dynamics of pertussis using sequence data

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Bordetella pertussis

- Most common vaccine preventable infection in US
- Causes respiratory infection; severe illness in babies and children
- Cases are mild/asymptomatic in older children and adults
- Six dose vaccine schedule recommended for children in US
The resurgence of pertussis

• 2012 saw the largest recorded incidence of pertussis since the pre-vaccine era
• Large outbreaks in several states
• Acellular vaccine protection appears to rapidly wane
Public Health Questions

• Can genetic adaptation of pertussis explain:
  • the resurgence in cases in recent years?
  • the relative lack of protection provided by the vaccines?

• Are pertussis outbreaks caused by the emergence and spread of fitter strains?

• Is case reporting capturing true pathogen dynamics?
Data

- 311 pertussis isolates from Massachusetts
- ~30 from each year, 2002-2012
- Age group, ZIP code, vaccination history information for each sample
Changes in genetic distribution

- Sequencing allows us to identify genetically similar groups

- Groups 2, 3, 5 disappear

- Groups 6, 7 emerge

- Without sequencing, strains cannot be differentiated at all
Is the expansion of the group 6/7 important?

- May be just random genetic drift...
- Or selective pressure resulting in emergence of new, fitter lineage
  - More transmissible
  - Vaccines offer less protection
Features of groups 6/7

• A number of mutations are unique to the groups 6/7, including in the *sphB1* gene, previously associated with virulence

• Furthermore, 11 strains in group 6 are pertactin negative
Pertactin (*prn*) disruption

- Vaccine target
- Commonly inactivated through insertion of repeated sequence (IS481)
- Negative strains observed in several other countries, from 2009
- Vaccine may potentially offer less protection against this strain
IS481 prn disruption

• 11/311 isolates have IS481 disrupted prn

• 2012: 4/32
• 2011: 3/27
• 2010: 4/29 (Earliest, March 2010)
US prevalence of *prn-*

- WA outbreak 2012: 63%
- Surveillance 2010-12: 12.1%
- CA outbreak 2010: 6% (n=33)
- OR surveillance 2010-12: 4.4%
- MA surveillance 2010-12: 1%
- NY surveillance 2010-12: 4.4%
- MA DPH 2010: 14%
  2011: 11%
  2012: 13%

*Different studies & different ascertainment methods*
Most recent common ancestors

**prn- strains MRCA:**

**Group 6/7 MRCA:**
Few clinical differences between clades

• Little difference in
  – Vaccine status
  – Age group
  – Symptoms
  – Geographic location

between clades

• However, disproportionate number of *prn*- strains among adults age >20 (p=0.001)
Transmission clusters
Conclusions

• Is the apparently limited protection provided by vaccines due to genetic adaptation?
  • No: no difference in vaccine status across clades.

• Do outbreaks occur due to emergence/importation of novel, fitter, strains?
  • No: all lineages successful in outbreak years

• However, emergence of prn- strains and rapid growth of groups 6/7 should continue to be monitored

• Sequencing can also be used as an outbreak investigation tool

• Future work will investigate whether most isolates are closely related to another detected isolate in MA
Collaborations

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