Machine Learning Approach Identifies Dysbiotic Oral Communities in Multiple Sclerosis

Feb 13th 2024
Objective

Uncover the oral microbial signatures of Relapsing Remitting Multiple Sclerosis
Multiple Sclerosis

- Neurodegenerative autoimmune disease of the CNS
- 2.8 million people worldwide
- Relapsing-Remitting makes up 85% of all MS cases
- Myelin sheath is attacked by immune cells and the regeneration is limited
- Linked to genetics and environment
  - Gut microbiome

Image from the National Multiple Sclerosis Society
Oral Microbiome

• Linked to neurodegenerative diseases
  • Alzheimer’s
  • Parkinson’s
• After gut, 2nd most diverse microbiome
  • ~700 bacterial species
• Limited current MS research (3 papers)
  • Small sample sizes
  • Only genus level resolution

Methods

- **Cohort**
  - RRMS, adults from the University of Iowa MS Clinic
  - HC, adults from the University of Iowa College of Nursing
    - No autoimmune disease or prior oral health conditions
  - Quit smoking at least 10 years ago (n=5), or never smoked
  - No antibiotics within the last 3 months

- **Saliva collection in clinic**
- **Shotgun metagenomic sequencing**
- **Data analysis with Argon and R**

<table>
<thead>
<tr>
<th></th>
<th>RRMS (n=48)</th>
<th>HC (n=49)</th>
<th>Stats</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BMI (avg +/- sd)</strong></td>
<td>28.68 +/- 5.16</td>
<td>26.21 +/- 5.36</td>
<td>Linear Regression (n.s.) *</td>
</tr>
<tr>
<td><strong>Age (avg +/- sd)</strong></td>
<td>42.02 +/- 8.64</td>
<td>43.08 +/- 18.66</td>
<td>T.test, p = 0.7197</td>
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<tr>
<td><strong>Female/Male/Intersex</strong></td>
<td>43:5:0</td>
<td>28:21:0</td>
<td>Linear Regression (n.s.) *</td>
</tr>
</tbody>
</table>

* Linear regression showed no significant difference at the species level
Is bacterial diversity altered in RRMS?

- Observe the richness and evenness of the present bacteria as well as the community structure.
- Alpha (Shannon) and beta (Aitchison) diversity significantly different between HC and RRMS.
What specific species are altered in RRMS?

- 96 bacteria significantly altered
  - 46 higher in RRMS
  - 50 higher in HC
What specific species are altered in RRMS?

- 96 bacteria significantly altered
  - 46 higher in RRMS
  - 50 higher in HC
- 28 *Streptococcus* species lower in RRMS
  - 1st inhabitants
  - Predominate the OM
  - High abundance associated with “health” in subgingival plaque studies *
  - *S. sanguinis* produces $H_2O_2$
What about the *community* of bacteria?

- Micro-ecosystem
  - Gene expression
  - Resources
- Topic Modeling: Unsupervised machine learning
  - Discover key patterns or themes within a set of data
- Community Patterns
What about the community of bacteria?

- Ideal topic number
- Built topic model with 33 topics
- 5 topics significantly more often assigned HC samples
5 significant bacterial communities

- Ideal topic number
- Built topic model with 33 topics
- 5 topics significantly more often assigned to HC samples
Topic 28 most often assigned to HC

- *S. salivarius* most often assigned species
- *S. parasanguinis* and *S. sanguinis* were associated with “health” in microbiome studies
- *P. melaninogenica* increased in oral microbiome of patients with RA and AD
- *V. parvula* and *S. gordonii* coaggregate and alter gene of one another

![Image of a heat map representing the community type 28 with Log2FC 6.442 in HC (p=1e-05 q=0.00044).]
Conclusions

• First oral microbiome study with:
  – large cohort of RRMS patients
  – Shotgun metagenomics
  – Unveiling dysbiotic communities linked to RRMS

• Many oral bacteria are linked to RRMS
  – Streptococcus species of interest
  – Coaggregation of species
  – Overlap with other chronic inflammatory diseases

• Future direction: Utilize a mouse model to explore if healthy communities (topics) can reduce severity of disease
Thank you!

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