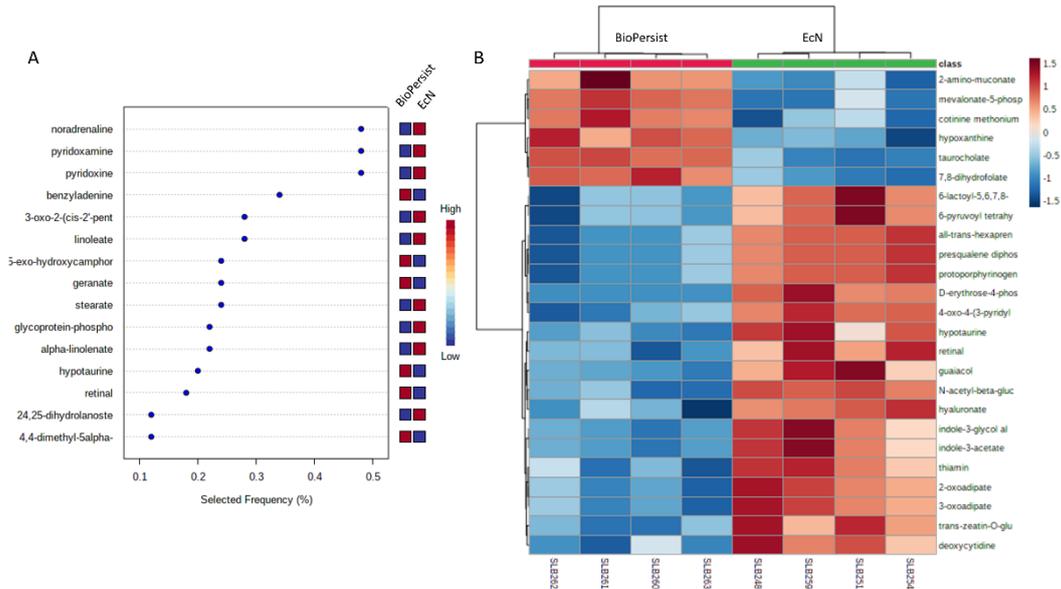
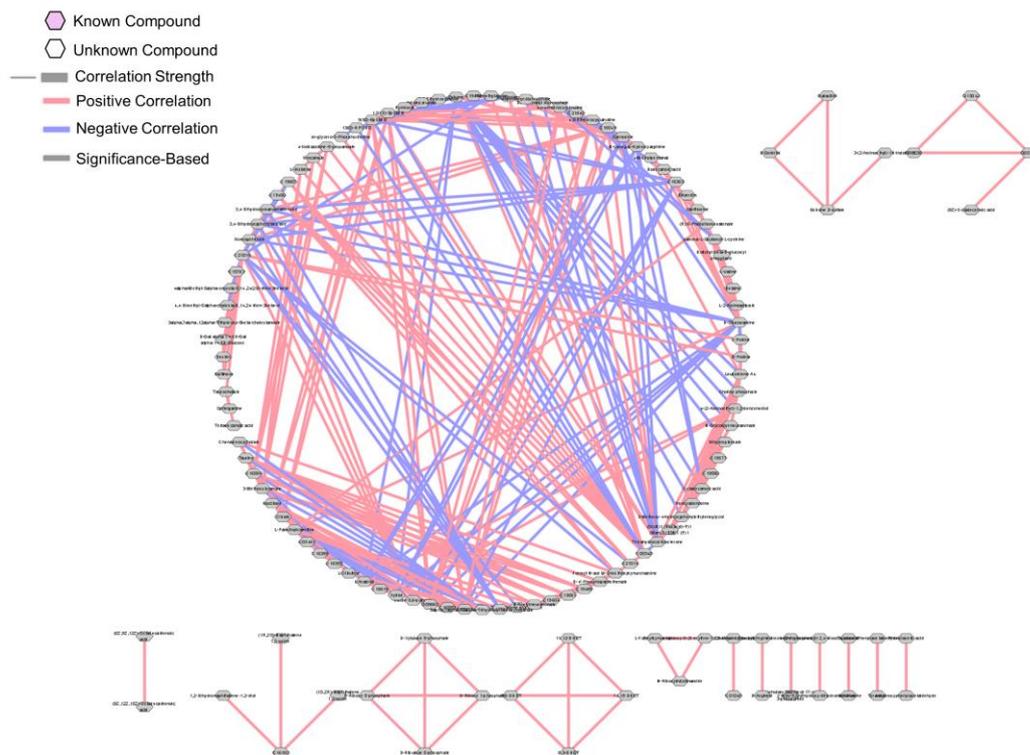


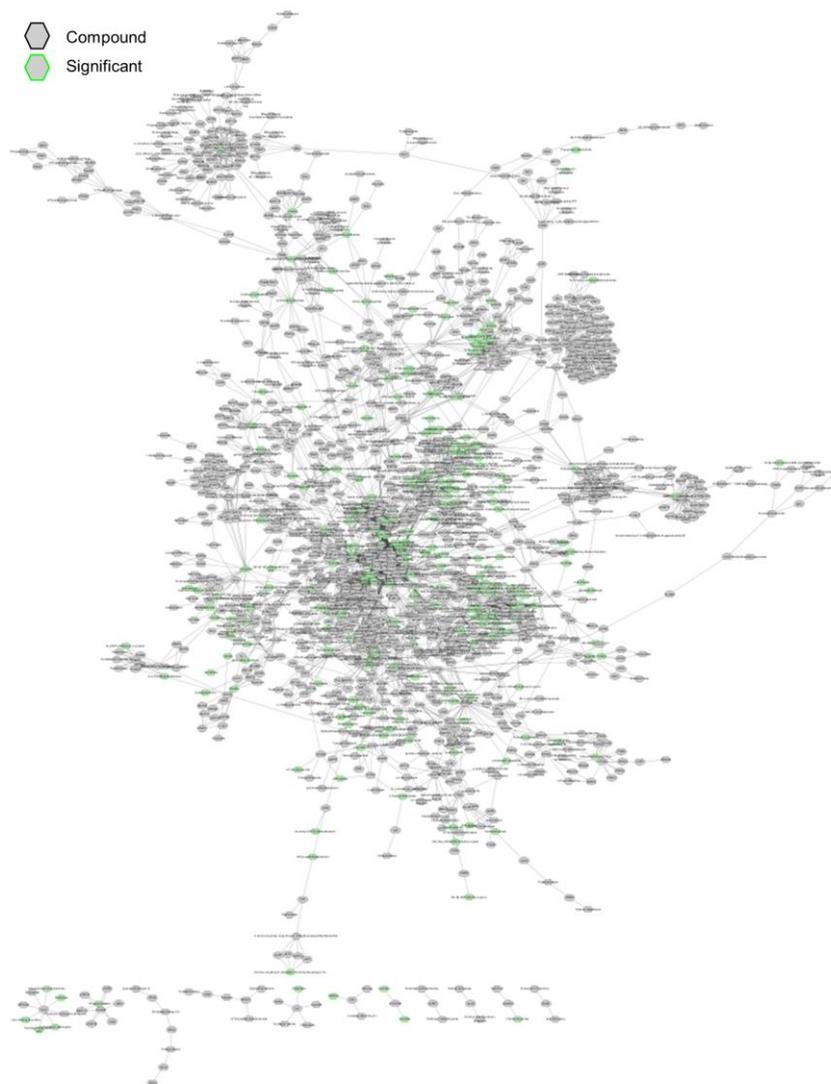
**Figure S1:** Non-Metric Multidimensional Scaling plot. QC samples are SLB246 and SLB247 labelled in red. SLB248, SLB251, SLB254 and SLB259 (labelled as green) represent mice colonic samples treated with EcN. SLB249, SLB 250, SLB 252 and SLB 253 shown in blue represent mice colonic samples treated with Lactobacillus probiotic. SLB 260, SLB261, SLB 262, SLB263 (labelled as pink) are samples treated with BioPersist. SLB255, SLB256, SLB257, SLB258 (light blue) are samples treated with BioColoniz.



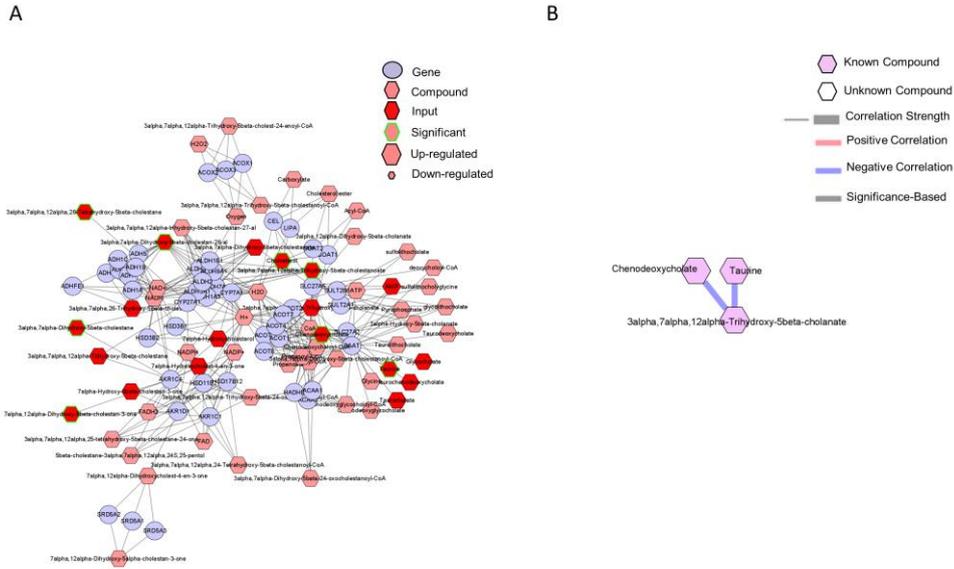
**Figure S2:** Distinct biomarkers and signature metabolites in mice treated with EcN and BioPersist. Top 15 biomarkers (A) and top 30 metabolites (B) in mice treated with EcN and BioPersist. AP: EcN; A: BioPersist.



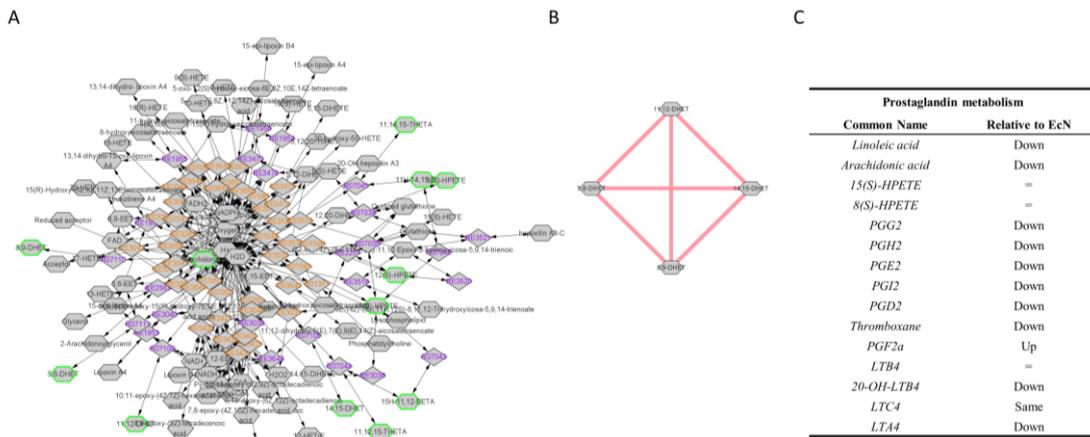
**Figure S3:** Correlation-based network of the metabolites annotated with KEGG mouse database. Red and blue represent positive and negative correlation, respectively. The thicker of the line, the higher correlation between the two metabolites. The correlation network was calculated based on the output of annotated metabolites of mice treated with EcN and BioPersist.



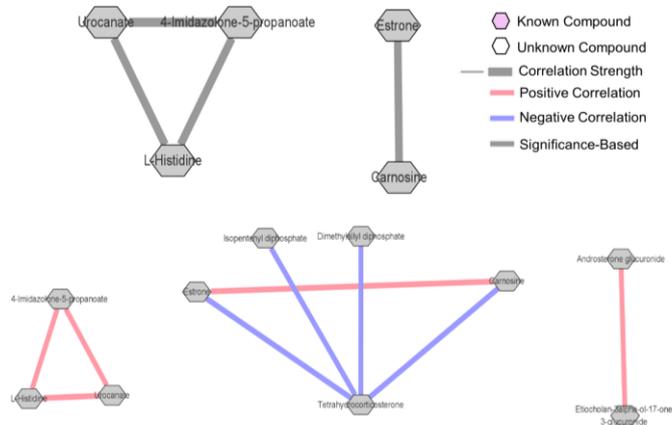
**Figure S4:** Pathway-based network of the metabolites annotated with KEGG mouse database. The metabolites highlighted in green indicate the statistically significant features. The network was built based on the normalized peak intensity output of mice treated with EcN and BioPersist.  $P < 0.05$ , fold change  $> 1.5$ . Cytoscape file is attached for better visualization.



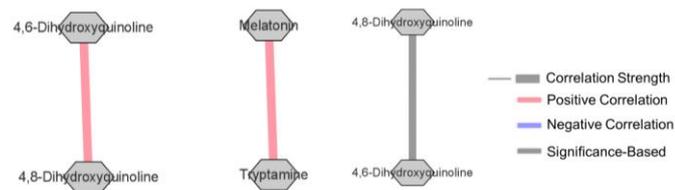
**Figure S5:** Networks of metabolites involved in bile acid biosynthesis pathway. A). Subnetwork of bile acid biosynthesis pathway, statistically significant features are highlighted in green. B). Correlation of metabolites annotated in bile acid biosynthesis pathway. Connection colored with blue indicated negative correlation between two metabolites



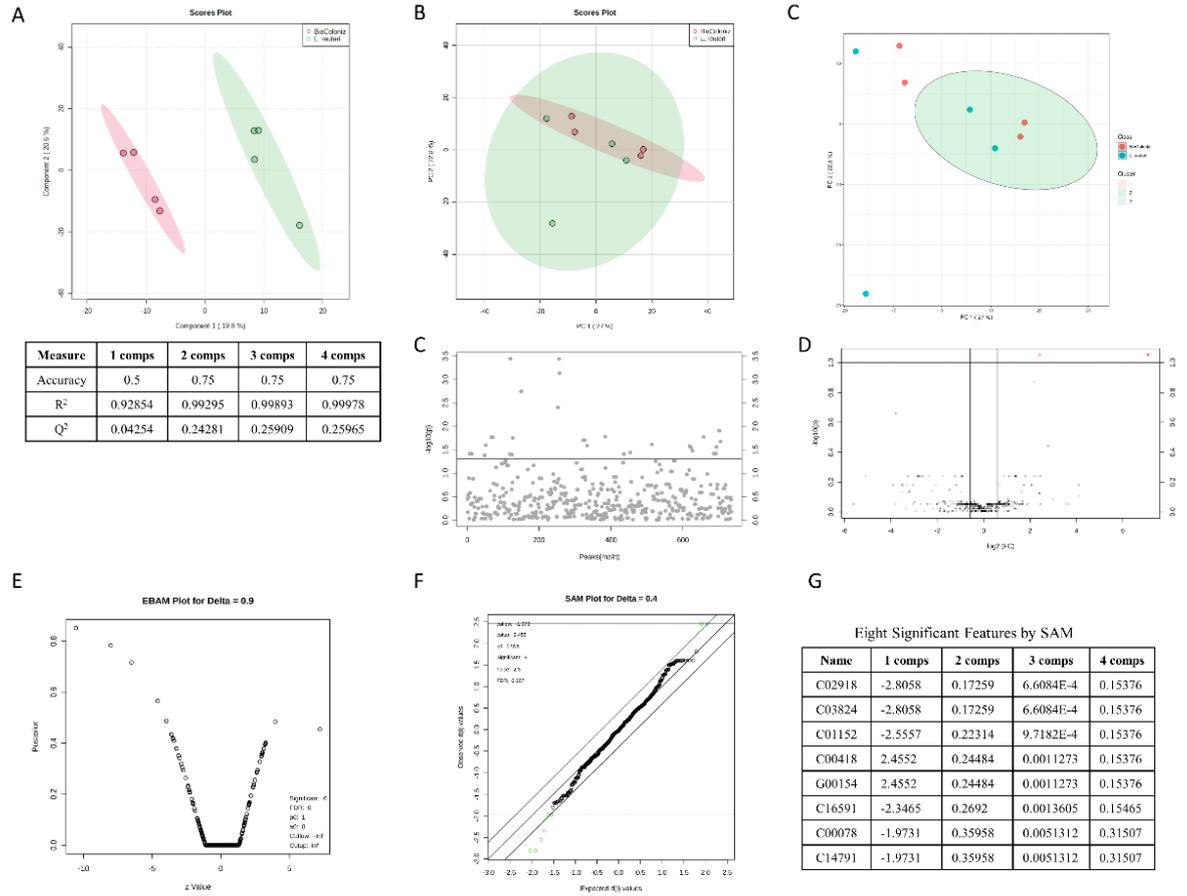
**Figure S6.** BioPersist reduces the production of pro-inflammatory prostaglandins. A) Subnetwork of arachidonic acid pathway. Metabolites highlighted in green indicated statistically significant features. B) Correlation of metabolites annotated in arachidonic acid pathway. Connection colored with red indicated positive correlation between two metabolites. C) List of metabolites annotated for prostaglandin biosynthesis.



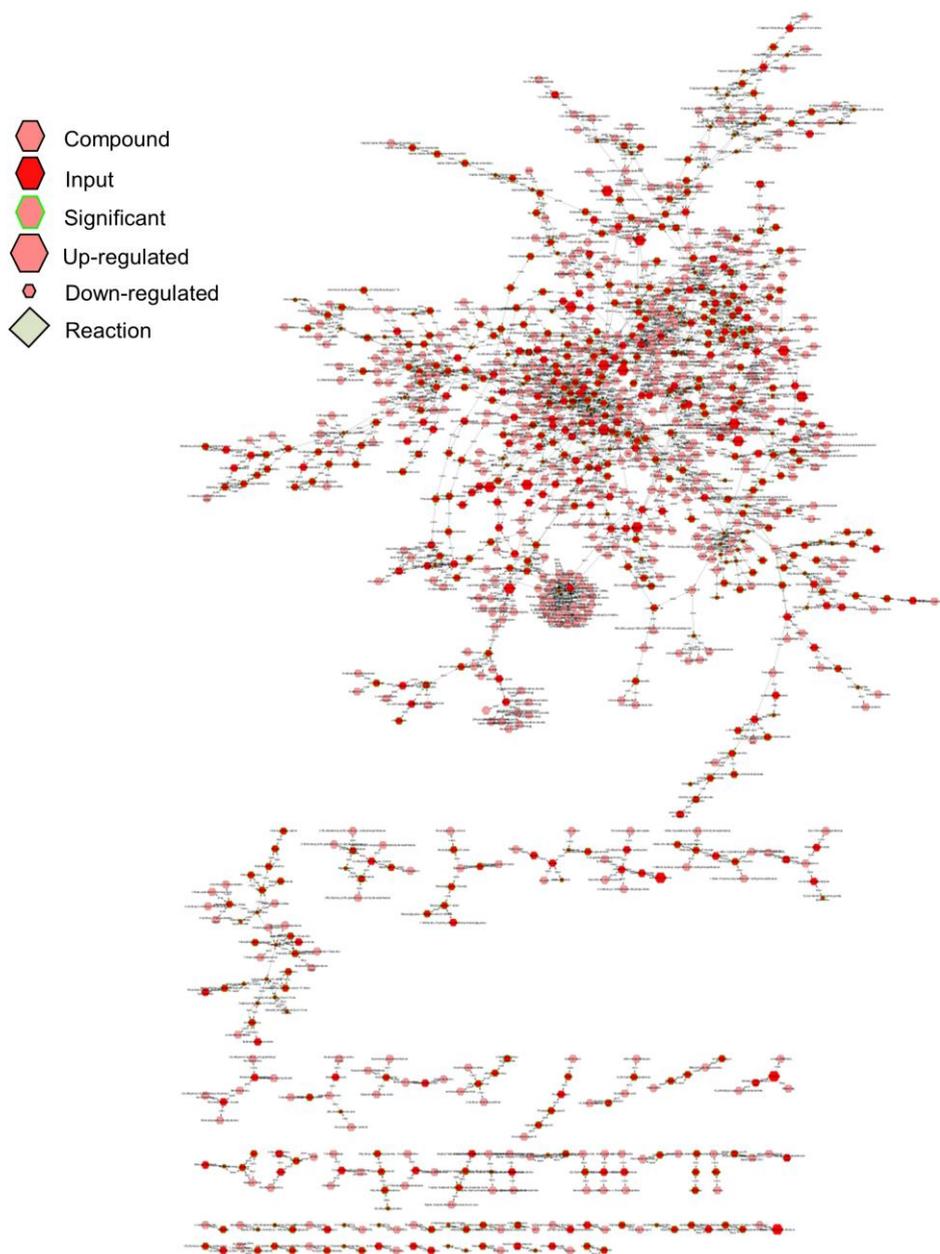
**Figure S7:** Correlation of metabolites annotated in steroid associated pathways. Connection colored with red and blue indicated positive and negative correlation between two metabolites, respectively. Statistically significant correlations of metabolites are highlighted with grey.  $P < 0.05$ .



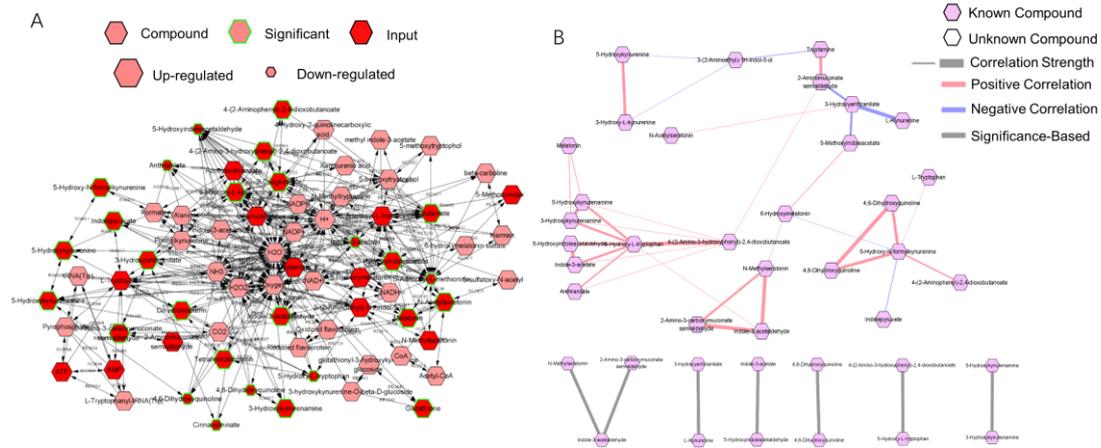
**Figure S8:** Correlation of metabolites annotated in tryptophan pathways. Connection colored in red indicated positive correlation between two metabolites. Statistically significant correlations of metabolites are highlighted with grey.  $P < 0.05$ .



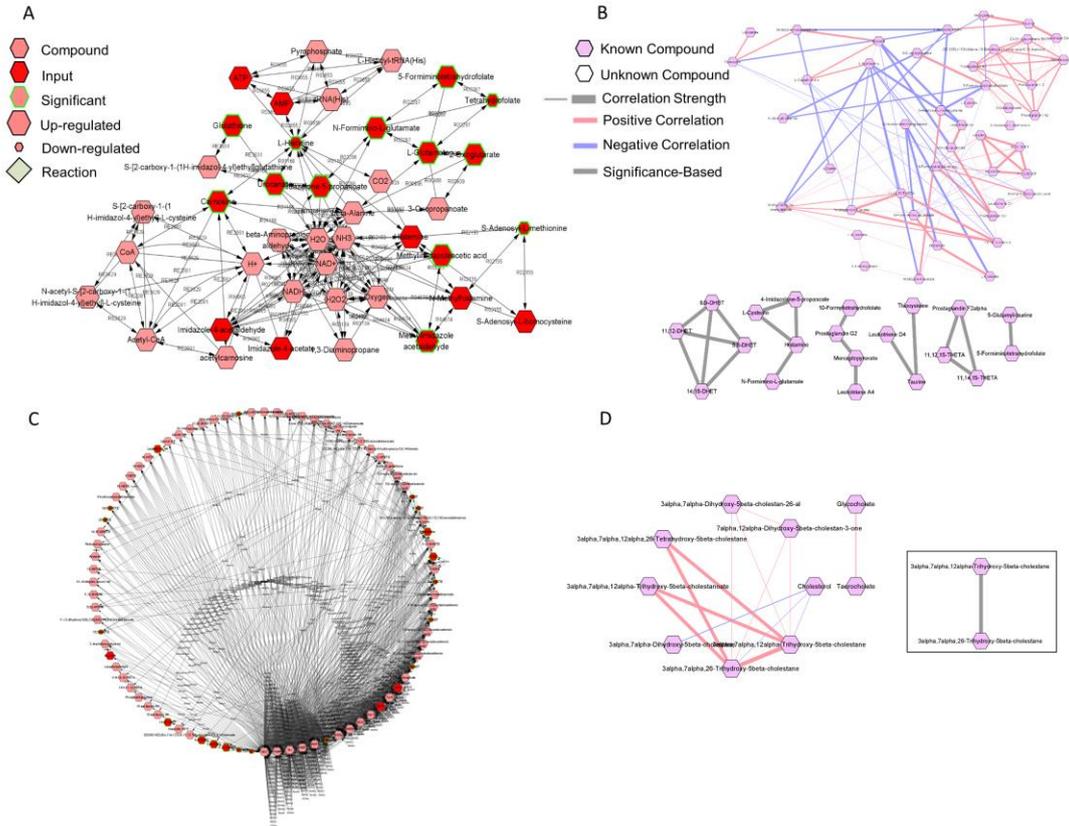
**Figure S9:** BioColoniz shows similar physiological effects with commercial *L.reuteri* strain. A) PL-SDA plot of mice treated with BioColoniz and *L. reuteri*. B) PCA plot of mice treated with BioColoniz and Lactobacillus. C). No statistical significant features were detected with t-test analysis. D) Volcano plot analysis for detecting differential metabolites between BioColoniz and Lactobacillus groups. Only three features were different between two treatments. E) No significant features were identified with empirical Bayesian method (EBAM). F-G) Eight significant features were observed with significance analysis of microarray (SAM).



**Figure S10:** Pathway-based network of mice treated with BioPersist and BioColoniz. Metabolites highlighted in green represent statistically significant features. The network was built based on the normalized peak intensity output of mice treated with BioPersist and BioColoniz.  $P < 0.05$ , fold change  $> 1.5$ . Cytoscape file is attached for better visualization.



**Figure S11.** The network of tryptophan metabolism. A) Subnetwork of tryptophan metabolism pathway. Metabolites highlighted in green indicated statistically significant features. B) Correlation of metabolites annotated in tryptophan metabolism pathways. Connections in red and blue indicated positive and negative correlation between two metabolites, respectively. Statistically significant correlations of metabolites were highlighted in grey.  $P < 0.05$ .



**Figure S12:** The network of histamine and prostaglandin metabolism. A) Subnetwork of histamine metabolism pathway. Metabolites highlighted in green indicated statistically significant features. B) Correlation of metabolites annotated in histamine and prostaglandin associated metabolism pathways. Connections in red and blue indicated positive and negative correlation between two metabolites, respectively. Statistically significant correlations of metabolites were highlighted in grey. C) Subnetwork of prostaglandin metabolism pathway. Metabolites highlighted in green indicated statistically significant features. D) Correlation of metabolites annotated in bile acid metabolism pathways. Connections in red and blue indicated positive and negative correlation between two metabolites, respectively. Statistically significant correlations of metabolites were highlighted with grey.  $P < 0.05$ , fold change  $> 1.5$ .