

# Gut microbial co-occurrence network in patients with peripheral artery disease

Sarbjee Niraula<sup>1</sup>, Jae W. Jang<sup>1</sup>, Jonathan Jung<sup>2</sup>, Spencer L. Stirewalt<sup>3</sup>, Megan E. Alagna<sup>1</sup>, James Du<sup>4</sup>, Christopher Staley<sup>5</sup>, Patrick C. Seed<sup>6</sup>, Stefan J. Green<sup>7</sup>, Karen J. Ho<sup>1</sup>

<sup>1</sup>Division of Vascular Surgery, Northwestern University; <sup>2</sup>University of Washington School of Medicine; <sup>3</sup>University of Chicago Crown Family School of Social Work, Policy, & Practice; <sup>4</sup>University of Illinois, Chicago; <sup>5</sup>University of Minnesota; <sup>6</sup>Stanley Manne Children's Research Institute; <sup>7</sup>Rush University, Chicago

## Background

- The human gut microbiome and microbe-derived metabolites are known to be associated with cardiovascular diseases
- However, their associations with lower extremity peripheral artery disease (PAD) are not well understood
- We hypothesized that clinical features of PAD are associated with unique gut microbiome and metabolome profiles

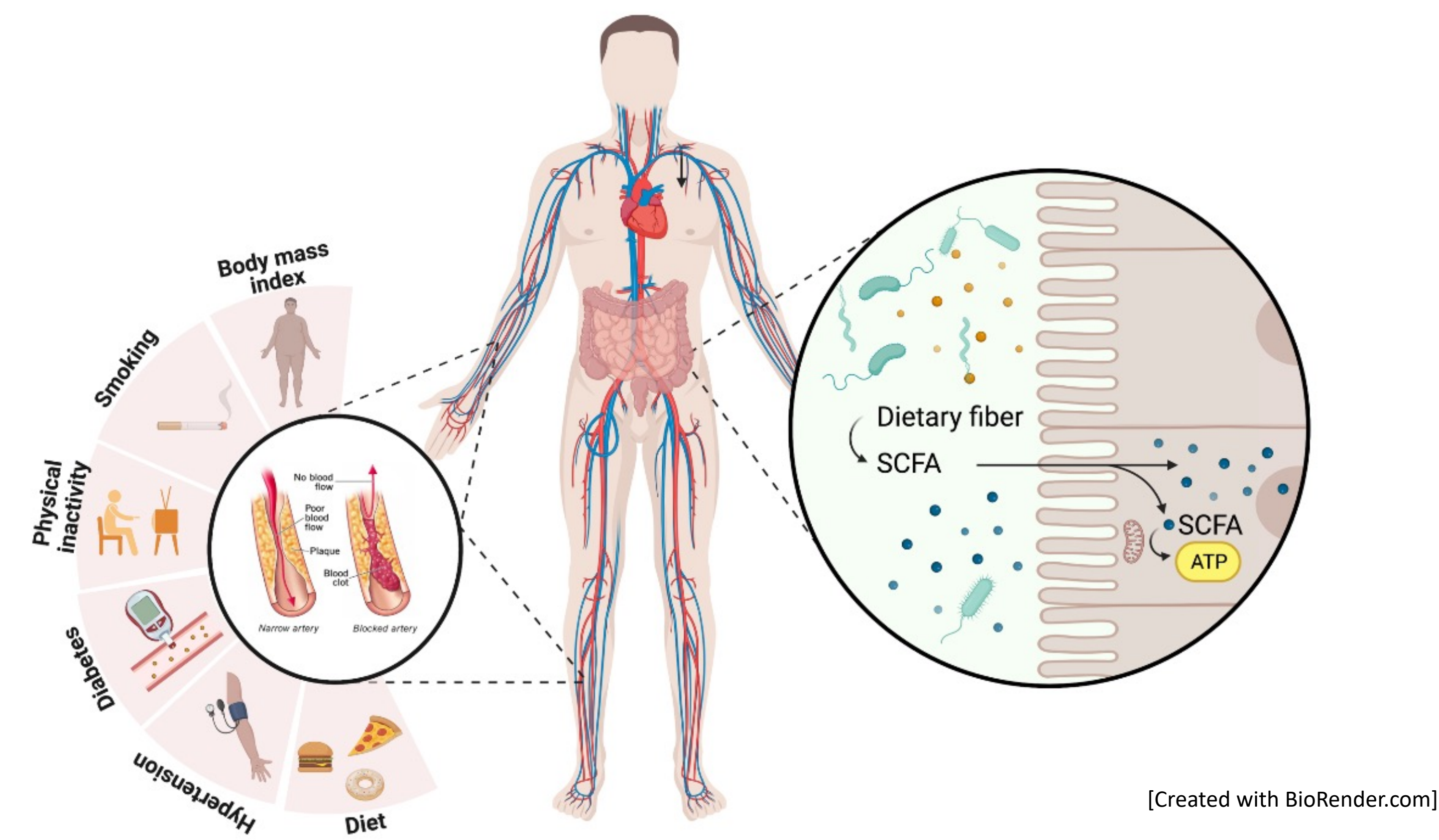


Figure 1. Peripheral artery disease (PAD) caused by atherosclerotic occlusions leads to pain and disability. SCFA, short chain fatty acids

## Objective

Identification of PAD associated microbial biomarkers using network-based co-occurrence pattern analysis

## Methods

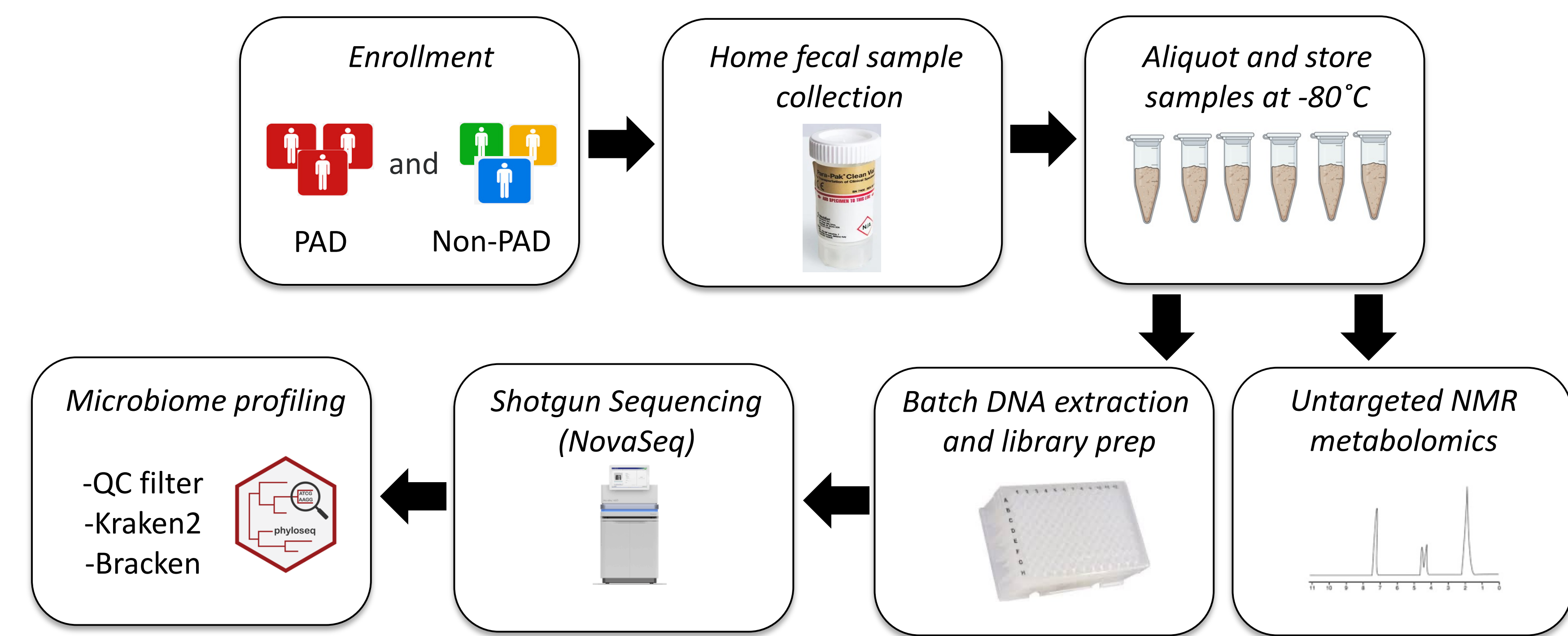


Figure 2. Schematic of overall workflow.

Figure 4. A. Correlation heatmap of PAD network modules with host characteristics and fecal metabolites. B. Preservation analysis of PAD network modules in non-PAD network.

## Results

### Networks represent complex interactions of gut microbial community members and host characteristics

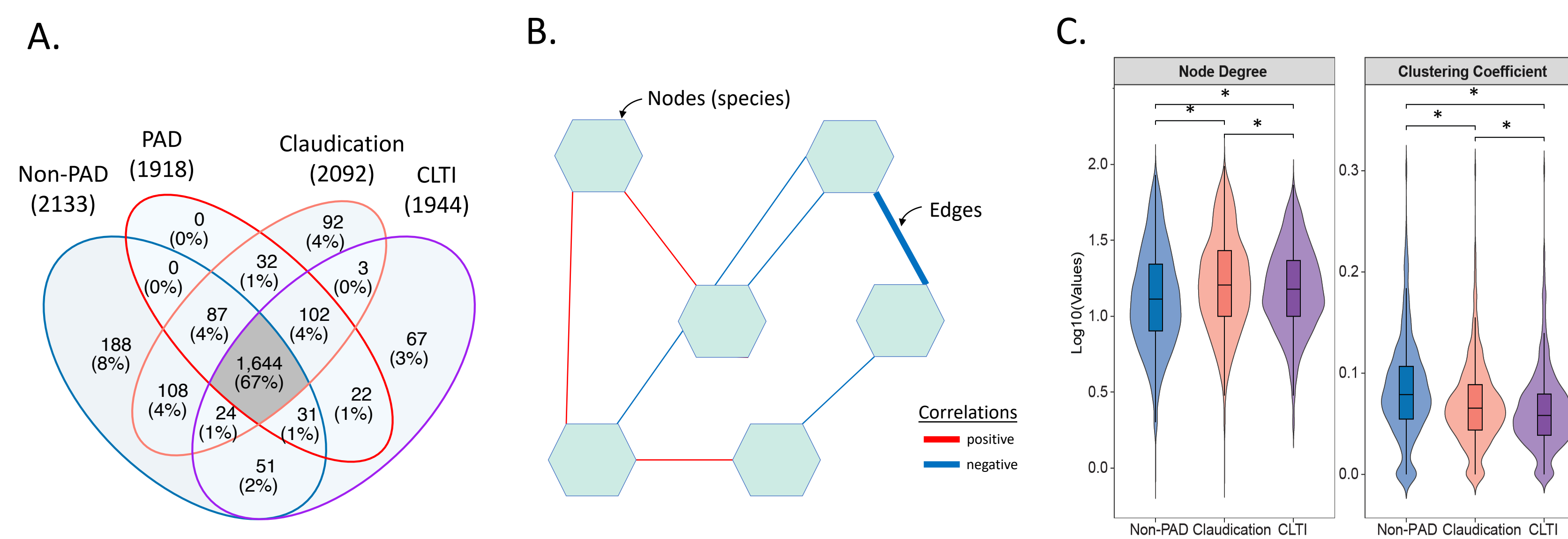
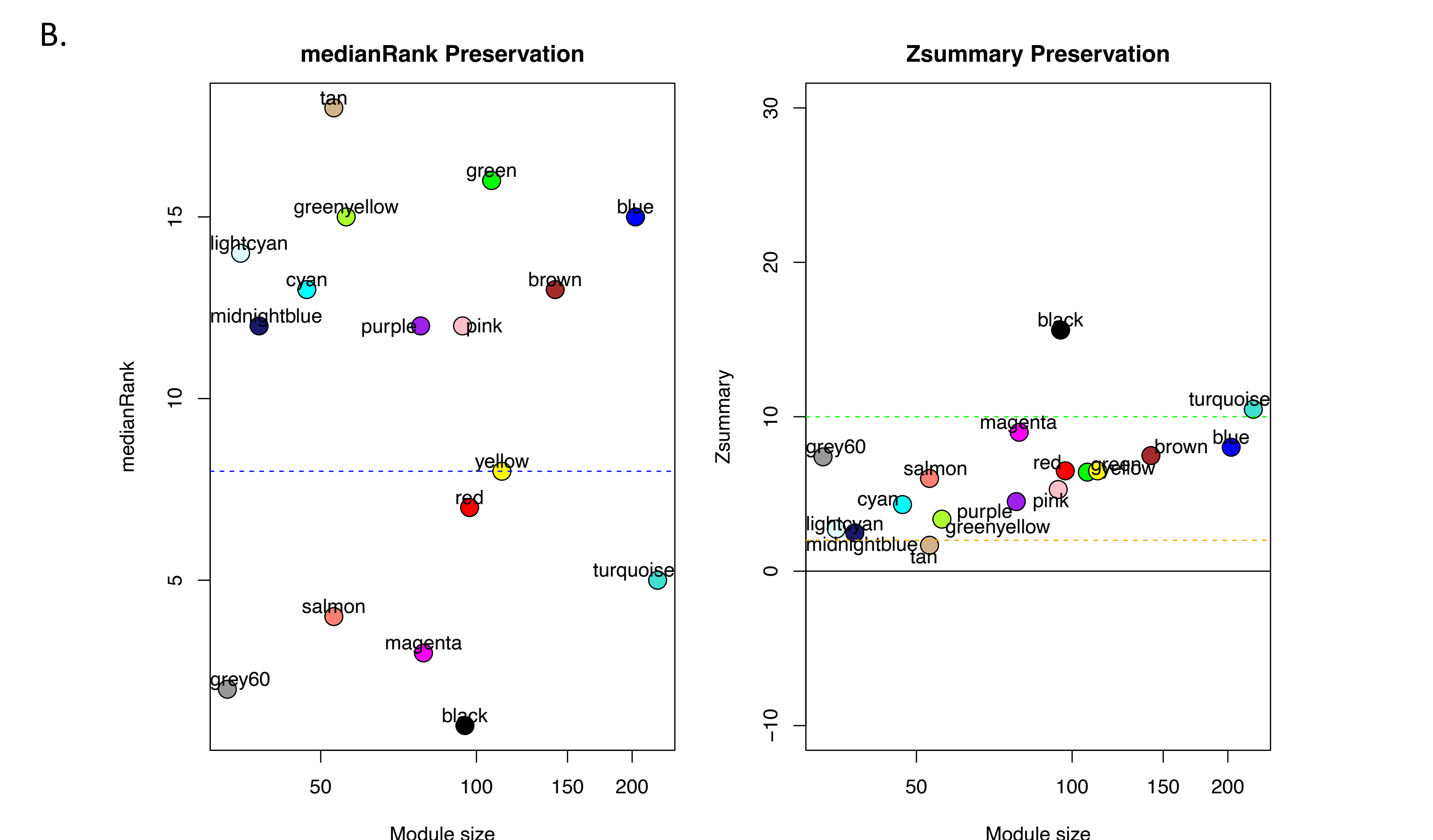
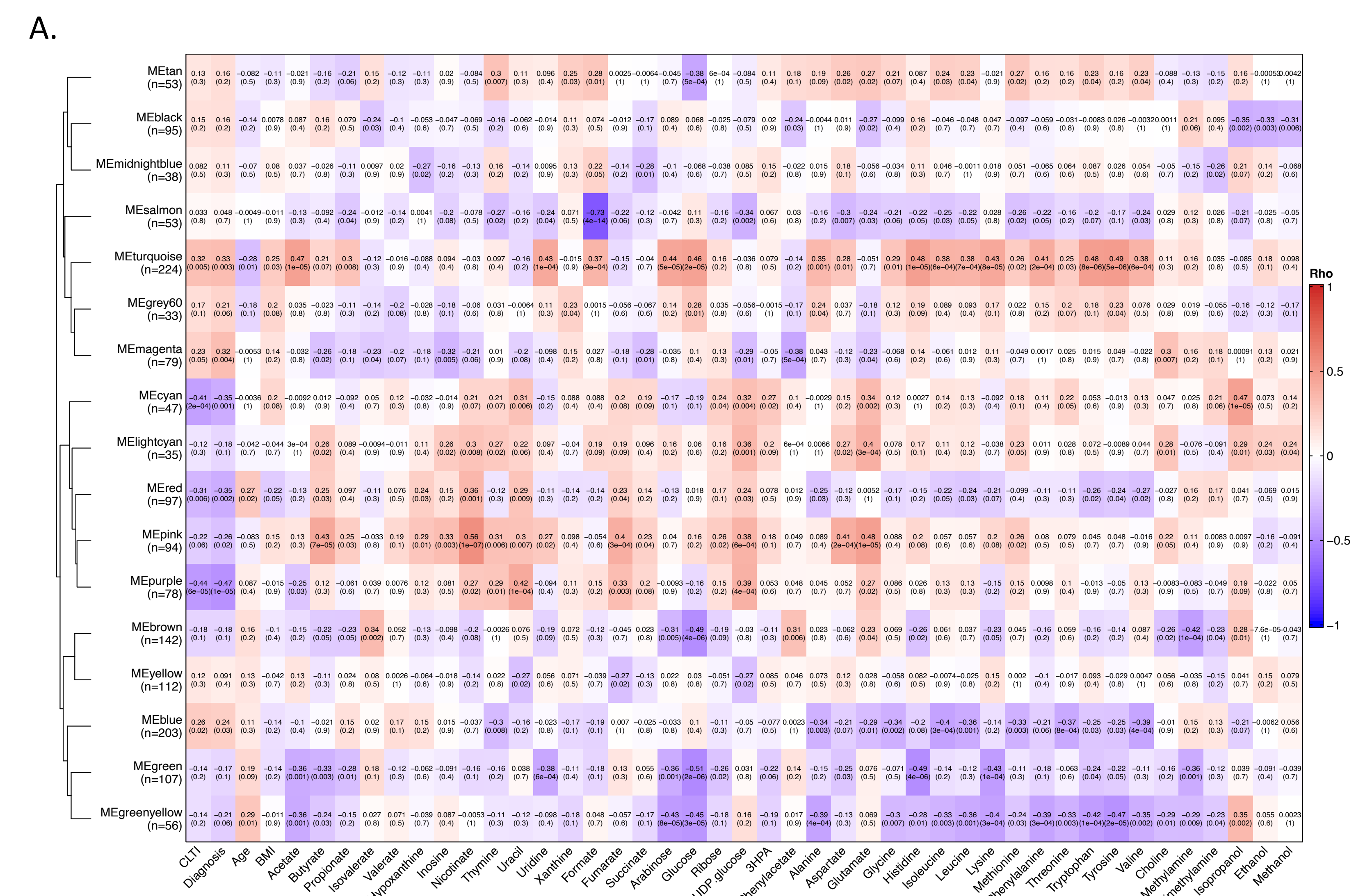


Figure 3. A. Common species among 4 groups for network construction. B. Basic network outline. C. Comparison of node degree and clustering coefficients between non-PAD, claudication and CLTI networks.

### PAD network modules show defined association pattern with PAD clinical presentation and potential for recovery



### Clostridium scindens is a key taxon in networks of all clinical subgroups of PAD

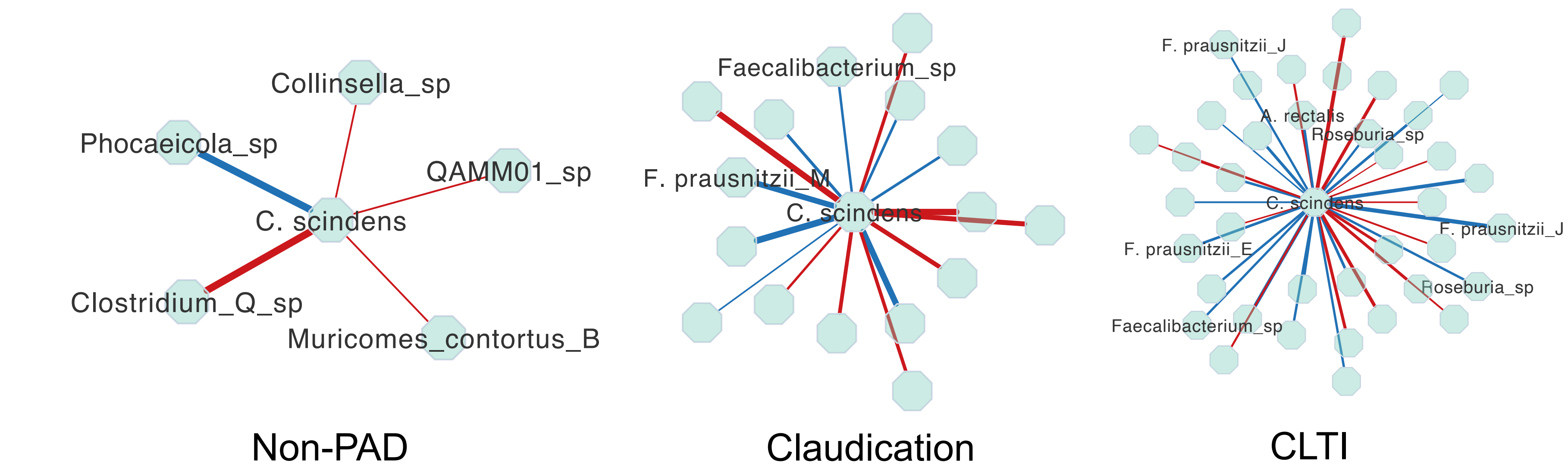


Figure 5. Connections of *C. scindens* in the non-PAD, claudication and CLTI networks.

### Clostridium scindens contributes to the enrichment of secondary bile acid pathways in CLTI

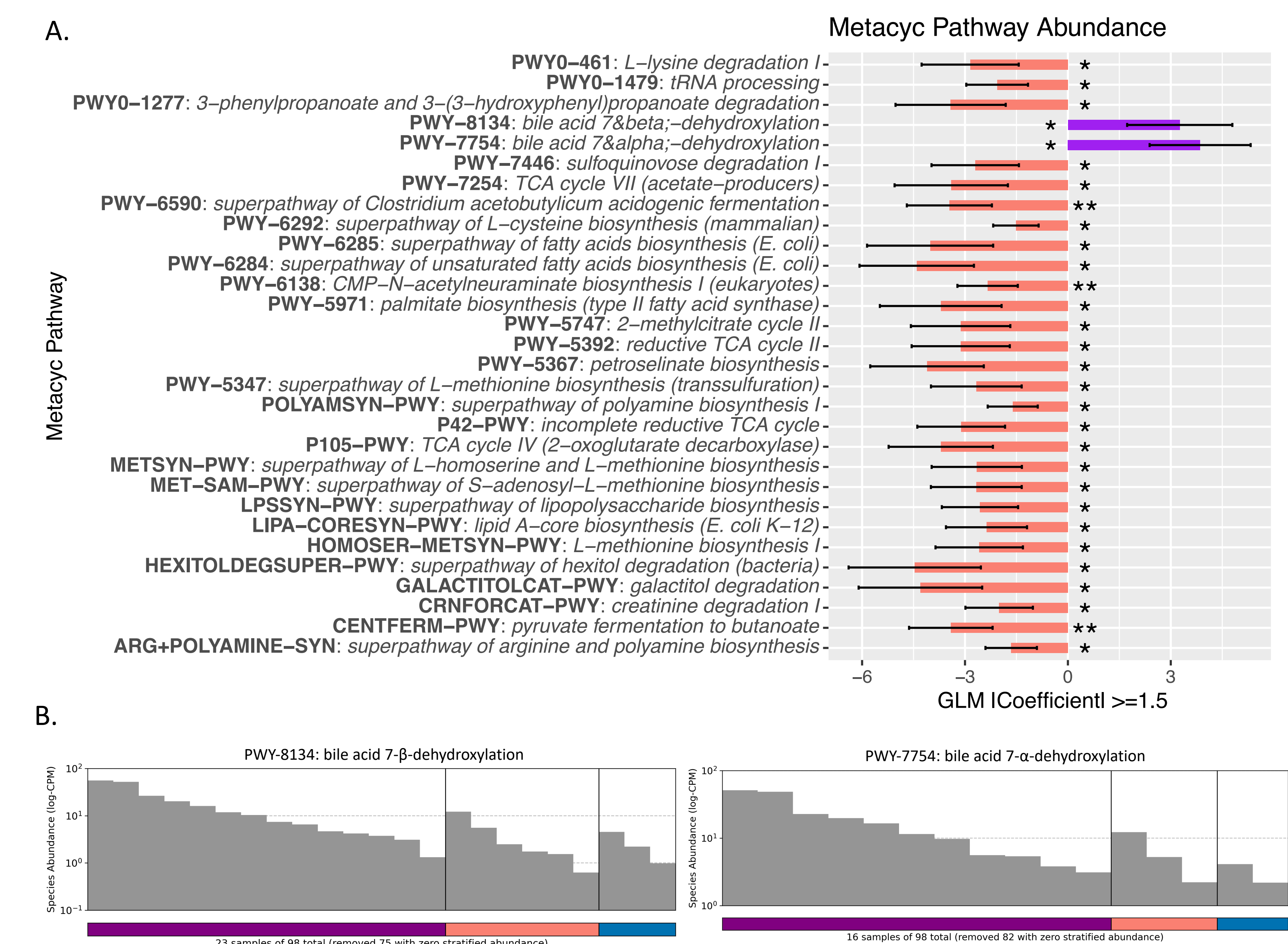


Figure 6. A. Pathway enrichment analysis between claudication and CLTI. B. Contributing taxa to secondary bile acid pathways. (Purple - CLTI, Salmon - Claudication, Blue - Non-PAD)

## Conclusions

- Differences in network architecture suggest dysbiosis associated with discrete clinical presentations of PAD
- C. scindens* is a key taxon in reshaping co-occurrence patterns in PAD networks by establishing negative correlations with butyrate producers in the gut and contributing to increased secondary bile acid pathway abundance in microbes in CLTI
- Future work is focused on validating these and other microbial biomarkers of PAD