A Potential Role of Serine-aspartate dipeptide repeat protein E (SdrE) in Immune Evasion of *Staphylococcus aureus*

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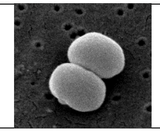

Background

- *Staphylococcus aureus*, a gram-positive, sphere-shaped (coccal) bacteria, is one of the most dangerous bacteria which causes skin infections, pneumonia, heart valve infections, and bone infections.
- Staphylococcus aureus surface proteins such as cell wall-anchored (CWA) proteins have been characterized as important virulence factors and have important roles in adhesion to host tissues, immune evasion, and biofilm formation in hosts.
- MSCRAMM (microbial surface components recognizing adhesive matrix molecules) proteins are members of the CWA family, which have serine-aspartate di-peptide repeats (Sdr). SdrE, a member of the MSCRAMM sub-family, is known to have an important role in *S. aureus* pathogenesis by inhibiting complement activation. However, the exact mechanism is unknown.
- In this study, we have characterized the interacting partner of the Sdr domain of SdrE through phage display and ELISA-based tools. We have characterized that SdrE binds to Complement Component C5 in a dose-dependent manner, suggesting a potential role in immune evasion.

Results

- Peptide sequence **WLWPVHSQHGFA** was enriched (~30%) in Phage display based characterization of the interacting partner which indicates to be part of Human complement component 5.
- For validation of Phage display results, an ELISA based binding assay was performed with 3 replicates using SdrE and other MASCRAMM proteins (SdrF and SesJ) as a negative control. ELISA results indicate that SdrE has dose-dependent binding with Human Complement Component 5

Conclusion

The interacting partner of the Sdr domain of SdrE was characterized. SdrE binds to Complement component C5 in a dose-dependent manner, suggesting a potential role in immune evasion

Phage Display

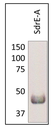

Fig. 1

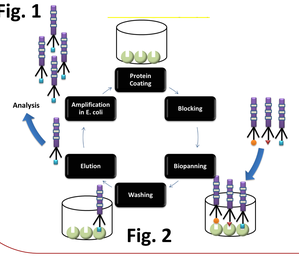

Fig. 2

Table 1

	Description	Max score	Total score	Query cover	E value	Ident	Accession
WLWPVHSQHGFA	**complement component C5 [Homo sapiens]**	**21.8**	**21.8**	**50%**	**61**	**83%**	**AAA51856.1**

Table 2

complement component C5 [Homo sapiens]

Sequence ID: AAA51925.1 **Length:** 1676 **Number of Matches:** 1

Range 1: 773 to 778 GenPept Graphics

Score	Expect	Identities	Positives	Gaps
21.8 bits(44)	69	5/6(83%)	5/6(83%)	0/6(0%)

```
Query  1    WLWPVH  6
           WLW VH
Sbjct  773  WLWEVH  778
```

Dose Dependent interaction

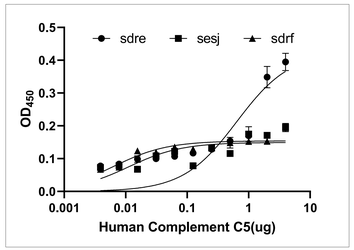

Fig. 3

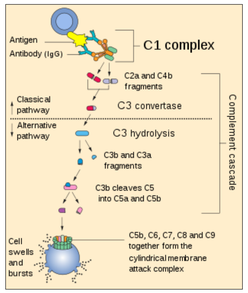

Fig. 4

Future Direction

- Validation of C5/ SdrE binding by Isothermal titration calorimetry (**ITC**)
- SdrE Knock-out studies for phenotype studies

References:

1-Foster, T. J., Geoghegan, J. A., Ganesh, V. K. & Ho¨ o¨ k, M. (2013). Adhesion, invasion and evasion: the many functions of the surface proteins of Staphylococcus aureus. Nat Rev Microbiol 12, 49–62

2-Patti, J. M., Allen, B. L., McGavin, M. J., and Höök, M. (1994). MSCRAMM-mediated adherence of microorganisms to host tissues. *Annu. Rev. Microbiol.* 48, 585–617.

3-https://commons.wikimedia.org/wiki/File:Complement_pathway.svg#file

Acknowledgements:

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