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# Evolution of *Streptococcus equi* the causative agent of equine strangles

## The importance of gene gain to disease

# *Streptococcus equi* evolution: quantification of the importance of key genome acquisition events



- Prj/758

- Dr. Andrew Waller



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# Strangles in horses

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- The most frequently diagnosed contagious equine disease worldwide
  - Caused by *Streptococcus equi*
  - Morbidity rates up to 100%
  - Case fatality rates up to 10% reported in some outbreaks
  - >1,000 outbreaks per year in the UK
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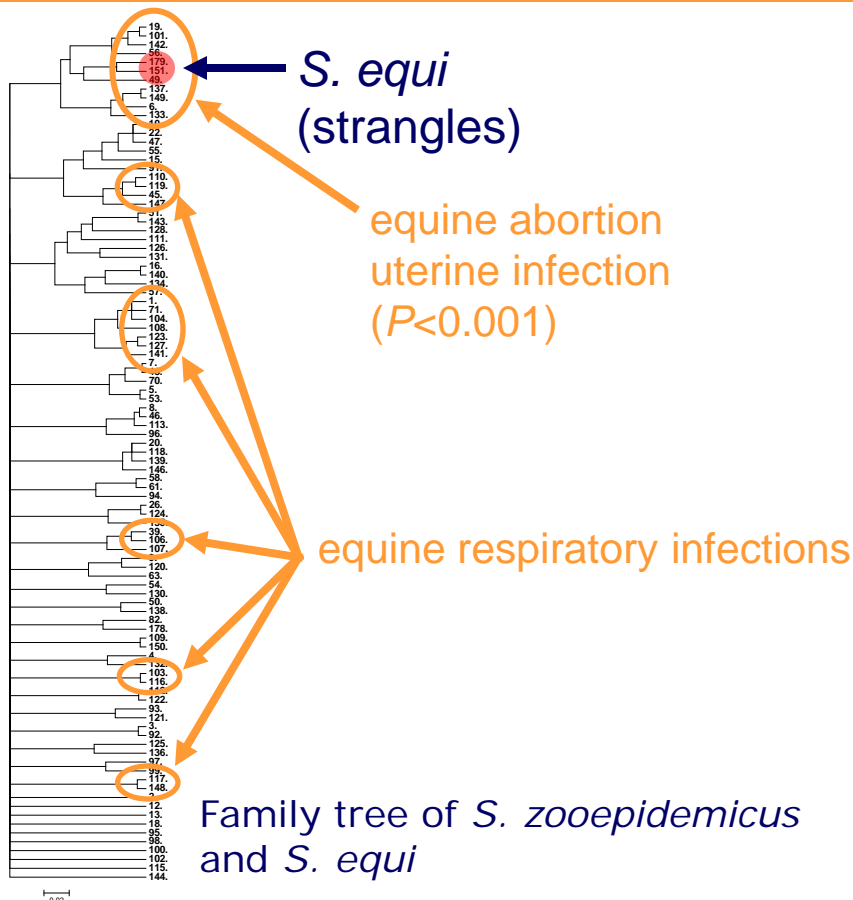
# Strangles in Thoroughbreds



- Common in horse populations
  - Spill-over into the Thoroughbred
  - Economic and welfare impact
- Quarantine and testing can prevent outbreaks
- Current vaccine interferes with diagnostic tests
  - Implications for horse movement
  - Need for new vaccines



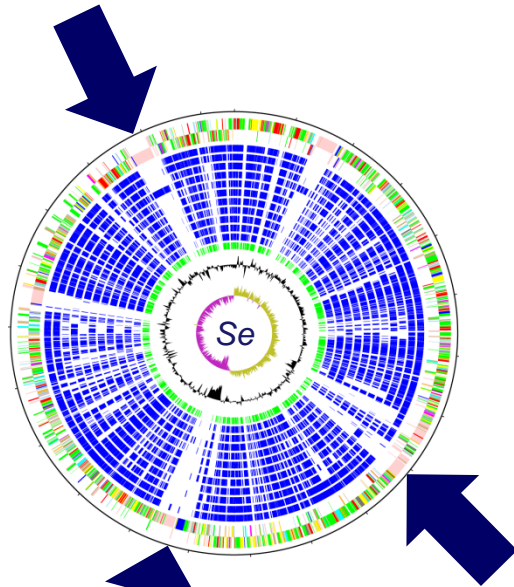
# *S. equi*: an aggressive member of the *S. zooepidemicus* family



- *S. equi* very closely related to *S. zooepidemicus*
  - Share 97% of their DNA
- Compare DNA to identify new genes
  - Provide an explanation to how *S. equi* causes strangles

# Gene gain in *S. equi*

Superantigens



Equibactin

Phospholipase toxins

- Superantigens
  - Misdirect the equine immune response
- Phospholipase toxins
  - Kill equine cells
  - Lead to inflammation
- Equibactin
  - Iron acquisition
  - Enhances growth of *S. equi* in the horse



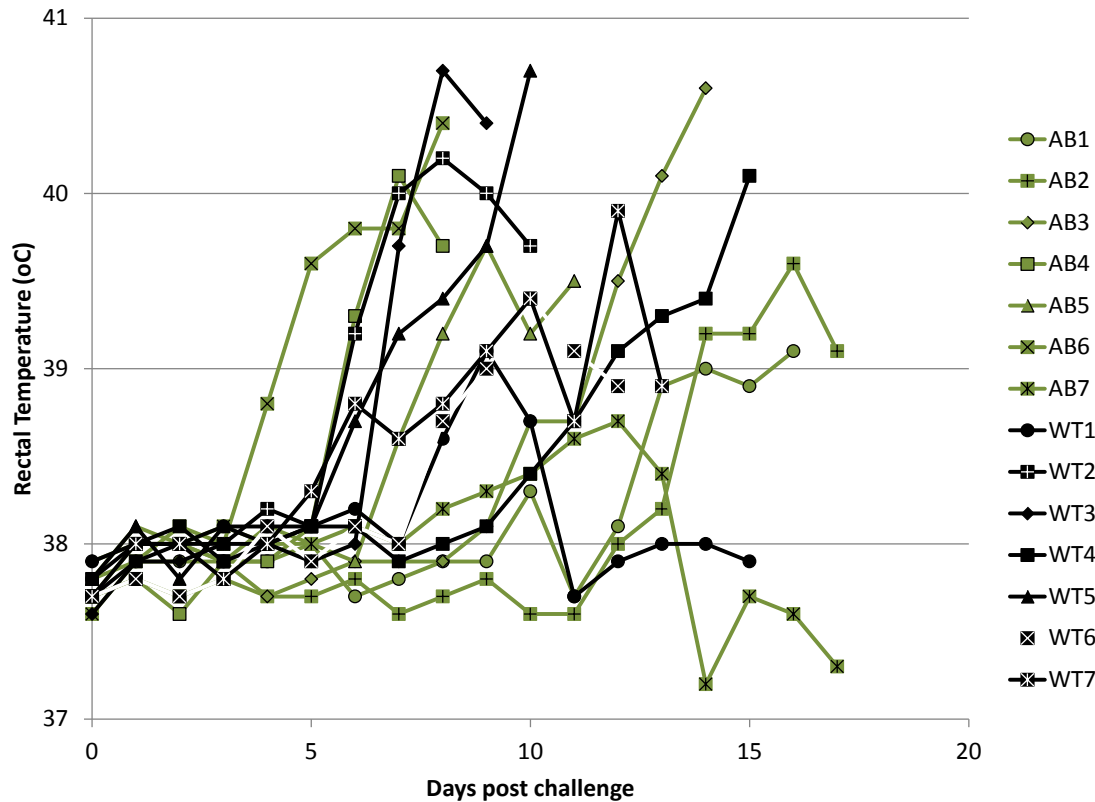
# Objective of this study

- To determine if superantigens, equibactin or phospholipase toxins are important for *S. equi* to cause strangles.
  - Delete genes (size of DNA band smaller vs. original (WT) in the picture below)
  - Test to see if these strains can still cause disease



WT: the original strain  
HILM: lacks superantigen genes  
AB: lacks phospholipase toxins  
E: lacks equibactin

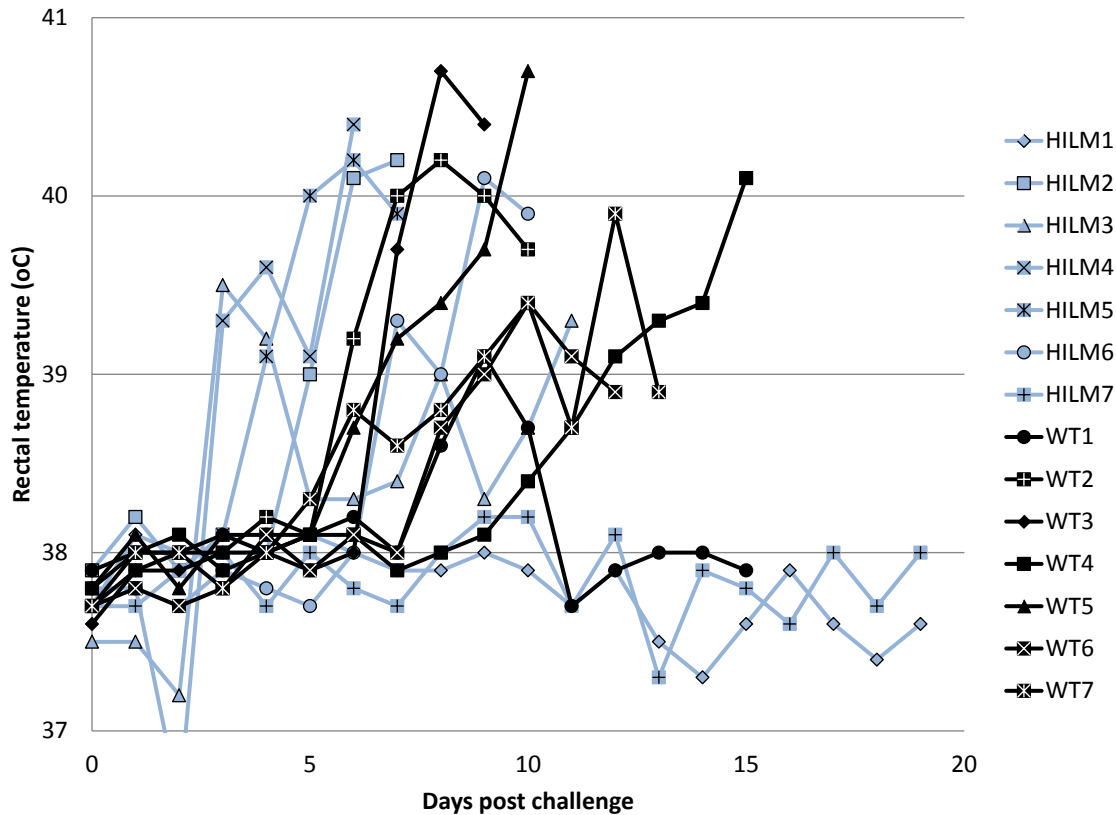
# Importance of phospholipase toxins



- No significant reduction in disease (AB = strain lacking the phospholipase genes *slaA* and *slaB*, compared to WT = original strain)
- Gain of phospholipase toxins was not the key event in the evolution of *S. equi*

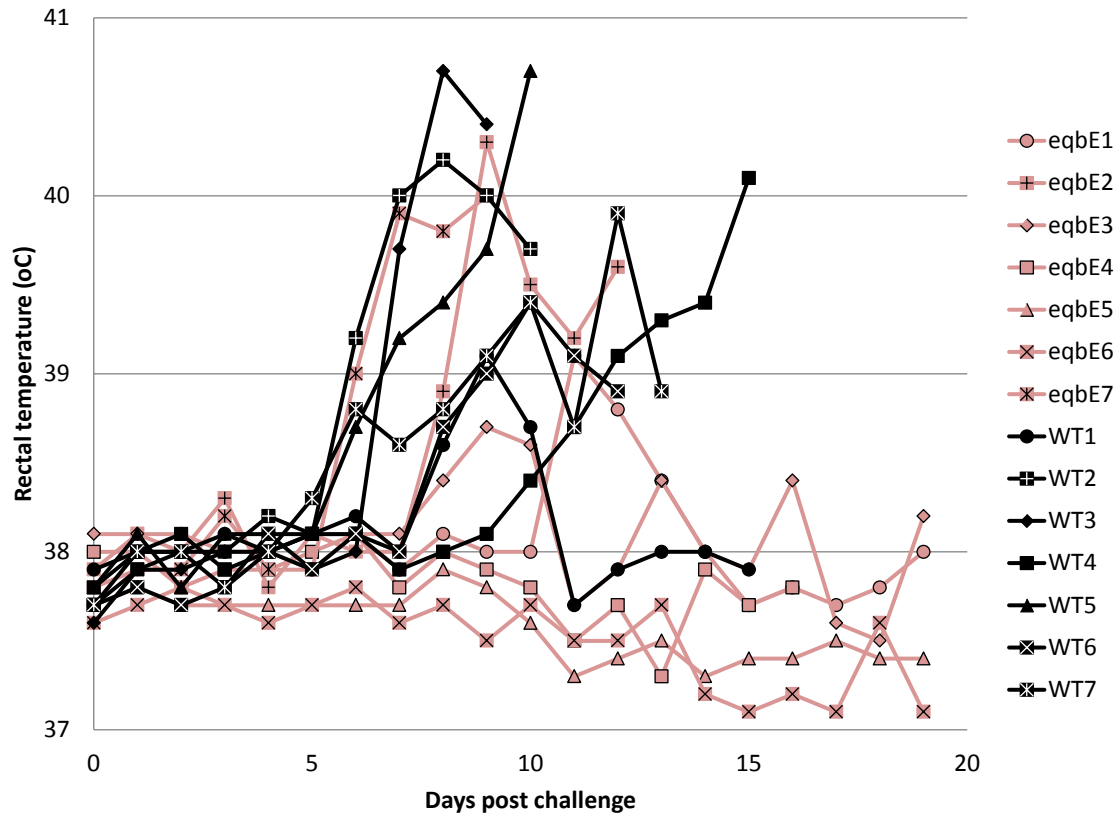


# Importance of superantigens



- 4 ponies developed clinical signs earlier! (HILM = strain lacking the superantigen genes *seeH*, *seeI*, *seeL* and *seeM*, compared to WT = original strain)
- 2 ponies had no clinical signs (HILM1 and HILM7)
- The role of superantigens is complex
  - Implications for vaccine design

# Importance of equibactin



- Loss of equibactin significantly reduced disease (eqbE = strain unable to make equibactin, compared to WT = original strain)
- Gain of equibactin was key to the evolution of *S. equi*
  - Informs the design of new vaccines



# Conclusions

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- Gain of equibactin was key to the evolution of *S. equi*
  - Superantigens play a complex role in disease
    - Ensure that all horses become infected
    - Reduce the severity of disease in some animals to help them survive and recover to become carriers
    - Maximise the opportunity for *S. equi* to transmit to new individuals
  - Gain of phospholipase toxins had a lesser effect on the ability of *S. equi* to cause strangles
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# Impact on the Thoroughbred

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- Strangles widespread in some horse populations
    - Potential for spill-over into the Thoroughbred
    - Significant welfare and economic impact
    - Vaccines must be safe, effective and not interfere with diagnostic tests
  - By understanding which genes are important to *S. equi*, this project informs vaccine design
    - Increase herd immunity
    - Reduce the welfare and economic cost of strangles
    - Improve safe movement of horses
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## Next steps

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- Incorporation of the equibactin deletion into a live vaccine strain in order to improve safety and avoid adverse reactions
  - Identification of the equibactin receptor, which could improve the effectiveness of new subunit vaccines
  - Investigate vaccine adjuvants and the application of superantigens
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