Using genomic sequences to develop new diagnostic methods for Glässer’s disease

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INTRODUCTION
Glässer’s Disease and *Haemophilus parasuis* (HPS)

**Symptoms:**
- Fibrinous polyserositis - Meningitis, Arthritis, Pericarditis, Septicaemia
- Also able to cause pneumonia

**Occurrence:**
- Used to be a sporadic disease in recently weaned pigs.
- Current production practices (multi-site, high health) have coincided with more frequent larger outbreaks, affecting various ages with increased mortality and morbidity
- Multisourcing of weaners has been a major driver to increased disease prevalence

**Diagnostics:**
- Most commonly used technique is serotyping, but no labs in the UK perform this test.

**Treatment & Disease Control**
- Antibiotics (penicillin based)
- Prophylactic antibiotic treatment in feed is common
- Several vaccines are available but they are serotype specific.

**Management of disease**
- Optimise maternal antibody delivery
- Optimise acquired immunity
- Minimise introduction of new strains of HPS
INTRODUCTION
Scale of Virulence by Serotype

Serotype: 1  2  3  4  5  6  7  8  9  10  11  12  13  14  15  NT

Avirulent

Moderately virulent

Highly virulent
OBJECTIVES

Aims to fill technology gaps in respiratory disease control by designing efficient diagnostics

Identify molecular markers from variation in the genetic sequences of *H. parasuis*

Two main strategies:

1. Molecular serotyping
   - Identify genes or markers characteristic of serotypes
   - Would indicate usefulness of vaccination & useful for stock mixing

2. Virulence Associated Gene Identification
   - Compare clinical and non-clinical strains of *H. parasuis*

**GENOME SEQUENCES + CLINICAL DATA + SEROTYPING DATA**
1. For diagnosis of HPS disease
2. For management of disease
3. For surveillance and herd monitoring prior to trade

Economic Impact on the UK Industry is ~£27/pig for an outbreak and £20/pig/year for vaccination (White 2010).

UK Statistics: 5% of systemic swine disease and 5% respiratory disease attributable to HPS in 2010 AHVLA surveillance report
1. Strains were collected by the AHVLA which were both disease-associated and non-disease associated (carrier strains), with clinical data.
2. Strains were also supplied by collaborators in Denmark & Spain including reference strains used in the current serotyping assays
3. All of these strains were sent for whole genome sequencing
4. Subset of strains sent for serotyping
5. Bioinformatics analysis
   - Assembly of sequencing data into draft sequences
   - Core genome built
   - Capsule loci identified & compared
   - Phylogenetic trees built for genes of interest
   - Pangenomes built – core & accessory genes identified – analysis continuing.
RESULTS
Core Genome – Disease association & Serotype

Preliminary whole genome sequences
- 103 clinical isolates (red)
- 47 non-clinical tonsil isolates (blue)
- 12 not defined (black)

Preliminary whole genome sequences
- Coloured by serotype
- Serotypes 4, 5 & 13 (most common disease causing serotypes) in bottom clade
RESULTS
Polysaccharide biosynthesis locus comparisons
**RESULTS**

Predicted Gene Functions between dominant serotypes

### SH0165
**Serotype 5**
- Gene Name: HAPS0039
  - Predicted Function: neA1, wzx, lsgB
- Possible variable region ~ 5kb

### HS238
**Serotype 4**
- Gene Name: HAPS0039
  - Predicted Function: neuA1, wzx
- Possible variable region ~ 5kb

### HS228
**Serotype 13**
- Gene Name: HAPS0039
  - Predicted Function: ADO96837.1, EIJ713
- Possible variable region ~ 5kb
CONCLUSIONS

Serotyped samples ONLY

Tree of Capsule Gene Cluster

All Strains
Serotyped samples ONLY

Predict serotype 4

5 & 12

6

14 Predict serotype 13

4 & 7

2

Predict serotype 5 or 12

13
NEXT STEPS
Virulence Gene Identification - Strategy

Non-Disease associated strains

Disease associated strains

Accessory genome

Core genome

Candidate virulence markers
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References


