CXCR2 perturbation promotes *Staphylococcus aureus* implant-associated infection

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MICROBIOLOGY, IMMUNOLOGY, AND PATHOLOGY

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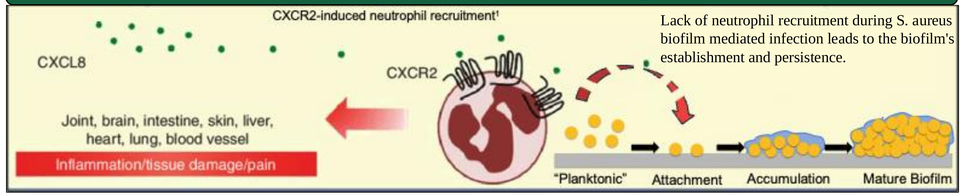
Background:

- *Staphylococcus aureus* is a major pathogen causing healthcare- and community-associated infections, including skin infections, sepsis, and osteomyelitis.[2] In patients with implanted medical devices, it poses a higher infection risk, leading to increased mortality, longer hospital stays, and significant healthcare costs.[3]
- Previous studies showed that *S. aureus* biofilms disrupt neutrophil chemotaxis, altering their migration patterns to prevent biofilm clearance. [4]
- This study investigates CXCR2 signaling in neutrophils as a potential novel approach to reduce morbidity and mortality from *S. aureus* biofilm-related implant infections.

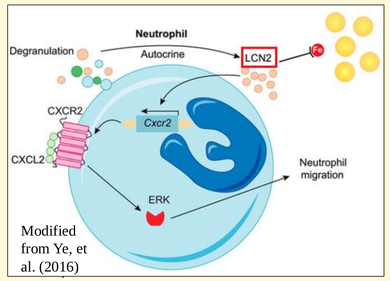
Overview:

CXCR2 interactions on neutrophils:



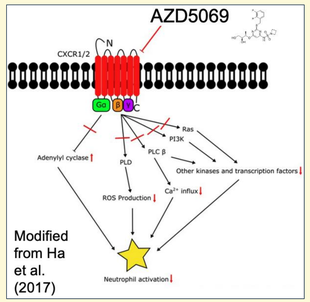
Lack of neutrophil recruitment during S. aureus biofilm mediated infection leads to the biofilm's establishment and persistence.

Lcn2 as a CXCR2 Inducer



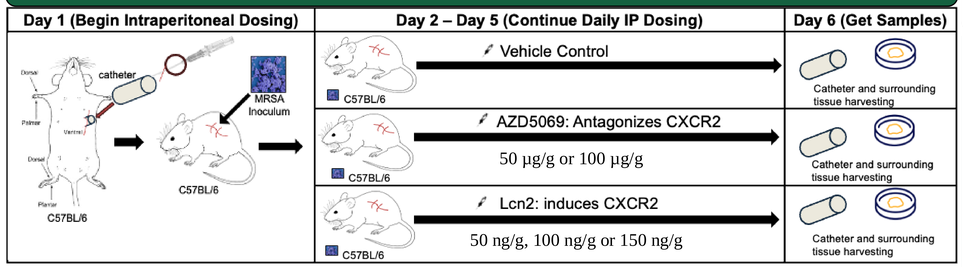
Modified from Ye, et al. (2016)

AZD5069 as a CXCR2 Antagonist



Modified from Ha et al. (2017)

Methods:



Results:

Lcn2 promotes spread of *S. aureus* from biofilm into soft tissue:

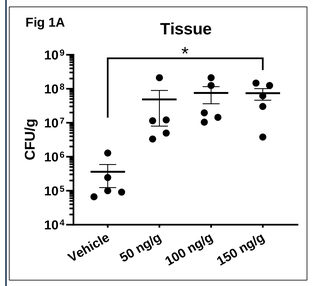


Fig 1A Bacterial burden associated with surrounding tissue infection

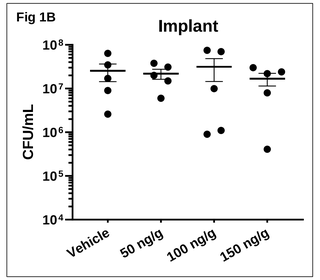


Fig 1B Bacterial burden associated with implant infection

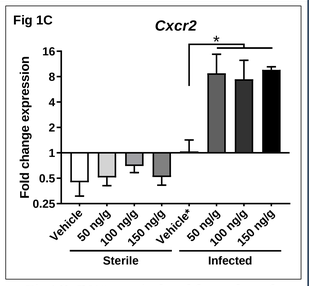
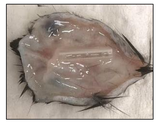
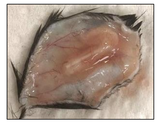


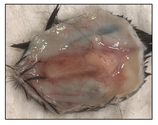
Fig 1C RNA was isolated from the soft tissues and *Cxcr2* expression quantified



Vehicle

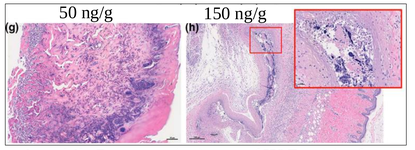


50 ng/g



150 ng/g

Gross tissue specimens from MRSA-infected subcutaneous catheters show increased surrounding tissue inflammation with higher Lcn2 doses



1g and 1h: Representative images of H&E staining for histopathology

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AZD5069 promotes *S. aureus* biofilm infection development:

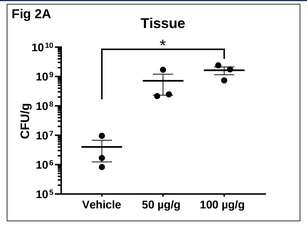


Fig 2A Bacterial burden associated with surrounding tissue infection

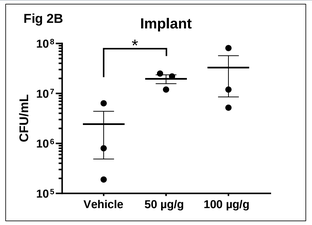


Fig 2B Bacterial burden associated with surrounding implant infection

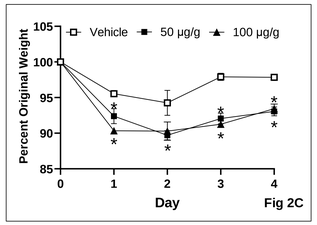


Fig 2C Animal weights during the study were recorded as a measure of health

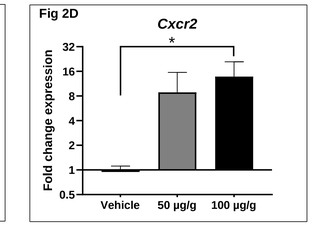
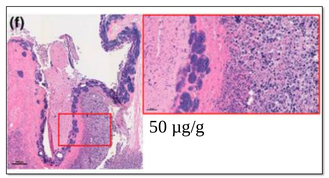
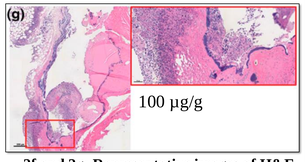


Fig 2D RNA was isolated from the soft tissues and *Cxcr2* expression quantified





2f and 2g: Representative images of H&E staining for histopathology

Discussion/Conclusions:

- CXCR2 is vital for controlling *S. aureus* implant infections, with both induction and inhibition leading to higher bacterial burdens, indicating the need for balanced CXCR2 signaling.
- Modulating CXCR2 activity with Lcn2 or AZD5069 may worsen infections, underscoring the need for further research to develop targeted treatments.