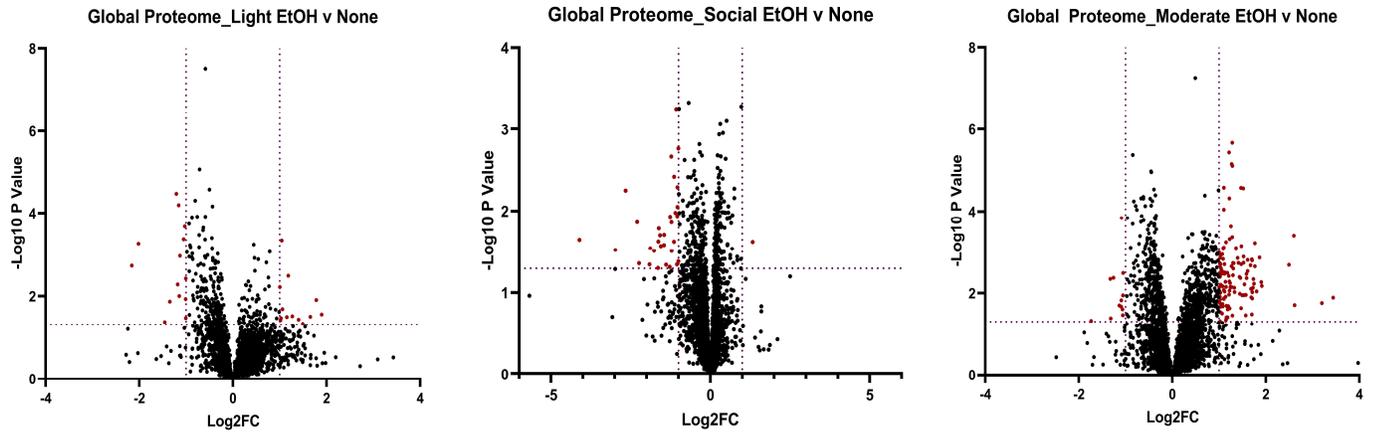


# Effects of alcohol consumption and tobacco smoking on the composition of the ensemble of drug metabolizing enzymes and transporters in human liver

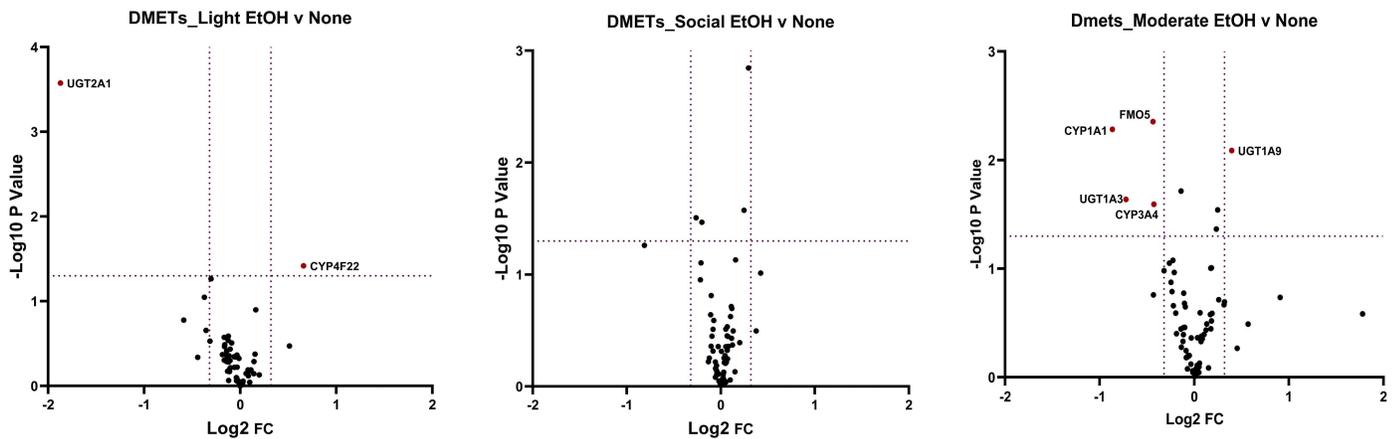
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## Supplementary figures

A



B



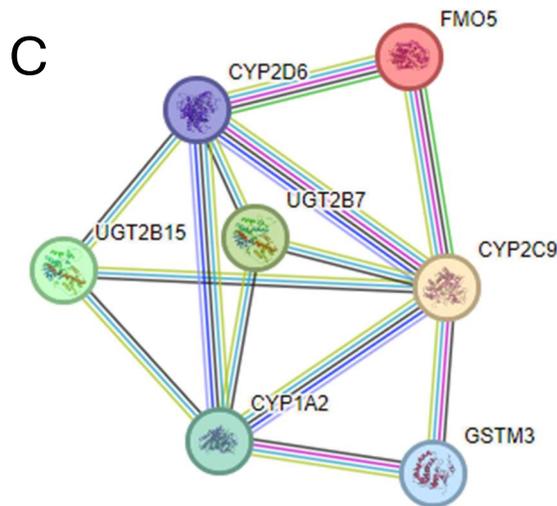
**Figure S1.** Global and DMET proteome analysis of HLM from light, social, and moderate alcohol drinkers. **(A)** Global proteomics of HLM from light drinkers vs non-drinkers showed little significant changes in proteins, similar to a comparison of social drinkers vs nondrinkers. There were moderate levels of significant differences in protein levels in HLM of moderate drinkers as compared to non-drinkers. (2.0 fold change (FC) cutoff, P-value<0.05) **(B)** The DMET proteome showed very little significant alteration in levels of expression in HLM from light drinkers, social drinkers, or moderate drinkers as compared to non-drinkers. (1.25 fold change cutoff, P-value<0.05)

### A KEGG Pathways Downregulated

Description	Count in network	Strength	FDR
Taurine and hypotaurine metabolism	2 of 11	1.44	3.28E-02
Starch and sucrose metabolism	5 of 32	1.37	1.20E-04
Drug metabolism - cytochrome P450	7 of 64	1.22	1.63E-05
Cholesterol metabolism	5 of 48	1.19	5.10E-04
Oxidative phosphorylation	12 of 128	1.15	4.96E-08

### B KEGG Pathways Upregulated

Description	Count in network	Strength	FDR
Proteasome	26 of 43	1.69	2.41E-30
Phenylalanine, tyrosine and tryptophan biosynthesis	3 of 6	1.61	1.20E-03
Valine, leucine and isoleucine degradation	22 of 46	1.59	6.63E-24
Propanoate metabolism	16 of 33	1.59	1.73E-17
Citrate cycle (TCA cycle)	12 of 28	1.54	8.50E-13



**Figure S2.** STRING analysis of significantly upregulated and downregulated proteins from global proteomics. **(A)** Downregulated KEGG Pathways include several key functions of the liver, including lipid metabolism, bile acid homeostasis, energy regulation and ATP synthesis, as well as drug metabolism. **(B)** Upregulated KEGG Pathways include those involved in proteolysis, amino acid metabolism, propanoate metabolism, and the TCA cycle. **(C)** Drug metabolism - cytochrome P450 KEGG Pathway. Seven members of this KEGG Pathway were significantly downregulated in the global proteomics data, indicating a strength of 1.22 and an FDR of  $1.63 \times 10^{-5}$ .