

LACSEF 2026 research poster

Historical presentation

This poster records the computational stage of the project presented at the 2026 Los Angeles County Science & Engineering Fair. The original poster is preserved on the following page.

How to read the findings

The overlap consists of directionally concordant metabolite annotations from two different rodent exposure studies. It suggests hypotheses about shared biology; it does not establish a common stress–immune mechanism. The primary model ranks predicted microbial mediator functions rather than demonstrating restoration of the nine annotations.

The poster's references to between-study variability should not be read as external validation. The executed training table reports one study identifier, so the reported cross-validation is internal. The permutation result ($p = 0.137$) was not definitive.

The later manuscript adds a separate experimental-priority model and preliminary animal work. Those additions are not part of this historical poster. Neither version establishes therapeutic benefit in humans.

Project page and current materials

<https://www.jalencai.com/research/gut-brain-axis/>

Reader note added September 21, 2026. The source document follows on the next page.

Abstract

Addiction is a chronic, relapsing disorder driven by neuroadaptations in reward, stress, and cognitive processes. Alcohol, nicotine, caffeine, and illicit drugs affect >270 million people globally and cost the U.S. >\$400 billion annually; however, treatments remain limited, and the mechanisms behind addiction are not well understood. An emerging topic in addiction biology is the gut–brain axis, the bidirectional link between the gut microbiome and the brain mediated by neural and immune pathways. Here, we asked whether addictive substances share a convergent metabolomic signature that could be targeted through the gut–brain axis. We integrated public metabolomics data and screened for metabolites exhibiting similar, consistent changes across alcohol and caffeine-exposed samples. Nine metabolites showed corresponding changes (seven increased, two decreased), including stress signaling (cortisone) and inflammatory lipid mediators (19-Hydroxy-PGE2), suggesting cross-substance convergence on stress and immune pathways. We then developed an AI-guided framework to rank probiotic strains by predicted capacity to restore the metabolite profile under diet-relevant conditions. Barrier-support features aligned most with the restorative label (Spearman $\rho = 0.438$), while neurocalming features were inversely associated ($\rho = -0.332$). The model achieved moderate discrimination (repeated-CV AUC mean = 0.749, best AUC = 0.755; ACC = 0.690), but limited capability ($p = 0.137$) and between-study variability. In strain ranking, Akkermansia muciniphila scored highest overall (mean 8.21; 95% interval 3.90–13.10), and closely related B. animalis strains were the most consistently top-ranked. Overall, this study provides a scalable pipeline linking cross-substance metabolomic convergence to probiotic candidates for future in vivo validation.

Introduction

Public health and economic burden:

Globally, an estimated 270 million adults reported using psychoactive substances in the past year. In the United States alone, the societal costs of SUDs—including healthcare, lost productivity, and law enforcement—are estimated to exceed \$400 billion annually.

The crucial role of the gut-brain axis:

Disruption of the microbiota (ecological imbalance) caused by exposure to substances (such as alcohol) can exacerbate systemic inflammation and affect the brain's reward and stress circuits, thereby promoting addictive behaviors.

Limitations of current research:

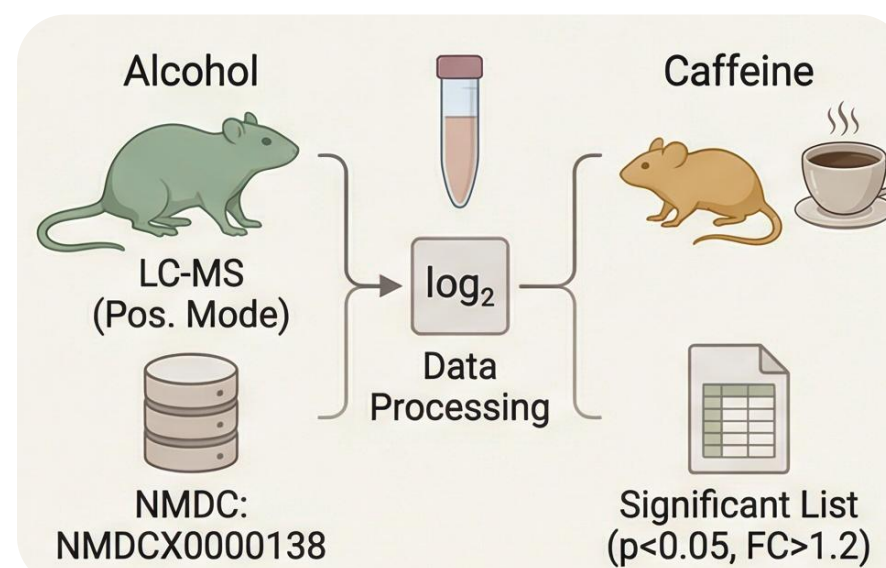
There are still limited effective treatments for SUDs, and the neurobiological mechanisms underlying their onset and persistence have not been fully elucidated.

The urgent unresolved issue:

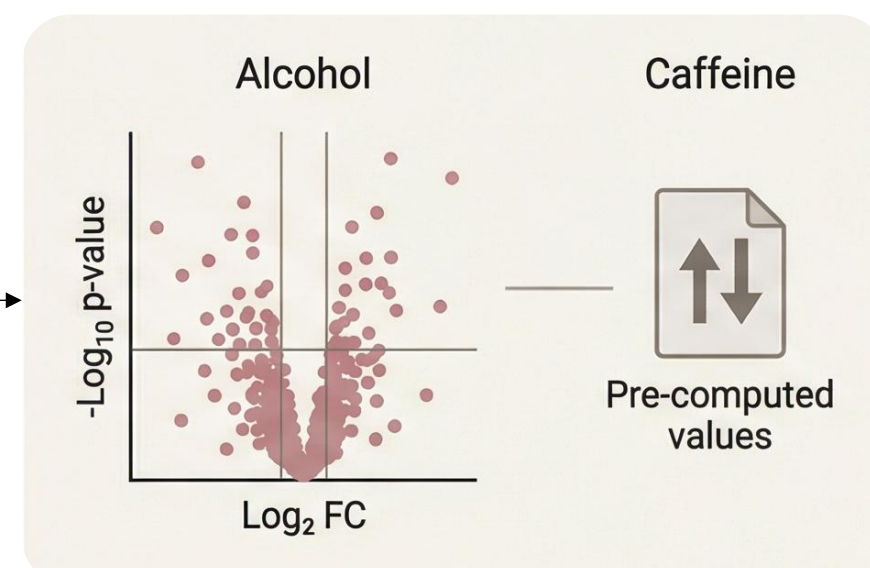
Although there is evidence suggesting that the gut microbiota plays a role in alcohol addiction, it remains unknown whether different types of widely used psychoactive substances (such as alcohol and caffeine) would lead to a common and quantifiable metabolic disorder feature (metabolomics feature).

Materials & Methods

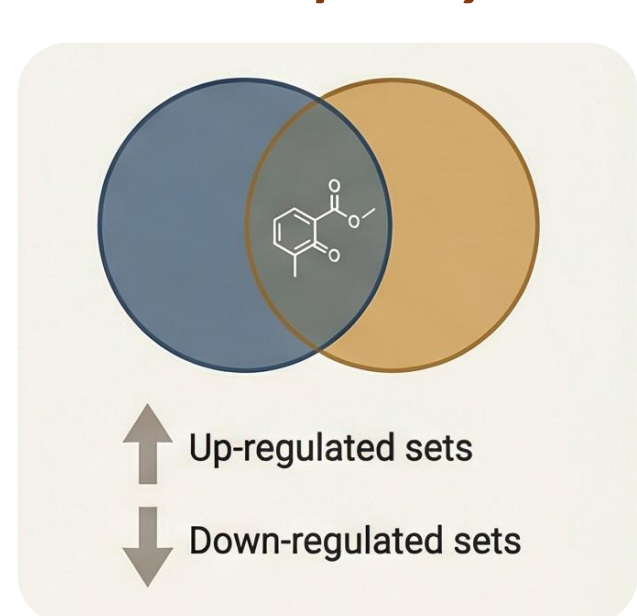
A. Data Acquisition and Preprocessing



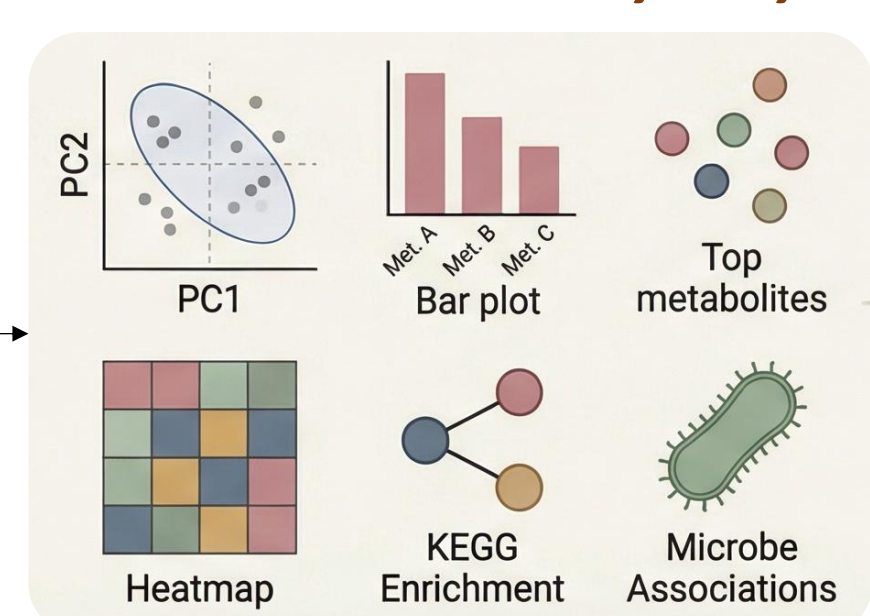
B. Differential Analysis



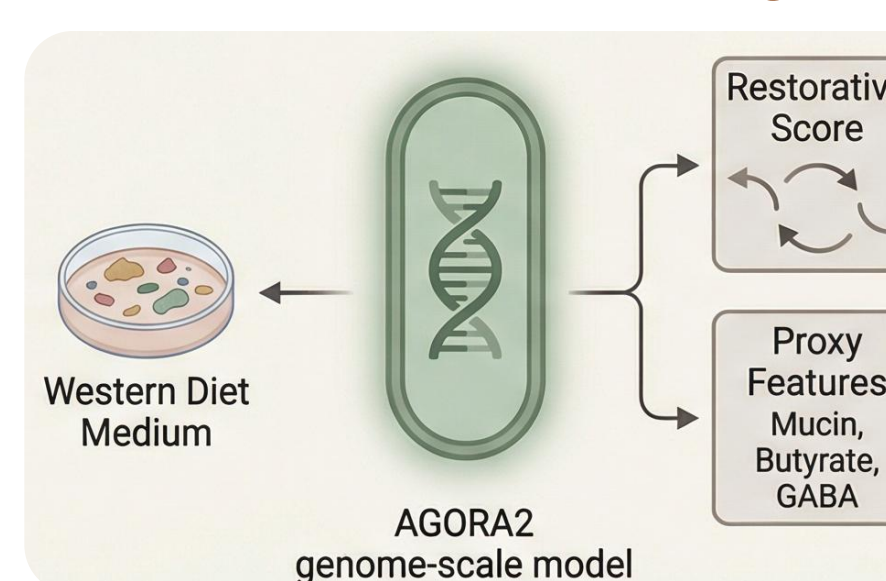
C. Overlap Analysis



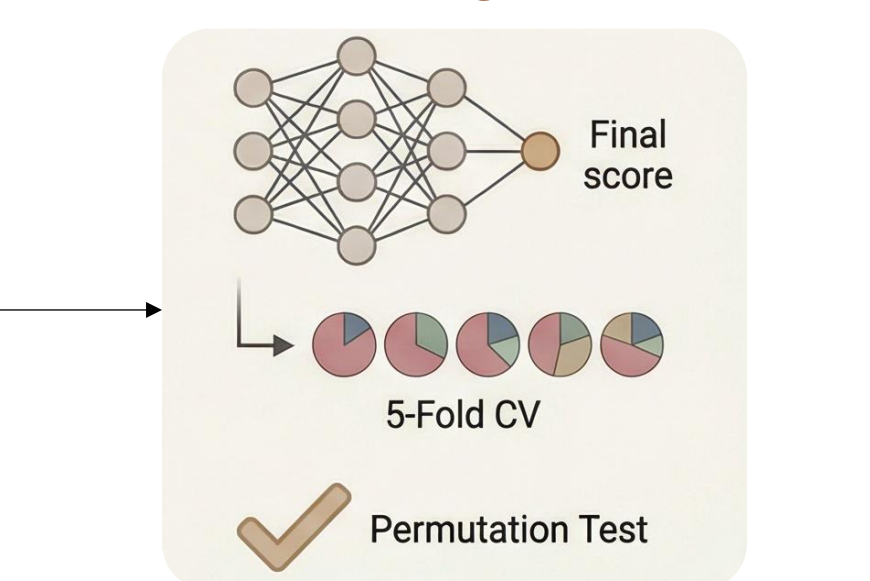
D. Visualization & Pathway Analysis



E. Genome-Scale Modeling



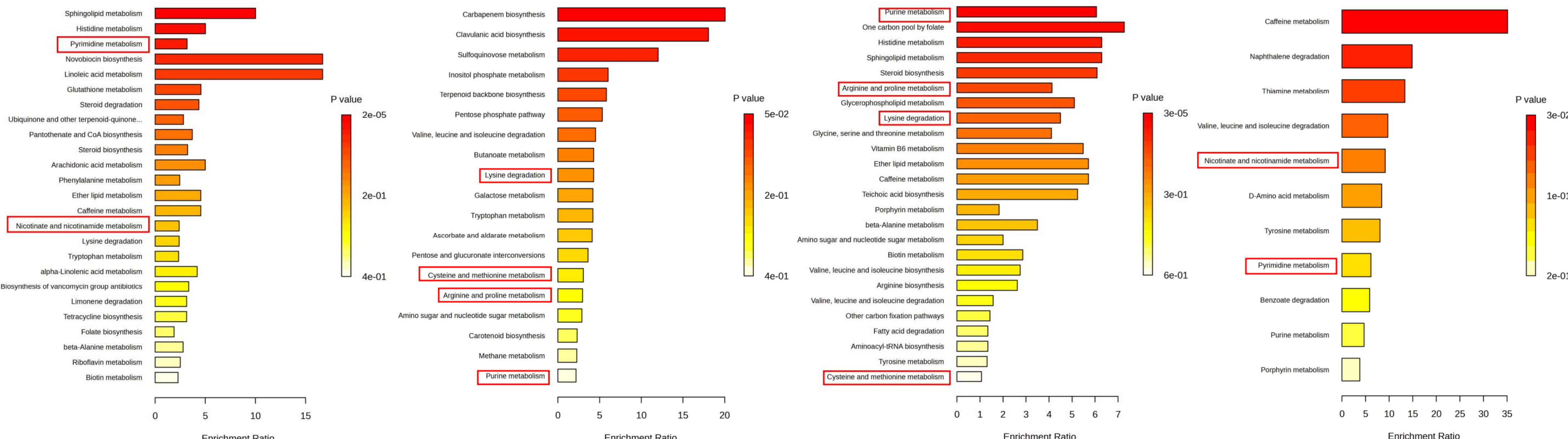
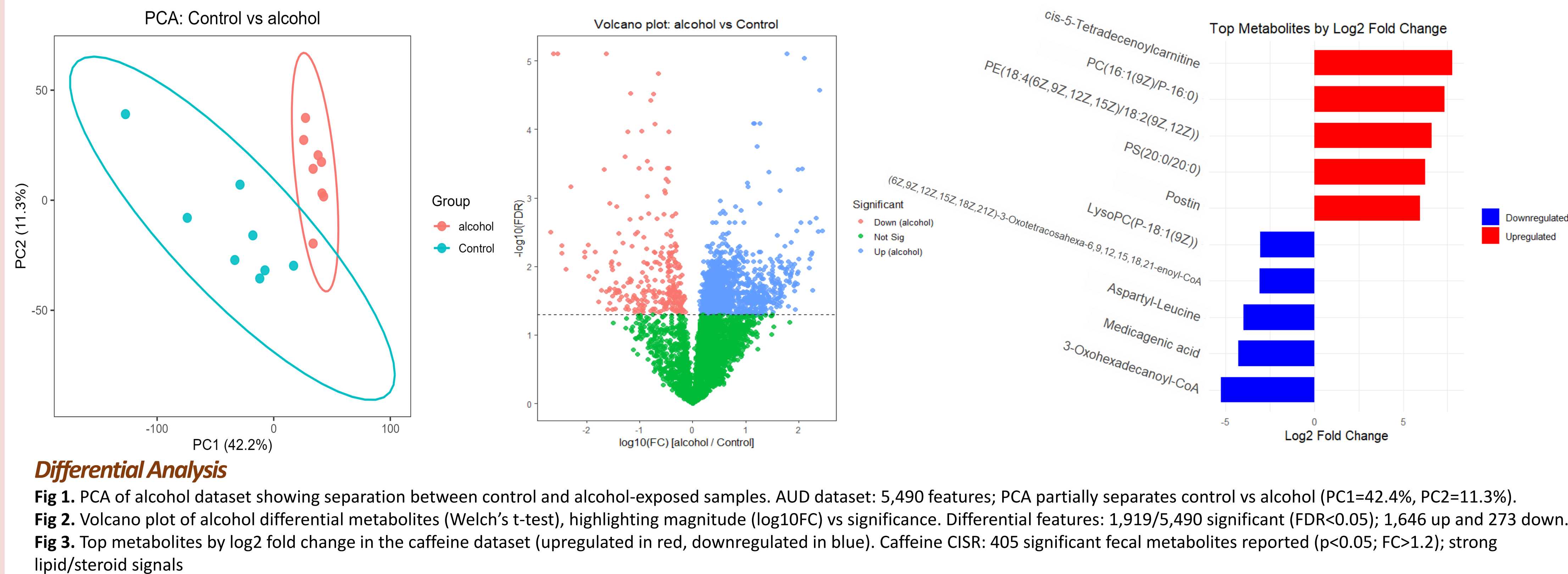
F. Model Training & Validation



Images courtesy of NanoBanana

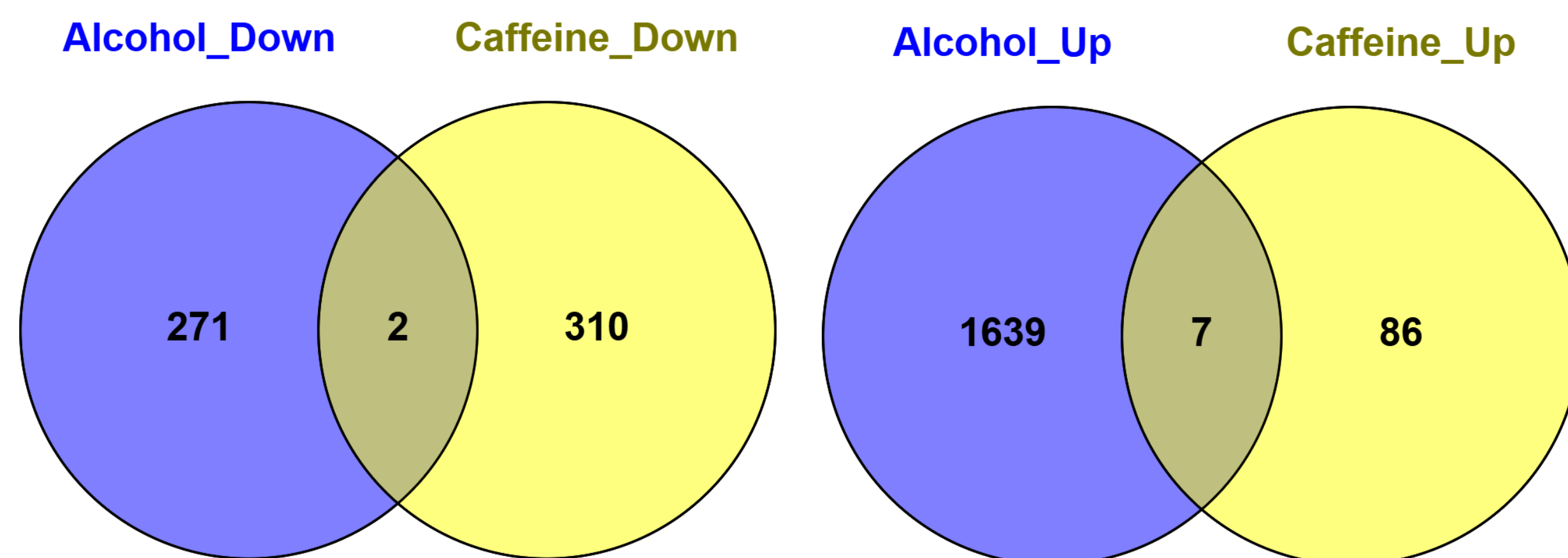
Identifying Shared Metabolomic Signatures Across Alcohol and Caffeine Exposure and Prioritizing Probiotic Candidates via Genome-Scale Modeling

Results



Pathway Analysis

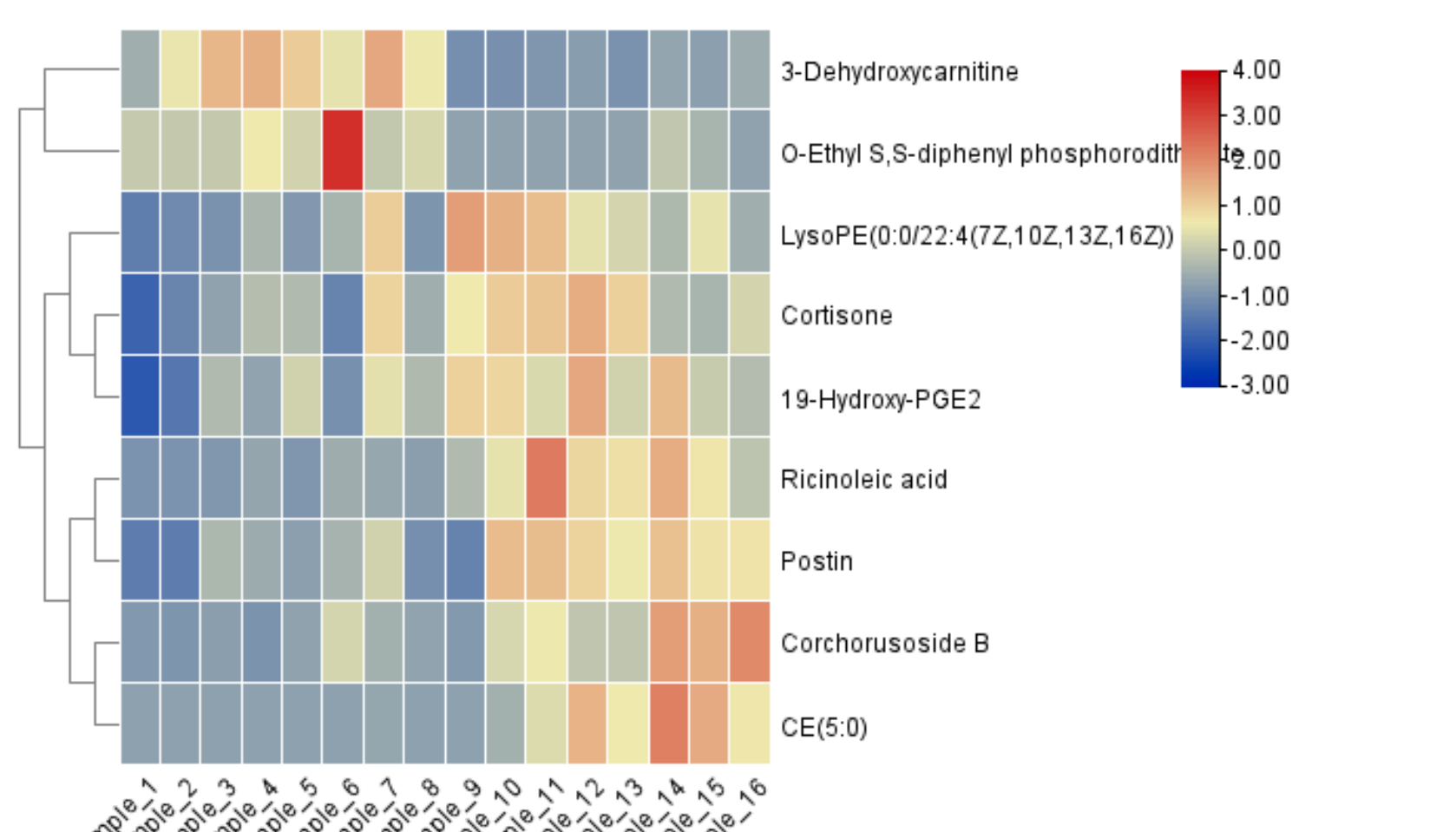
Fig 4. Gut enrichment overview for downregulated + upregulated metabolites in the alcohol and caffeine datasets. Corresponding metabolism pathways were found to be highly correlated with both alcohol and caffeine intake. Downregulated: lysine degradation; cysteine and methionine metabolism; arginine and proline metabolism; and purine metabolism. Upregulated: pyrimidine metabolism; nicotinate and nicotinamide metabolism.



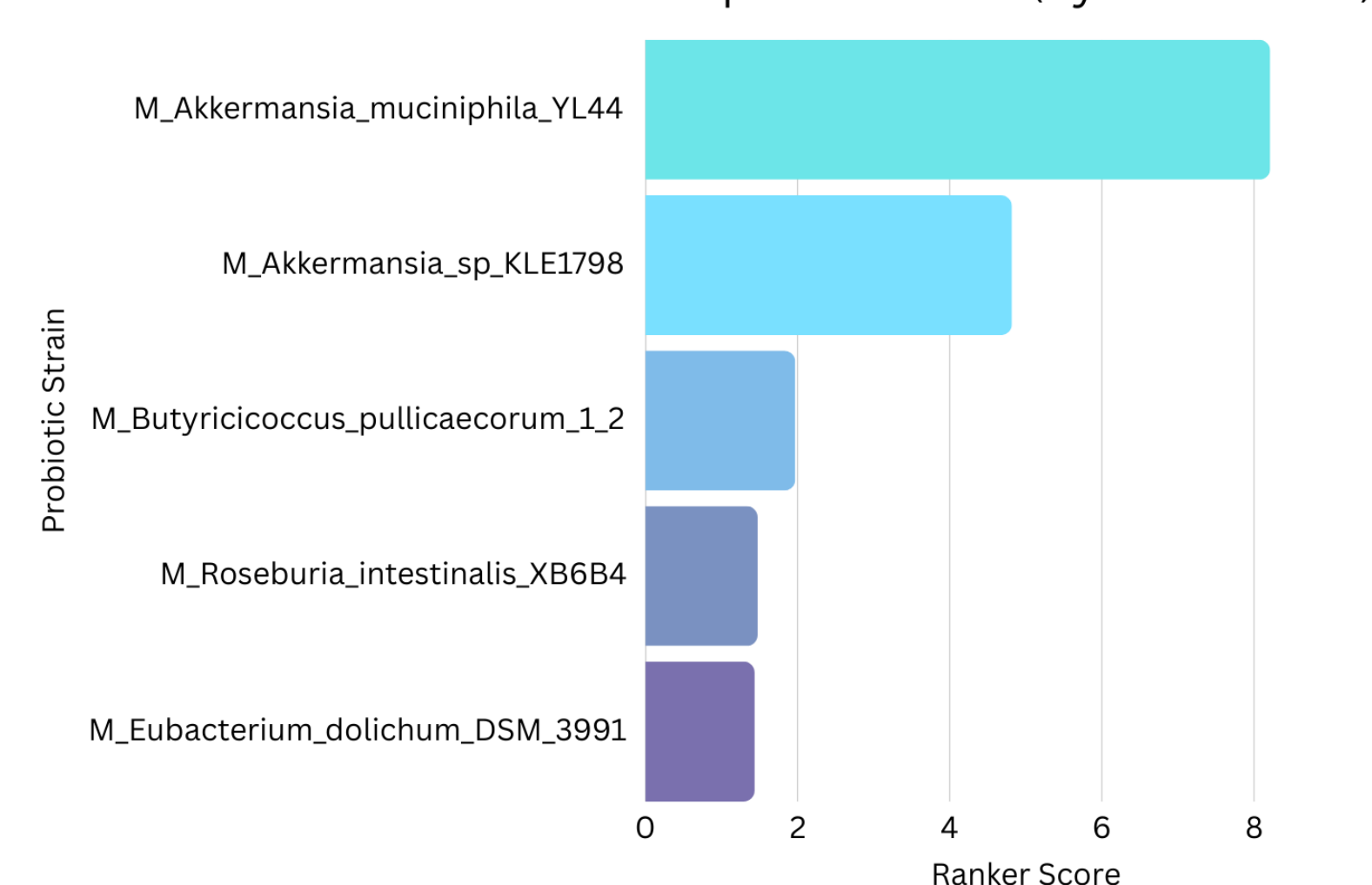
Overlap Analysis

Fig 5. Venn diagram of shared downregulated + upregulated metabolites between alcohol and caffeine/CISR datasets. Downregulated: 3-Dehydroxycarnitine; O-Ethyl S,S-diphenyl phosphorodithioate. Upregulated: Ricinoleic acid; Cortisone; Corchoroside B; Postin; CE(5:0); 19-Hydroxy-PGE2; LysoPE(0:0/22:4(7Z,10Z,13Z,16Z)).

Fig 6. Heatmap of the nine shared metabolites across alcohol control and alcohol-exposed samples.



Top 20 species-level representatives (by mean score)



Machine Learning Model Analysis

Fig 7. AI predictions: Akkermansia muciniphila scored highest overall; Bifidobacterium animalis strains consistently top-ranked among probiotic-filtered candidates (model performance: repeated-CV AUC ≈ 0.75; ACC ≈ 0.69).

Discussion

Key findings

- Alcohol and caffeine exposure showed consistent metabolic change directions in two different animal models.
- There is a common stress-immune-lipid remodeling mechanism at play.

Key metabolites and pathways

- Upregulated metabolites (LysoPE, 19-hydroxy-PGE2, cortisone):
 - Reflect membrane remodeling, immune activation, and HPA axis stress response;
 - The endocrine (cortisone) and immune (steroidal aliphatic acids) pathways work synergistically.
- Downregulated metabolite (3-dehydroxy-carnitine):
 - It indicates abnormal fatty acid transport or mitochondrial metabolism.

Limitations

- Cross-study heterogeneity (species, exposure methods, sample types);
- Based solely on the matching of metabolite names, no effect size was combined.
- Some metabolite annotations are uncertain.

Improvement Direction

- Use standardized metabolite identifiers (HMDB/InChIKey);
- Include more datasets and conduct a random effects meta-analysis;
- Targeted quantitative verification of key metabolites (such as cortisol, 20-hydroxycholesterol, etc.).

Conclusion

Across alcohol and caffeine-related exposures, we identified a small panel of metabolites with concordant directionality, implicating stress-hormone and inflammatory lipid mediator pathways that plausibly interface with the gut–brain axis. Genome-scale modeling and AI-guided ranking prioritized candidate strains—particularly Akkermansia (overall) and Bifidobacterium/ Lactobacillus (probiotic-deployable)—that may counteract this shared signature. These results provide a testable, mechanistically grounded shortlist for future probiotic intervention experiments.

References

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