Chronic Rhinosinusitis and Disturbed Microbial Homeostasis

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Chronic Sinusitus (CRS)

- Chronic sinus inflammation affects 30 million Americans annually
- Persistent inflammation of the paranasal sinuses lasting > 12 weeks.
- Sinus pressure
- Headache
- Breathing difficulties
- Lost sense of smell/taste

Sinus Microbiology

- Single species studies
- In vitro examination

Bacterial and fungal species implicated:
- Staphylococcus
- Streptococcus
- Moraxella
- Mycobacterium spp.
- Aspergillus spp.

Culture-Independent Microbial Analyses

"The great plate count anomaly"

- Small subunit rRNA (16S rRNA)

The Human (Bacterial) Microbiome

- Composition
  10%
- Function
  1%

Microbiome contributes functions critical to host health:
- Metabolism of indigestible carbohydrates
- Vitamin and hormone production
- Immune development
- Immune homeostasis
- Ancillary mucosal protection
- Microbiome dysbiosis associated with chronic inflammatory diseases
**Sinus Microbiome**

- Surgical samples obtained from twenty patients
- 10 CRS patients, 10 healthy control
- Undergoing open maxillary sinus surgery
- Varying pre-operative antimicrobial administration

*16S rRNA-based bacterial burden was not significantly different between CRS and healthy groups*

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**CRS is Associated with Microbiome Collapse**

- **Loss of microbiota membership and structure in CRS patients**

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**CRS Microbiome Tracks with Disease Status**

- Community composition tracks is associated with sinus health status Based on SNOT-20 score
- Antibiotics are not the primary driver of community membership
- Nasal allergy microbiome similar to CRS
Specific Bacteria Characterize Health Status

- Pseudomonadaceae, Lachnospiraceae, Ralstoniaceae, Mycobacteriaceae and Helicobacteriaceae detected in both groups.
- > 1,000 bacterial types depleted in CRS ptx.
  - Loss of Lactobacillales
    - Phylogenetically distinct Lactic Acid Bacteria
      - Carnobacterium, Enterococcus, Pediococcus spp.
    - Lactobacillus sakei (t value = 7.036; p < 0.00002; q < 0.00014)
  - Single taxon significantly increased in relative abundance in CRS ptx.
    - Actinobacteria
      - Corynebacterium tuberculostearicum (t value = -2.652; p < 0.034; q < 0.003)

Specific Bacteria Are Related to SNOT-20 Score

- Correlations between SNOT-20 score and taxon relative abundance
- Total of 228 taxa significantly negatively correlated SNOT-20 scores:
  - Lactic acid bacteria
    - Lactobacillus sakei (r = -0.620; p < 0.018; q < 0.035)
  - Taxa positively correlated with SNOT-20:
    - C. tuberculostearicum (r = 0.622; p < 0.018; q < 0.035)
    - C. segmentosum (r = 0.551; p < 0.041; q < 0.035)

Corynebacterium tuberculostearicum

- Gram-positive, rod/club-shaped bacterium (Actinobacteria)
- Non-motile, non-spore-forming, aerobic/facultative anaerobe
- Fatty acid profile contains tuberculostearic acid
- Do not typically cause disease
  - Part of normal human skin microbiome
  - Related to other pathogenic groups
Sinus Mouse Model

Sinus Mucosal Pathogenesis and Protection

Summary

- Sinuses house a diverse microbiome
- Microbiome composition is related to sinus health
- Microbiome collapse is associated with chronic sinusitis
- Loss of protective Lactic acid bacteria is a hallmark of chronic disease
- Corynebacterium tuberculostearicum represents an overlooked pathogen in CRS

• C. tuberculostearicum is a pathobiont
• L. sakei protects mucosal surface from pathogenesis

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