*Candida albicans E*nhances the Proliferation and Virulence of *Staphylococcus aureus* in Implant-Associated Infections.

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Background

- Polymicrobial implant-associated infections are becoming increasingly common and lead to greater morbidity and worse clinical outcomes compared to monomicrobial infections.
- We investigated how co-infection of *Staph aureus* (SA) and *Candida albicans (CA)* influences the in-vitro growth of these microorganisms on stainless steel implants and the in-vivo growth in a murine model of spinal implant infection.

Methods

In-vitro

- SA and CA were incubated on stainless steel pins for 1h.
- The pins were transferred onto fresh RPMI media and incubated for 1h, 3h, 6h and 24h and then homogenized to detach biofilm.
- Colony forming unit (CFU) counting was performed using the IVIS (PerkinElmer, Waltham, MA).
- Minimum inhibitory concentration (MIC) testing for vancomycin was performed in a 96-well plate on SA alone and SA+CA, with and without antifungal amphotericin B (AMB).

In-vivo

- 8 week-old C57BL/6 mice underwent survival surgery in which a surgical-grade 0.1 mm diameter L-shaped stainless-steel implant was press-fit into the L4 spinous process. There were 5 mice in each SA, CA, and SA+CA groups and 2 mice in the sterile group. Bioluminescent strains of methicillin resistant SA, AH4775, and CA, CEC749 were used in this study. An inoculum of 1×10^3 CFUs of SA alone, CA alone, SA + CA, or sterile saline (sterile control) were inoculated directly onto the implant.
- Infection burdens were measured by longitudinal tracking of the bioluminescence on post-operative day (POD) 0-35 using the IVIS.
- On POD35, all animals were sacrificed. Implants and soft tissue were harvested for CFU analysis.

Conclusion

- SA infection significantly increased in the presence of CA in both in-vitro and in-vivo models. Moreover, the susceptibility of SA to vancomycin was decreased in the presence of CA.

References

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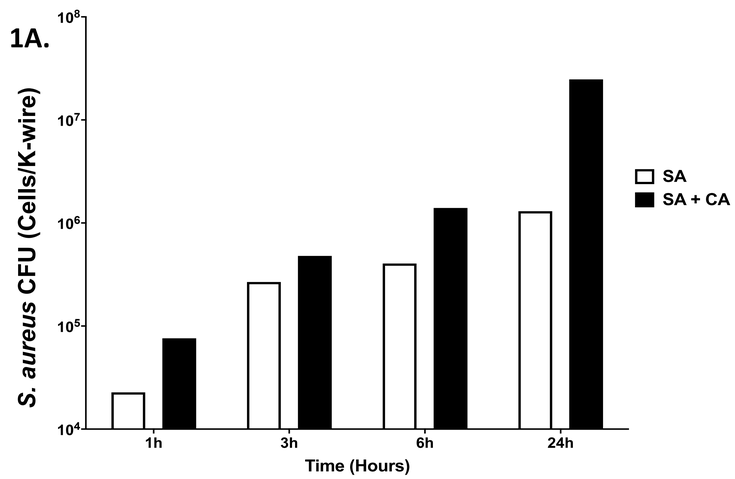
Results



In-vitro

1B.

Minimum inhibitory concentration (MIC) assay		
	VAN (ug/ml)	VAN (ug/ml) (in combination with AMB)
SA	800	800
SA+CA	>3200	1600 (Van)+16 (AMB)

1C.

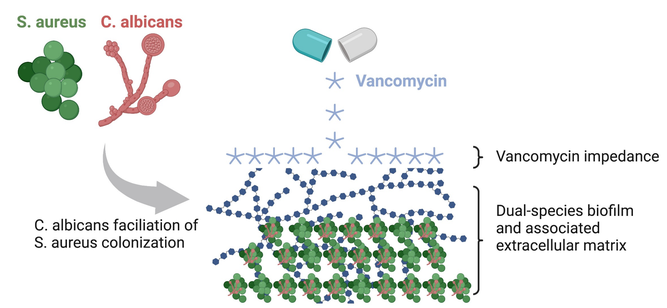


Figure 1. (A) Incubation of SA alone and SA + CA on stainless steel pins showed significantly higher SA CFU in the co-infection group.
(B) MIC assay showed reduction in SA vancomycin susceptibility when co-infected with CA.
(C) Illustration of SA and CA synergy leading to increased SA colonization and decreased SA vancomycin susceptibility.

In-vivo

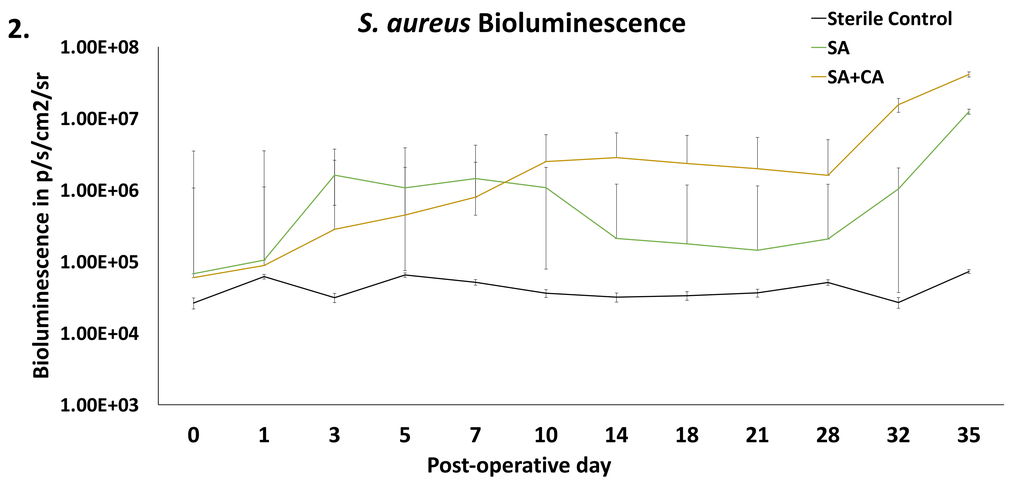


Figure 2. Bioluminescent signal over time representing SA bacterial infection.
Co-infection of SA with fungal pathogen CA increased the infection of this bacterial pathogen.

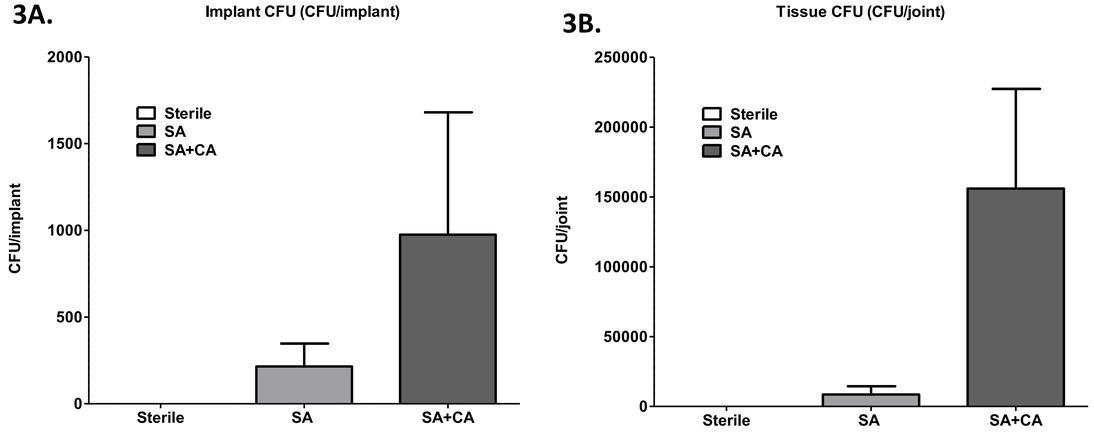


Figure 3. In-vivo SA CFU results at POD35 for (A) spine implants and (B) soft tissue.

CFUs were 0.5-log and 1.5 log greater in the SA+CA co-infection group compared to the SA only group for implant and tissue, respectively.