Chronic nasal inflammation induces dysbiosis of the nose and gut microbiota

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Introduction

- Chronic nasal inflammation increases the risk of psychiatric disorders.
- Our previous studies have indicated that LPS-induced chronic nasal inflammation causes dysbiosis of gut microbiota in adult male mice.
- Bacteria live on all mucosal surfaces of the host body including the nasal mucosa.

Hypothesis

Chronic nasal inflammation changes the composition of nose microbiota, which affects the gut microbiota.

Aims

① Identify the differences in the components of microbiota between nose and gut.

② Clarify whether and how eosinophilic chronic rhinosinusitis (ECRS) induces dysbiosis in nose and gut.

Methods

➤ **Animal**: C57BL/6J (8w) male mice

➤ **Experimental protocol**

Topical application
- CONT: 100% ethanol + PBS
- ECRS: vitamin D analog (MC903) + ovalbumin (OVA)

Intranasal administration
- CONT: PBS (20μL)
- ECRS: OVA (20μL)

Kagoya et al. Allergy. (2020)

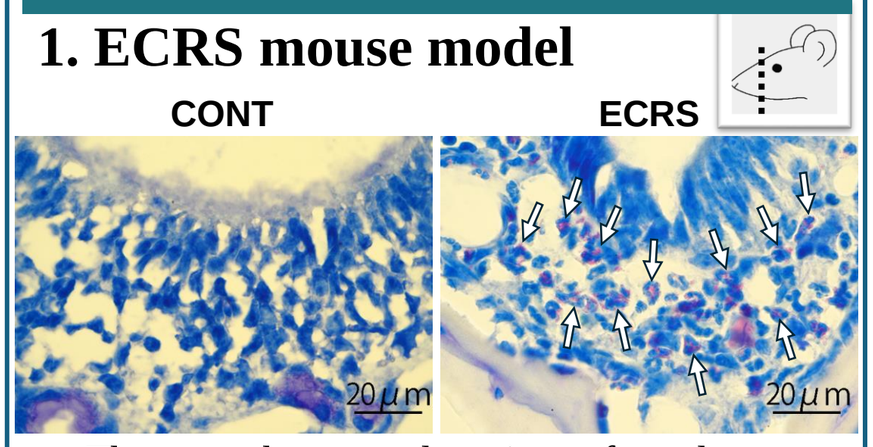
➤ **Histology**: Wright staining

➤ **Bacterial DNA extraction**
- Nose microbiota
  QIAmp DNA Microbiome Kit (QIAGEN)
- Gut microbiota
  QIAmp PowerFecal Pro DNA Kit (QIAGEN)

➤ **16S metagenomic analysis**
- The V3-V4 region of 16S rRNA was amplified and sequenced on an Illumina MiSeq.
- Database: Silva-132-99
- α-diversity: Shannon index
- β-diversity: Bray-Curtis index
  PCoA (Principal Coordinate Analysis) plots were prepared using Bray-Curtis distances.
- LEfSe (Linear discriminant analysis Effect Size)

Results

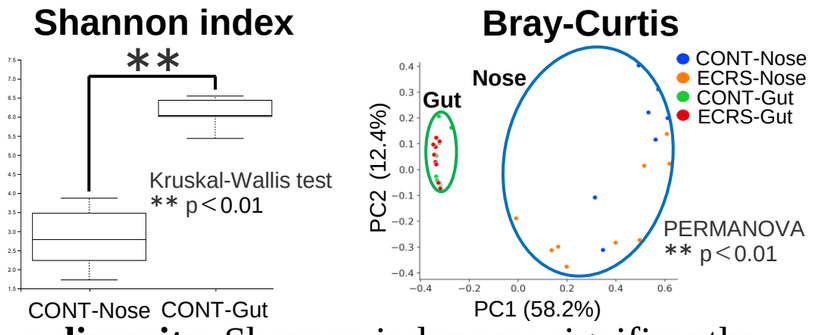
1. ECRS mouse model



These are the coronal sections of nasal mucosa. Eosinophils (pink cells) infiltrated the olfactory mucosa in ECRS mice.

2. Nose vs Gut microbiota

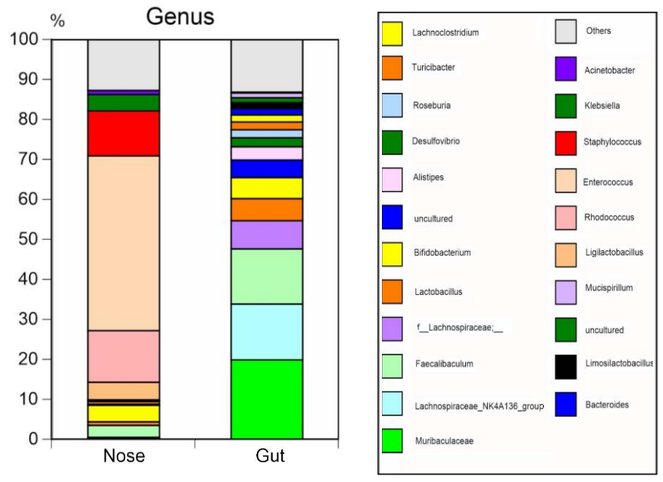
◈ Diversity



α-diversity: Shannon index was significantly higher in the gut microbiota, indicating that diversity of microbiota was significantly higher in the gut than nose.

β-diversity: Bacterial composition was significantly different between the nose and gut in both control and ECRS.

◈ Abundance

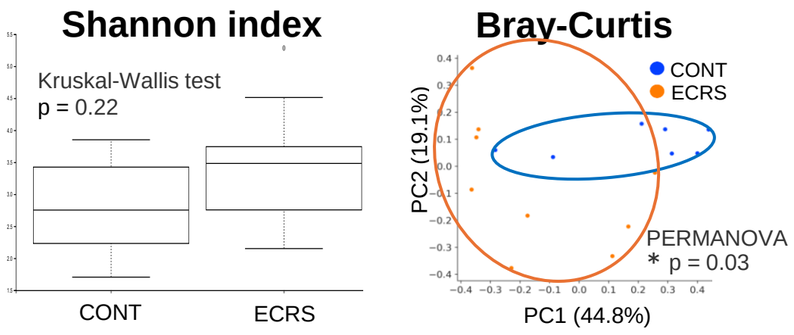


Bacterial components were clearly different between nose and gut in the genus level.

3. Control vs ECRS microbiota

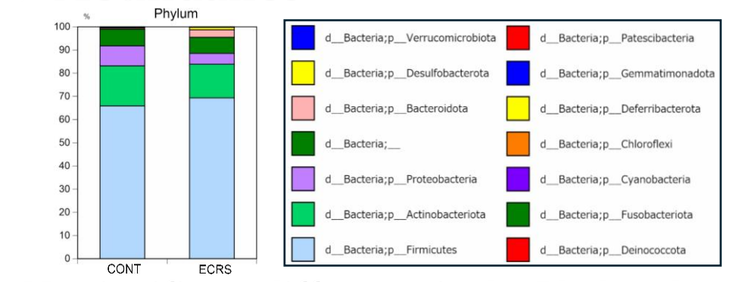
3-1. Nose

◈ Diversity



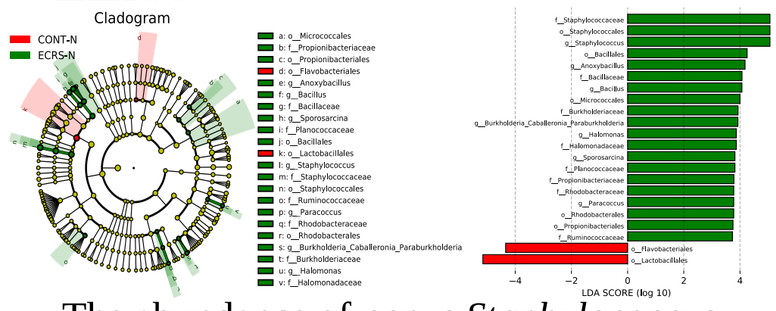
α-diversity: No significant difference
β-diversity: Significant difference

◈ Abundance



No significant difference in the Phylum level

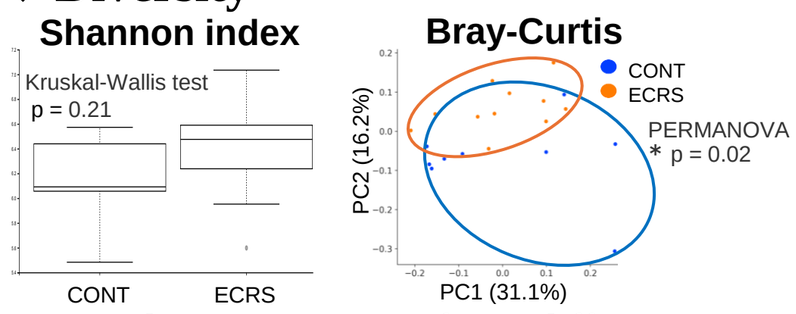
◈ LEfSe



The abundance of *genus Staphylococcus* increased significantly in ECRS mice. (11.3% in CONT, 34.5% in ECRS)

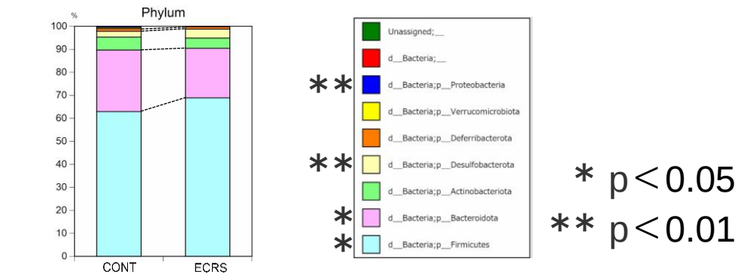
3-2. Gut

◈ Diversity



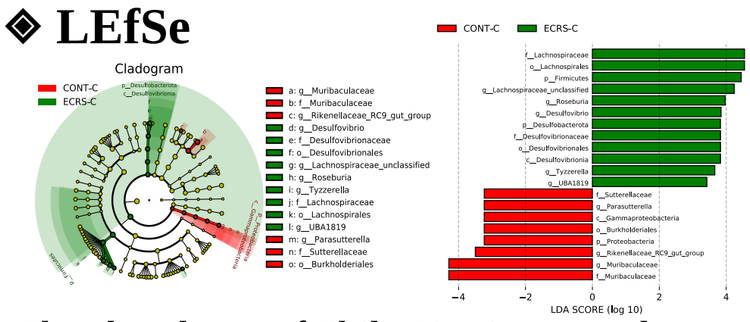
α-diversity: No significant difference
β-diversity: Significant difference

◈ Abundance



Significant difference in the Phylum level

◈ LEfSe



The abundance of Phila Firmicutes and Desulfobacterota significantly increased, while that of Phylum Proteobacteria significantly decreased in ECRS mice.

Take home messages

- Mouse nose microbiota was identified. It had clearly different components from those of gut microbiota.
- Dysbiosis was induced in nose and gut microbiota in ECRS mice.
- ECRS-induced dysbiosis may be the first step to lead to psychiatric disorders by chronic nasal inflammation.