Comparison of oral microbial diversity and metabolic pathways between patients with Inborn Errors of Immunity (IEI) and healthy controls: A pilot study in a Thai population

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Abstract

Inborn Errors of Immunity (IEI) are genetically determined immune disorders associated with disruptions in host–microbiome homeostasis, particularly in the oral cavity, yet their microbial characteristics and functional consequences remain poorly understood. This study compared the taxonomic diversity and functional potential of the oral microbiome between **15 Thai patients with IEI and 18 age- and sex-matched healthy controls** using 16S rRNA gene amplicon sequencing. Alpha-diversity (Chao1, Shannon, Simpson and Evenness) was analyzed using the Wilcoxon rank-sum test, while Beta-diversity was evaluated with Bray–Curtis distance, visualized by Principal Coordinates Analysis (PCoA), and validated by Permutational Multivariate Analysis of Variance (PERMANOVA). Functional profiling was performed using linear discriminant analysis effect size (LEfSe; score > 2.0). A total of 6 phyla and 372 species were identified. Although All Alpha-diversity showed no significant difference, Beta-diversity (p = 0.0120) revealed distinct microbial community structures between groups. LEfSe analysis identified 27 health-associated species enriched in controls, whereas *Streptococcus gordonii* was enriched in the IEI group. Additionally, 7 metabolic pathways, including Inosine 5'-monophosphate degradation and Fatty acid biosynthesis initiation, were significantly elevated in IEI and may support the survival of *S. gordonii*. These findings suggest that IEI is associated with shifts in the oral biofilm microbiota and metabolic activity, **highlighting** *S. gordonii* as a potential biomarker for further investigation.

Background

Thailand has increasingly implemented newborn screening for immunodeficiency using T-cell Receptor Excision Circles (TRECs) and developed a national patient registry; however, diagnostic delay and limited studies on the oral microbiome in primary immunodeficiency remain challenges. This study aims to improve understanding of the relationship between the oral microbiome, immune system, and metabolic pathways to support future advances in diagnosis and treatment.



OBJECTIVE

To comprehensively characterize and compare the taxonomic diversity and functional potential of the oral microbiome in patients with Inborn Errors of Immunity (IEI) and healthy controls.

Methodology

Sample Collection

- **Study groups:** IEI:15 VS CT:18
- **Sample type:** 33 Oral biofilm samples
- **Technique:** 16S rRNA Gene Amplicon Sequencing

Diversity Analysis

statistical analyses were performed in R

Normality test

- **Alpha-diversity** — Indices: Chao1, Shannon, Simpson, Evenness
- **Beta-diversity** — Bray–Curtis distance

Statistical Validation: PERMANOVA

Visualization: PCoA

Functional Profiling

Species, Metabolic Pathways

LEfSe

Threshold: LDA Score > 2 and *P-value* < 0.05

Results & Discussion

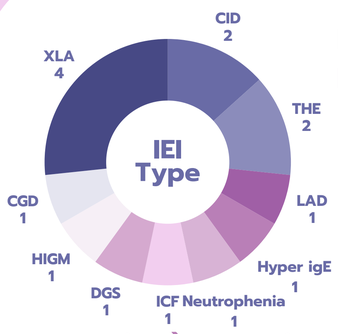


Fig.1) Types of diseases in the IEI study group

The most common disease was XLA (26.67%), followed by Combined CID and THE (13.33%)

Fig.2) Venn diagram of expressed species

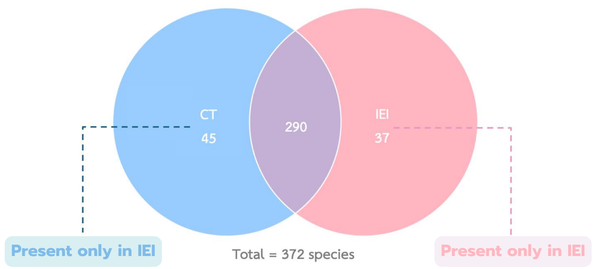
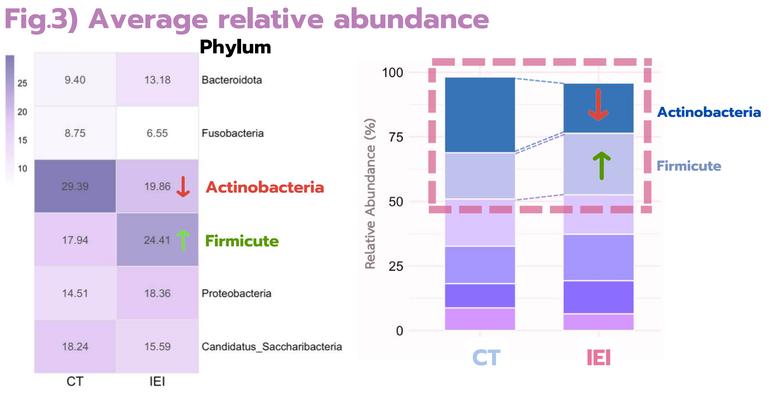


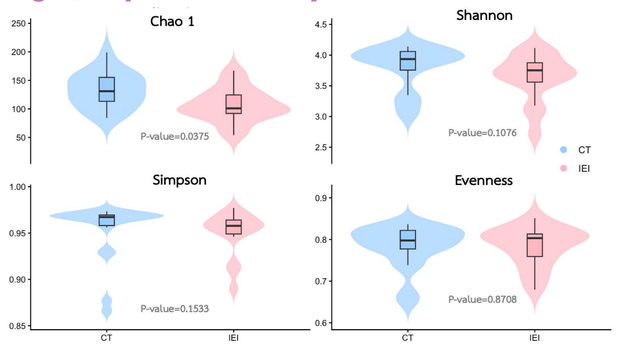
Fig.3) Average relative abundance



At the taxonomic level from **Actinobacteria** in the control group to **Firmicutes** in the IEI group.

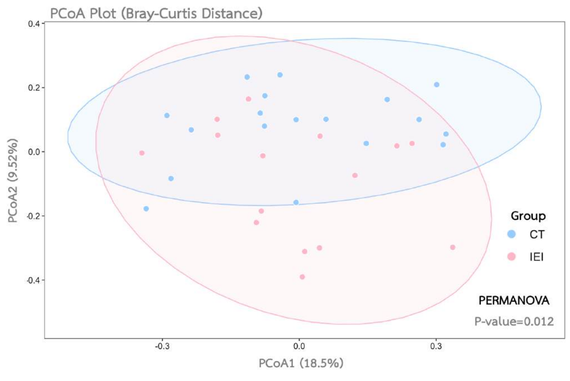
Diversity Analysis

Fig.4) Alpha-diversity



Alpha-diversity based on Chao1 showed a significant difference between groups (p = 0.0375), whereas Shannon (p = 0.1076), Simpson (p = 0.1533), and Evenness (p = 0.8708) indices showed no significant differences .

Fig.5) Beta-diversity



Beta-diversity revealed distinct microbial community structures between groups, although most species and core phyla were shared with differing relative abundances.

Functional Profiling

Fig.6) Analysis of microbial species using LEfSe.

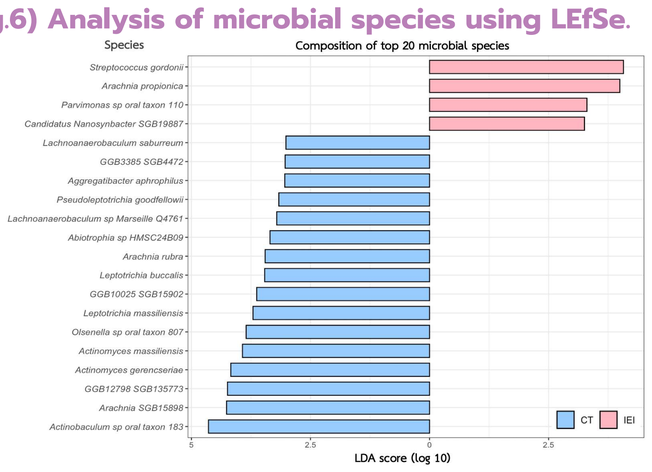
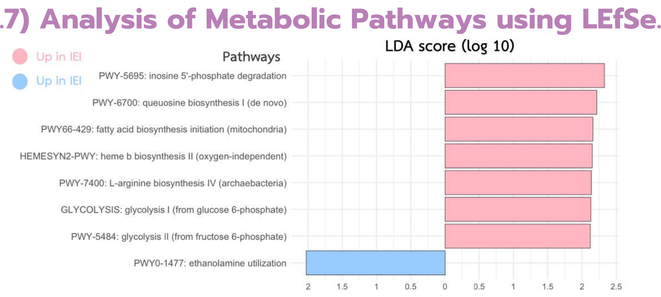


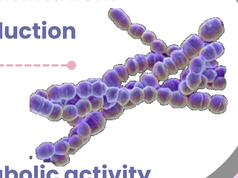
Fig.7) Analysis of Metabolic Pathways using LEfSe.



LEfSe (LDA > 2, P<0.05) identified *S. gordonii* as the most significantly enriched species in the IEI group (Fig.6). **Functional profiling** revealed 7 metabolic pathways significantly upregulated in the IEI group, including Inosine 5′-phosphate degradation, Queuosine biosynthesis I, and Fatty acid biosynthesis initiation; these pathways are primarily associated with energy metabolism, cell component synthesis, and bacterial adaptation within the oral biofilm. In contrast, the control group exhibited only one prominent pathway, Ethanolamine utilization (Fig.7).

Conclusions

- **Dominant Pathogen:** *S. gordonii* enriched in IEI, driving oral dysbiosis and inflammation.
- **Functional Enrichment:** 7 pathways upregulated in IEI, supporting energy production and biofilm growth.
- **Survival Strategy:** Enhanced fatty acid biosynthesis promotes *S. gordonii* persistence.
- **Main Finding:** IEI significantly alters both oral microbial composition and metabolic activity.



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REFERENCES