

# Microbiome study of Systemic Lupus Erythematosus patients

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## Introduction

The role of microbiome in an autoimmune disease like Systemic Lupus Erythematosus (SLE) remains under-explored. Microbiota studies reveal strong association of healthy and disease states to microbiome composition and functionality. SLE association with diseased microbiota is investigated in this study.

## Hypothesis

Changes induced in the microbiota by SLE could be marked by taxonomic composition, as well as on a higher levels of functional hierarchy - metabolic pathways.

## Study design and analysis

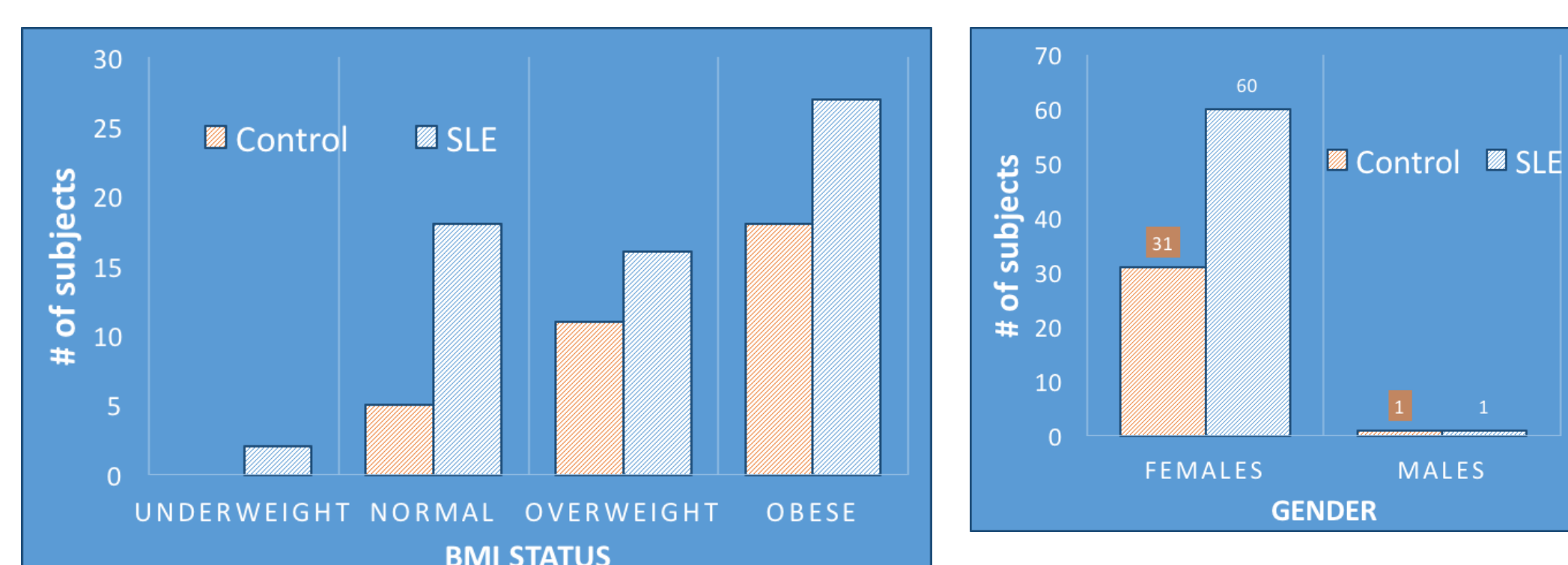
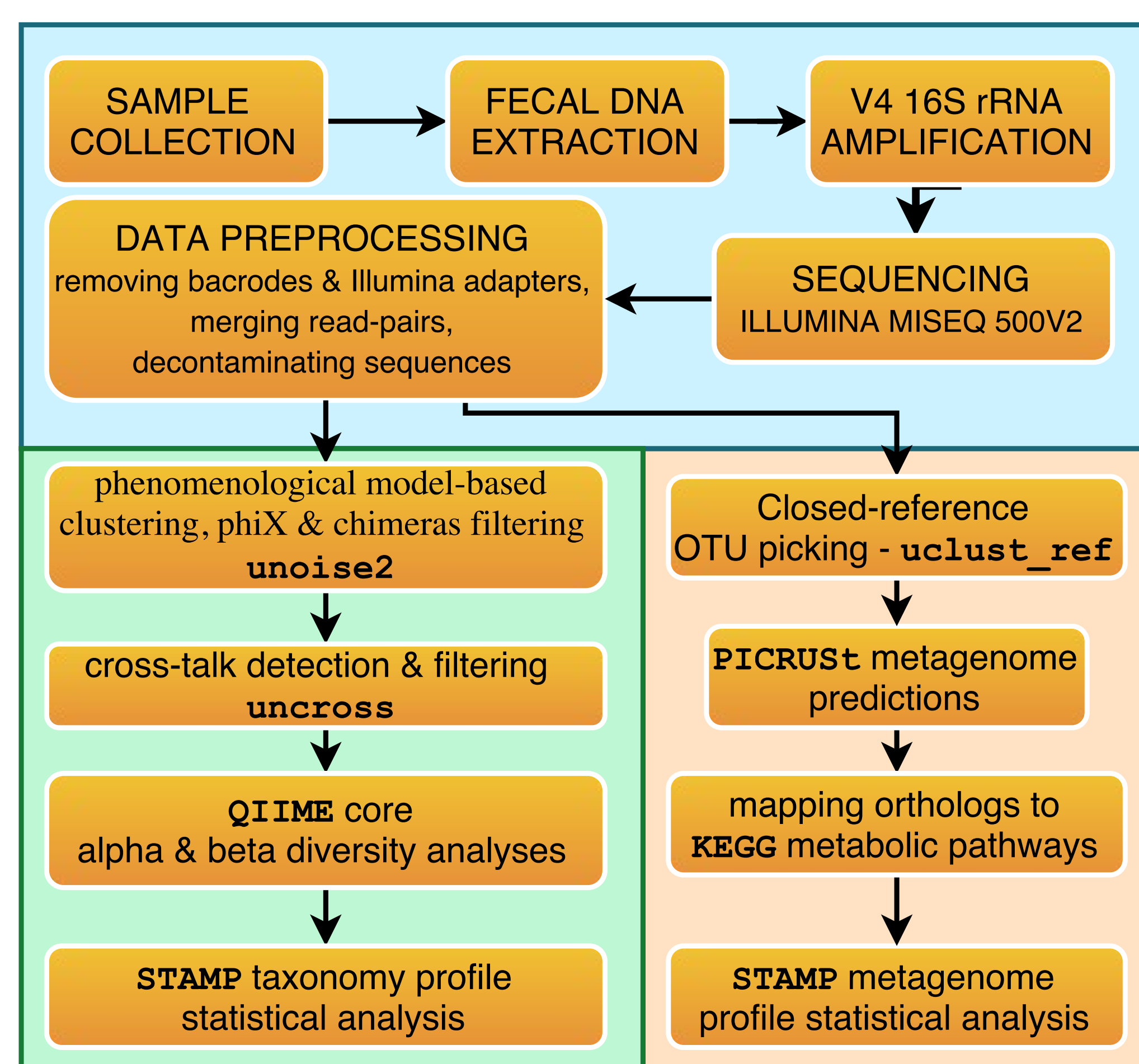


Figure 1: BMI status in study subjects

Figure 2: Gender of study subjects

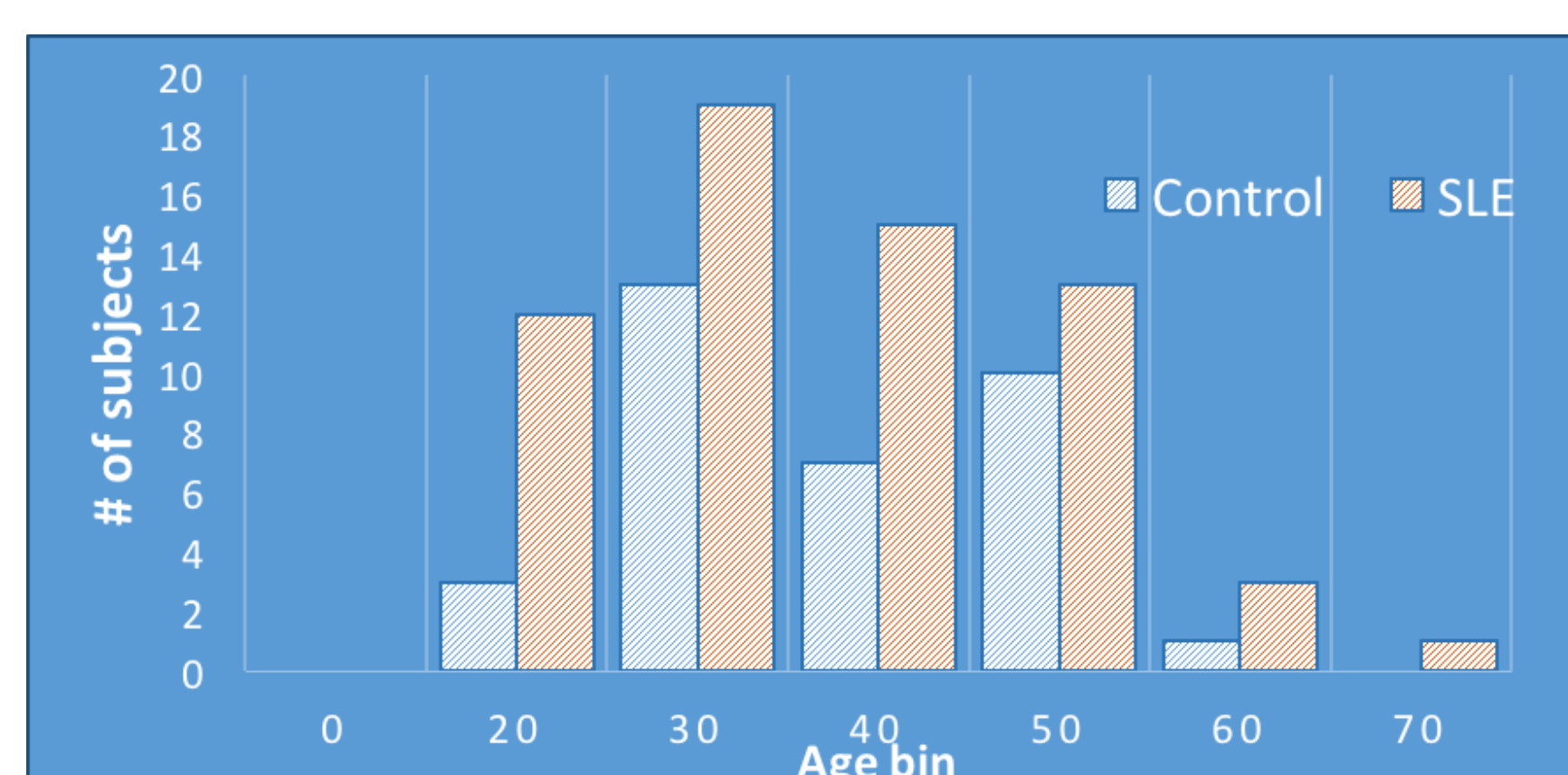


Figure 3: Age status in study subjects

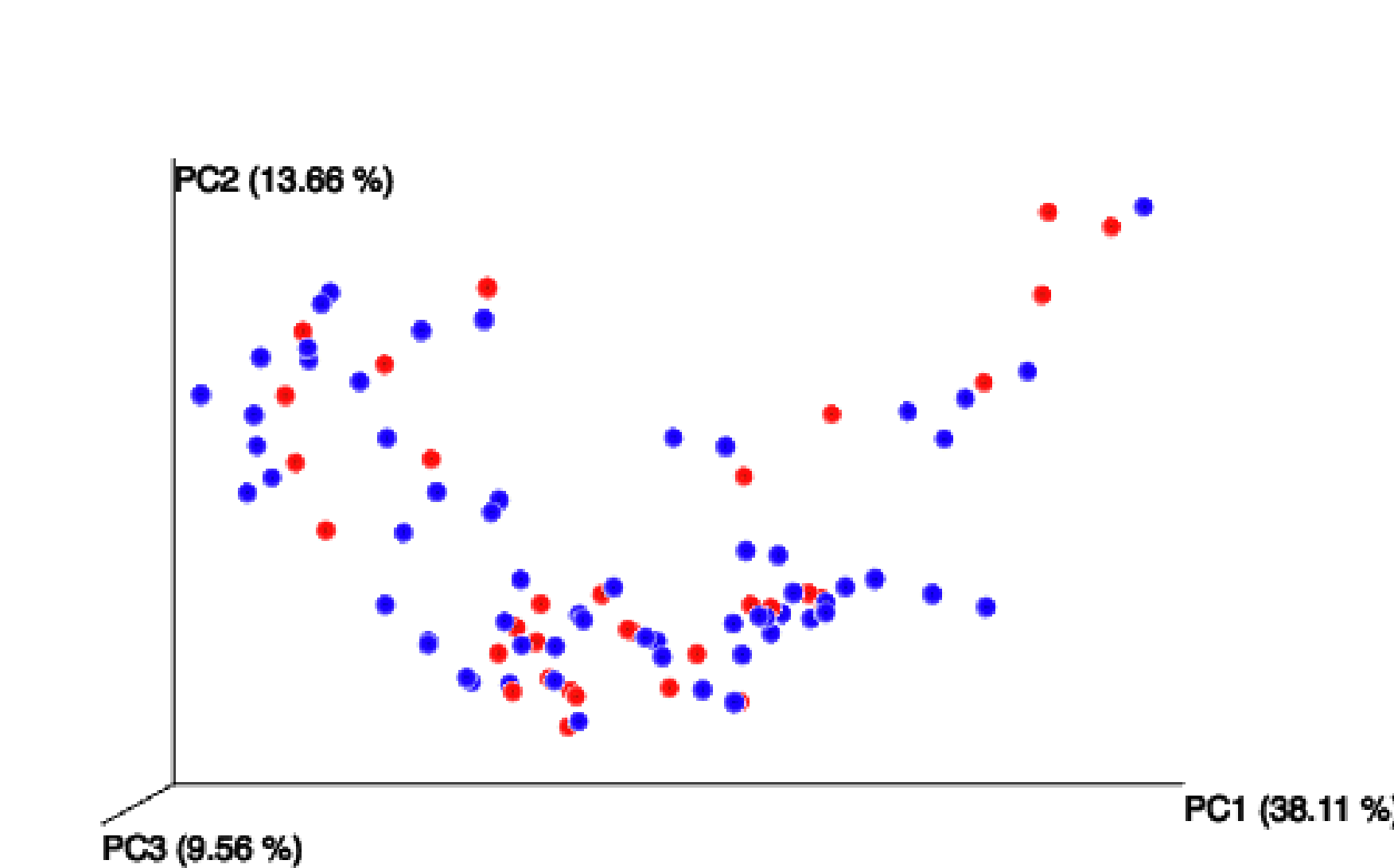


Figure 4: Weighted UniFrac PCoA plot (HC/SLE) showing no clear separation in terms of phylogenetic composition.

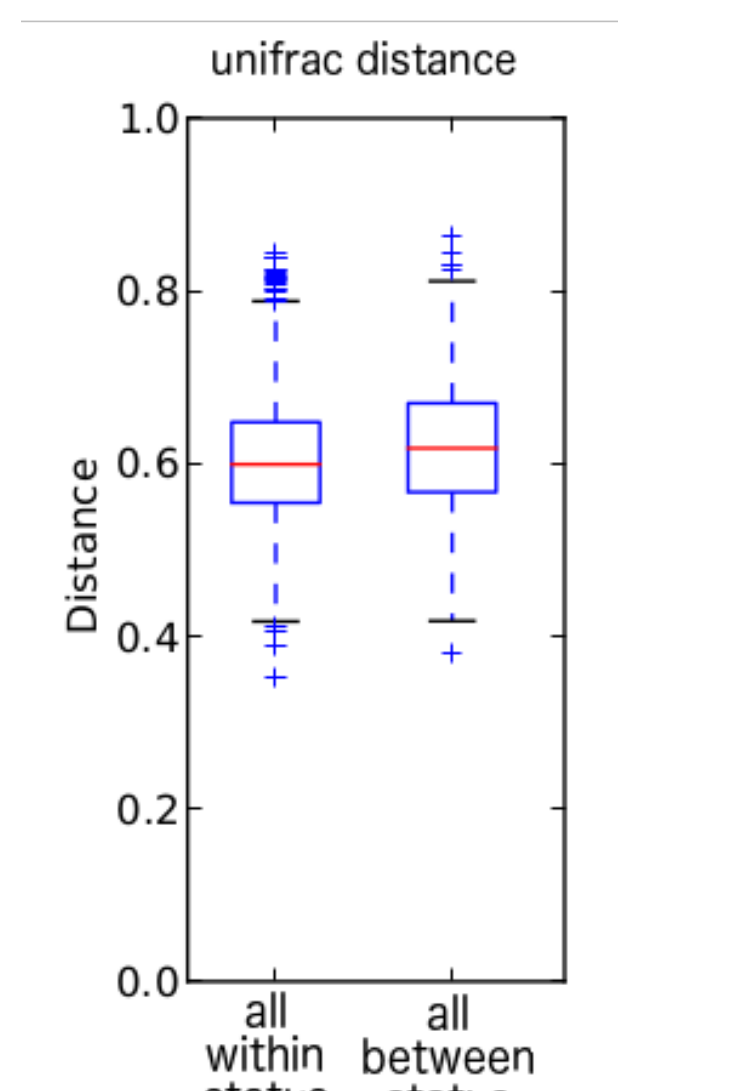


Figure 5: Unifrac distance within and between status (SLE/HC).

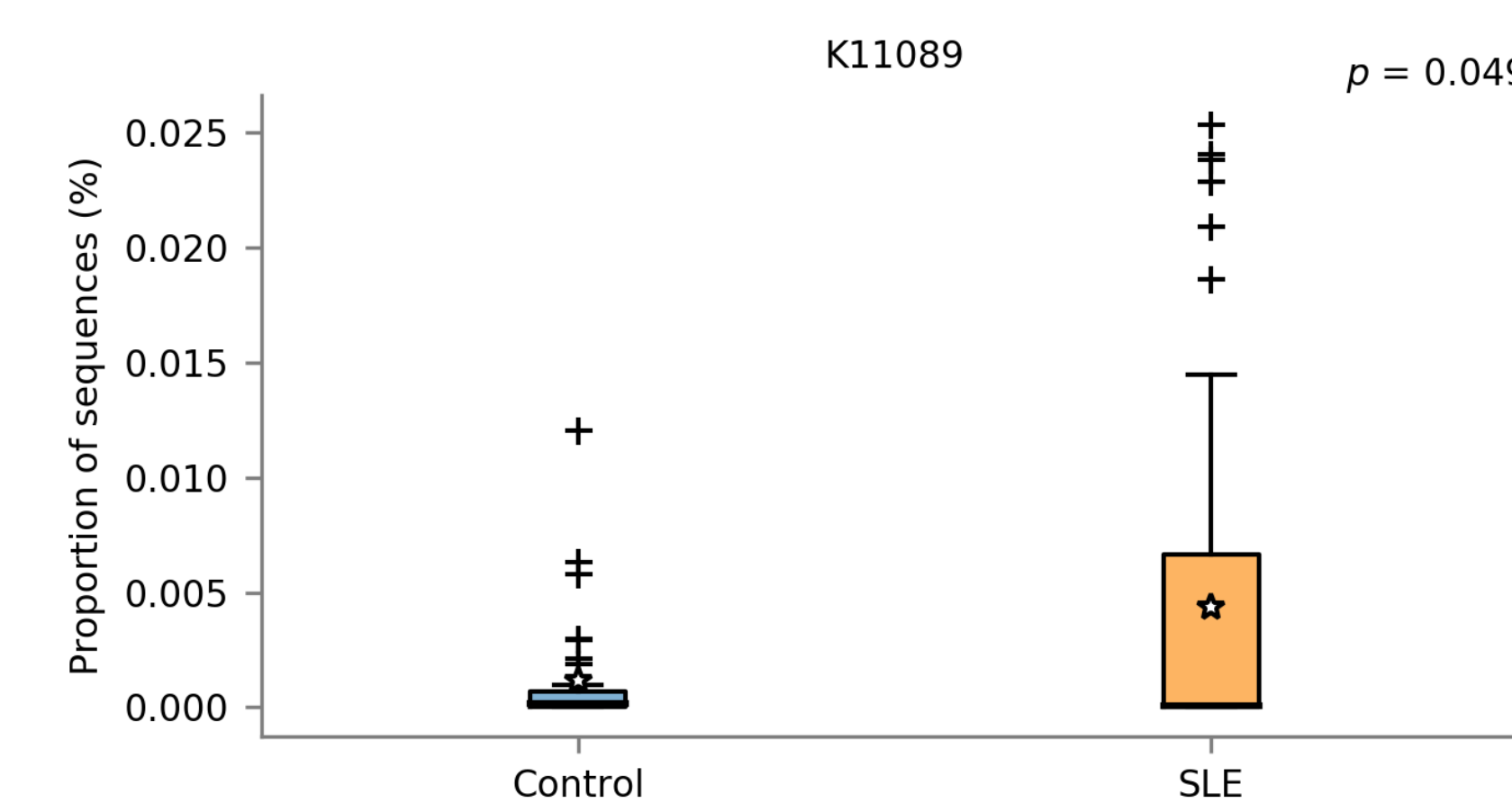


Figure 6: Enriched K11089 ortholog belonging to SLE pathway in affected subjects compared to HC. This ortholog is Ro60 (Trove2) gene.

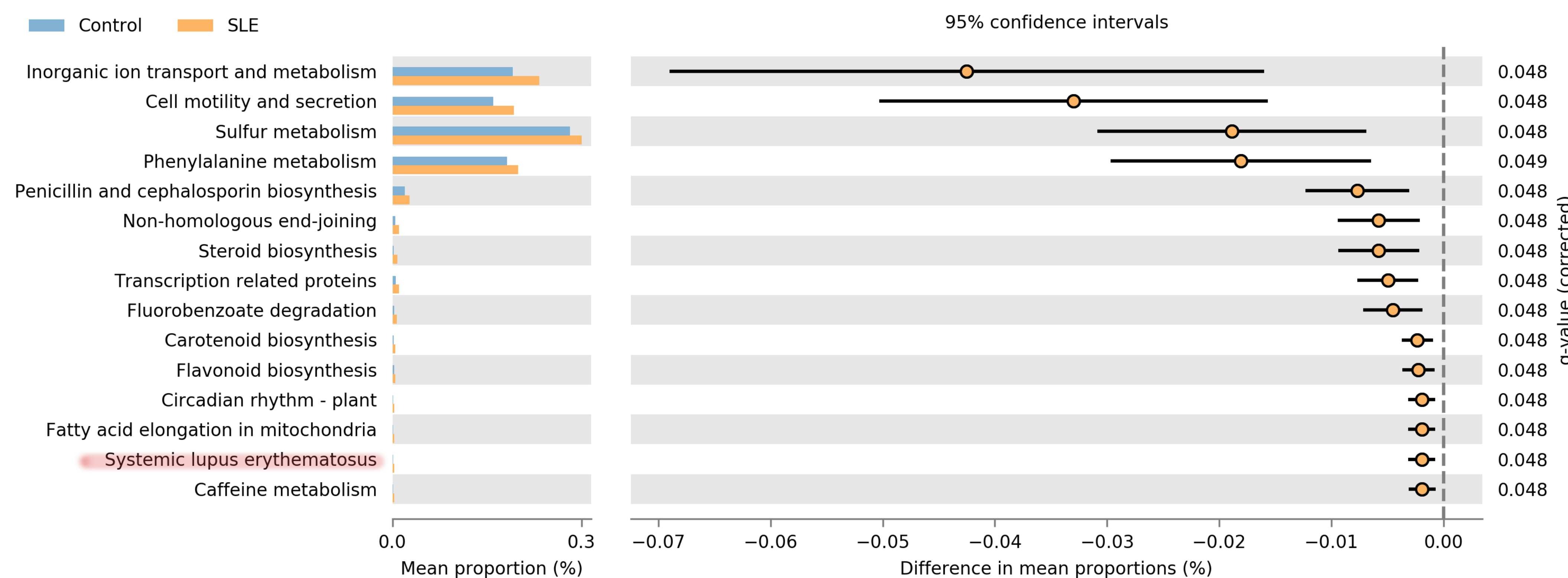


Figure 7: Significantly enriched metabolic pathways in SLE subjects compared to HCs.

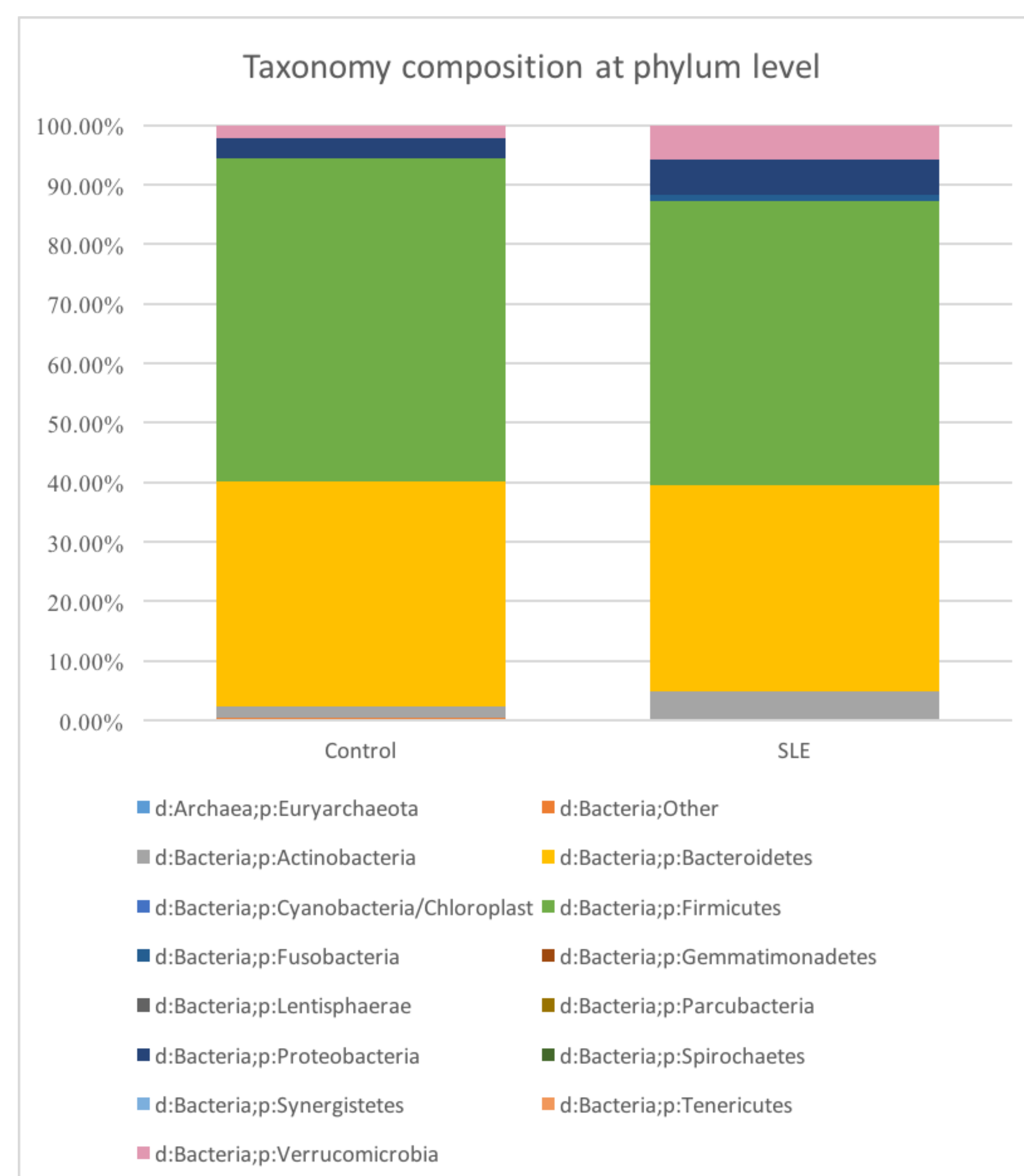


Figure 8: Taxonomic summary at phylum level.

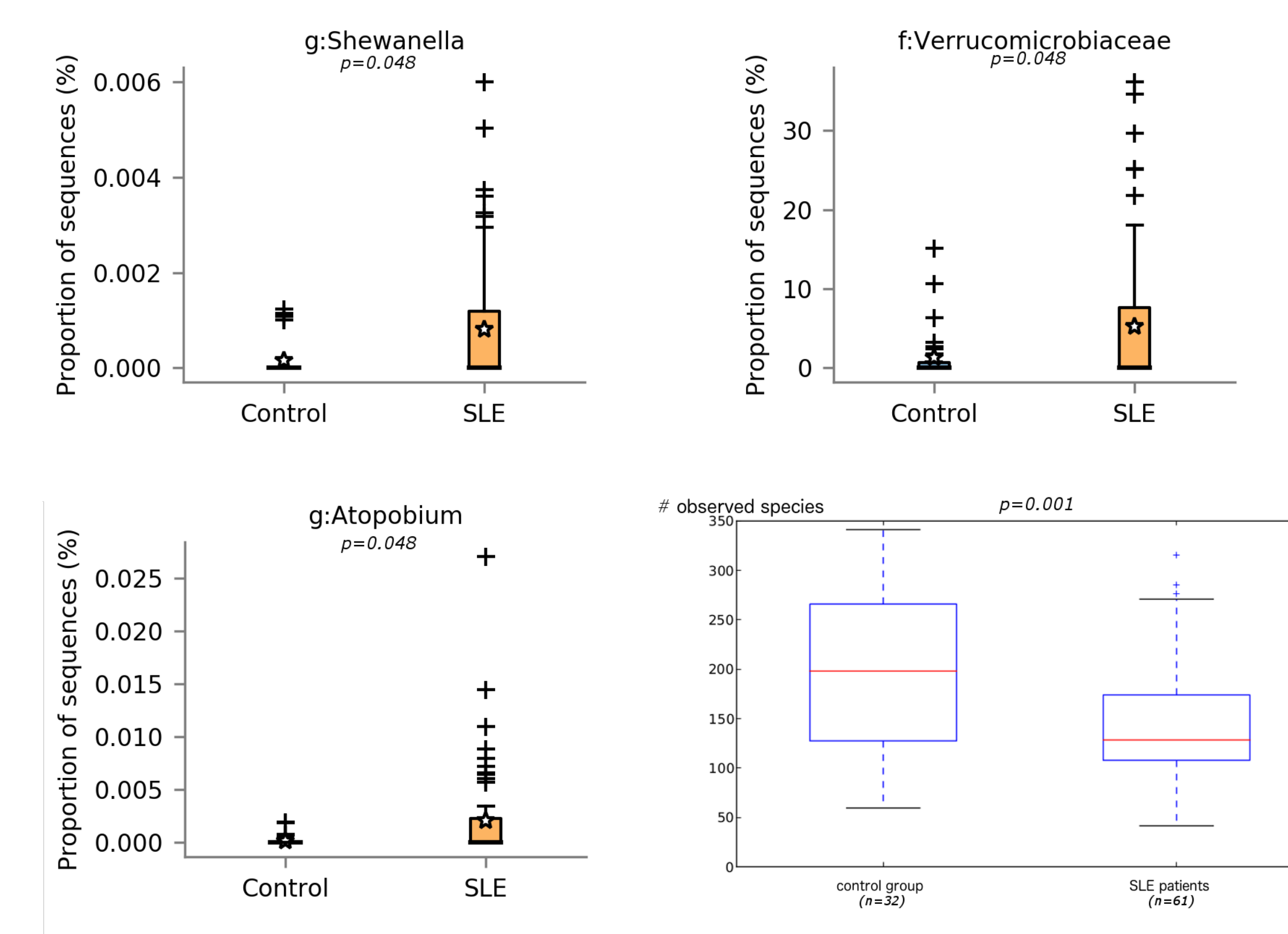


Figure 9: Bacterial abundance comparison for differently abundant taxa belonging to genus (g) and family (f) level. Observed number of species comparison between HC/SLE.

## Discussion

- SLE patients exhibit smaller alpha diversity compared to HCs, but do not separate in beta diversity metrics,
- Observed statistically significant increase of Ro60 gene (KEGG K11089 ortholog) abundance in SLE patients,
- Commensal bacteria residing in the gut microbiota of SLE patients might produce mimicking Ro60 peptides,
- Molecular mimicry has been hypothesized to play an important role in the activation of Ro60 reactive B/T cells[1],
- Infection-induced autoimmunity hypothesis assumes an activation of autoreactive T-cells when encountering a viral or bacterial pathogen,
- This activation might be caused by epitopes cross-reactive with self antigens (like Ro60).

## Ro60

- Encodes Trove2/Ro60 RNA binding protein,
- Clinically important member of the nuclear antigen family,
- Performs quality control of misfolded ncRNA (such as Alu RNAs and pre-5S rRNAs),
- Major auto-antigen most frequently found in SLE and in Sjogren's Syndrome (SjS) patients,

- Mimicry peptides might lack components of pathways involved in cleaning extracellular debris,
- Undisrupted functioning of Ro60 prevents autoimmunity progression by removing defective Ribonucleoproteins (RNPs) [2],
- PICRUSt analyses point to several bacterial taxa contributing to SLE in which *akkermansia muciniphila* from *Verrucomicrobiaceae* family is the strongest contributor,

## Summary & Future Studies

Presented metagenomic predictions need to be regarded as "suggestive only", however we hypothesise that SLE state might be associated with microbiota changes at higher functional hierarchy - i.e. metabolite level. Metagenomic analysis of fecal microbiota in SLE state is an ongoing experiment. This analysis would allow for detailed study of differences in functional repertoire between SLE and HCs, explore the role of virome, and the importance of Ro60 microbial gene.

## References

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