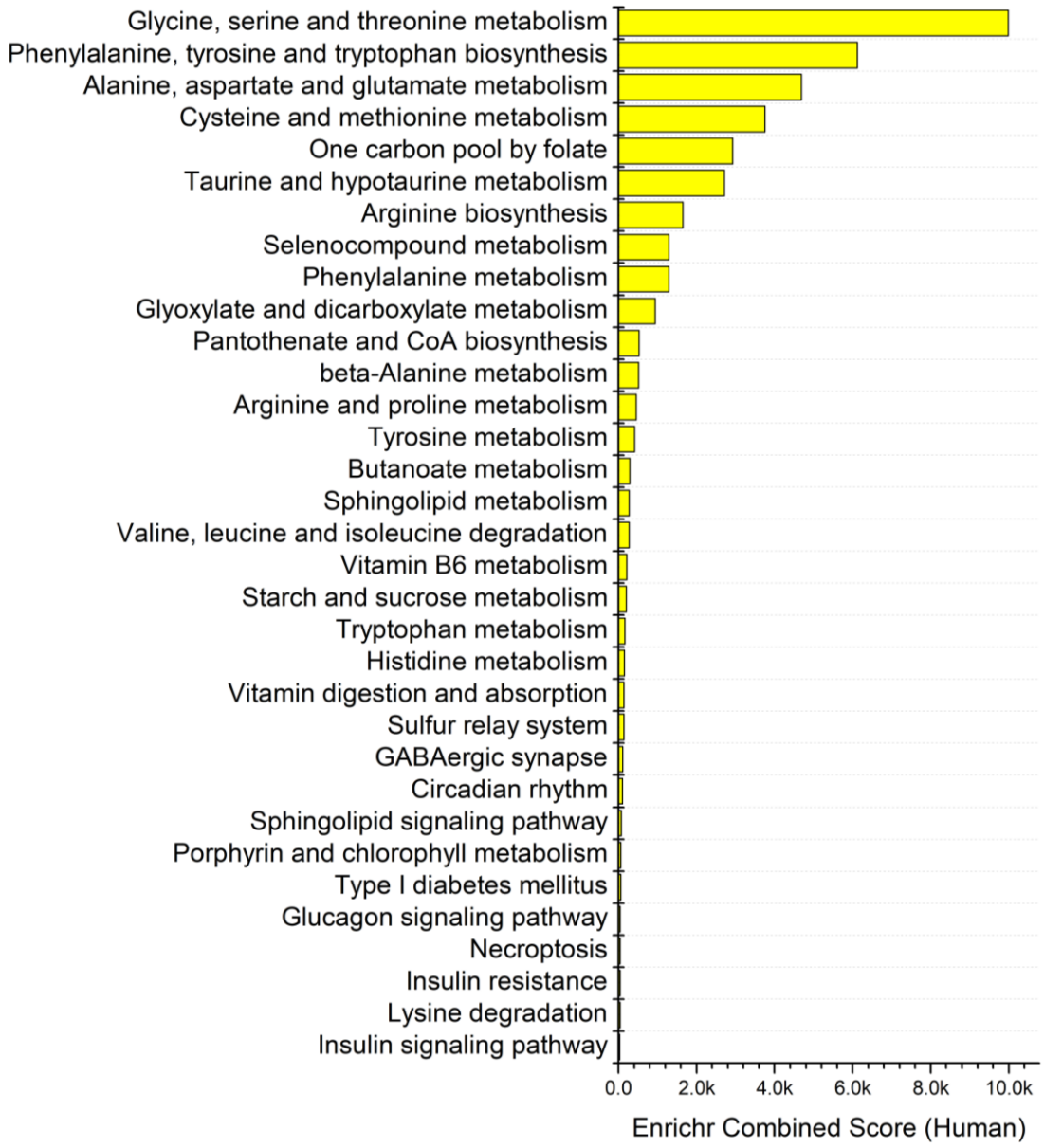
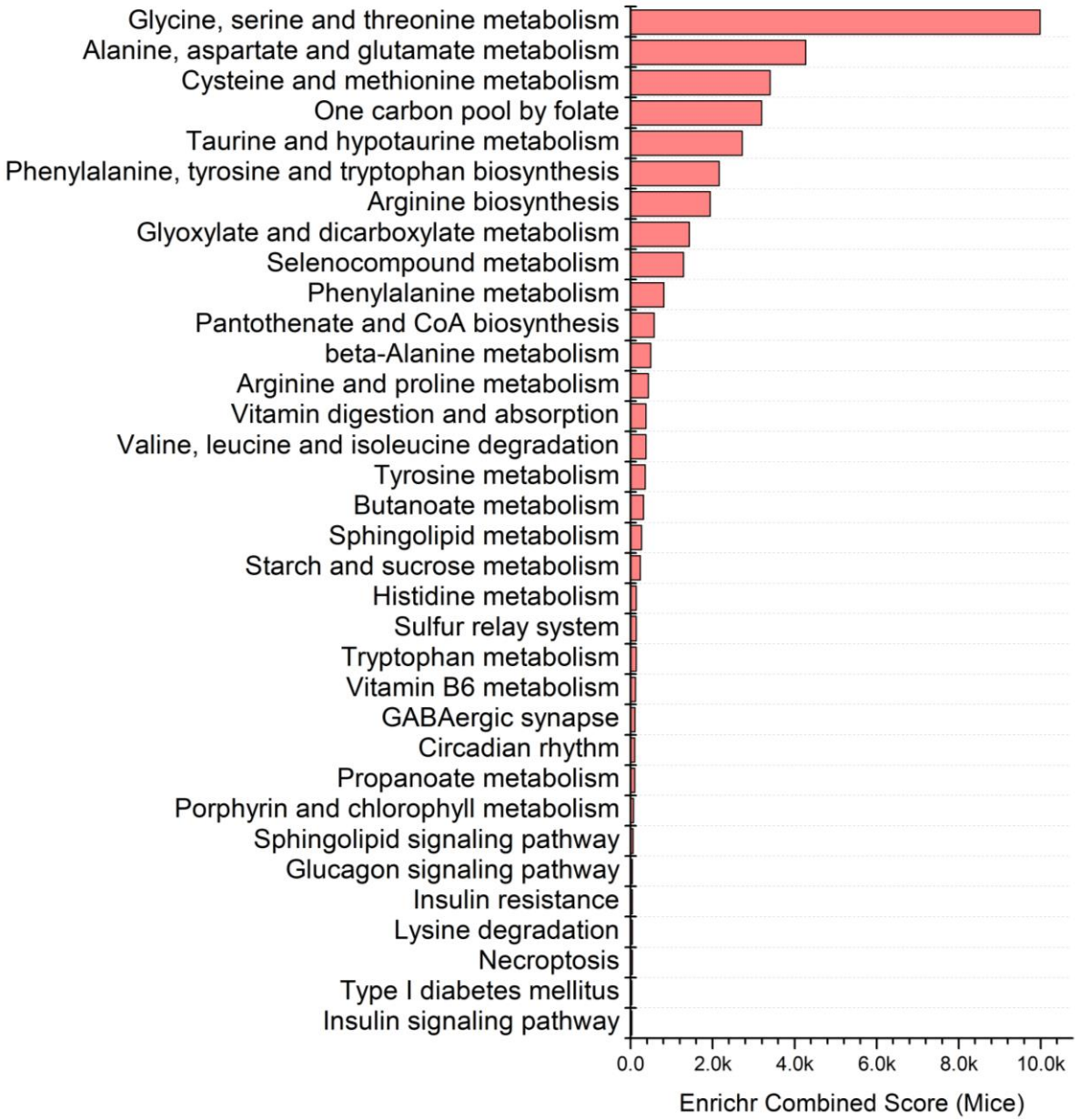
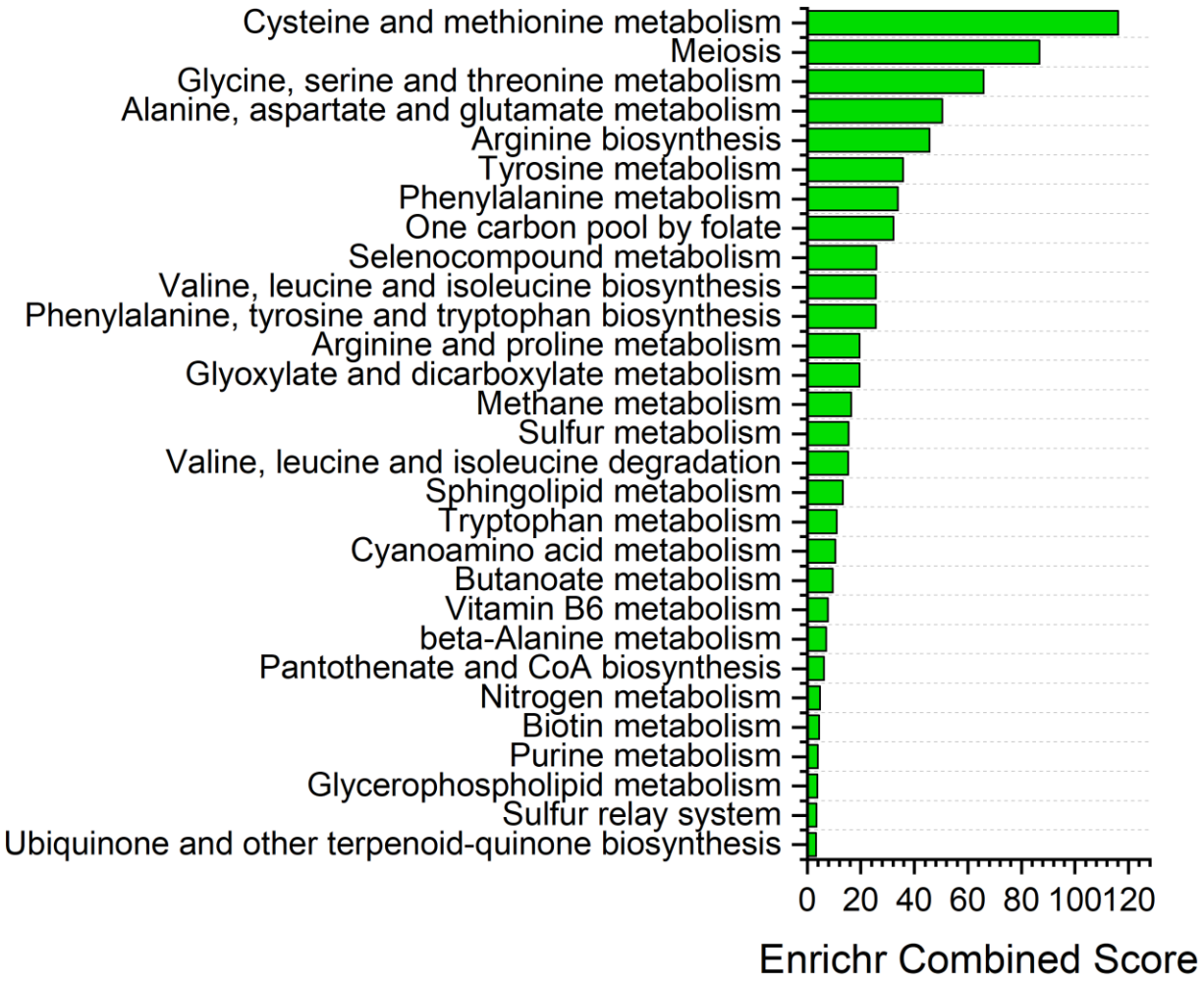


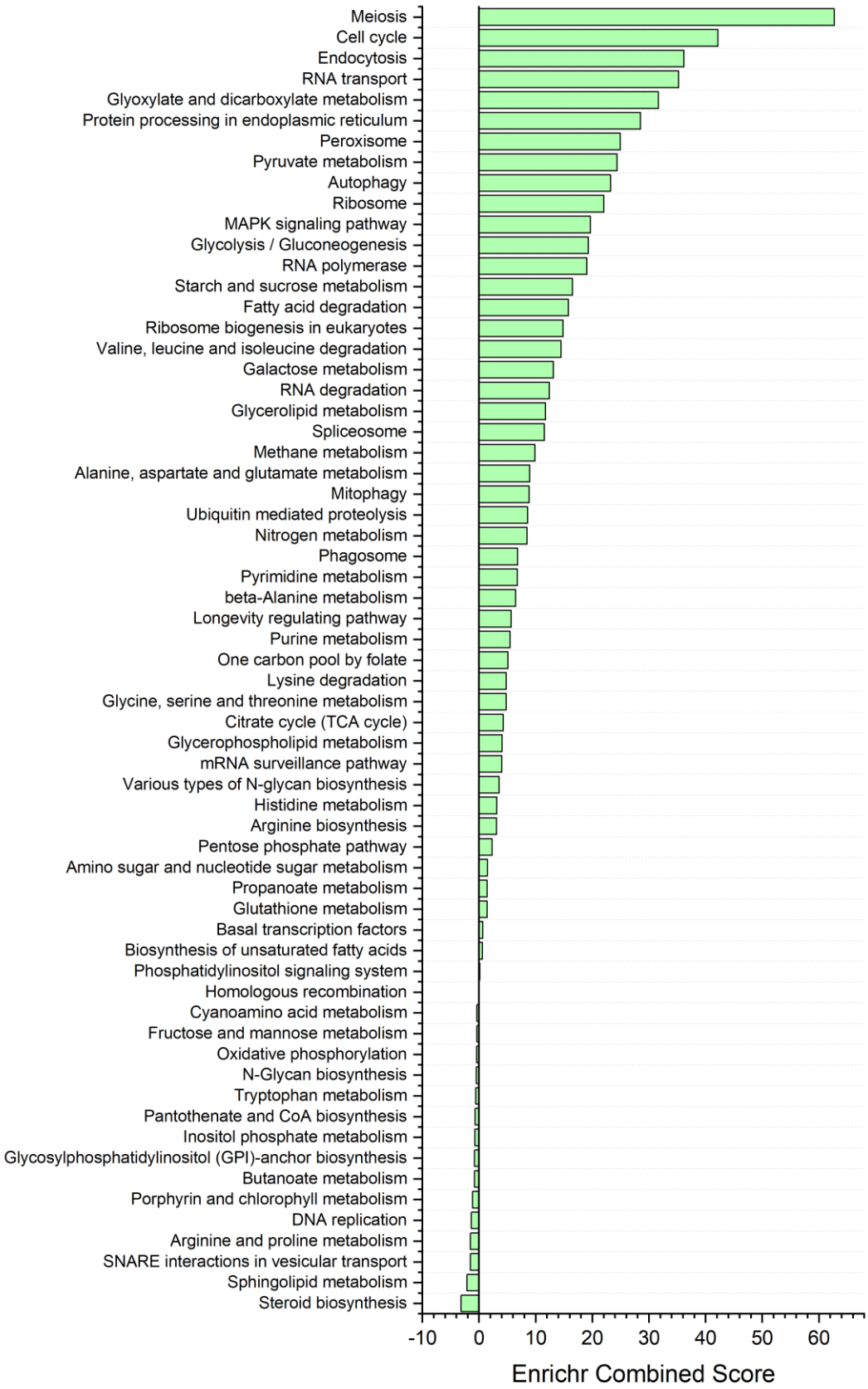
a. Vitamin B_6, B_{12} and folate cofactor-protein interacting protein enrichment analysis result in human. Plot made using Origin software.



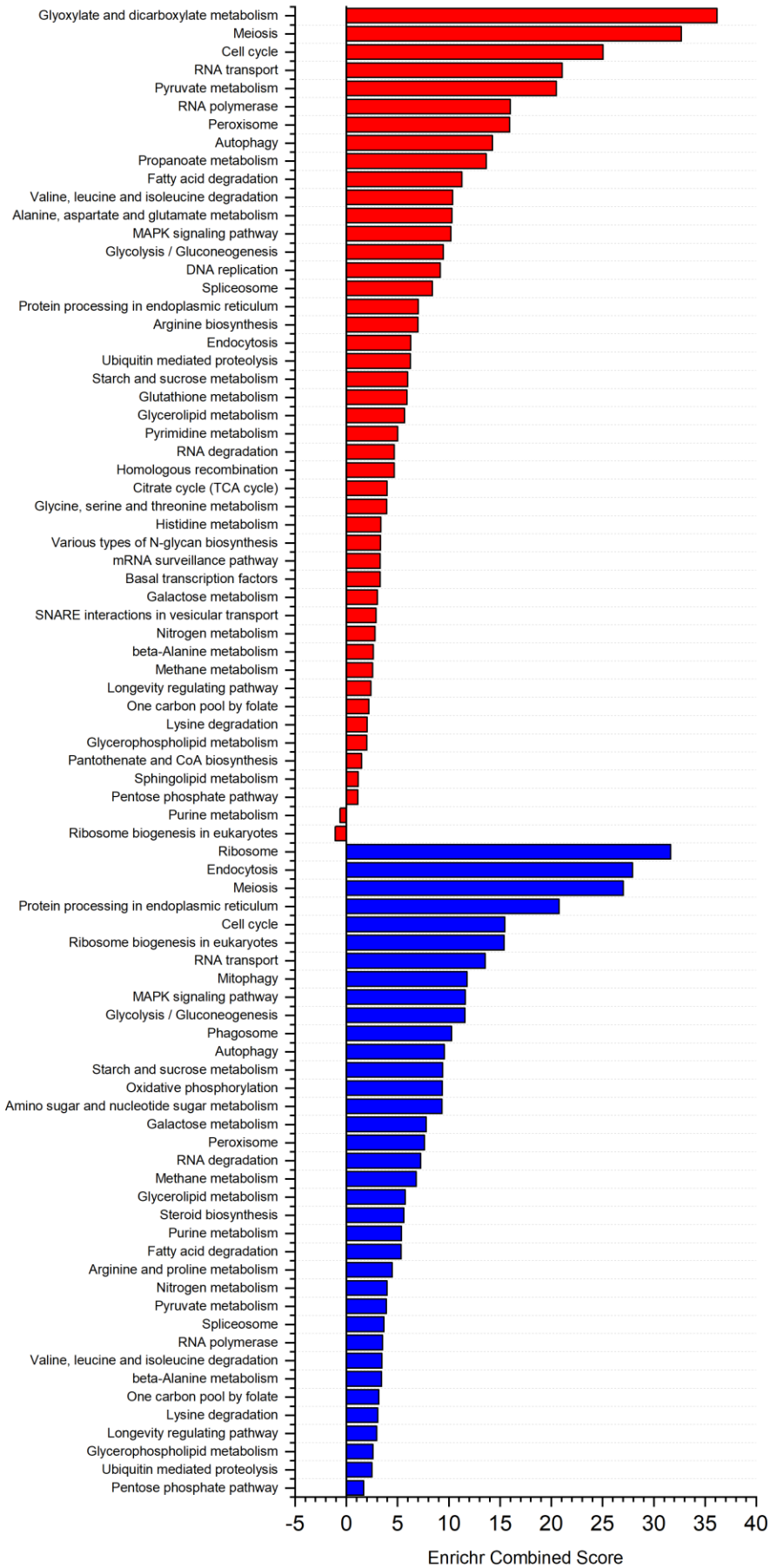
b. Vitamin B_6, B_{12} and folate cofactor-protein interacting protein enrichment analysis result in mice. Plot made using Origin software.



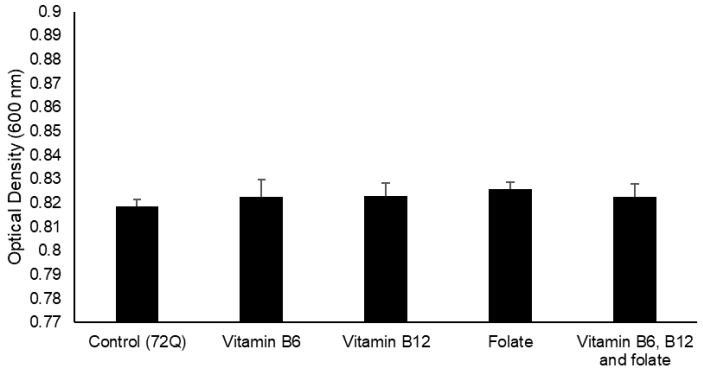
c. Vitamin B_6, B_{12} and folate cofactor-protein interacting protein enrichment analysis result in yeast. Plot made using Origin software.



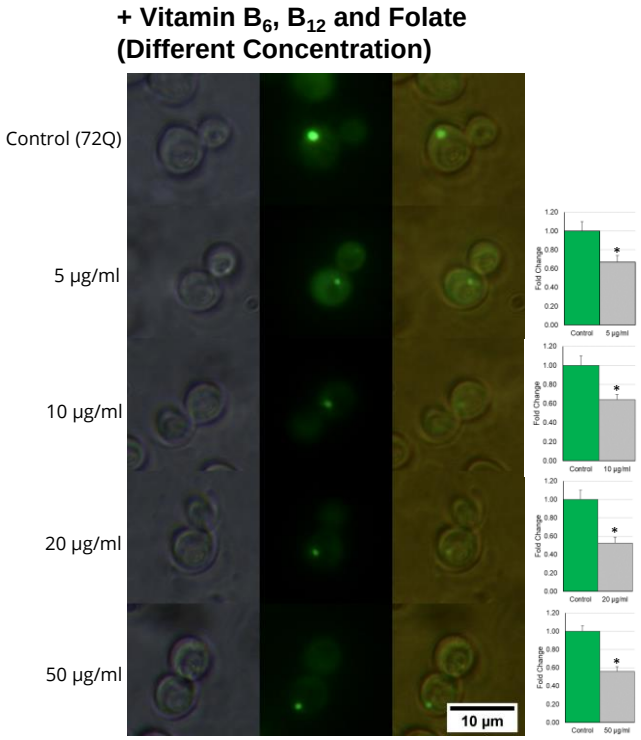
d. Enrichment analysis of transcriptomic data of control (72Q) and experimental sets treated with a combination of B_6, B_{12} and folate showing 63 significant pathways deregulated. Plot made using Origin software.



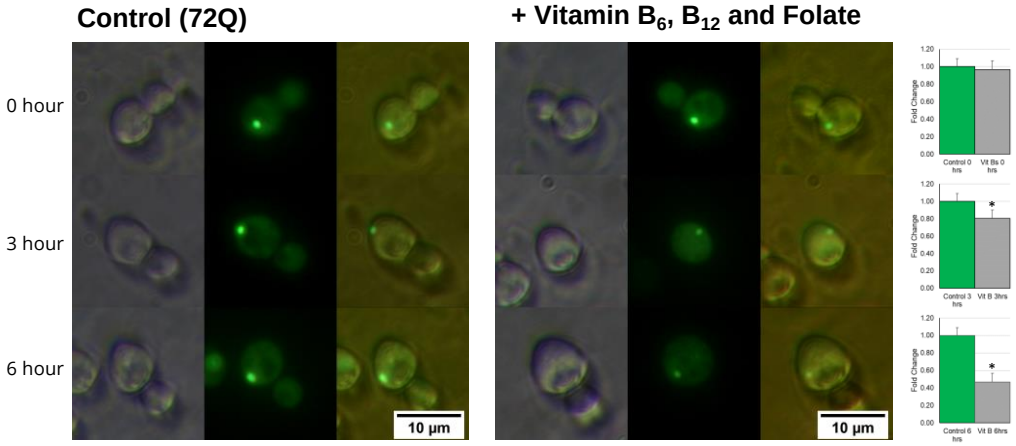
e. Enrichment analysis of upregulated and downregulated genes separately showing 46 and 36 pathways enriched respectively in 72Q treated with a combination of B_6, B_{12} and folate when compared to 72Q. Plot made using Origin software.



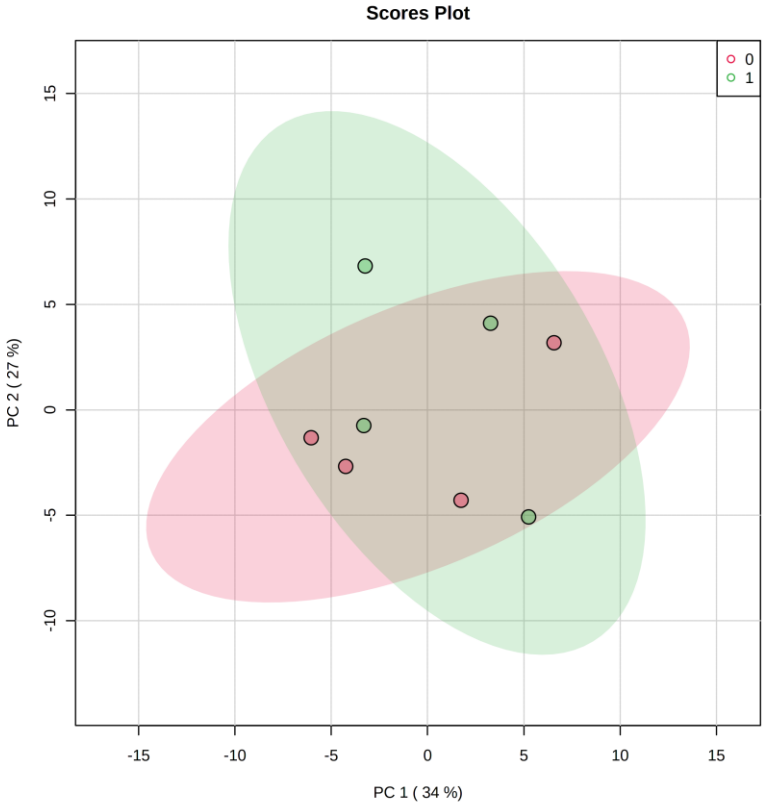
f. Absorbance graph of yeast transformed with Htt 72Q and Htt 72Q treated with vitamin B_6, B_{12} and folate individuals or in combination. Absorbance taken at OD_{600} show no significant difference between sample cultures at the time of imaging and quantification after treatment.



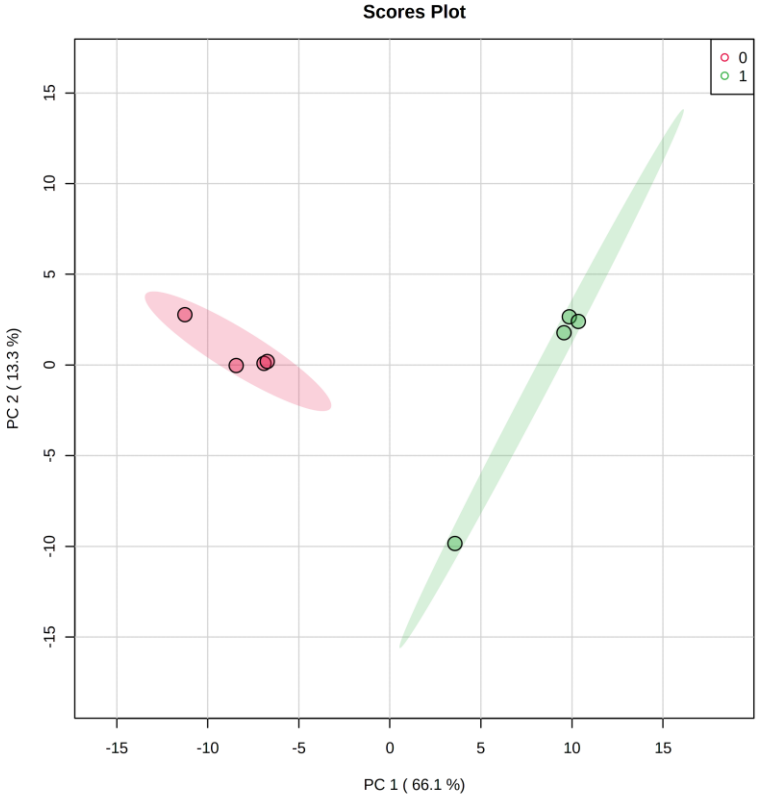
g. Yeast transformed with Htt 72Q. Fluorescence data showing reduction of protein aggregation when treated with different concentration of vitamin B_6, B_{12} and folate in combination. Fluorescence quantification show significant reduction in protein aggregation on treatment with (i) 5 µg/ml concentration [0.668 fold, $p \leq 0.00087$], (ii) 10 µg/ml concentration [0.639 fold, $p \leq 0.00024$], (iii) *20 µg/ml concentration [0.525 fold, $p \leq 1.22E^{-05}$], (iv) 50 µg/ml concentration [0.561 fold, $p \leq 3.35E^{-08}$].



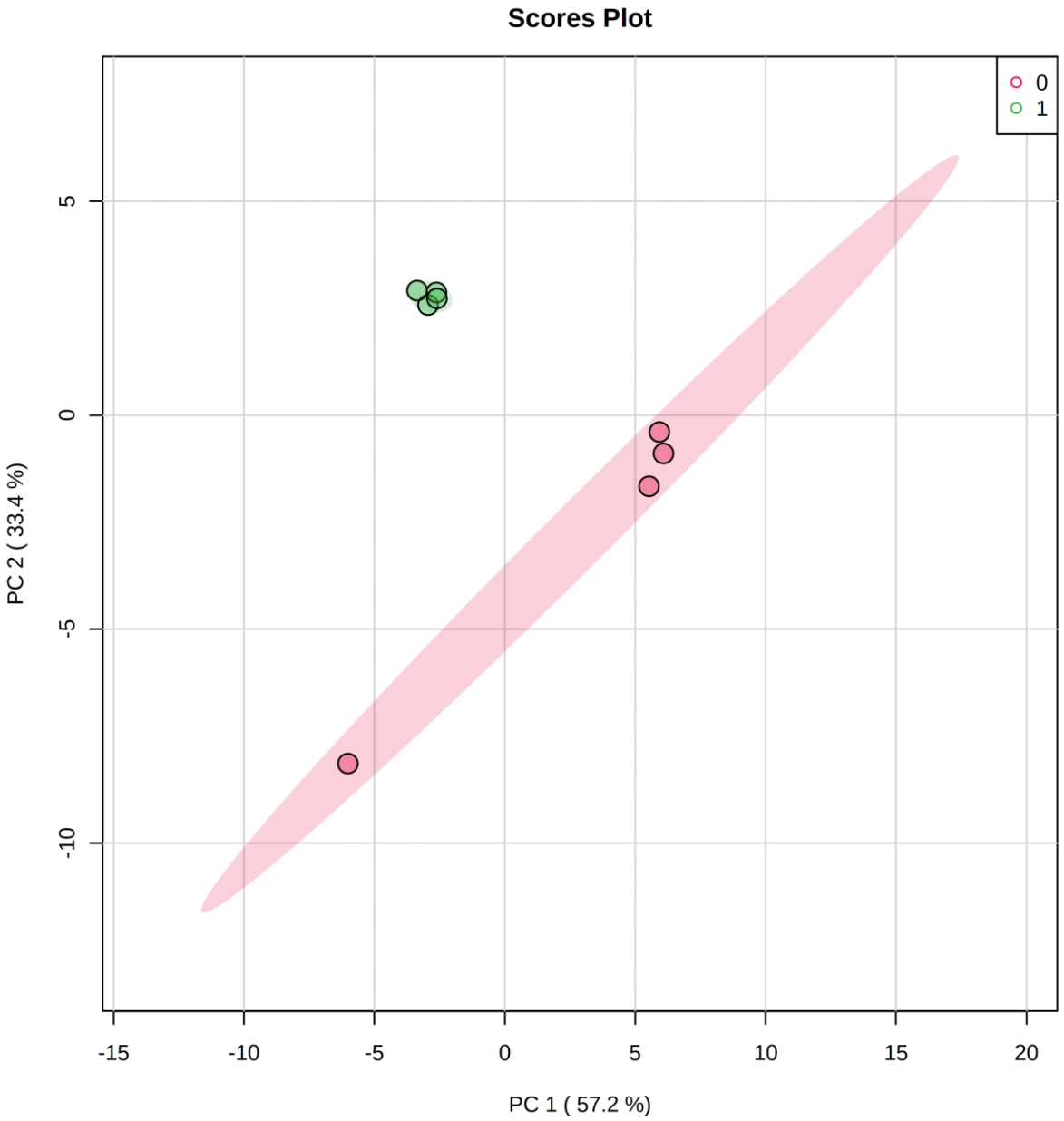
h. Yeast transformed with Htt 72Q. Fluorescence data showing reduction of pre-formed protein aggregation when treated with vitamin B_6, B_{12} and folate in combination. Fluorescence quantification results show significant reduction in protein aggregation at 3 hours [0.803 fold, $p \leq 0.0207$] and 6 hours [0.469 fold, $p \leq 6.74E^{-12}$] from treatment.



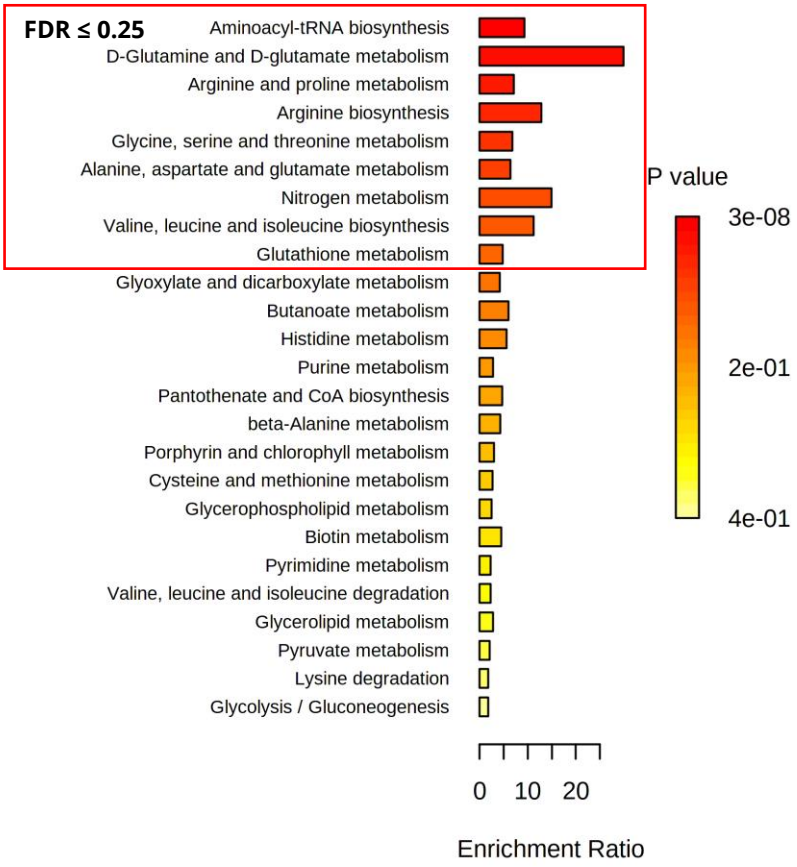
i. PCA Plot representing grouping and separation between samples (0=25q; 1= 25q Treatment). Plot created using MetaboAnalyst 5.0.



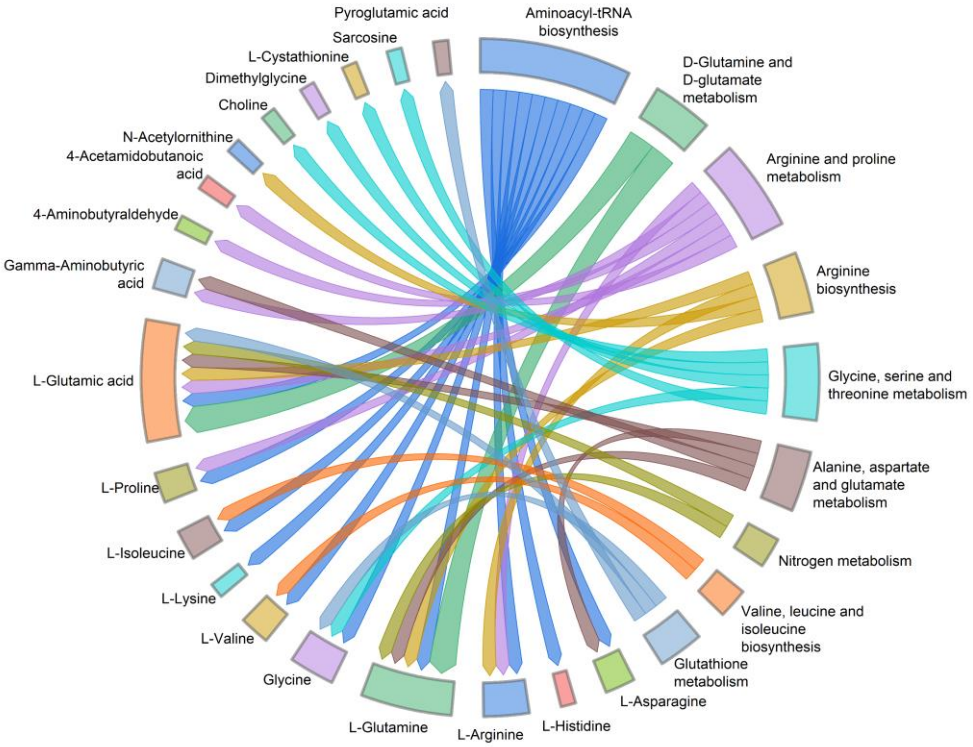
j. PCA Plot representing grouping and separation between samples (0=25q; 1= 72q). Plot created using MetaboAnalyst 5.0.



k. PCA Plot representing grouping and separation between samples (0=72q; 1= 72q Treatment). Plot created using MetaboAnalyst 5.0.



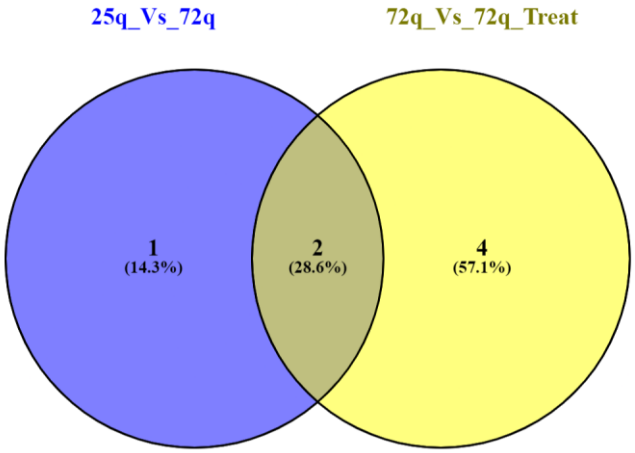
l. Metabolite set enrichment analysis (MSEA) of significant differential metabolites in 72Q vs 72Q B_6 +B_{12}+folate treated samples showing 9 pathways enriched with a FDR ≤0.25. Plot created using MetaboAnalvst 5.0.



m. Chord diagram showing a link between the metabolites altered and pathways deregulated in 72Q vs 72Q Treatment samples. Diagram made using Origin software.

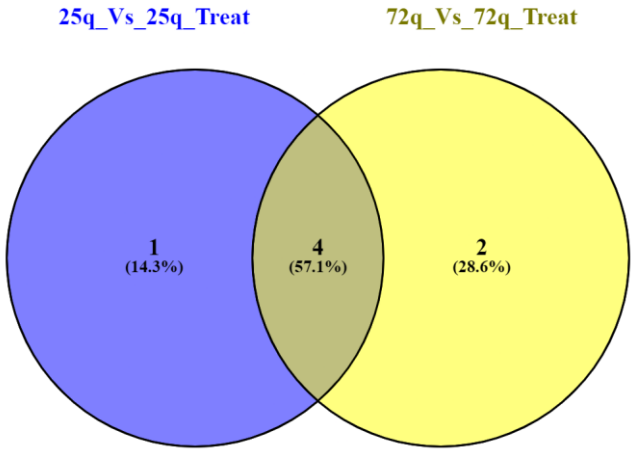
PATHWAY	METABOLITES
Aminoacyl-tRNA biosynthesis	L-Asparagine↓, L-Histidine↓, L-Arginine↓, L-Glutamine↓, Glycine↓, L-Valine↓, L-Lysine↓, L-Isoleucine↓,L-Proline↓, L-Glutamic acid↓
D-Glutamine and D-glutamate metabolism	L-Glutamic acid↓, L-Glutamine↓
Arginine biosynthesis	L-Glutamic acid↓, L-Arginine↓, N-Acetylornithine↓, L-Glutamine↓
Alanine, aspartate and glutamate metabolism	L-Asparagine↓, L-Glutamic acid↓, Gamma-Aminobutyric acid↓, L-Glutamine↓
Nitrogen metabolism	L-Glutamic acid↓, L-Glutamine↓
Valine, leucine and isoleucine biosynthesis	L-Isoleucine↓, L-Valine↓

n. Deregulated pathways with the levels of associated metabolites as observed in and 72Q vs 72Q Treatment samples. Table created using Microsoft Excel.



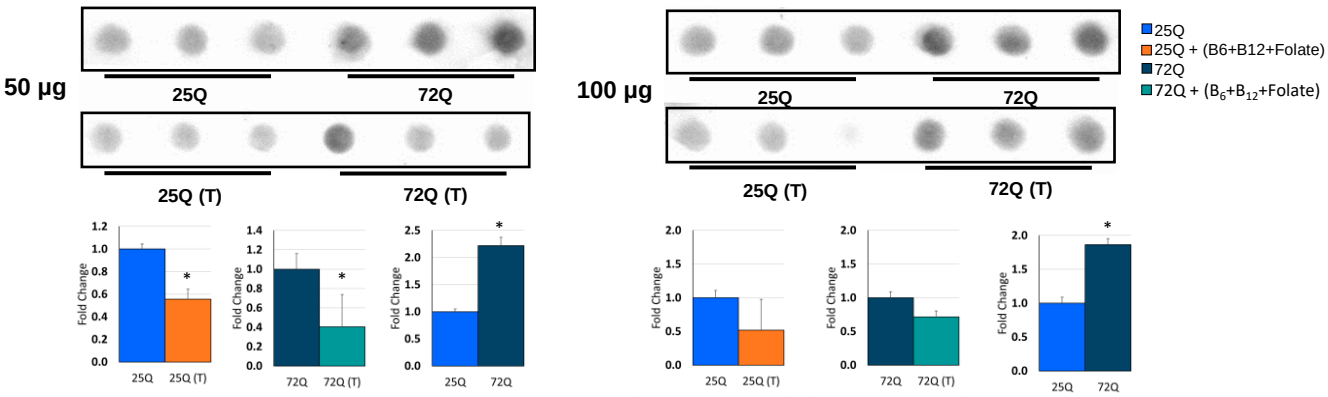
NAMES	TOTAL	ELEMENTS
25q_Vs_72q 72q_Vs_72q_Treatment	2	D-Glutamine and D-glutamate metabolism Aminoacyl-tRNA biosynthesis
25q_Vs_72q	1	Phenylalanine, tyrosine and tryptophan biosynthesis
72q_Vs_72q_Treatment	4	Valine, leucine and isoleucine biosynthesis Alanine, aspartate and glutamate metabolism Arginine biosynthesis Nitrogen metabolism

o. Common Pathways – 25Q vs 72Q and 72Q vs 72Q Treatment (FDR = 0.25). Venn diagram made using Venny- https://bioinfogp.cnb.csic.es/tools/venny/.

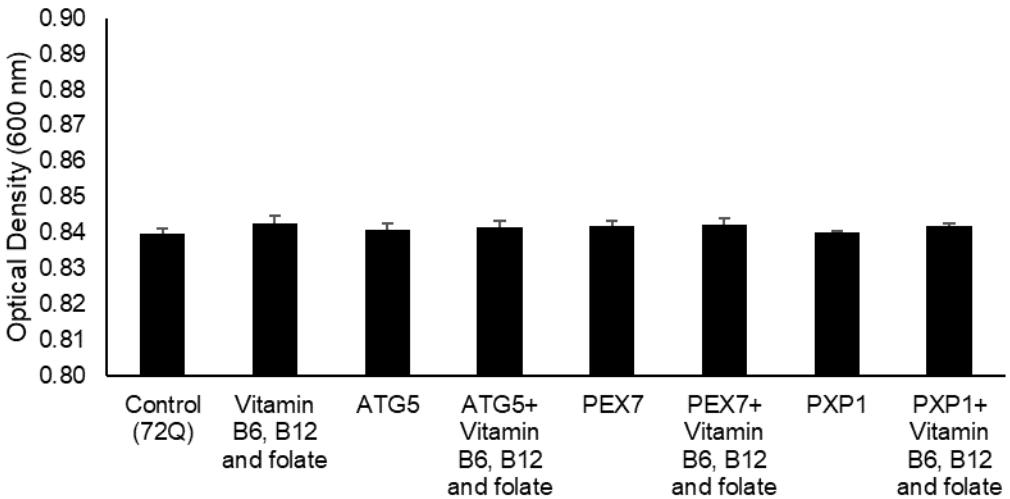


NAMES	TOTAL	ELEMENTS
25q_Vs_25q_Treatment 72q_Vs_72q_Treatment	4	Valine, leucine and isoleucine biosynthesis Arginine biosynthesis D-Glutamine and D-glutamate metabolism Aminoacyl-tRNA biosynthesis
25q_Vs_25q_Treatment	1	Histidine metabolism
72q_Vs_72q_Treatment	2	Alanine, aspartate and glutamate metabolism Nitrogen metabolism

p. Common Pathways – 25Q Vs 25Q Treatment and 72Q vs 72Q Treatment (FDR = 0.25). Venn diagram made using Venny- https://bioinfogp.cnb.csic.es/tools/venny/.



q. Filter retardation assay for yeast Htt 25Q/72Q and B_6, B_{12} and folate treated samples in two concentrations (50 µg and 100 µg). The intensity of the blot shows aggregation in control and its attenuation in B_6, B_{12} and folate treated yeast samples. The intensity of the blot was calculated and shown to be significantly reduced in the treated sample at a *p-value <0.05 and n=3. The quantification for mean intensity was done using ImageJ and the plots were made using Microsoft Excel.



r. Absorbance graph of yeast control strain, knockout strain transformed with Htt 72Q and transformed yeast treated with vitamin B_6, B_{12} and folate in combination. Absorbance taken at OD_{600} show no significant difference between sample cultures at the time of experiment, imaging and quantification after treatment.