Can genetics explain how *Staphylococcus aureus* causes disease?

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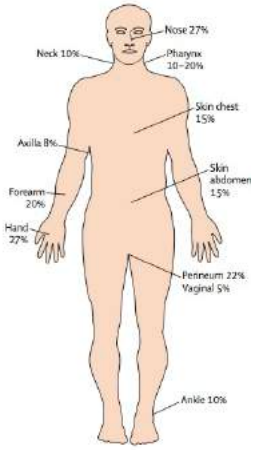
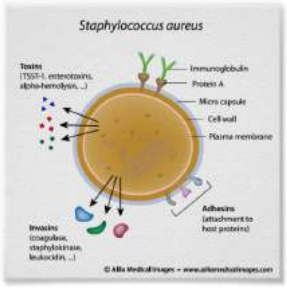
Staphylococcus aureus



- Approximately 1/3 people carry on skin and surfaces at any time
- Carriage may be persistent or intermittent
- Carriage itself does not cause any symptoms

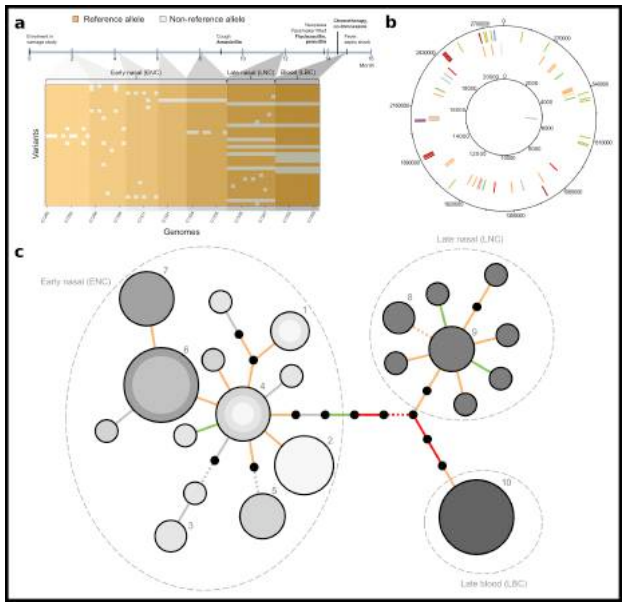
S. aureus disease



- Toxin-mediated disease
  - Food poisoning
  - Toxic Shock Syndrome
- Skin and soft tissue infections (eg boils, impetigo)
- Invasive infections: bloodstream, joints, bone, devices, heart
  - 12500/year cases of bloodstream infection in UK

Who gets disease?

- The relationship between carriage and disease is complex
  - Carriage is associated with skin and soft tissue infections
  - Decolonisation treatment for carriers at the time of surgery decreases infections
  - Carriers more likely to develop bloodstream infection than non-carriers (1.2% vs 0.4%),
    - 80% of these are the carried strain were 'the same' as bloodstream infection



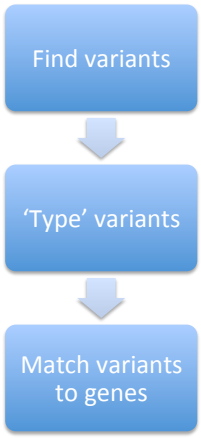
Our study

- "Paired" samples growing S. aureus
  - Nasal swabs collected on admission for MRSA carriage
  - Samples from individuals with S. aureus infection
- 112 individuals from Oxford and Brighton
- Bacteria grown from multiple colonies,

DNA extracted and sequenced

(>1400 seqeunces!)

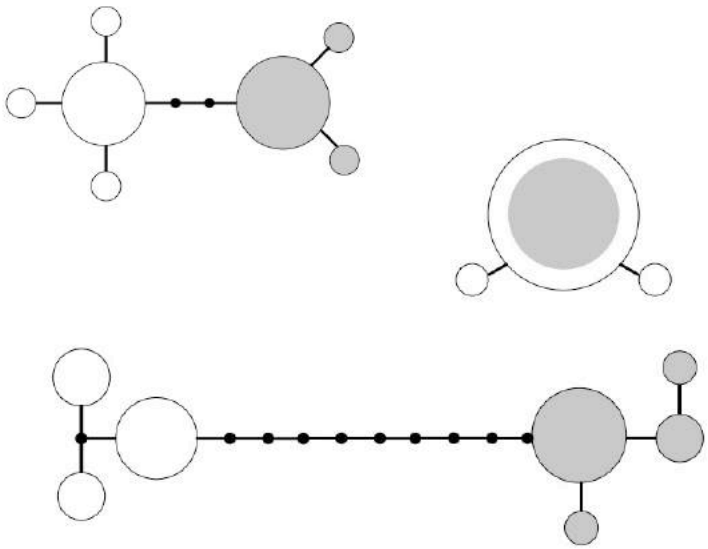
Analysis



- All sequences of S .aureus grown from an individual are compared
- Use a number of methods to identify differences between sequences to ask
  - Are the bacteria grown in disease different from those that are carried in the nose?
  - If they are different, do those differences cause change in bacterial behaviour?
  - If so, in what genes to those differences occur?

Initial results – hot off the press!

- Sequences returned for 62 individuals – in differing stages of analysis
- 85% - nasal bacteria are closely related to disease bacteria
- 35% - the same genotype in carriage and disease
- 50% - small number of differences separate nasal carriage from disease
  - Majority of those are <10 differences across the whole genetic code (2.8 million bases)



Forward…

- Annotation work is in early stages
- So far, no definite statistical difference in the types of variants seen (but 1000's more to be added)
- However mutations regulatory proteins are seen more frequently between carriage from disease than in other groups of variants (10% of variants between carriage and disease)

Conclusions

- Whole genome sequencing is allowing us to see in previous unrealisable detail the processes that accompany transition from harmless carriage to disease
- By better understanding how this process occurs, we hope to inform strategies to combat disease, both prevention and possibly treatment.