The amyloidogenic and prionic secretomes of staphylococci: A new insight in their prions role.

Universitat Autònoma de Barcelona

Marc Ramos-Sala (m.ramos.sala@gmail.com)

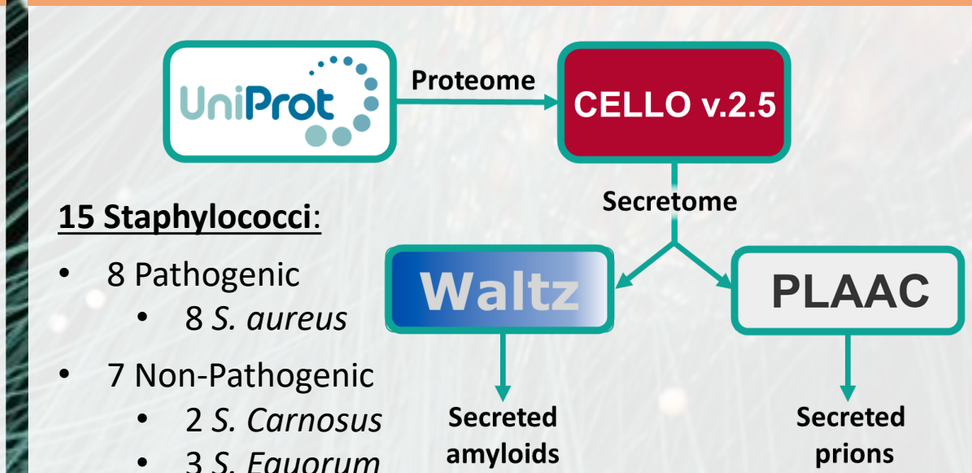
INTRODUCTION

Prions are a subset of amyloids able to transmit their misfolding to amyloid state to other soluble proteins.

Staphylococcus is a genus of gram+ bacteria. Some species are pathogenic (*S. aureus*) while others are not (*S. carnosus, S. equorum*, *S. xylosus*). Although extracellular amyloids in staphylococci have been described as a major biofilm component (PSMs, Bap, SuhB), no staphylococci extracellular prion has been described yet. However, I hypothesize that the prion transmissibility of misfolding to amyloid state could synchronize the phenotype of the whole bacteria community (quorum sensing-like).

For that reason, an *in silico* study of pathogenic and non-pathogenic staphylococci extracellular prions was made in order to identify them and elucidate their possible role.

METHODS



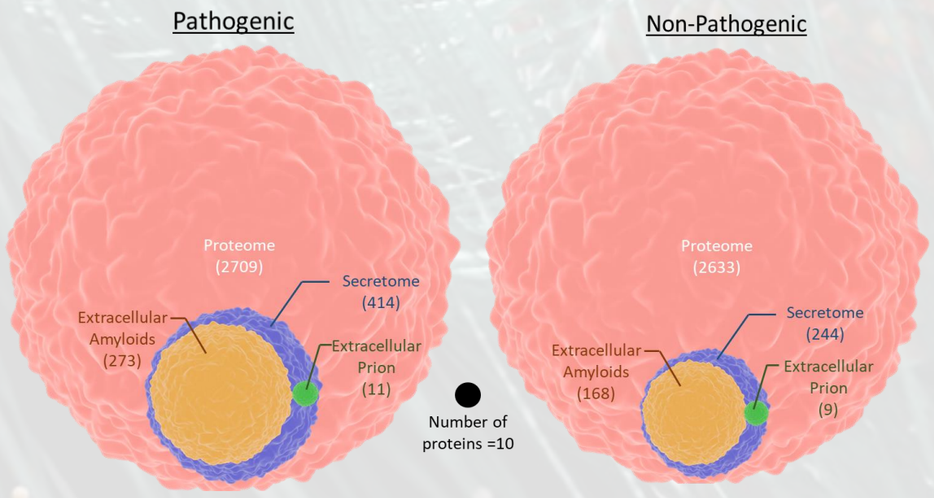
15 Staphylococci:

- 8 Pathogenic
  - 8 *S. aureus*
- 7 Non-Pathogenic
  - 2 *S. Carnosus*
  - 3 *S. Equorum*
  - 2 *S. Xylosus*

RESULTS

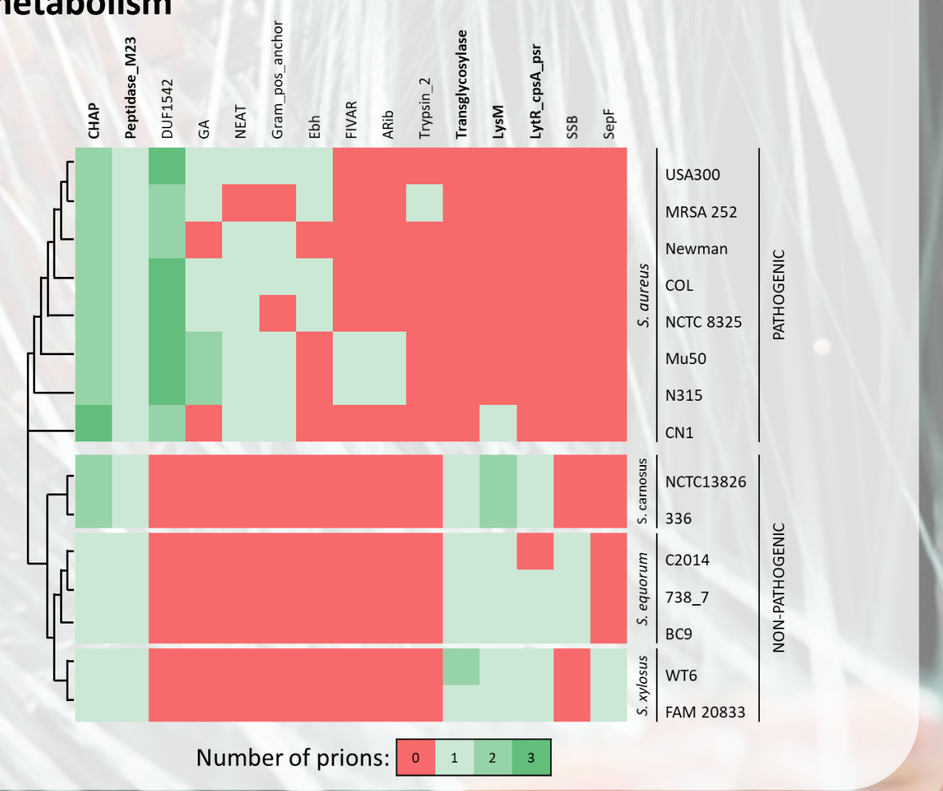
Variation in the number of extracellular prions

- The number of prions are conserved in all staphylococci.
- Prions are not related with pathogenicity → possible role in cell homeostasis.



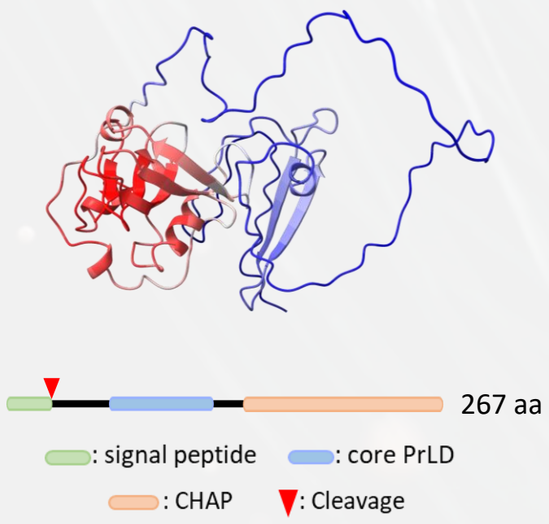
Main PFAM domains of extracellular prions

- Extracellular prionic functions are related with **cell wall metabolism**



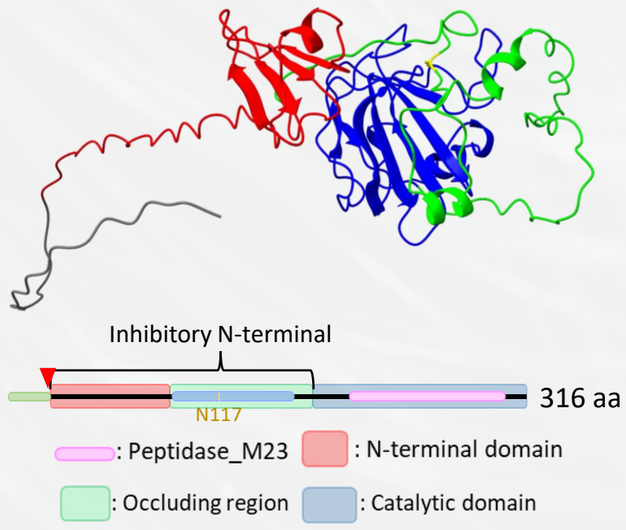
Conserved extracellular prions in staphylococci

SsaA (CHAP-containing protein)



- Amidase + peptidase activity (cell wall metabolism)
- 2 isoforms in pathogenic, 1 isoform in non-pathogenic

LytM (Peptidase M23-containing protein)



- Endopeptidase activity (cell wall metabolism)
- Prion domain regulates LytM activity

- Further evidence of the role of ssaA and LytM in cell wall metabolism was found when, after inhibition of WalKR (peptidoglycan metabolism regulator), only overexpression of ssaA and LytM was able to restore growth (Delaune et al., 2010)

CONCLUSIONS

- No difference in the number of prions is observed, despite pathogenic staphylococci having 1.6 fold more extracellular proteins than non-pathogenic.
- Extracellular staphylococcal prions do not seem to be related with pathogenicity.
- Most staphylococci extracellular prions display functions related with cell wall metabolism.
- The transmissibility of this prion cell wall modulators could be a method synchronizing whole colonies phenotypes, regulating bacterial growth and death.

BIBLIOGRAPHY

1. Yu et al. Prediction of protein subcellular localization. Proteins: Structure, Function, and *Bioinformatics*. 2006;64(3):643-651. doi:10.1002/PROT.21018
2. Oliveberg M. Waltz, an exciting new move in amyloid prediction. *Nature Methods.* 2010;7(3):187-188. doi:10.1038/NMETH0310-187
3. Lancaster et al. PLAAC: a web and command-line application to identify proteins with prion-like amino acid composition. *Bioinformatics.* 2014;30(17):2501-2502. doi:10.1093/BIOINFORMATICS/BTU310
4. Delaune et al., Peptidoglycan Crosslinking Relaxation Plays an Important Role in Staphylococcus aureus WalKR-Dependent Cell Viability. *PLOS ONE*. 2011;6(2):e17054. doi:10.1371/JOURNAL.PONE.0017054