Gut Microbiome Diversity Impacts the Response to Periprosthetic Joint Infection

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Background

Commensal gut bacteria support host immune function by promoting cytokine production, myelopoiesis and wound healing. Gut microbiome diversity is decreased by antibiotic exposure. This study aimed to investigate how gut microbiome diversity, depleted by antibiotics, or supported by probiotics, affects the immune response to periprosthetic joint infection (PJI), in a pre-clinical model.

Methods

Mice were randomized into four groups: sterile (n=2), infected control (IC; n=4), antibiotic-treated (Abx; n=4) and Co-treated (Co-Tx; n=4). Subjects underwent four weeks of pre-operative treatment consisting of ampicillin and neomycin (Abx group), ampicillin, neomycin and probiotics (Co-Tx group), or no treatment (sterile and IC groups). Surgery consisted of placement of a titanium pin into the right distal femur. The distal aspect of the implant was inoculated with 1000 colony forming units of bioluminescent *Staphylococcus aureus* in the IC, Abx, and Co-Tx groups. Bacterial burden was quantified via bioluminescence imaging from post-operative day (POD) 0-28. Stool samples were collected on POD0 and POD28, and gut microbiome diversity was examined via 16s sequencing.

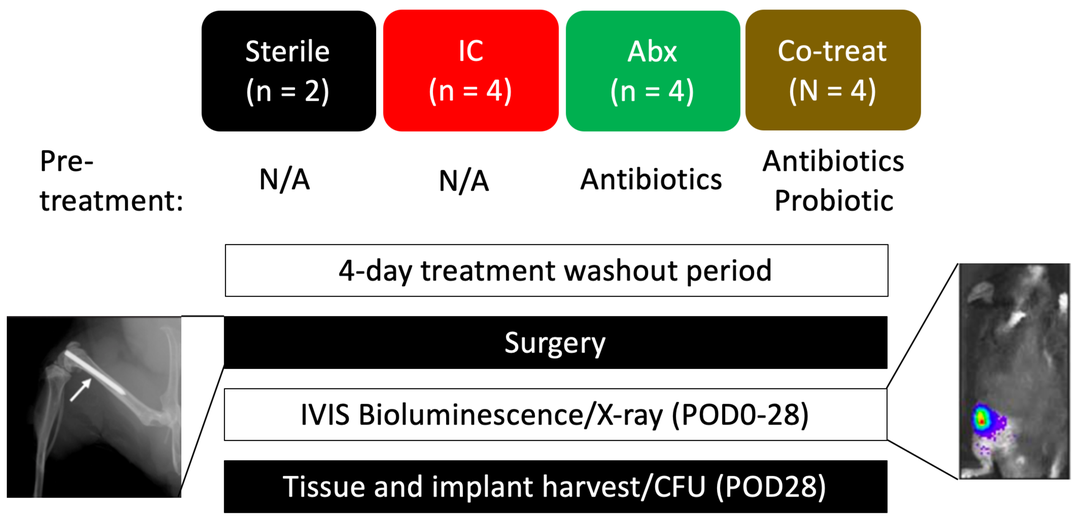

Figure 1: Experimental overview showing treatment groups, representative x-ray demonstrating proper implant placement (bottom left), and example of bioluminescence imaging (bottom right).

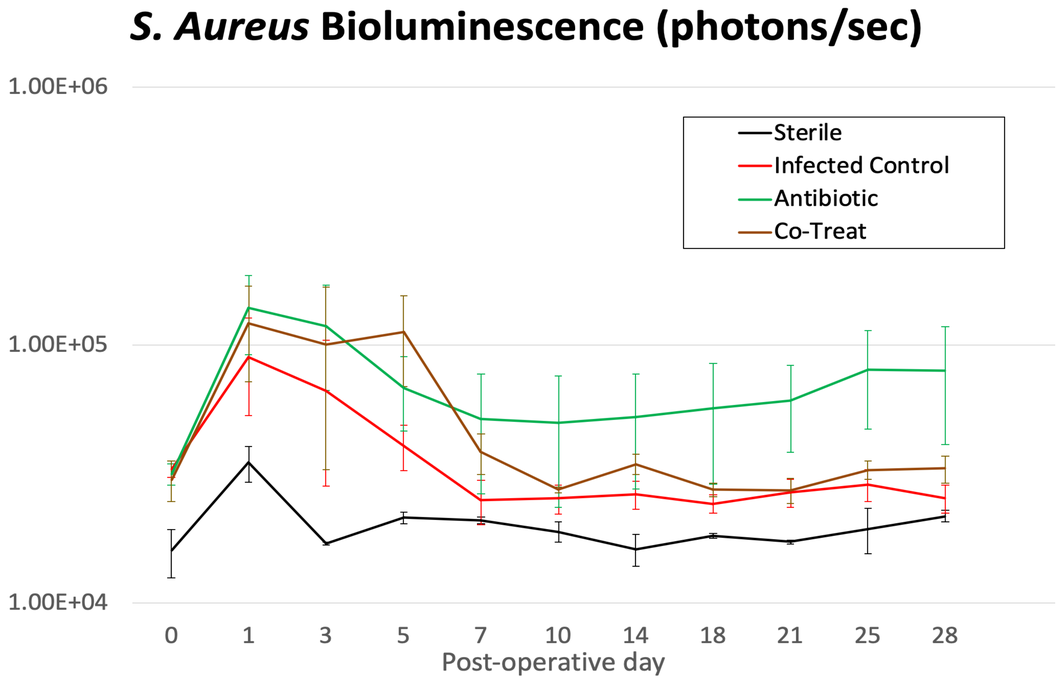

Figure 2: In vivo *S. aureus* burden demonstrating increased bacterial load in antibiotic pre-treated mice.

Results

As measured by Chao1 diversity, compared to the IC group, gut microbiome diversity was significantly decreased in the Abx group ($p<0.001$), but not in the Co-Tx group ($p>0.05$). Compared to the IC group, as measured by bioluminescence imaging, bacterial burden was higher in the Abx group at all time points after POD0. Bacterial burden in the Co-Tx group was greater than in the IC group from POD1-7, but was similar to that of the IC group at all later time points.

Discussion

This study demonstrates that gut microbiome diversity may play a role in supporting the ability to mount an effective immune response to PJI. This study underscores the need to consider the totality of the impact of medical interventions, and to better understand the mechanisms underlying the beneficial contributions of a diverse gut microbiome.

References

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