

# Comparative genomic study of *Staphylococcus aureus*: Lessons from its gene contents

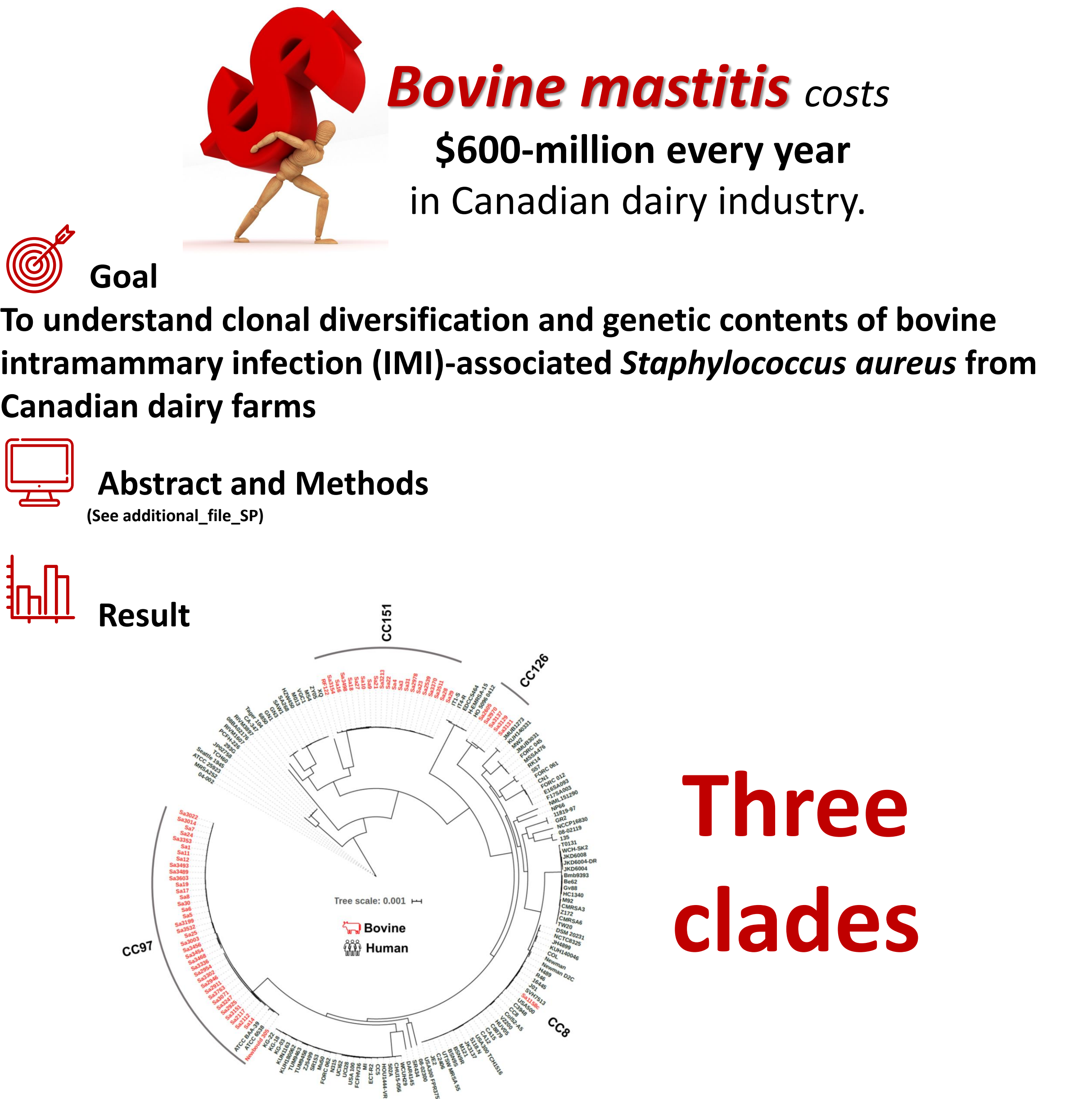
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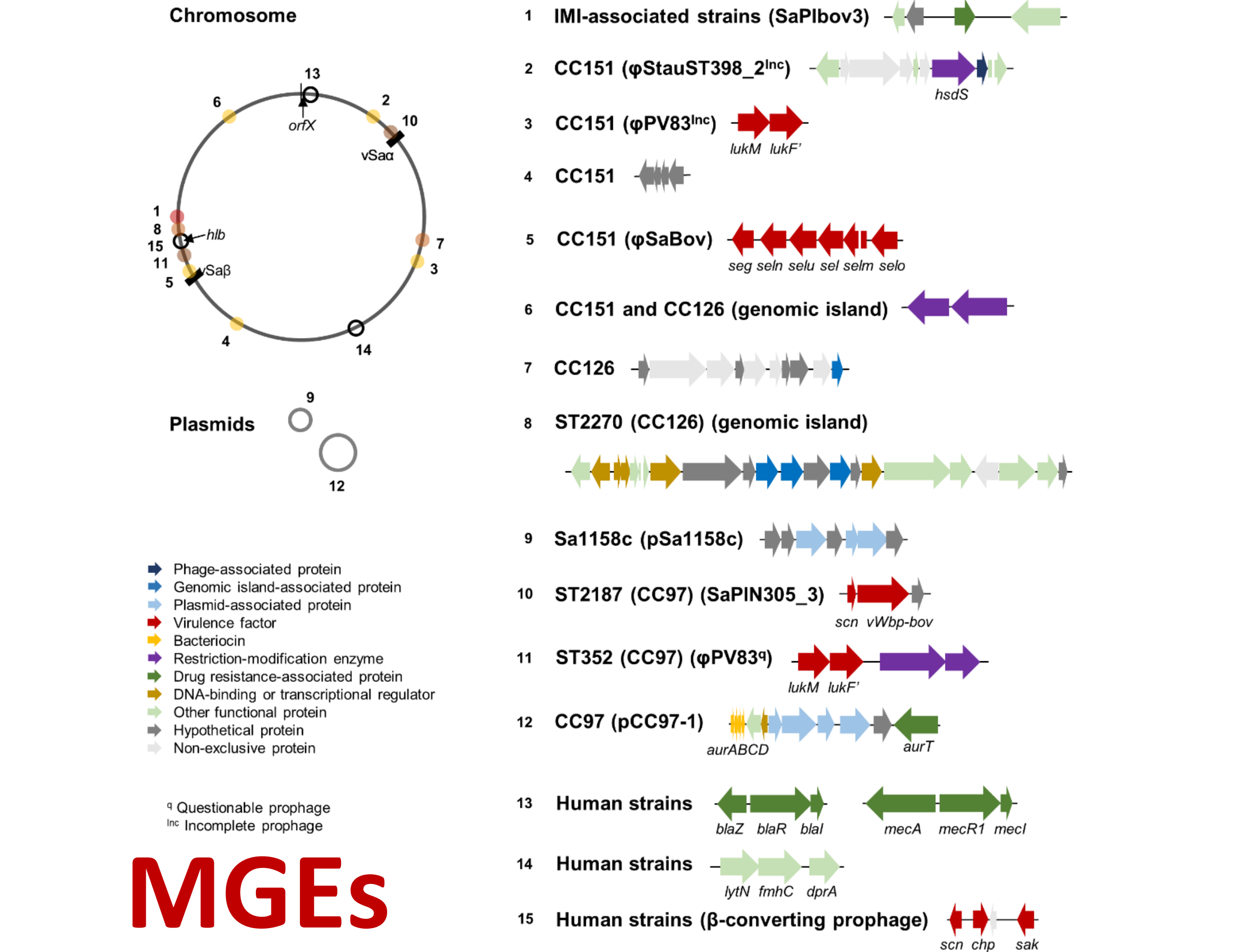
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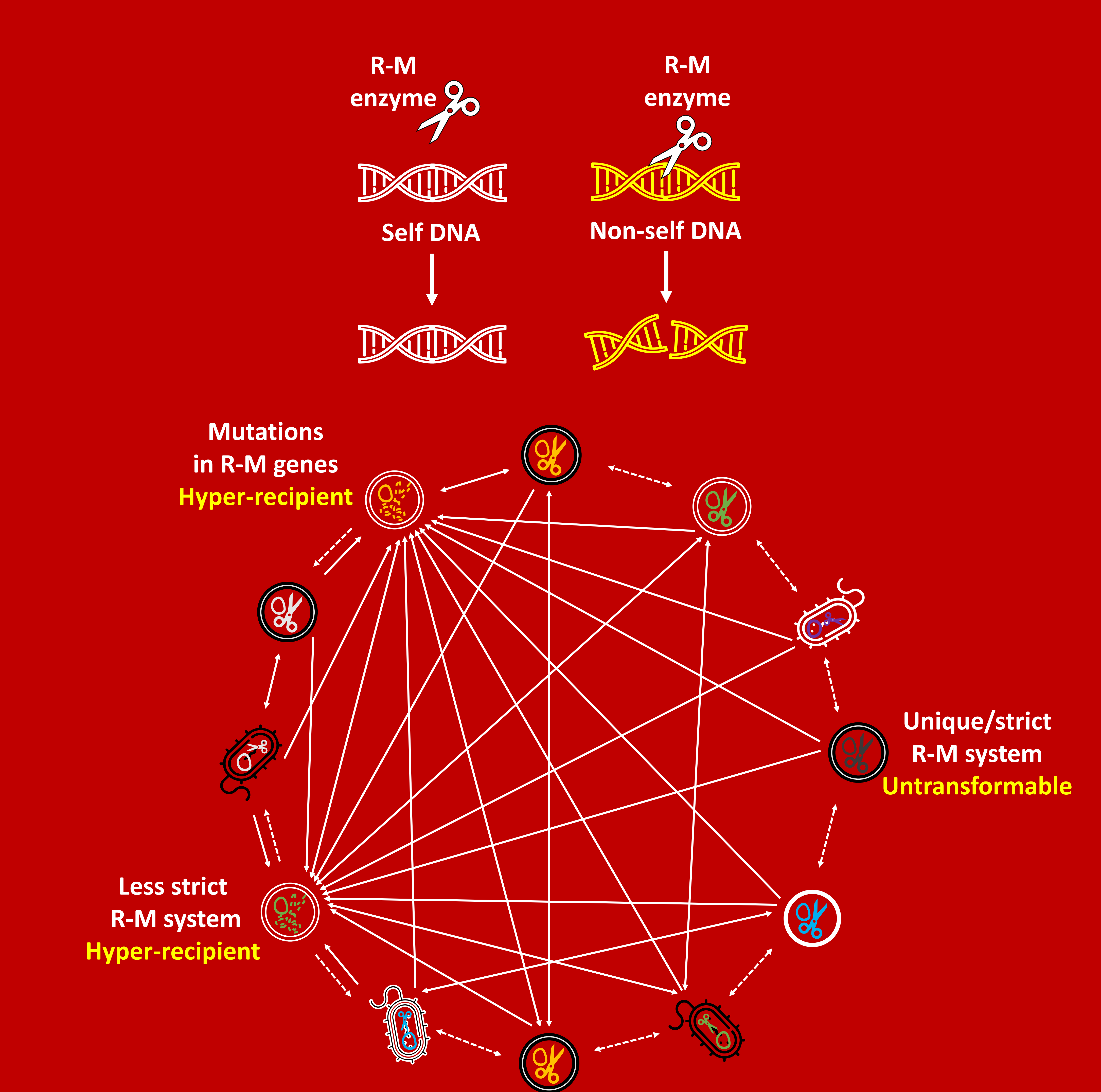


**Figure 1. Phylogenetic tree of 187 *S. aureus* from human and bovine.** All IMI-associated *S. aureus* strains cluster into three main clades except for ST8 (CC8) and belong to **CC51, CC126, and CC97**.

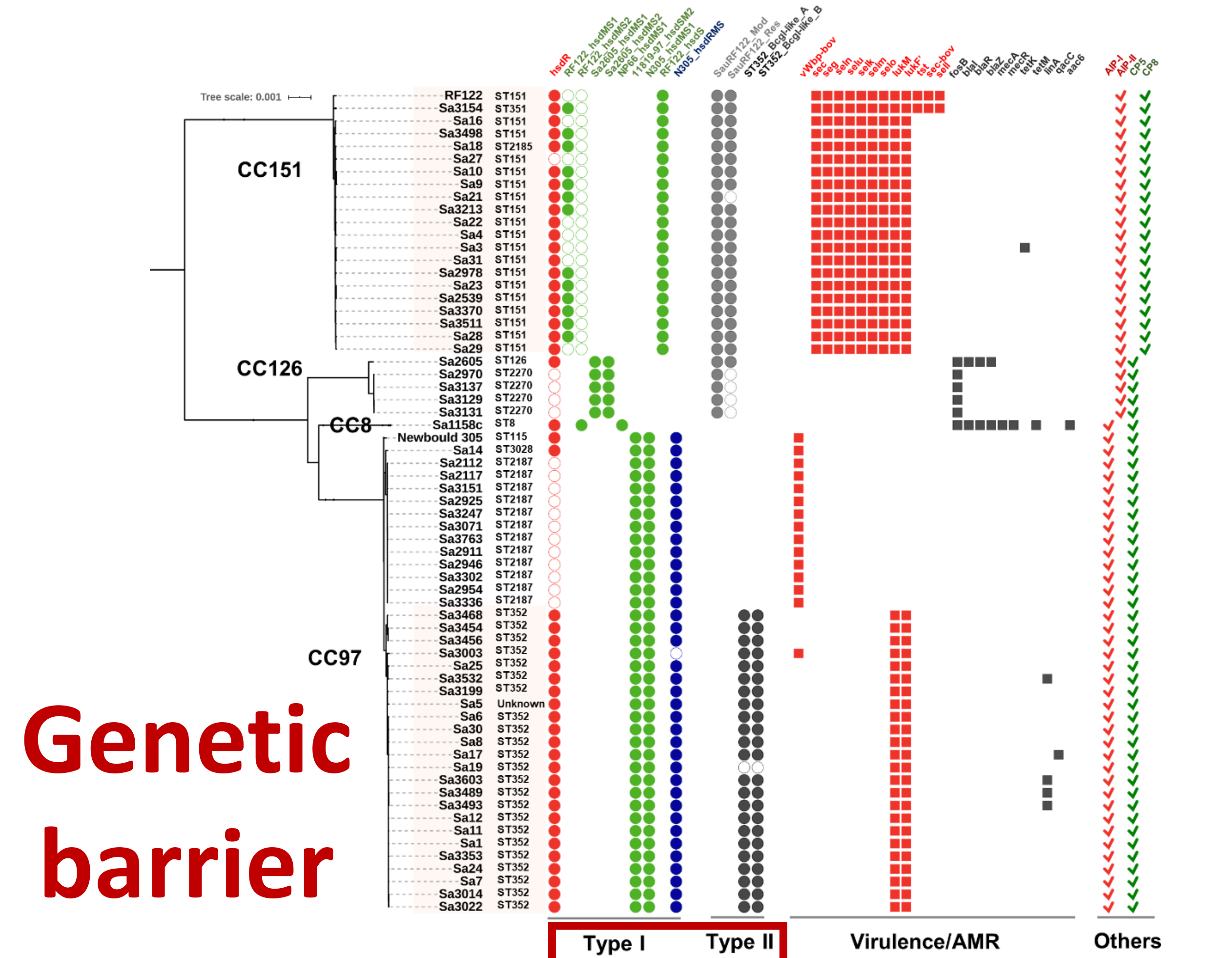


**Figure 2. Distribution of lineage-specific exclusive genes in *S. aureus*.** This figure illustrates the exclusive genes present mainly in bovine IMI-associated strains. The exclusive genes are shown with their associated lineages and **mobile genetic elements (MGEs)**. A reference genome of RF122 was used to identify the relative location of these genes with the corresponding numbers (1-15).

# *Staphylococcus aureus* favors to share exclusive/virulence/AMR genes with closely related strains with comparable restriction-modification (R-M) systems.



## Horizontal Gene Transfer Network



**Figure 3. Distribution of restriction-modification (R-M) genes and virulence/AMR genes in IMI-associated *S. aureus*.** The phylogenetic tree of 65 IMI-associated *S. aureus* and aligned genes show lineage-specific **R-M genes**, which serve as a **genetic barrier of horizontal gene transfer**. The virulence/AMR genes are either sequence type (ST)-specific or strain-specific. Circular and square boxes indicate R-M genes and virulence/AMR genes, respectively. Open circular box indicates pseudogenes. Checkmarks indicate other elements (signal molecule AIPs and capsular polysaccharide) associated with *S. aureus* pathogenicity. The highlighted strains were mostly associated with clinical mastitis.

- Summary**
1. Bovine *S. aureus* are **phylogenetically distinct** from human strains.
  2. **Lineage-specific and exclusive genes** are mainly located in **MGEs**.
  3. **Virulence/AMR genes** in IMI-associated *S. aureus* are **confined within lineage, ST, or strain**.
  4. **R-M systems** in IMI-associated *S. aureus* are **lineage/ST-specific**.
  5. Distribution of MGEs that encode exclusive/virulence/AMR genes links to **R-M systems as they serve as a genetic barrier** of horizontal gene transfer.
  6. *BlaZ* was found from two strains and **ST8 was the only MRSA**.

- Conclusions**
1. IMI-associated *S. aureus* has evolved in **multiple directions** and **MGEs** are associated with clonal diversification.
  2. **R-M systems** in *S. aureus* contribute to **shaping the clonal diversification and pathogenicity** by discriminating MGEs.
  2. **Sa1158c (ST8)** is the only bovine MRSA strain found in this study that **originated from humans**, suggesting the need for modifications to current dairy farm management programs.

**Significance**

**ACADEMICAL**

Moving closer to a "post-antibiotic era"

**BIOLOGICAL**

Understanding bacterial symbiosis

**INDUSTRIAL**

Reducing a burden of clinical bovine mastitis