

SUPPLEMENTARY DATA

Supplementary Table 1. Co-variation of *Staphylococcus aureus* relative abundance with anaerobic species-level taxa and *Corynebacterium* relative abundance. Rho (ρ) represents the Spearman rank correlation coefficient. *P*-values were calculated by a permutation test. These *P*-values were then corrected for multiple testing by applying false discovery rate (FDR) control ($q=0.05$).

| | ρ | <i>P</i> -value | FDR-adjusted <i>P</i> -value |
|----------------------------------|--------|-----------------|---------------------------------|
| Anaerococcus | -0.43 | 0.001 | 0.038 |
| Anaerococcus.1 | -0.42 | 0.002 | 0.047 |
| Anaerococcus.2 | -0.46 | 0.001 | 0.024 |
| Clostridium | -0.06 | 0.657 | 0.917 |
| Enterococcus | -0.15 | 0.293 | 0.731 |
| Fastidiosipila | -0.18 | 0.194 | 0.631 |
| Finegoldia | -0.15 | 0.284 | 0.725 |
| Fusobacterium | -0.16 | 0.245 | 0.693 |
| Gemella | -0.10 | 0.460 | 0.844 |
| Helcococcus | -0.30 | 0.030 | 0.248 |
| Helcococcus.1 | -0.40 | 0.003 | 0.061 |
| Parvimonas | -0.43 | 0.002 | 0.042 |
| Peptoniphilus | -0.34 | 0.013 | 0.156 |
| Peptostreptococcus | -0.35 | 0.011 | 0.135 |
| Porphyromonas | -0.48 | <0.001 | 0.014 |
| Porphyromonas.1 | -0.22 | 0.124 | 0.531 |
| Porphyromonas.2 | -0.41 | 0.002 | 0.051 |
| Prevotella | -0.38 | 0.005 | 0.082 |
| Prevotella.1 | -0.51 | <0.001 | 0.007 |
| unclassified.Clostridiales | -0.51 | <0.001 | 0.006 |
| unclassified.Clostridiales.1 | -0.10 | 0.469 | 0.848 |
| unclassified.Incertae.Sedis.XI | -0.38 | 0.006 | 0.089 |
| unclassified.Incertae.Sedis.XI.1 | -0.17 | 0.223 | 0.663 |
| Veillonella | 0.14 | 0.325 | 0.753 |
| Corynebacterium | 0.47 | <0.001 | 0.02 |
| Corynebacterium.1 | -0.05 | 0.703 | 0.93 |
| Corynebacterium.2 | 0.30 | 0.031 | 0.26 |

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Supplementary Table 2. Analysis of molecular variance (AMOVA) F statistic values and Bonferroni corrected *P*-values. AMOVA was performed on data clustered by the weighted and unweighted UniFrac metric, the Jaccard index, and the Theta index. The UniFrac metric measures shared phylogeny among samples, weighted or unweighted for abundance. The Jaccard index measures shared community membership. The Theta index measures shared community structure. AMOVA detects differences in microbial communities (as measured by the above metrics) with respect to the clinical factor specified. *P*-values are adjusted for multiple testing using a Bonferroni correction.

| | UniFrac-weighted | | UniFrac-unweighted | | Jaccard | | Theta | |
|----------------|------------------|---------|--------------------|---------|---------|---------|-------|---------|
| | Fs | p-value | Fs | p-value | Fs | p-value | Fs | p-value |
| Depth | 1.31 | 0.06 | 1.03 | 0.27 | 0.99 | 0.60 | 1.35 | 0.02 |
| Hemoglobin A1c | 1.30 | 0.05 | 1.02 | 0.30 | 1.06 | 0.11 | 1.19 | 0.10 |
| Tissue oxygen | 0.71 | 0.94 | 1.01 | 0.45 | 1.01 | 0.40 | 0.87 | 0.73 |
| Necrosis | 1.82 | 0.01 | 1.01 | 0.44 | 0.94 | 0.75 | 1.38 | 0.07 |
| Surface area | 1.32 | 0.12 | 0.85 | 0.99 | 0.93 | 0.90 | 1.27 | 0.12 |
| Duration | 1.20 | 0.12 | 0.98 | 0.67 | 0.97 | 0.77 | 1.21 | 0.08 |

Supplementary Table 3. Spearman correlation coefficients (ρ) between DFU clinical factors and bacterial diversity and dominant bacterial taxa. * Indicates significance at a threshold of $P < 0.05$ by permutation test.

| | Staphylococcus | Streptococcus | Proteobacteria | Anaerobes | Shannon Index | Richness |
|---------------|----------------|---------------|----------------|-----------|---------------|----------|
| Duration | -0.31* | 0.12 | 0.38* | 0.05 | 0.32* | 0.41* |
| Depth | -0.47* | 0.11 | 0.25 | 0.33* | 0.27* | 0.16 |
| HGBA1c | 0.07 | 0.18 | -0.22 | -0.07 | -0.18 | -0.06 |
| Necrosis | -0.16 | -0.05 | -0.08 | 0.15 | 0.20 | 0.11 |
| Tissue oxygen | -0.12 | -0.04 | 0.12 | 0.11 | 0.21 | 0.24 |
| Surface area | -0.26 | 0.11 | 0.20 | 0.23 | 0.24 | 0.27* |

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Supplementary Figure 1. Co-variation of species-level OTUs colonizing DFUs. Spearman rank correlation coefficients were calculated for the 72 taxa present in >10% of DFU samples and containing greater than 100 sequence counts. Purple and red denote positive and negative correlation, respectively. Columns and rows were hierarchically clustered, as indicated by the dendrograms at the top and to the left of the heatmap. OTUs are classified as Staphylococcus, Anaerobes, Proteobacteria, Streptococcus, or Other, and are indicated by the color strips at the bottom and to the left of the heatmap. Rho values significant after false discovery rate (FDR) control of 5% are indicated by dots.

