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Immunochemical diagnosis of *S. aureus* infections targeting quorum sensing autoinducing peptides

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1 Introduction

Staphylococcus aureus is one of the leading causes both of healthcare-associated and community-acquired infections[1]. Up to now, there is still a need of reliable **diagnostic tools** able to early detect and monitor these infections.

Quorum-sensing (QS) is a cell-to-cell communication process based on the release and sensing of low molecular weight chemical signals, called autoinducers (AIs)[2]. In *S. aureus*, these molecules correspond to cyclic thiolactone **autoinducing peptides** (AIPs I-IV), whose production is regulated by the accessory gene regulator (agr) system during an infection process[3]. AIPs control its own biosynthesis and modulate the genetic expression of virulence factors and survival mechanisms[4].

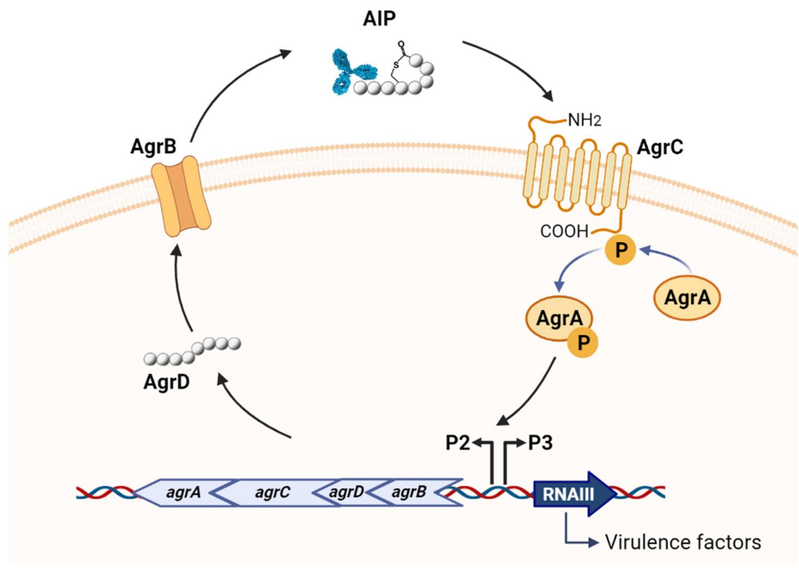


Fig. 1. Schematic representation of *S. aureus* agr QS system.

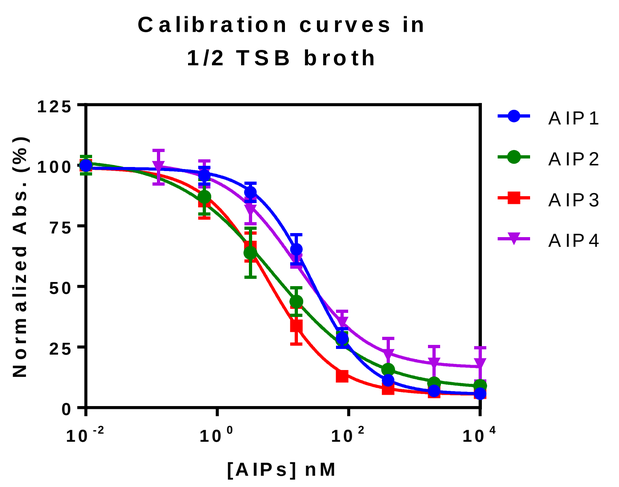
2 Principal objective

Improve the **diagnosis** of ***S. aureus* infections** based on the better understanding of QS mechanisms involved on its pathogenesis.

3 Strategy presented: Immunochemical assay for AIP detection

Production of specific **antibodies** for the **detection** of **AIPs** and their implementation for the development of **competitive indirect microplate-based ELISAs** to **speed up** the **diagnosis** of infections caused by *S. aureus* in clinical settings.

4 Results: analysis of bacterial isolates



	AIP1	AIP2	AIP3	AIP4
IC_{50} (nM)	28.16 ± 8.10	7.81 ± 3.95	6.68 ± 3.38	3.18 0.95
Slope	-1,02 ± 0.04	-0.62 ± 0.08	-0.86 ± 0.11	-0.80 ± 0.12
LOD (nM)	**3.12 ± 1.08**	**0.41 ± 0.22**	**0.70 ± 0.59**	**0.30 ± 0.12**
R^2	0.99 ± 0.001	0.99 ± 0.004	0.99 ± 0.003	0.99 ± 0.01

Fig. 2. ELISA Calibration curves for the detection of each AIP and their analytical parameters.

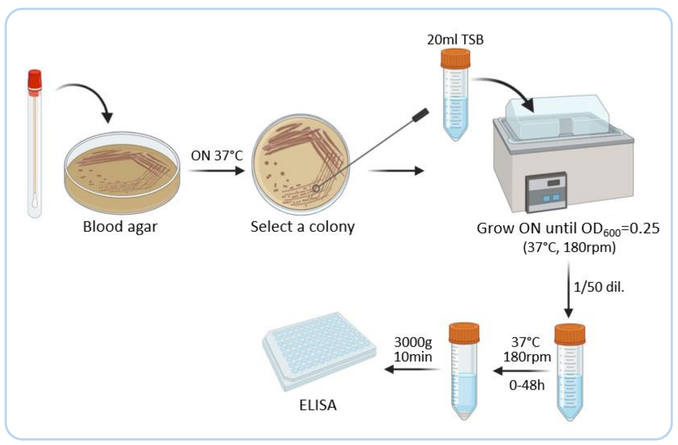


Fig. 3. Procedure of growth curves and supernatant extraction for AIP quantification.

Main features of the ELISAs developed:

- **Robust** and **reproducible**
- **High sensitivity** (low nM range)
- **High specificity** to each of the AIPs

AIP profile in ½ TSB broth

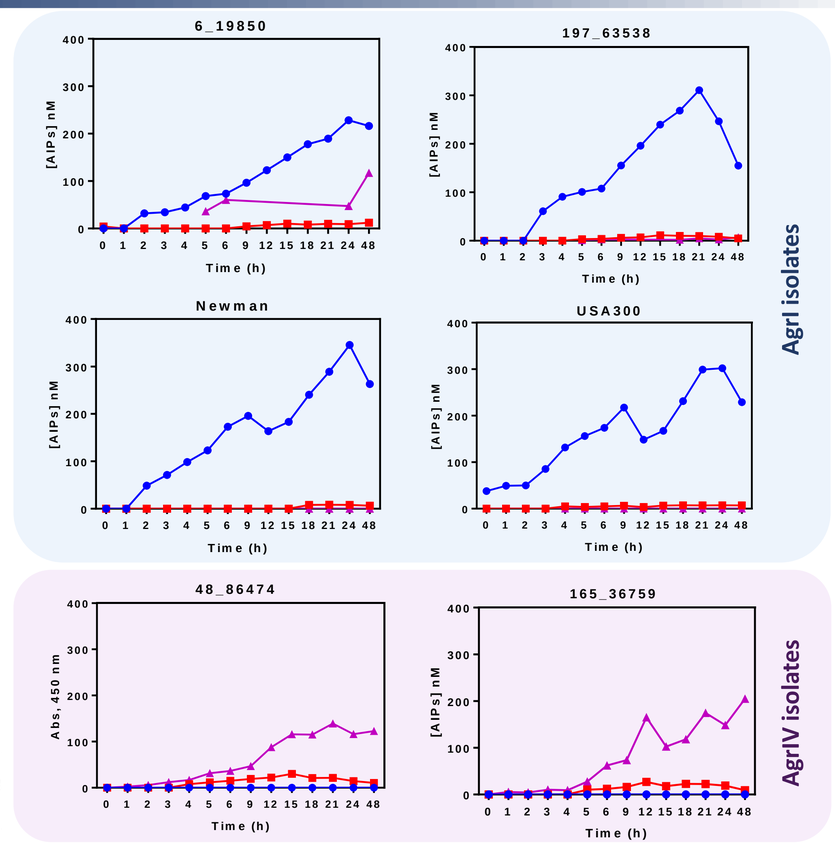


Fig. 4. AIP profile of bacterial isolates belonging to agrI and agrIV genotypes in ½ TSB.

AIPs have been quantified with **high accuracy** in **½ culture broth** samples where clinical isolates have been grown after a **short incubation** period.

5 Conclusion

The results shown in this communication bring to light the potential of the immunochemical technique developed to **early diagnose *S. aureus* infections**. Likewise, the specificity profile towards the different AIPs gives possibility of using this method in **genotyping studies**.

6 Future work

Further studies will be carried out to validate the diagnosis and genotyping capability of the present technology.

Future steps will be addressed to the detection of AIPs directly from clinical samples and the implementation of this technique on bio-sensing technologies.

CONTACT

Literature

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Aknowledgments

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