### **1. INTRODUCTION**

### **Bovine Mastitis**



Bacterial infection (Staphylococcus aureus)

**Costly disease** 

#### Abstract

Staphylococcus aureus is a major etiological agent of clinical and subclinical bovine mastitis. Versatile adaptative strategies of this bacterium have challenge mastitis control and prevention globally and raise the concern of antimicrobial resistance (AMR) and zoonosis. We performed a phylogenetic analysis of 187 S. aureus strains isolated from bovines and humans. Our results revealed that S. aureus associated with bovine intramammary infections (IMI) showed distinct clades from human S. aureus strains. From a pan-genome analysis, we found 2,070 genes as a core genome out of 6,182 gene clusters. We also found host-specific genes and clonal-specific genes within bovine S. aureus strains, which were mainly located in mobile genetic elements (MGEs), and showed genetic potents of IMI-associated S. aureus. We analyzed restriction-modification (R-M) systems in IMI-associated S. aureus and revealed Type I R-M system is lineage-specific and Type II R-M system is sequence type (ST)-specific. Distribution of exclusive/virulence/AMR genes linked to R-M systems in S. aureus, suggesting R-M systems might contribute to shaping clonal diversification by providing a genetic barrier to the horizontal gene transfer (HGT). Our findings suggest the dissemination of virulence/AMR genes between bovine-adapted S. aureus might limit between different lineages due to the lineage-specific R-M systems. Additionally, we reported ST8 strain positive to both *blaZ* and *mecA*, which was originated from the human. This ST8 in the bovine niche raises a concern regarding reverse zoonosis and the need for dairy farm management programs that reflect the current status in Canadian dairy farms.



# To understand genetic contents of bovine intramammary infection (IMI)-associated *Staphylococcus aureus*

#### Only one comparative genomic study in IMI-associated S. aureus from Canadian dairy cows

- 1. What sequence types (STs) are common in Canadian dairy farms?
  - 2. Are they related to human *S. aureus* isolates?
  - 3. What unique/exclusive genes do they have?
- 4. What virulence/antimicrobial resistance (AMR) genes do they carry?
  - 5. What does the distribution of those genes look like?

### 2. METHODS



Bovine-associated strains (n = 65) Human-associated strains (n = 122)

### **3. RESULTS 1. Phylogenetic tree of** *S. aureus*



GOAL

Study the evolutionary relationship **between bovineassociated strains** and **human-associated strains** using core gene alignment



Bovine-associated strains (n = 65) Human-associated strains (n = 122)



Three clades

#### RESULTS

Bovine-associated lineages are branched from human-associated lineages and diverged

Suspicious spillover strains exits (e.g., Sa1158c, ATCC6538, and ATCC BAA-39).

#### 3. RESULTS 2. Unequally distributed genes



GOAL

Study differences in genetic

15

11



**Exclusive** genes in **MGEs** 

#### RESULTS

Within bovine isolates, exclusive genes are present in different STs.

Several exclusive genes are known virulence factors and antagonistic factors.

#### **3. RESULTS 3. Distribution of virulence/AMR genes**



Study other mastitis-associated elements in 65 IMI-associated *S. aureus* 

#### Virulence/AMR genes

Total of 103 virulence genes  $\rightarrow$  most of them conserved in all *S. aureus*   $\rightarrow$  bovine-specific vWbp (n = 1) and toxins (n = 12) in MGEs

Total of 25 AMR genes

- $\rightarrow$  common AMR genes (n = 14)
- $\rightarrow$  other AMR genes (n = 11)

 $\rightarrow$  fosB in non-MGEs and others in MGEs



## **Restriction-modification (R-M) systems**



### **3. RESULTS** 3. Distribution of R-M genes

**GOAL** 

Study R-M systems in 65 IMIassociated S. aureus

#### Type I and II R-M systems

Type I R-M genes as a part of core genes  $\rightarrow$  > 95% of amino acid identity

Additional Type I R-M genes and Type II R-M genes in MGEs



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#### **4. CONCLUSIONS**

S. aureus R-M systems are associated with dissemination of virulence and resistance elements although they are not the only elements deciding horizontal gene transfer.

Identification of bovine-adapted STs in dairy herds is an important aspect in a risk assessment, prevention, and treatment because the distribution of virulence factors varies in STs.

The dissemination of AMR genes from human to bovine via host transmission occurs in Canadian dairy farms and it needs to be considered in farm management programs.



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