Comparison of Oral Microbiome In Stable vs Declining Kidney Function In Renal Transplant Recipients

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Introduction

- Transplantation causes dysbiosis of the oral microbiome and has been correlated with worse allograft outcomes.
- Hypothesis: There are differences in dental subgingival plaque microbes between renal transplant recipients with stable versus declining allograft function.

Primary Objective:
- To compare the subgingival dental plaque taxa of renal transplant recipients with stable versus declining allograft function.

Secondary Objective:
- To compare transplant subjects’ plaque and other oral microbiomes to those of healthy subjects.

Methods

- Case-control study evaluated subgingival plaque samples from 20 adult patients from two existing prospective study cohorts (DeKAF Genomics) at the University of Minnesota in Minneapolis, MN.
- Stable kidney function (SKF): creatinine (SCr) stable from 3 month post-tx baseline
- Declining kidney function (DKF): SCr ≥ 25% above 3 month post-tx baseline
- DNA extracted from plaque and other oral sites (nasal, buccal swab, hard palate, tongue), amplified, and compared to 16S V4 bacterial rRNA libraries.
- Healthy subject data taken from the Human Microbiome Project (HMP) 16S V3V5 rRNA.
- Samples were grouped into operational taxonomic units (OTUs) and compared to known reference libraries of microorganisms.

Statistical Analysis

- For each individual OTU, we applied the Wilcoxon rank-sum test to compare differences between SKF and DKF groups.
- We also looked at the aggregated OTU distribution difference at the genus level between the two groups using the kernel RV test.

Results

Selected participant data is listed below.

Table 1: Selected demographics of study participants

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>SKF (n=15)</th>
<th>DKF (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>8 (53.3%)</td>
<td>11 (100%)</td>
</tr>
<tr>
<td>Multiracial</td>
<td>7 (46.7%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Sex:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>7 (46.7%)</td>
<td>2 (18.2%)</td>
</tr>
<tr>
<td>Female</td>
<td>8 (53.3%)</td>
<td>9 (81.8%)</td>
</tr>
<tr>
<td>Donor age, mean (std)</td>
<td>41.3 (12.8)</td>
<td>44.6 (11.9)</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>1.01 (0.25)</td>
<td>1.76 (0.49)</td>
</tr>
</tbody>
</table>

Subgingival Plaque in SKF vs DKF

- In 11 cases of DKF, genus Tannerella was more prevalent in subgingival plaque samples compared to those with SKF (p=0.046, KRV – not significant if FDR 0.05).
- By oligotyping, Tannerella forsythia.

Subgingival Plaque in HMP vs Transplant

- 20 transplant (TX) recipient subgingival plaque samples were compared to 30 healthy subjects found in the Human Microbiome Project (HMP).
- The overall subgingival plaque microbiome is significantly different in TX vs HMP hosts (KRV, p=1.28x10^-12).

Conclusions

- There are distinct signatures in the subgingival plaque of renal transplant recipients compared to those of healthy subjects.
- There is a significant prevalence of both Cellulosimicrobium and Pseudomonas in the non-plaque oral sites of transplant recipients compared to healthy hosts (Wilcoxon, p<0.0001).
- There is a non-significant greater prevalence of Tannerella forsythia in the plaque of DKF vs SKF renal transplant recipients (KRV, p=0.046, not significant if FDR 0.05).

References