

IOWA

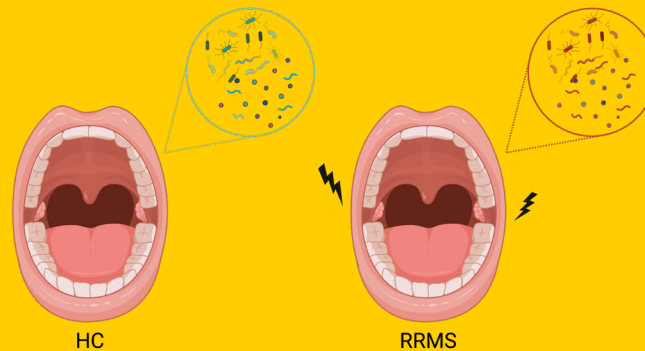
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Machine Learning Approach Identifies Dysbiotic Oral Communities in Multiple Sclerosis

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

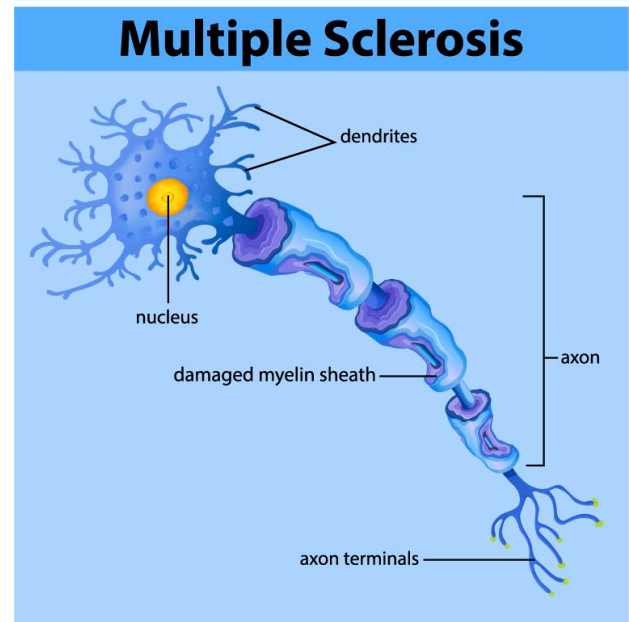
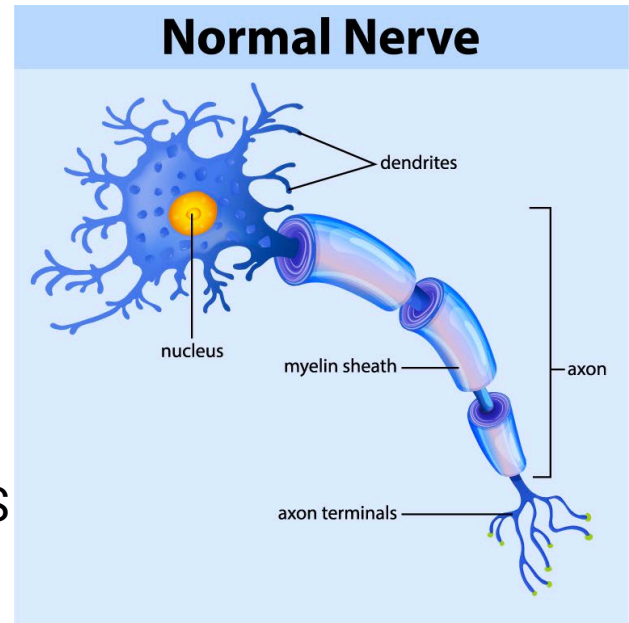


Image from the National Multiple Sclerosis Society

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

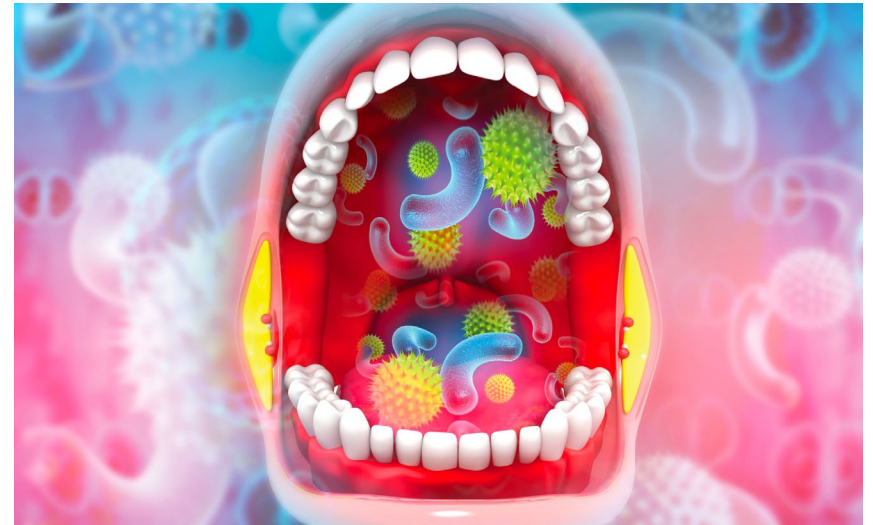


Image <https://www.dentalproductsreport.com/view/9-members-of-the-oral-microbiome-rogues-gallery>

Methods

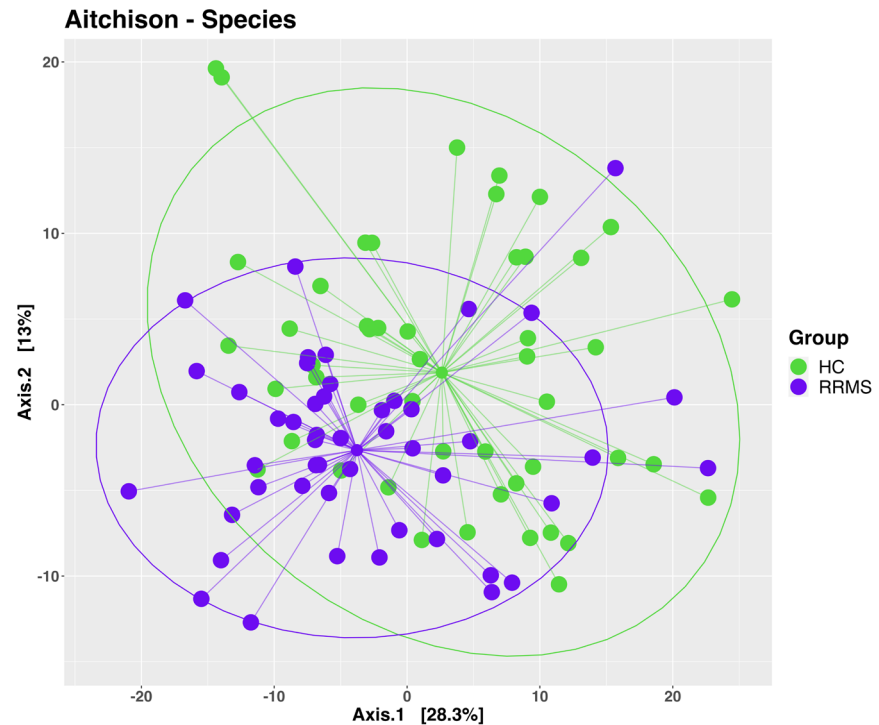
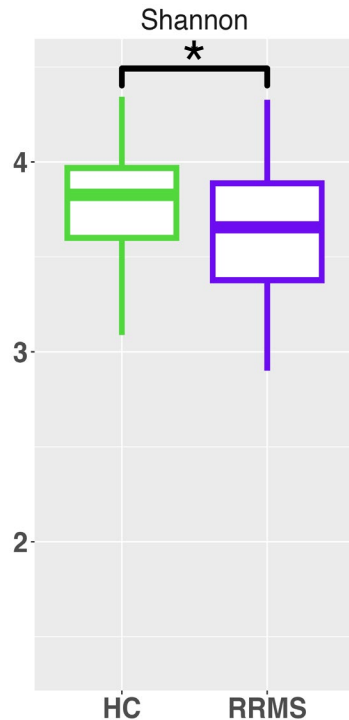
- Cohort
 - RRMS, adults from the University of Iowa MS Clinic
 - HC, adults from the University of Iowa College of Nursing
 - No autoimmune disease or prior oral health conditions
 - Quit smoking at least 10 years ago (n=5), or never smoked
 - No antibiotics within the last 3 months
- Saliva collection in clinic
- Shotgun metagenomic sequencing
- Data analysis with Argon and R

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

* Linear regression showed no significant difference at the species level

Is bacterial diversity altered in RRMS?

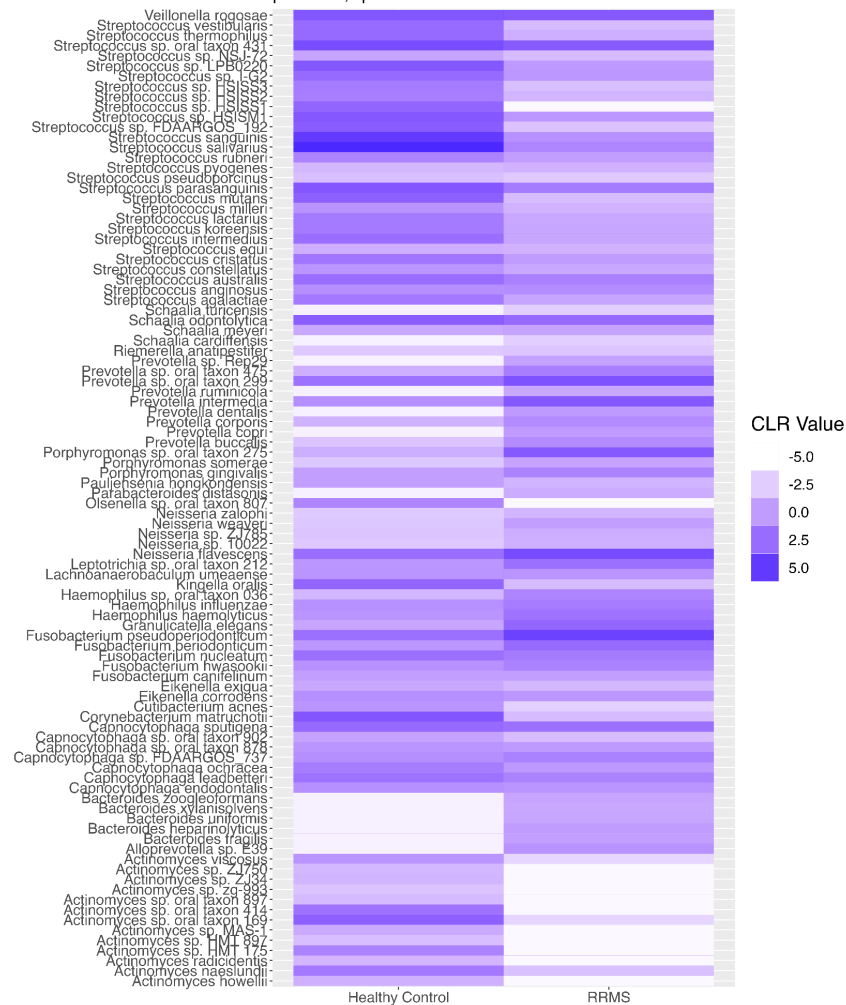
- Observe the richness and evenness of the present bacteria as well as the community structure
- Alpha (Shannon) and beta (Aitchison) diversity significantly different between HC and RRMS



What specific species are altered in RRMS?

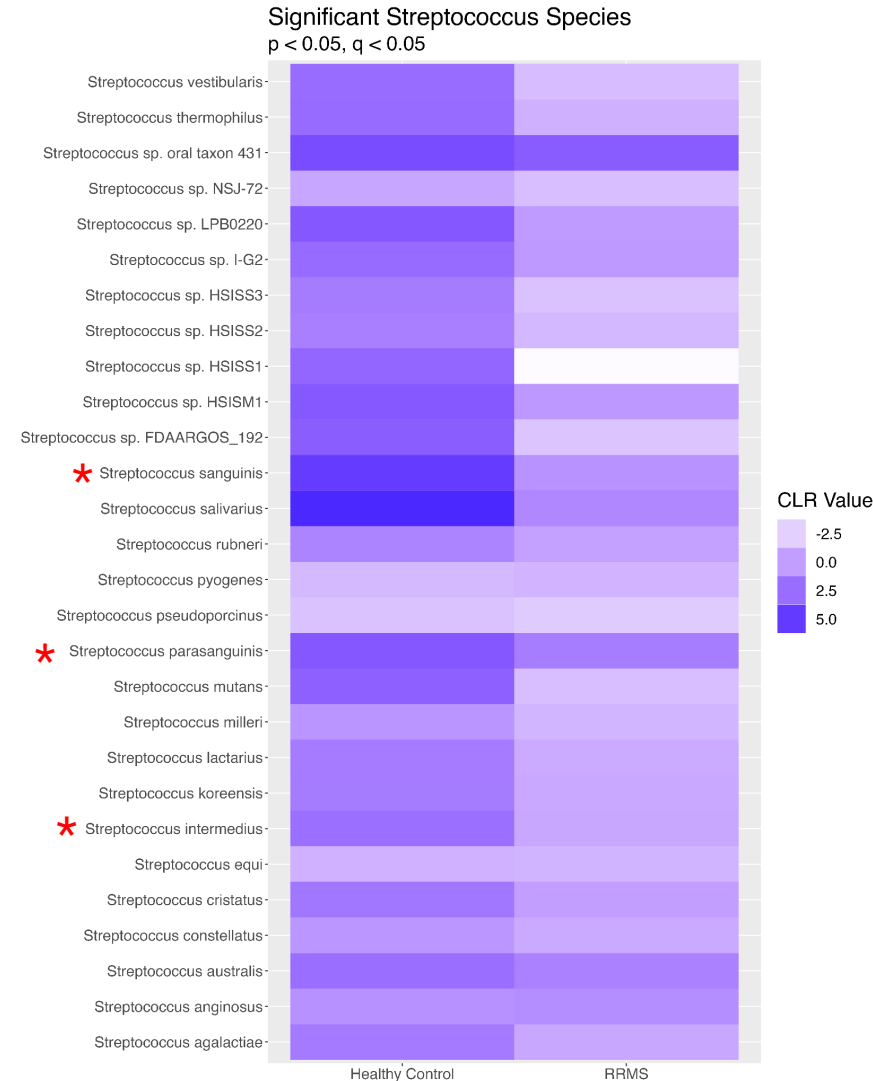
- 96 bacteria significantly altered
 - 46 higher in RRMS
 - 50 higher in HC

Wilcox Significant Species
 $p < 0.05, q < 0.05$



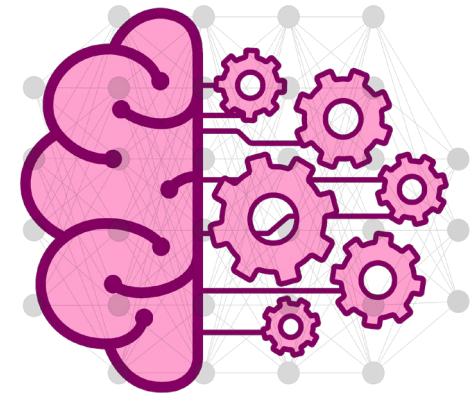
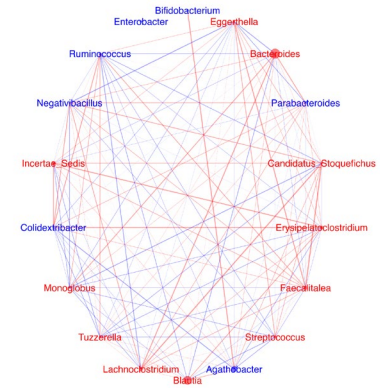
What specific species are altered in RRMS?

- 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



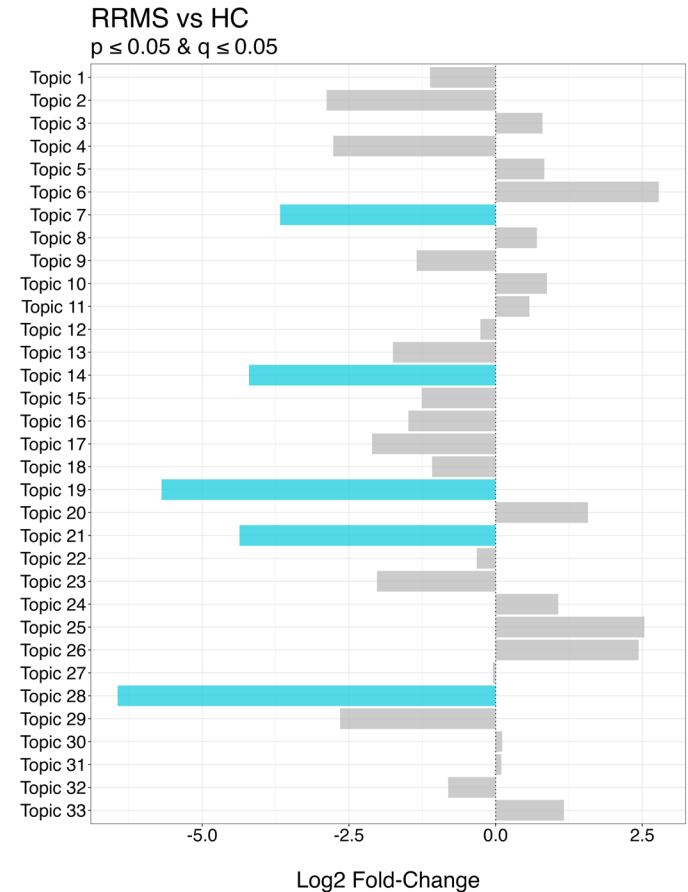
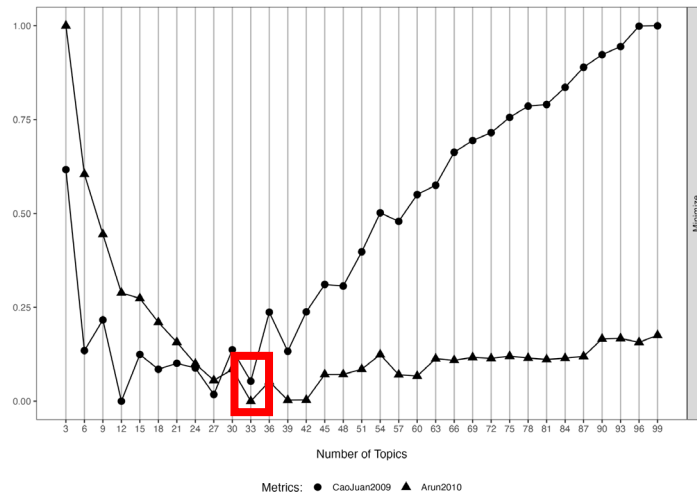
What about the *community* of bacteria?

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



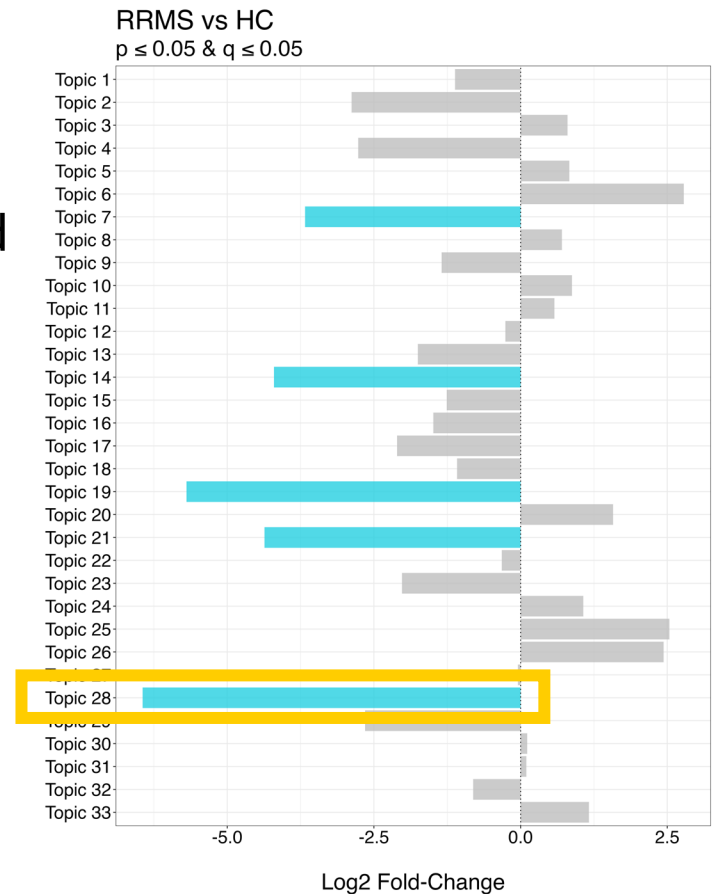
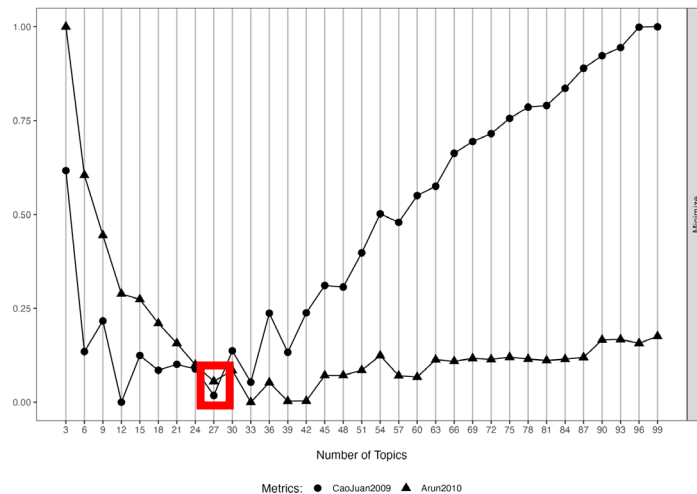
What about the *community* of bacteria?

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



5 significant bacterial communities

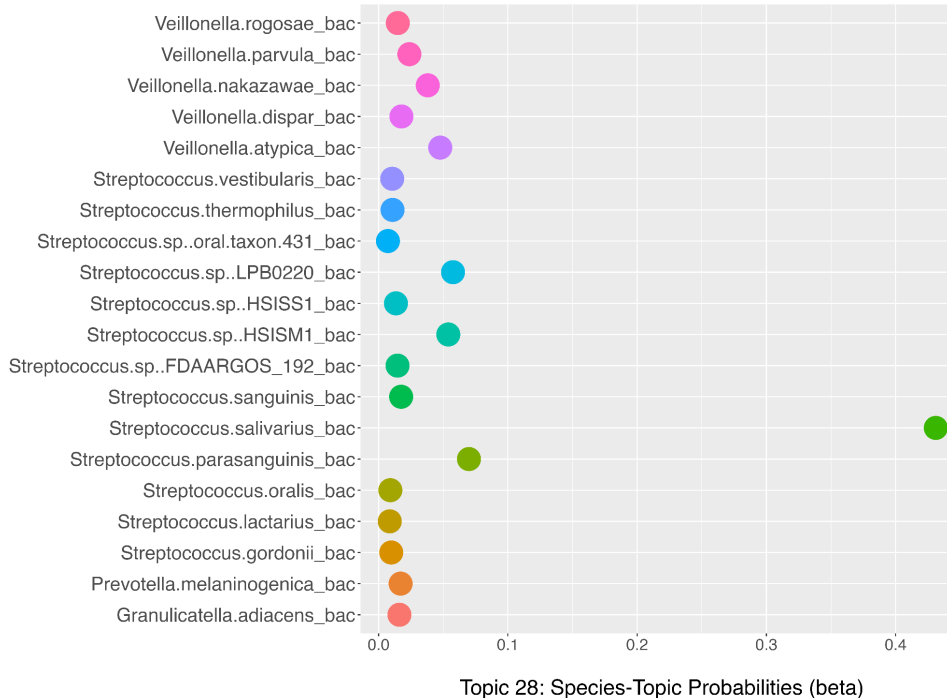
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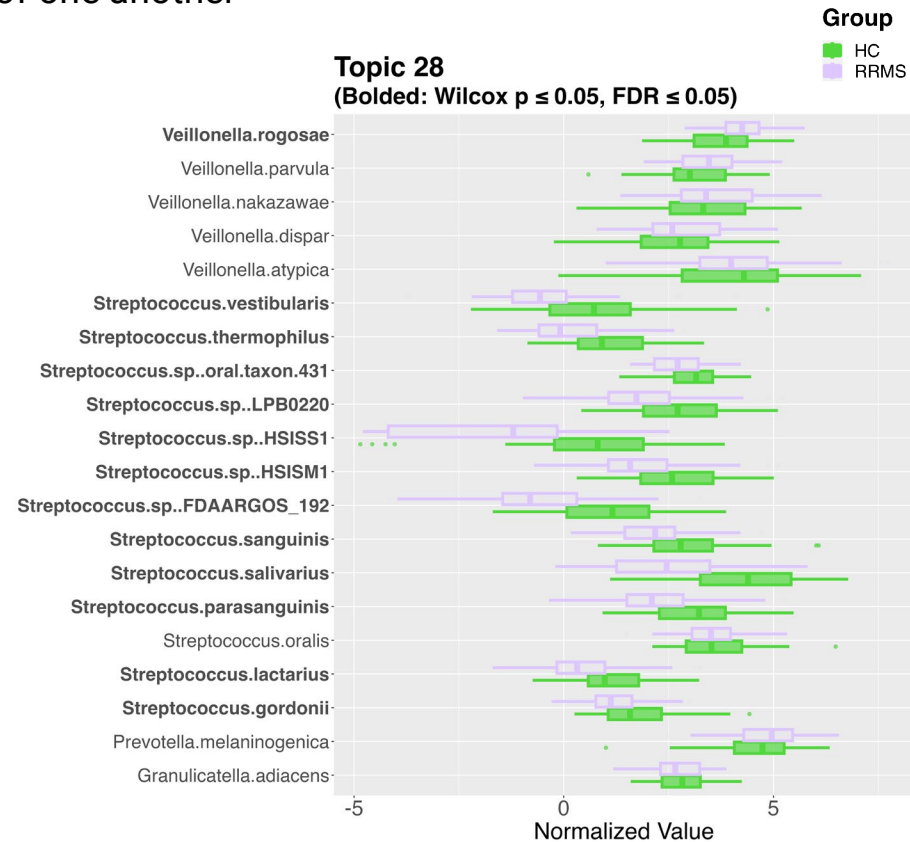
Topic 28 most often assigned to HC

- *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

Community Type 28
Log2FC 6.442 in HC ($p=1e-05$ $q=0.00044$)



Topic 28
(**Bolded: Wilcox $p \leq 0.05$, FDR ≤ 0.05**)



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

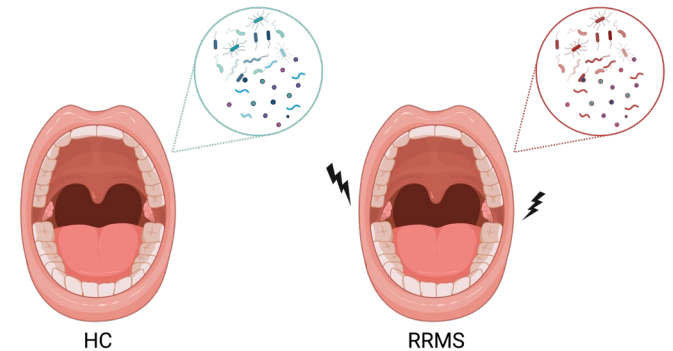


Image made with BioRender

Thank you!

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- Dr. Albert Erives
- Mangalam Lab

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