



Exfoliative toxin E, a new *Staphylococcus aureus* virulence factor with host-specific activity

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MICROBES
15^e congrès national
de la SFM ●●●●●

Société Française
de Microbiologie

Du
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au 2 octobre
2019

Cité des sciences et de l'industrie, Paris 19^{ème} ●●●

Déclaration de conflit d'intérêt

Pour cette présentation, je déclare n'avoir
aucun conflit d'intérêt.

Mastitis



Huge economic loss

Animal Health
Mastitis

4896€/year for a herd of 100 dairy cows⁽¹⁾
(~200 M€/year in France)

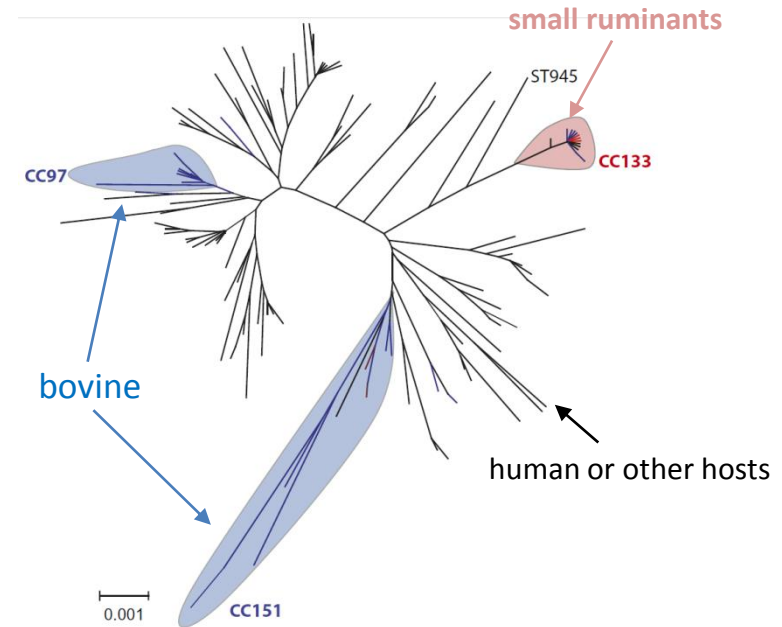
Lower « cheesability »⁽²⁾

Food Safety
SFP outbreaks

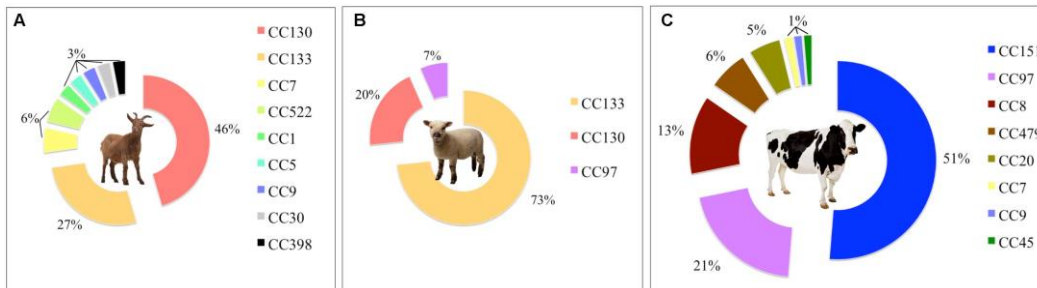
(1) Halasa et al., 2009. Livest. Sc.
(2) Le Maréchal et al., 2011. DST

S. aureus genotypes and host adaptation

MLST: some clonal complexes predominate in animal hosts



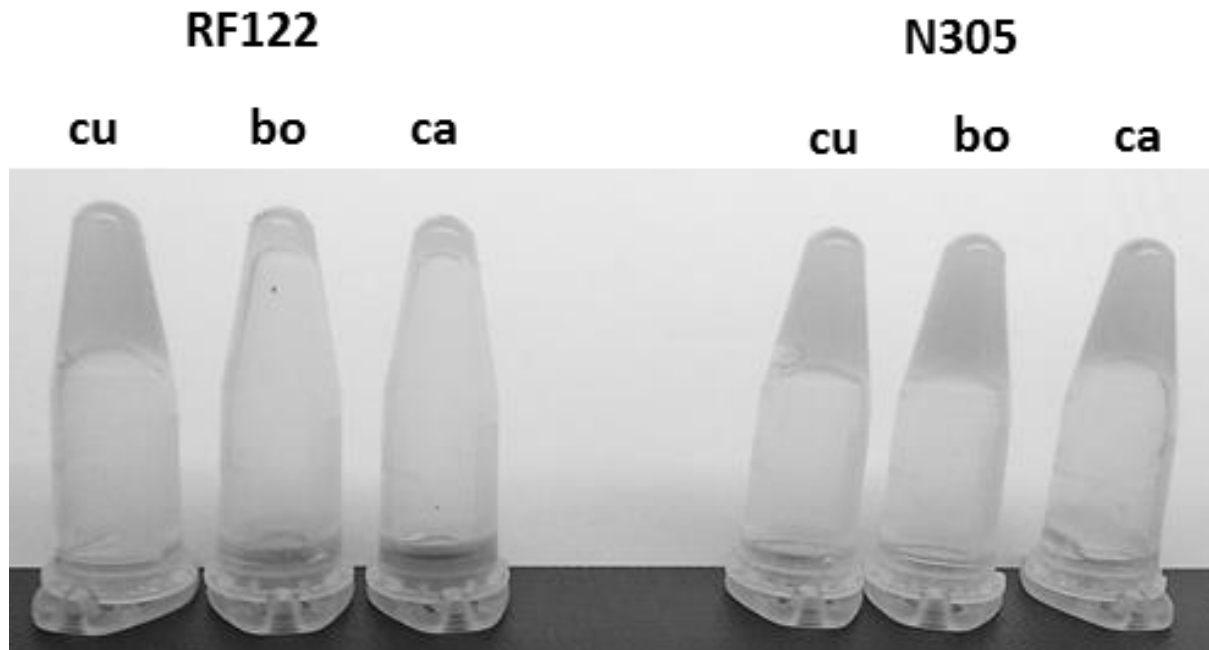
After Guinane et al., 2010. Genome Biol. Evol. 2:454



After Merz et al., 2016. Front. Microbiol. 7:319.

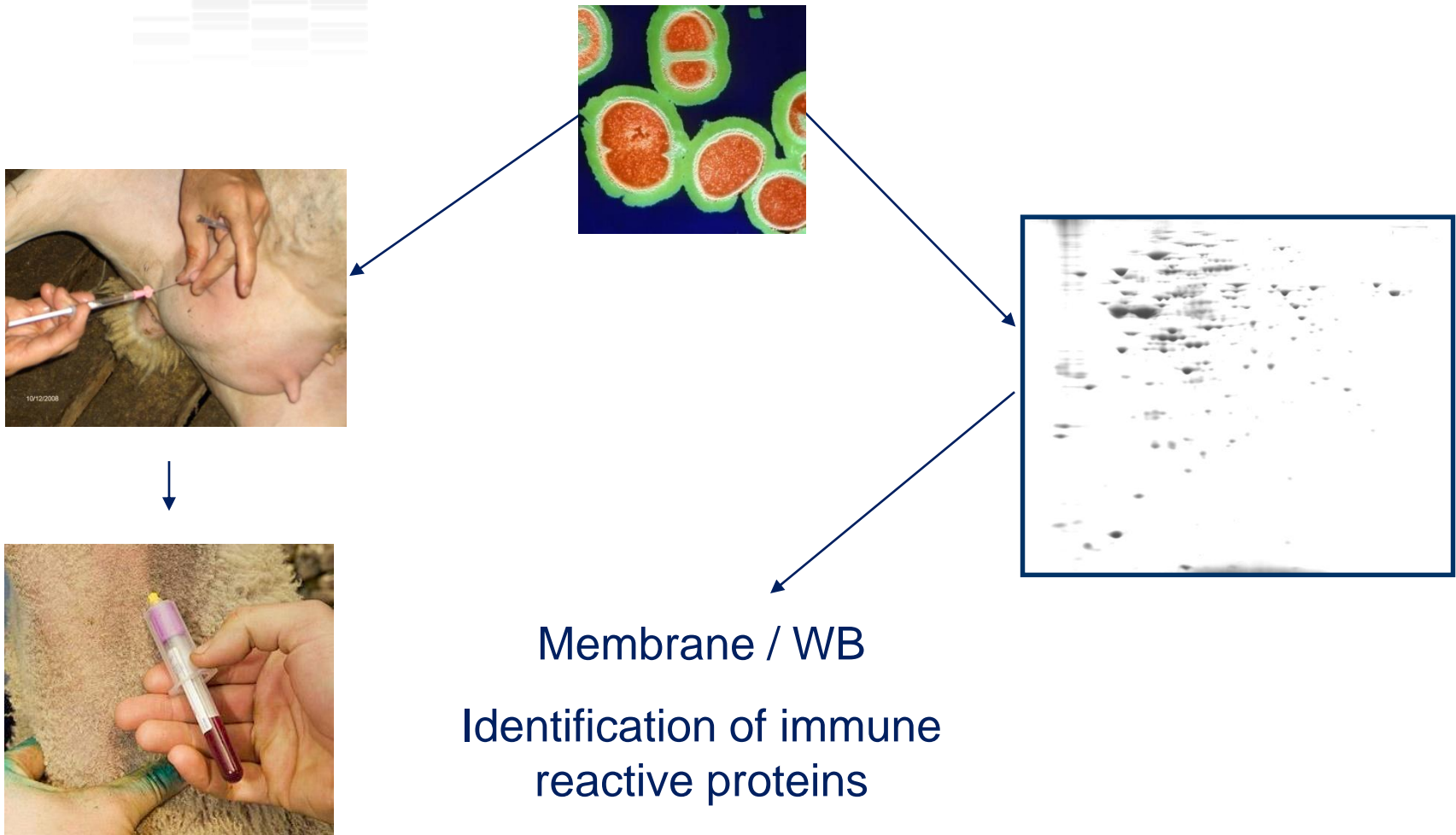
S. aureus virulence factors and host adaptation

Bovine variant of the von Willebrand-binding protein



Peton *et al.*, 2014. *Vet Res.* 45(1):106

SERological Proteome Analysis (SERPA)



Le Maréchal et al., 2009. J. Mic. Meth. 79:131-136.

Comparative SERPA on 2 *S. aureus* strains

severe



O11

O46

mild



12

74

3

Immune reactive proteins

Produced during mastitis

1st time: 37 proteins identified as potential antigens in *S. aureus*



74 proteins produced during mastitis (whatever the acuteness)
→ Role? Vaccine candidates, treatments?

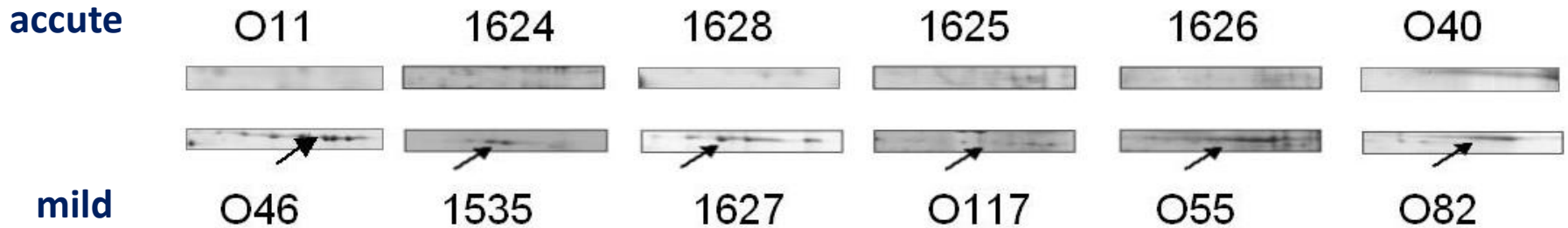


Candidates linked to mastitis acuteness

Le Maréchal et al., 2011. Vet. Res.

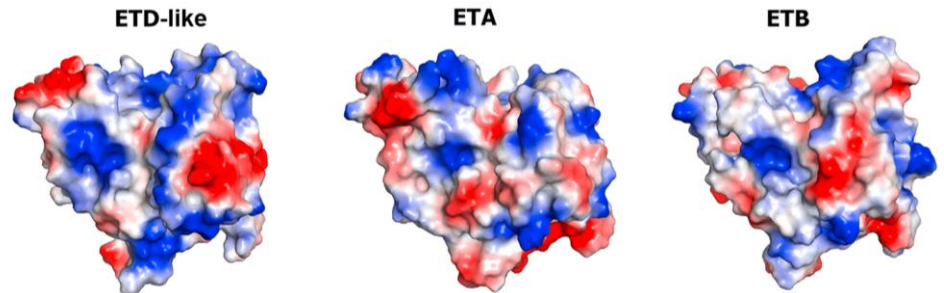
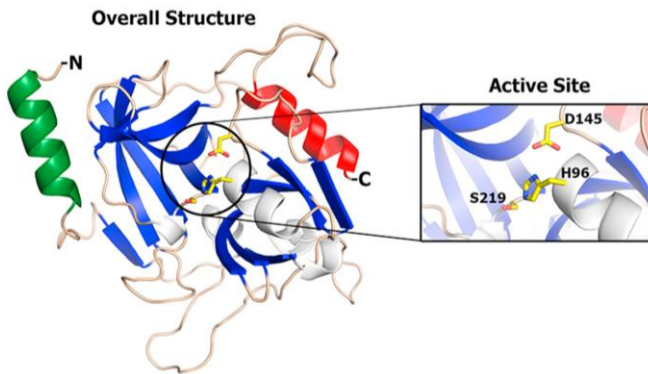
Le Maréchal et al., 2011. PLoS ONE 6(11): e27354.

S. aureus strains isolated from ewe mastitis



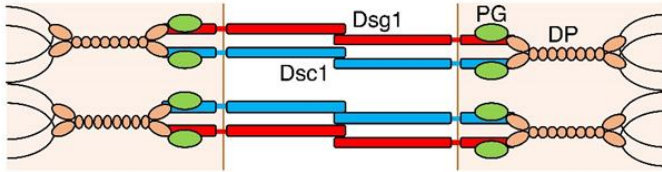
Similarity with Exfoliative toxins

59% sequence identity to ETD

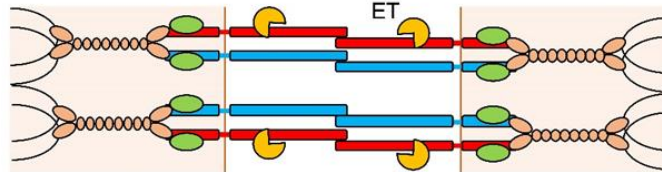


Mariutti et al., 2016. Biochem. Biophys. Res. Comm. 467(1):171-7

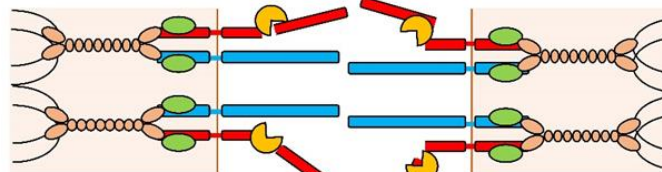
1. Intact desmosome



2. ET cleavage of desmoglein 1



3. Initial keratinocyte separation



4. Expansion of intercellular spaces

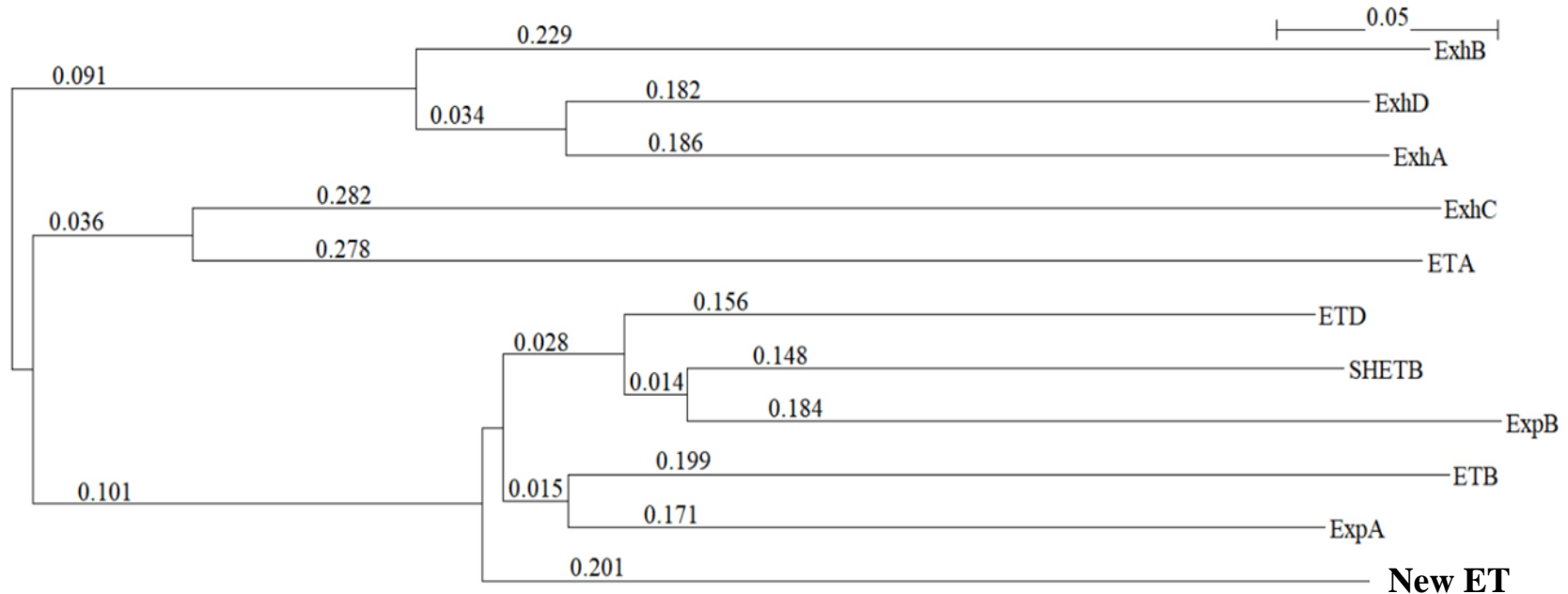


S. aureus Scalded Skin Syndrome



S. hyicus Exudative epidermitis

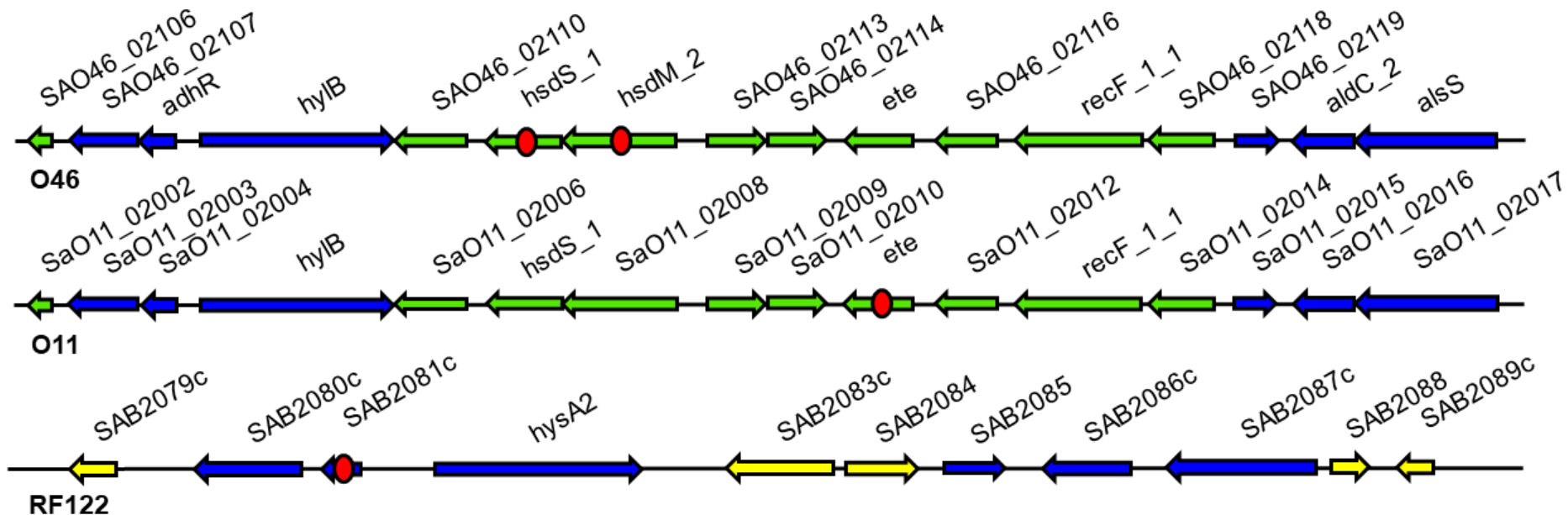
A new *S. aureus* exfoliative toxin?



Phylogenetic analysis based on the amino acid sequences of ETs

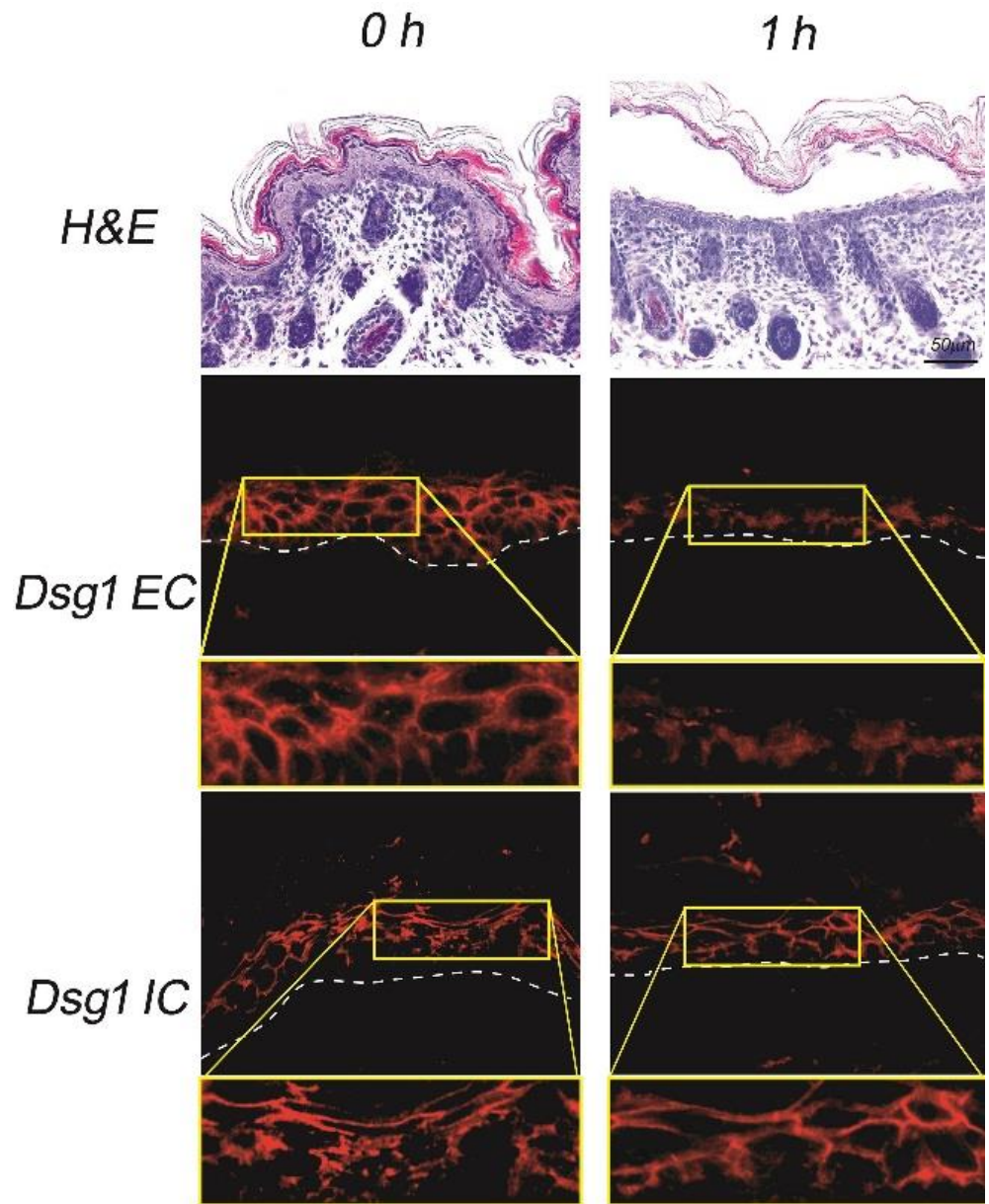


Genetic vicinity of ETD-like gene in *S. aureus*

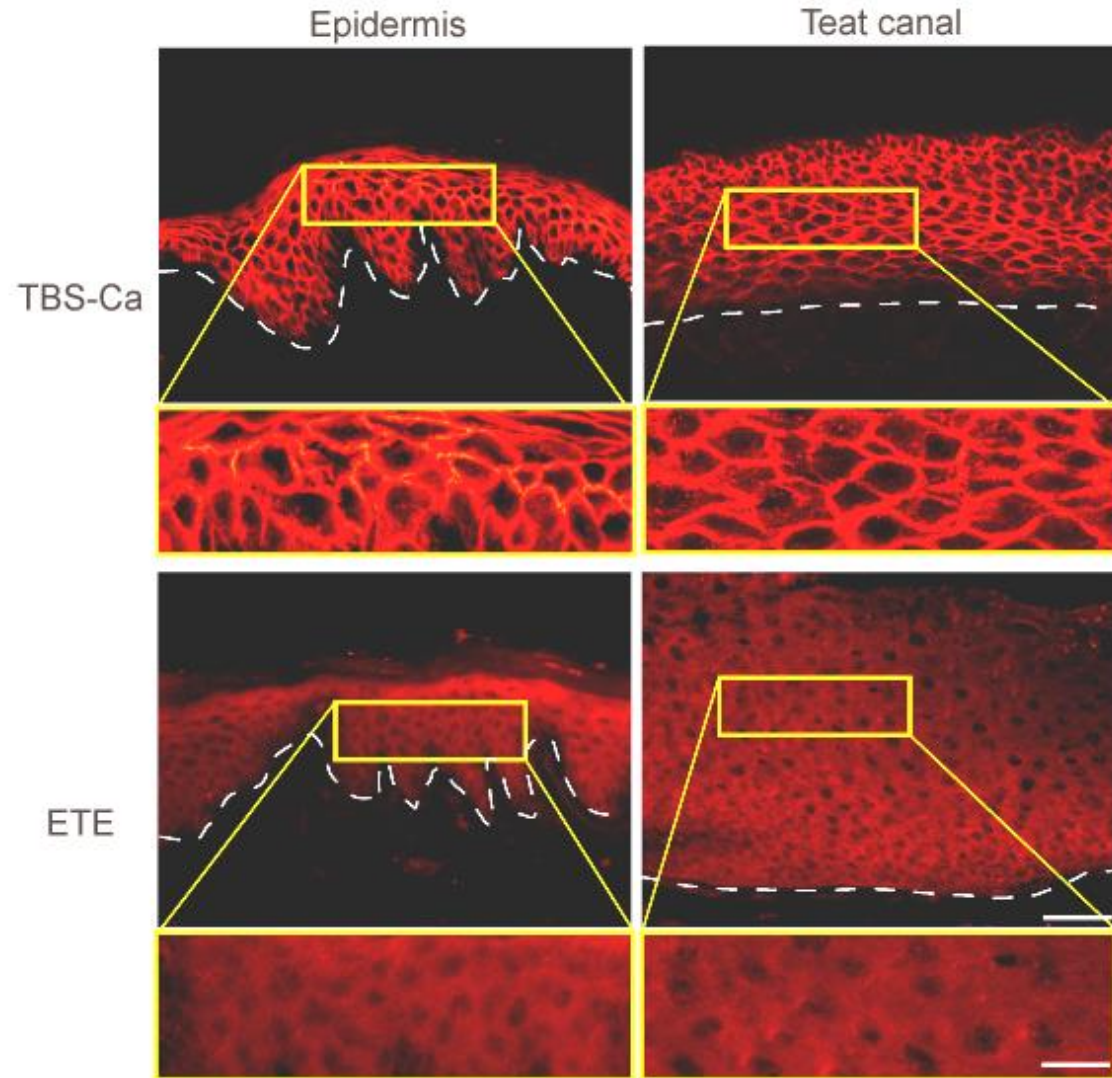


Exfoliative activity of the new ET in neonatal mice.

ETD-like → ETE



ETE degrades Dsg1 in caprine teat canal epithelia.

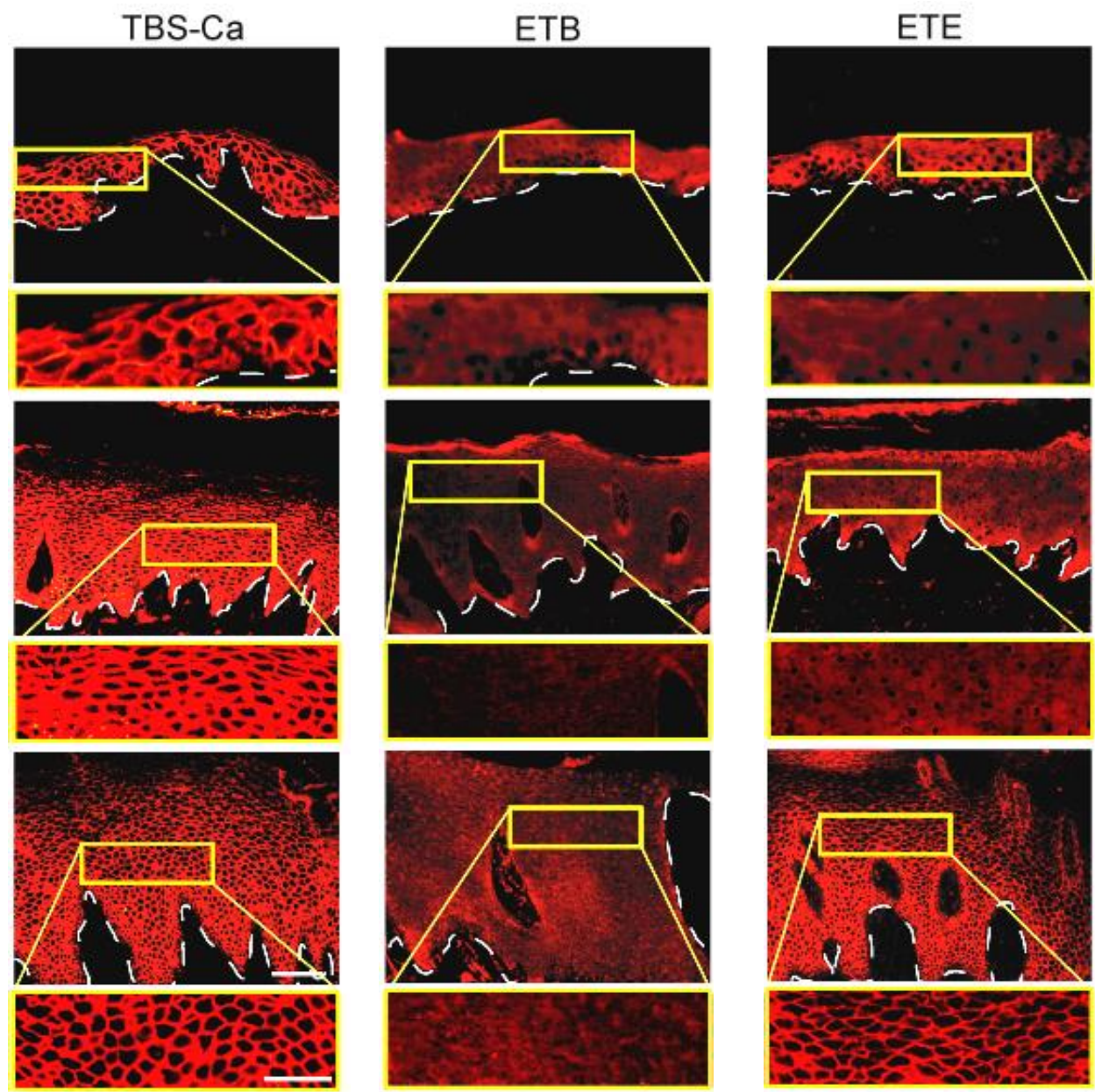


ETE degrades Dsg1 in ovine and caprine epidermis...

Ovine

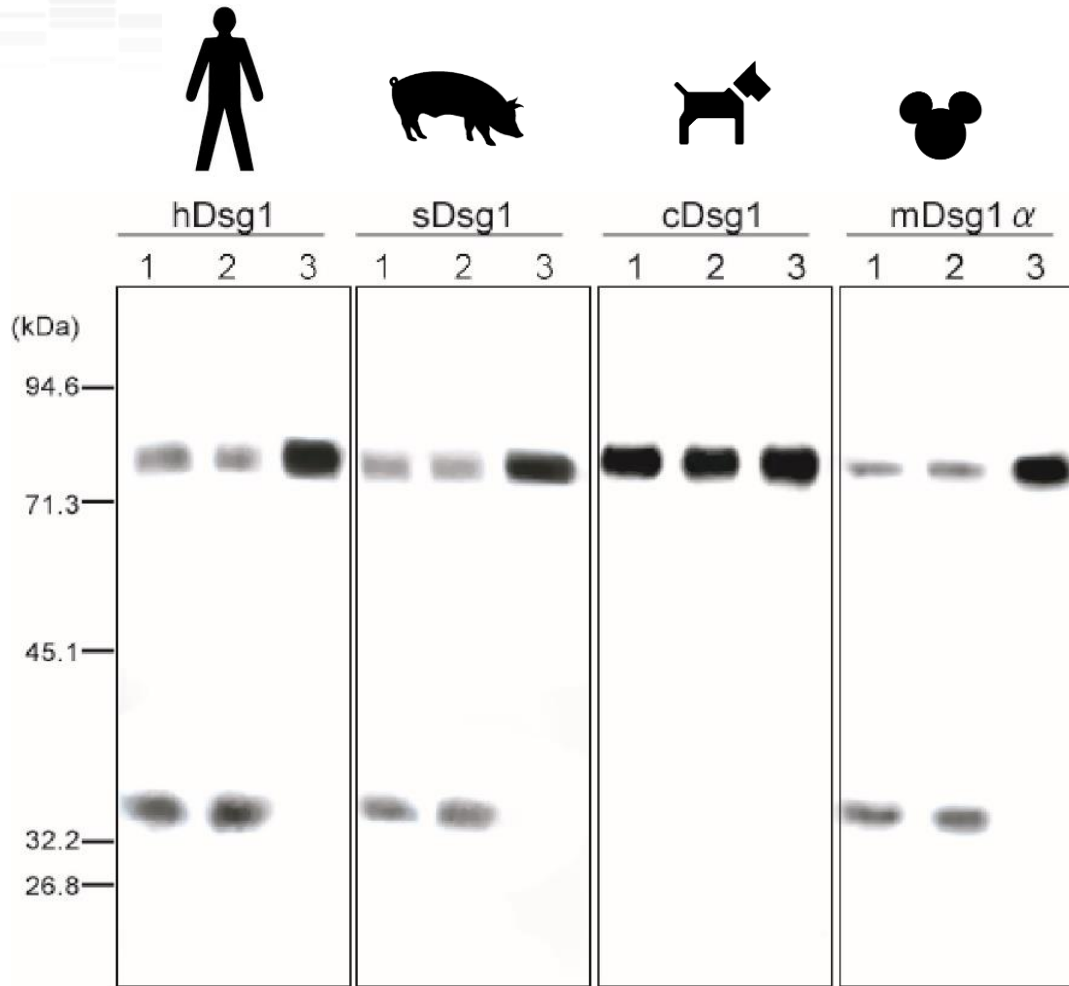
Caprine

Bovine

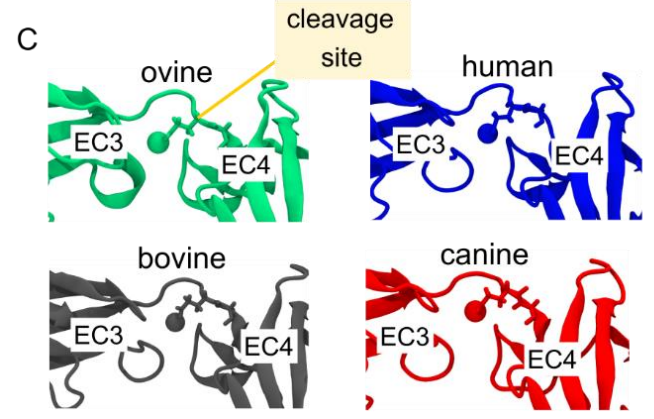
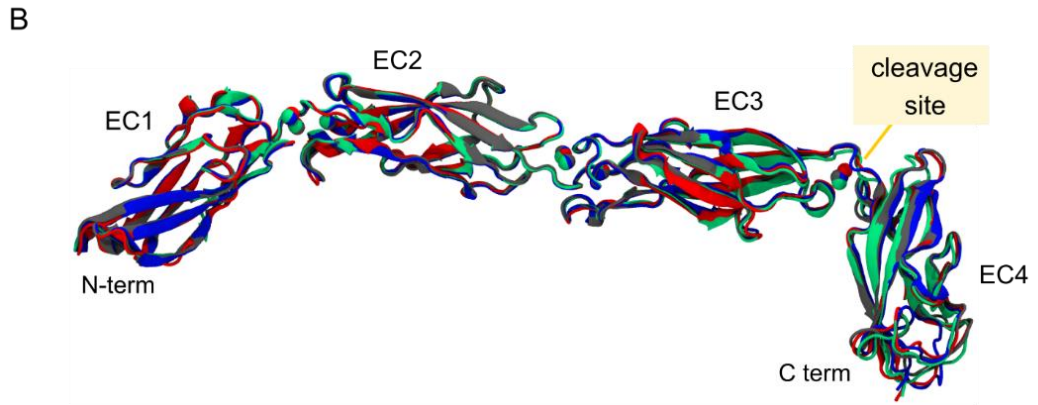
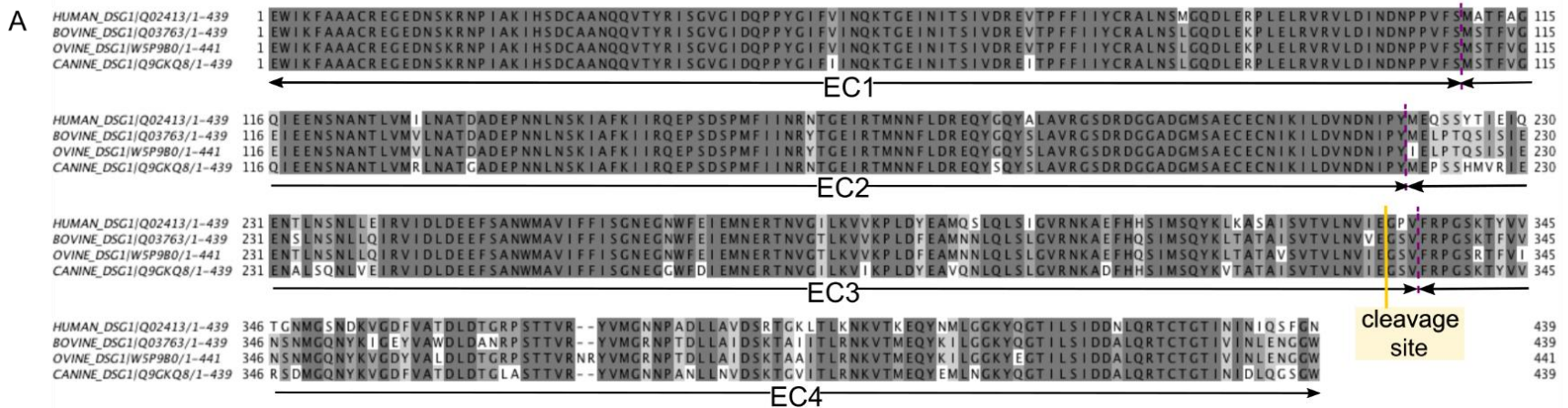


...but not in bovine epidermis

In vitro digestion of recombinant Dsg1s with ETE.



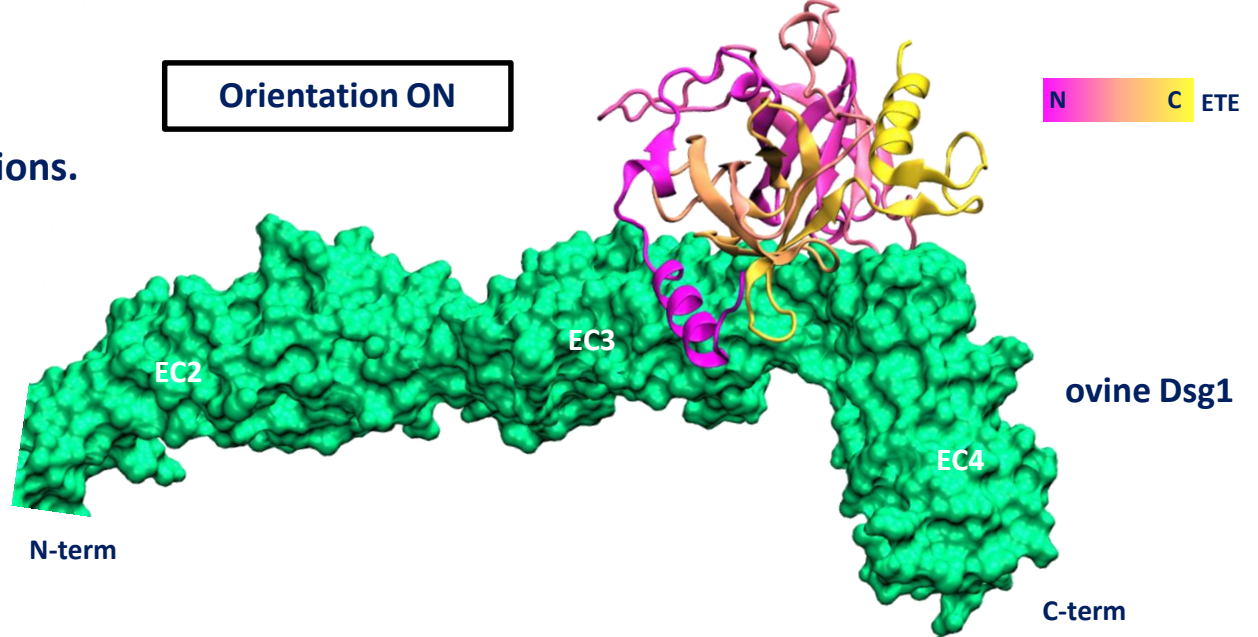
Molecular modeling



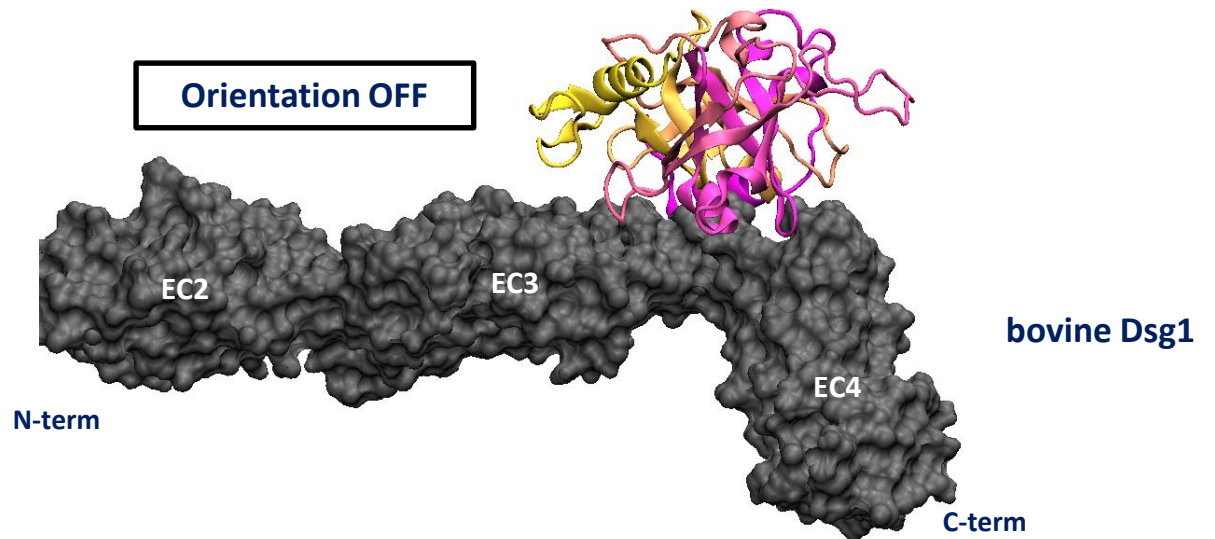
Molecular docking

Best HADDOCK docking solutions.

95 % of docking solutions



100 % of docking solutions



Docking step preceding cleavage accounts for the ETE species-specificity?

Conclusion

ETE, a new *S. aureus* virulence factor

Frequently associated with ovine *S. aureus* isolates

New example of host specialization in *S. aureus*

Found in *S. aureus* strains associated with mild mastitis in ewes

Marker of *S. aureus* virulence in ewe mastitis (diagnosis)?

ETE provides selective advantages for *S. aureus* colonization and persistence in the udder?



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Thank you for your attention

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