

Microbial Interspecies Associations in Open Fracture and Subsequent Infection Using Next Generation Sequencing

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Purpose: Multispecies interactions and polymicrobial biofilm formation (both on foreign material as well as bone and soft tissue) are poorly understood but are increasingly thought to be prognostically important. The purpose of this study was to evaluate the co-occurrence or clustering of microbial taxa in open fracture and subsequent fracture related infection wounds using data derived from next generation sequencing (NGS). Our hypothesis is that specific microbes that tend to co-occur are likely to demonstrate synergistic and potentially clinically relevant intermicrobial interactions.

Methods: This is a secondary analysis of patients enrolled in the METRC Bioburden Study with polymicrobial NGS results (n = 94 total, 55 baseline open fracture patients, and 39 follow-up infection or nonunion patients). Baseline open fracture wound specimens were collected at time of definitive wound closure. The primary outcome was number of co-occurring microbial pairs. Number of co-occurrences in this cohort was totaled to create a heat map.

Results: Among polymicrobial open fracture wounds probed at definitive wound closure, there were no microbe species pairs that co-occurred together in more than 4 patients. However, there were many low-frequency (51 unique) co-occurring pairs of species. In follow-up specimens collected at time of nonunion or infection, there were 4 dominant co-occurring microbial species that were each seen in 8-16 patients (Staphylococcus-Enterococcus (12%), Staphylococcus-Enterobacter (9%), Staphylococcus-Serratia (6%) and Staphylococcus-Streptococcus (7%)) and accounted for 30% of all follow-up infections (some polymicrobial infections contained more than one microbial pair).

Conclusion: The present study indicates that among polymicrobial specimens, there was a conversion from a diverse array of polymicrobial species in the baseline open fracture specimens to a very dominant Staphylococcus-Enterococcus, Staphylococcus-Enterobacter, Staphylococcus-Serratia or Staphylococcus-Streptococcus co-occurring species. These frequent microbial co-occurrences in patients with infection likely represent an evolutionary or survival benefit associated with these microorganisms. Understanding and potentially disrupting these antimicrobial relationships could result in improvement in both prevention and treatment for infection.

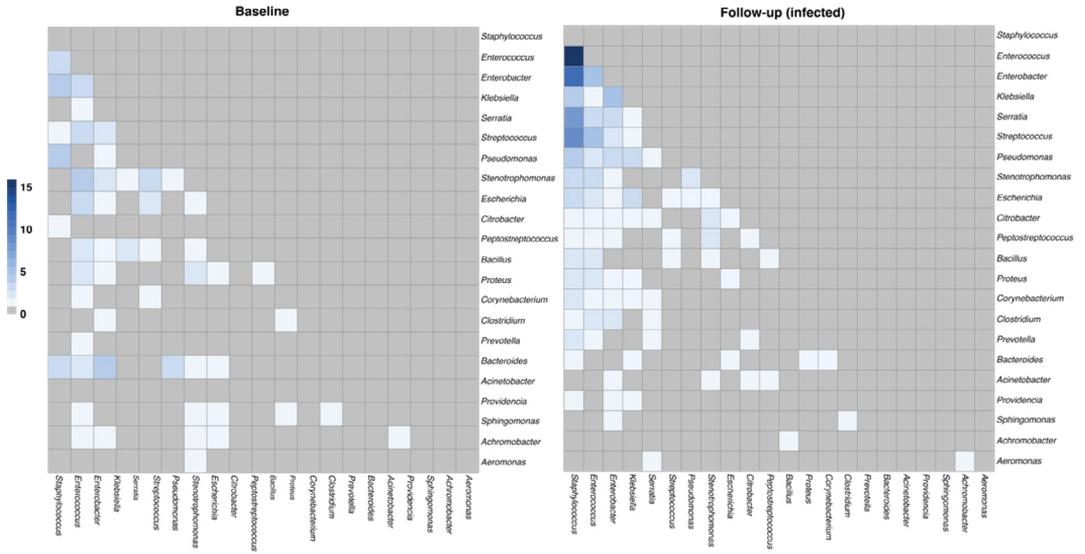


Figure. Heatmap indicating the frequency of co-occurring of the genera listed from baseline (left) and follow-up (right, infected) specimens from the Bioburden cohort.