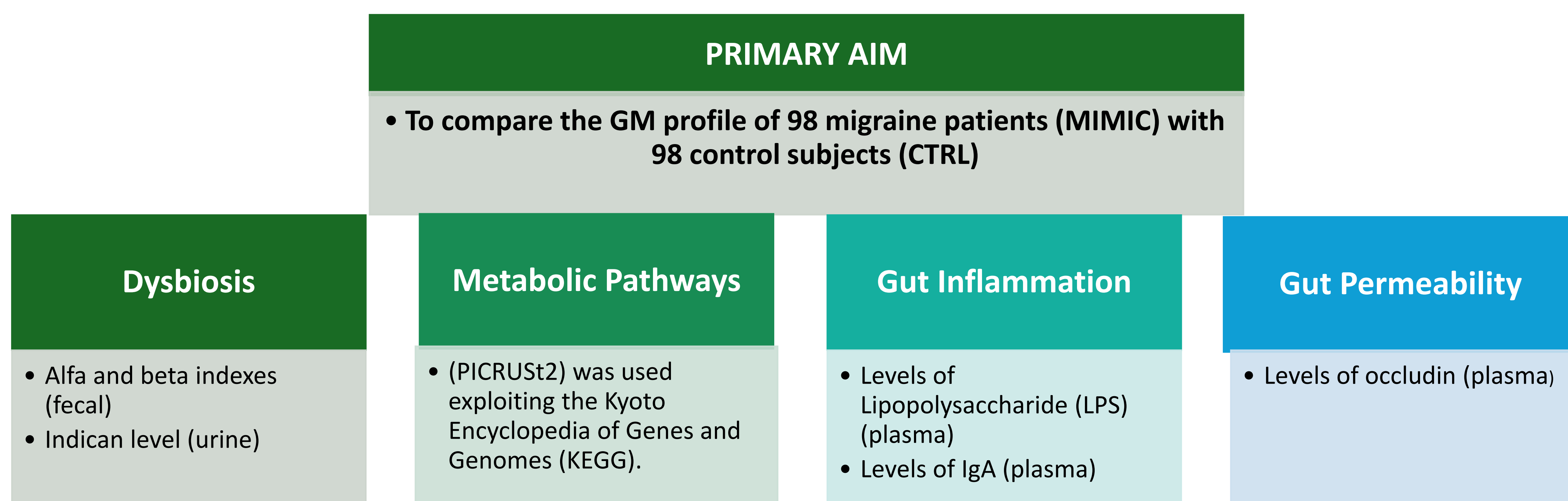# Gut microbiota ecosystem in pediatric migraine.
How are dysbiosis, inflammation and intestinal metabolites involved?

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PRIMARY AIM

- To compare the GM profile of 98 migraine patients (MIMIC) with 98 control subjects (CTRL)

Dysbiosis
- Alfa and beta indexes (fecal)
- Indican level (urine)

Metabolic Pathways
- (PICRUSt2) was used exploiting the Kyoto Encyclopedia of Genes and Genomes (KEGG).

Gut Inflammation
- Levels of Lipopolysaccharide (LPS) (plasma)
- Levels of IgA (plasma)

Gut Permeability
- Levels of occludin (plasma)

RESULTS

Total Patients:	98
Age: mean (median±SD; range)	12.24 years (12.5±2.87; 6-17)
Female: male (%)	64:34 (females 65.3% - males 34.7%)
Headache diagnosis	
Migraine without aura	91 (92.9%)
Migraine with aura	7 (7.1%)
Migraine Features	
Mean (median±SD; range) age at onset	9.35 (9 ± 3.2; 6-17)
Early Onset (≤ 10 years of age)	61 (62%)
Late Onset (>11 years of age)	37 (38%)
MMD	
Low frequency (<4/m)	54 (55.1%)
High Frequency (>4/m)	44 (44.9%)
Nausea/Vomiting	70 (71.4%)
Photophobia	74 (75.5%)
Phonophobia	74 (75.5%)

Figure 1. Altered gut microbiota biodiversity in MIMIC. A: α-diversity analysis based on the Shannon-Weiner, Simpson and Chao1 indexes. B: β-diversity was calculated by the Bray-Curtis algorithm and presented by PCoA plots. PERMANOVA test results are statistically significant, p-value = 0.001; C: receiver operating characteristic (ROC) analysis of the PLS-DA model. The value of AUROC=0.969 indicates a high accuracy of the prediction model.
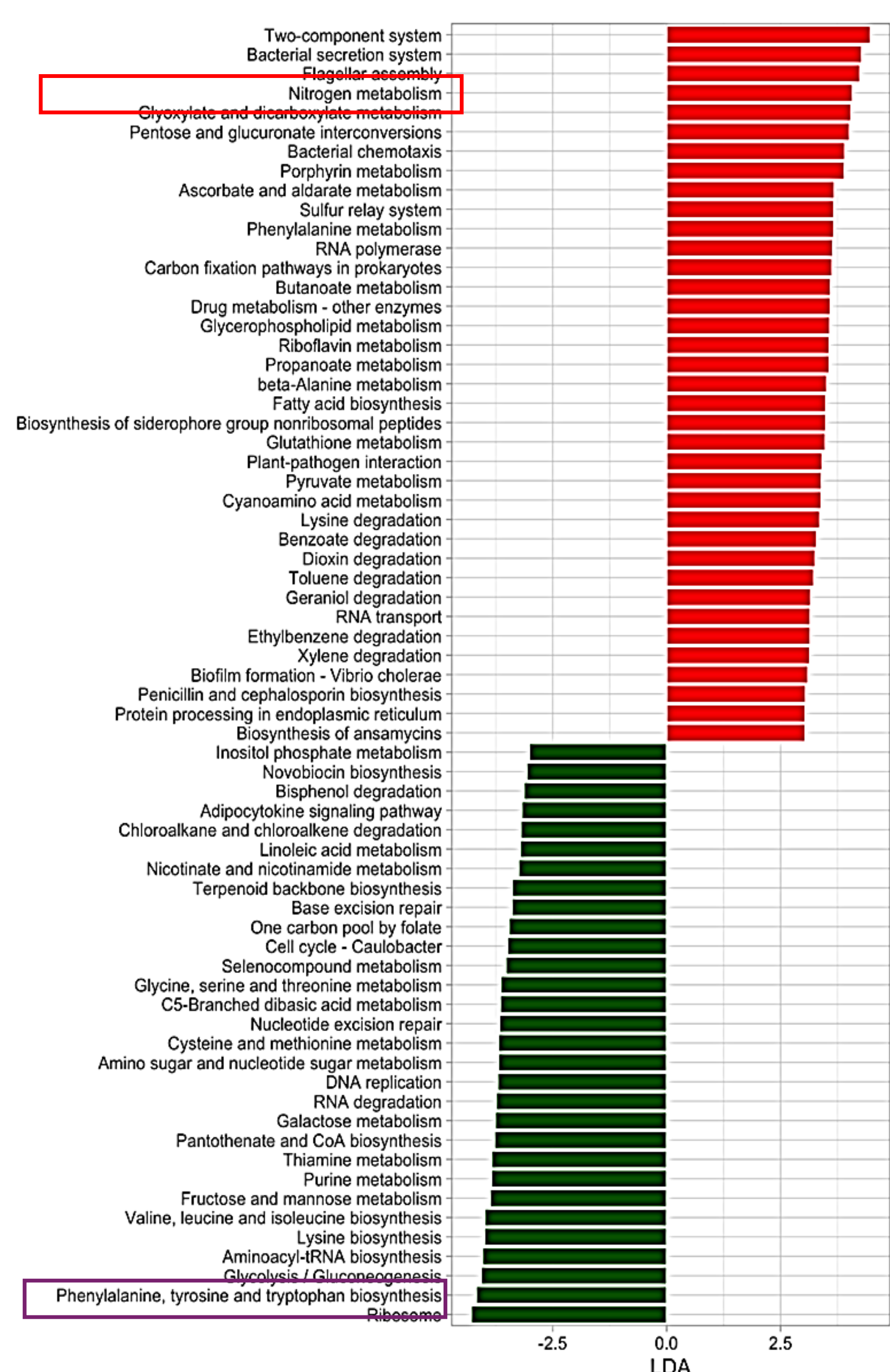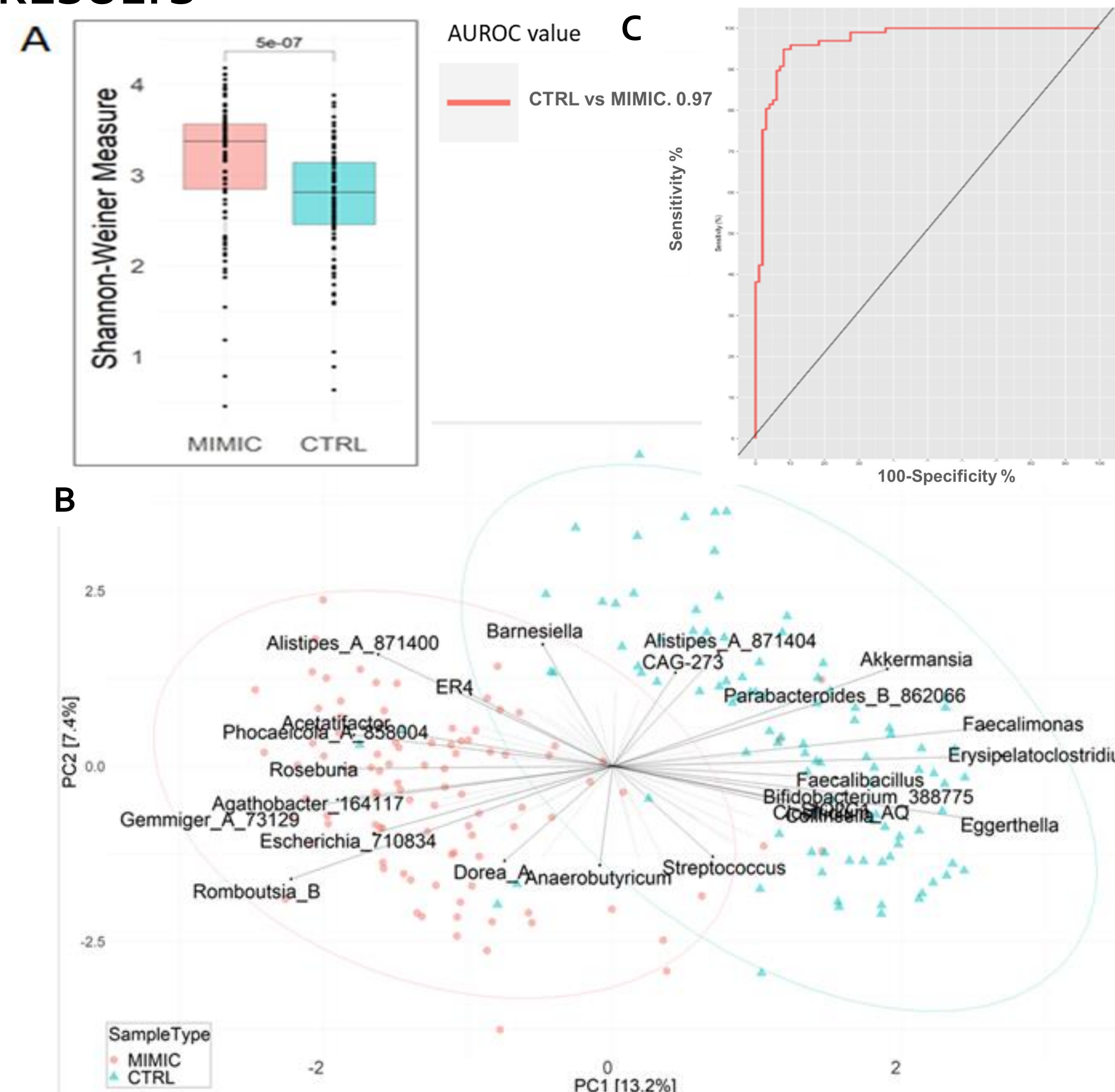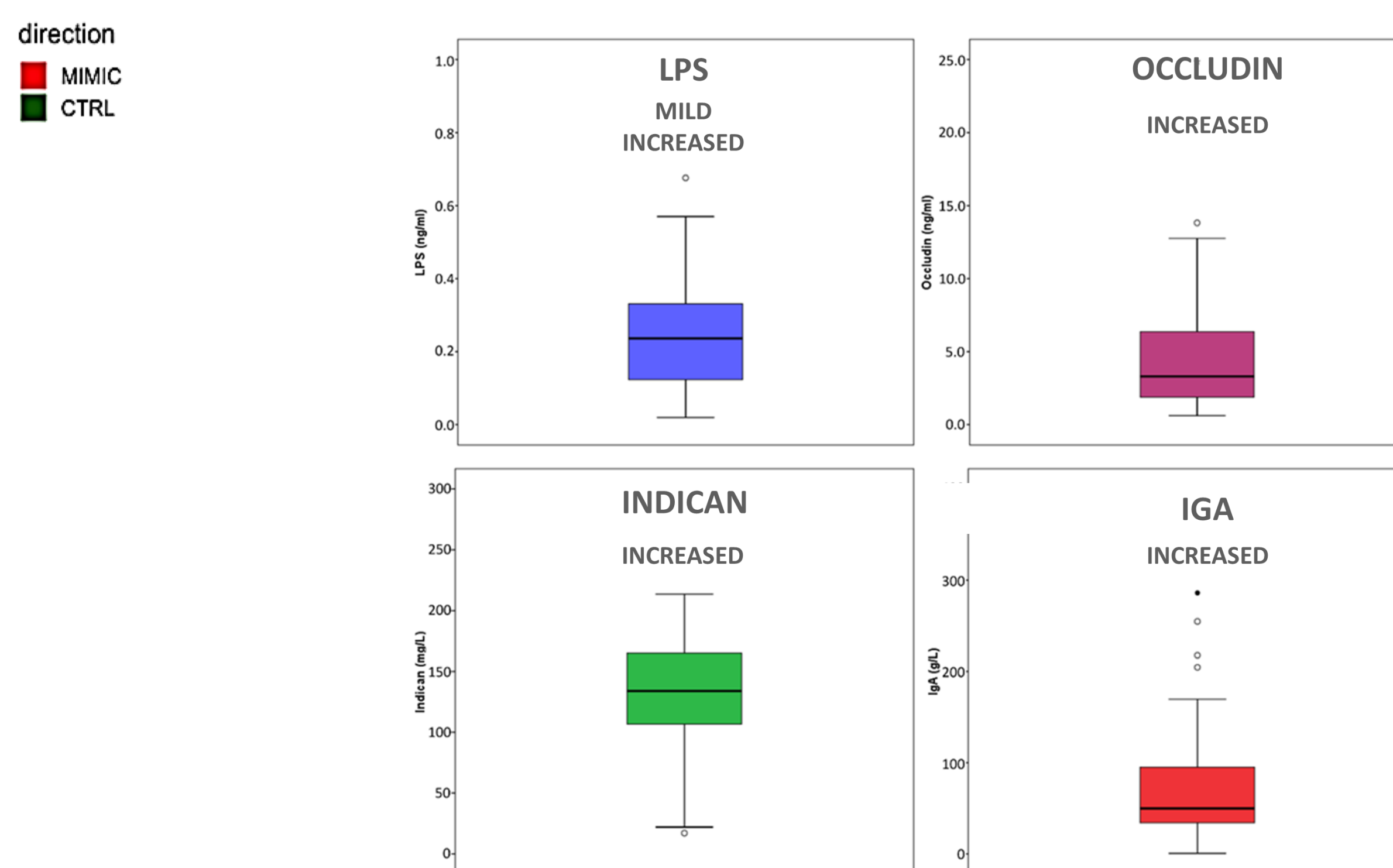

Figure 2. Predicted metabolic pathways statistically associated to MIMIC and CTRL. Red bars represent pathways increased in MIMIC; green bars represent pathways increased in CTRL. LDA, linear discriminant analysis.

Figure 3. Plasmatic levels of LPS occludin and IgA and urinary level of indican. Bar plots of LPS (ng/ml), occluding (ng/ml) and IgA (g/L) plasmatic concentrations and of urinary indicant concentration (mg/dL).

CONCLUSIONs

- MIMIC patients present different GM profiles than CTRLs.
- These profiles are connected with metabolic pathways important for migraine.
- The low levels of intestinal inflammation associated with increased intestinal permeability suggest that the products of these metabolic pathways should play a role in the onset of migraine more than intestinal inflammatory mediators.

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