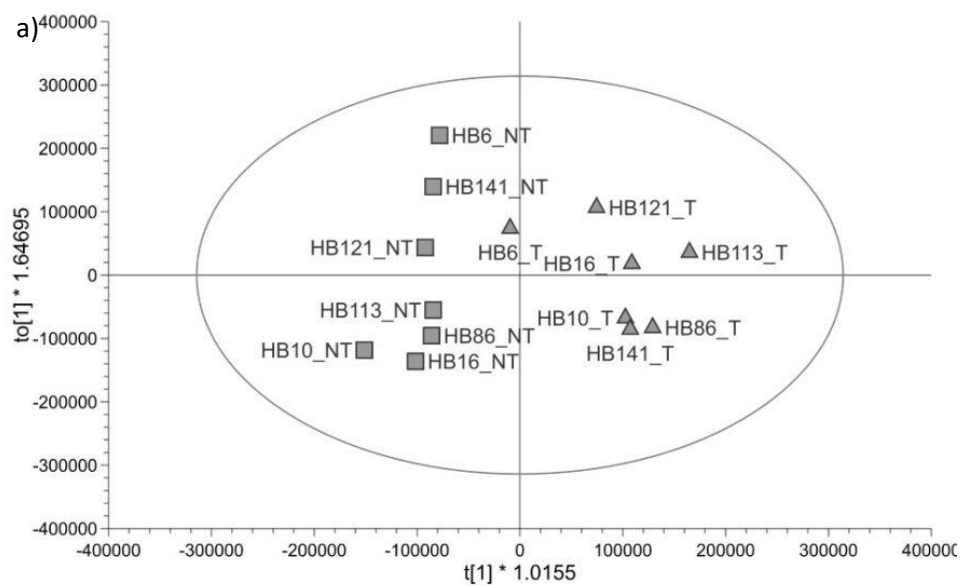


Figure S1: Permutation test of OPLS-DA model shown in Figure 1b.



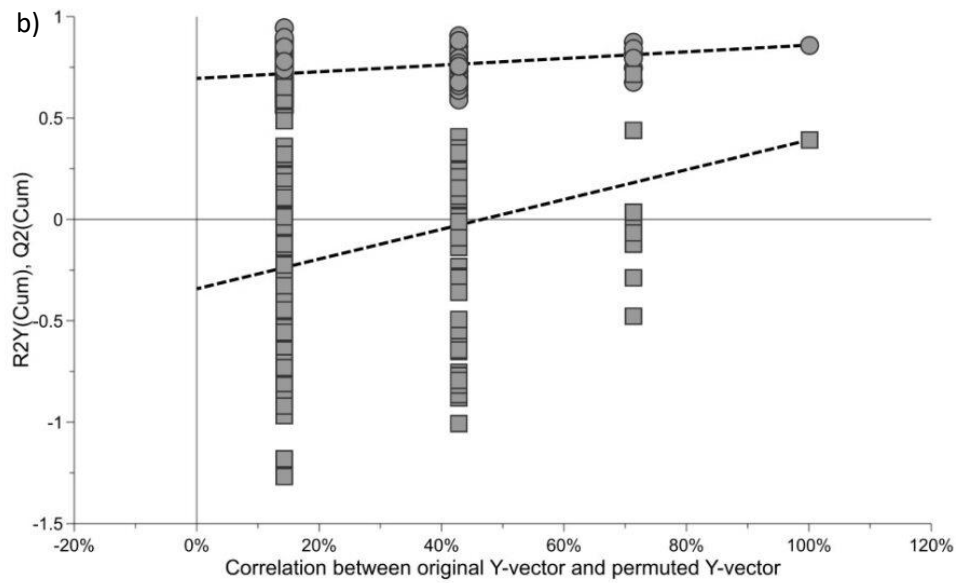


Figure S2: a) OPLS-DA scores plot showing hepatoblastoma ▲ and healthy liver ■ paired samples from paediatric patients omitting patient HB83 (R^2Y 0.859, Q^2 0.392). b) Permutation test of the model.

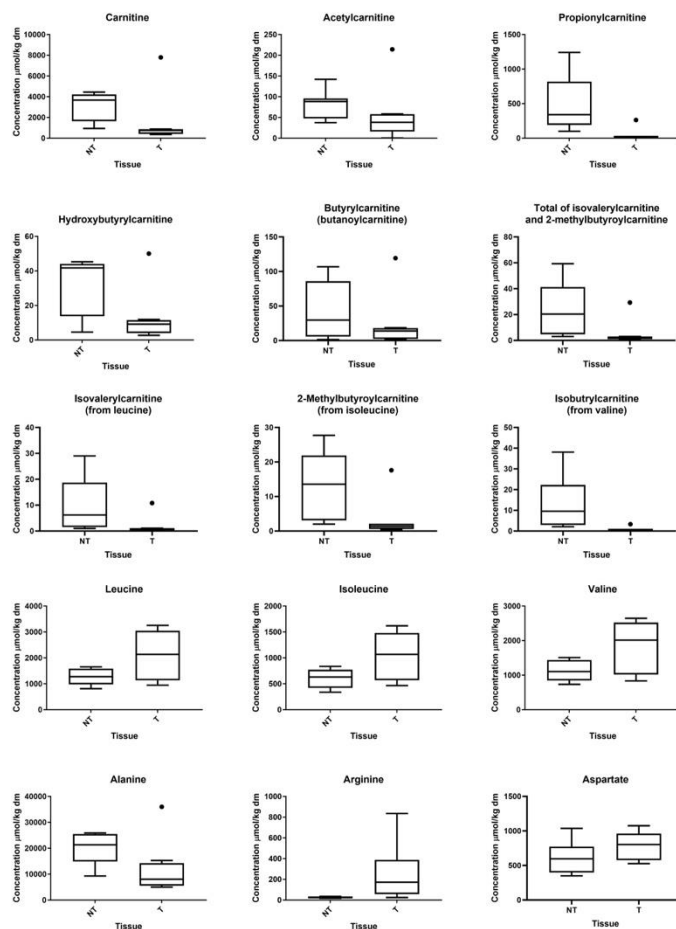


Figure S3: Box and whisker plots with Tukey's whiskers showing HB83_T is an outlier in targeted metabolomics in the case of multiple metabolites, thereby allowing us to remove patient HB83 from our analysis.

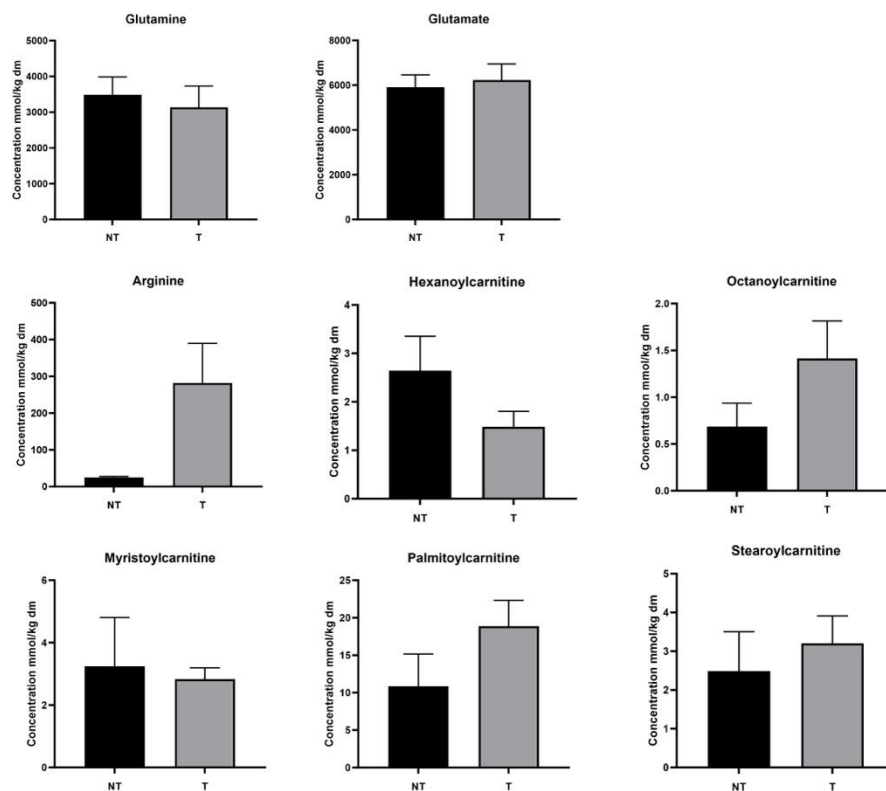


Figure S4: Amino acids and acylcarnitines concentrations in hepatoblastoma (T) and paired healthy liver tissue (NT). Values are means \pm standard deviation; (n = 7 paired samples) None were significant.

Table S1: Summary of metabolic pathway analysis with Metaboanalyst (www.metaboanalyst.ca) of the statistically significant metabolites identified by untargeted metabolomics.

Pathway Name	Match Status	p	-log(p)	Holm p	FDR	Impact	Details
Alanine, aspartate and glutamate metabolism	5/12	0.014506	1.8385	0.85584	0.5812	0.3109	KEGG SMP SMP S MP
Nitrogen metabolism	2/2	0.019702	1.7055	1	0.5812	0	KEGG SMP

D-Glutamine and D-glutamate metabolism	2/3	0.05401	1.2675	1	0.832 4	0.5	KEGG SMP
Glyoxylate and dicarboxylate metabolism	3/7	0.0608	1.2161	1	0.832 4	0.0317 5	KEGG
Butanoate metabolism	2/4	0.09875 9	1.0054	1	0.832 4	0	KEGG SMP
Glutathione metabolism	2/4	0.09875 9	1.0054	1	0.832 4	0.0267 5	KEGG SMP
Citrate cycle (TCA cycle)	2/4	0.09875 9	1.0054	1	0.832 4	0.1231 1	KEGG SMP
Selenocompound metabolism	1/1	0.14407	0.8414 3	1	0.85	0	KEGG SMP
Ether lipid metabolism	1/1	0.14407	0.8414 3	1	0.85	0	KEGG
Propanoate metabolism	1/1	0.14407	0.8414 3	1	0.85	0	KEGG SMP
Lysine degradation	2/6	0.20675	0.6845 6	1	1	0.1455 4	KEGG SMP
Pyrimidine metabolism	2/7	0.26512	0.5765 5	1	1	0.0158 4	KEGG SMP

Arginine biosynthesis	2/7	0.26512	0.57655	1	1	0.11675	KEGG
Glycerolipid metabolism	1/2	0.26843	0.57116	1	1	0.04361	KEGG SMP
Nicotinate and nicotinamide metabolism	1/2	0.26843	0.57116	1	1	0.1943	KEGG SMP
Glycerophospholipid metabolism	2/8	0.32403	0.48942	1	1	0.12907	KEGG
Aminoacyl-tRNA biosynthesis	3/15	0.36987	0.43195	1	1	0	KEGG
Purine metabolism	3/15	0.36987	0.43195	1	1	0.01451	KEGG SMP
Porphyrin and chlorophyll metabolism	1/3	0.37565	0.42522	1	1	0	KEGG
Glycolysis / Gluconeogenesis	1/3	0.37565	0.42522	1	1	2.10E-04	KEGG SMP SMP

Table S2: Table of results from the analysis of metabolic pathways using GSEA (Gene Set Enrichment Analysis) confirmed the dysregulation of these specific pathways (FDR<0.25) in HB as compared to NT tissues

Gene Set	Enrichment Score (ES)	Normalized Enrichment Score (NES)	Nominal p-value	FDR q-value	FWER p-Value
WP_ALANINE_AND_ASPARTATE_METABOLISM	- 0.90693 47	- 1.79820 53	0	0	0
KEGG_BETA_ALANINE_METABOLISM	- 0.87722 74	- 1.99104 81	0	0	0
KEGG_ALANINE_ASPARTATE_AND_GLUTAMATE_METABOLISM	- 0.71576 357	- 2.01453 1	0.001 908	0.001 908	0.001
GOBP_ALPHA_AMINO_ACID_CATABOLIC_PROCESS	- 0.76589 84	- 2.00925 47	0.003 883	0.003 883	0.002
GOBP_BRANCHED_CHAIN_AMINO_ACID_CATABOLIC_PROCESS	- 0.88882 774	- 1.68914 09	0.009 921	0.009 921	0.005
GOBP_AMINO_ACID_CATABOLIC_PROCESSES	- 0.78353 465	- 2.00170 87	0.002 053	0.002 053	0.001
REACTOME_TRANSPORT_OF_FATTY_ACIDS	- 0.43739 185	- 0.91982 87	0.564 007	0.564 007	0.304
GOBP_POSITIVE_REGULATION_OF_FATTY_ACID_TRANSPORT	- 0.41594 616	- 1.32859 29	0.108 607	0.108 607	0.053
GOBP_NEGATIVE_REGULATION_OF_FATTY_ACID_TRANSPORT	- 0.75177 634	- 1.56687 06	0.021 739	0.021 739	0.011
GOBP_FATTY_ACID_TRANSPORT	- 0.42737 868	- 1.71218 41	0.006 061	0.006 061	0.003
KEGG_GLUTATHIONE_METABOLISM	- 0.56139 565	- 1.65766 38	0.037 422	0.037 422	0.018
GOBP_GLUTATHIONE_METABOLIC_PROCESS	- 0.63098 53	- 1.90510 76	0.008 048	0.008 048	0.004
GOBP_GLUTATHIONE_CATABOLIC_PROCESSES	- 0.26168 445	- 0.61140 496	0.907 975	0.907 975	0.444
HALLMARK_GLYCOLYSIS	- 0.41626 13	- 1.51795 7	0.07	0.07	0.035
REACTOME_GLYCOLYSIS	- 0.39208 227	- 1.27930 45	0.225 352	0.225 352	0.112

KEGG_GLYCOLYSIS_GLUONEOGENESIS	- 0.66981 17	- 1.92805 65	0.001 898	0.001 898	0.001
REACTOME_CITRIC_ACID_CYCLE_TCA_CYCLE	- 0.75022 274	- 1.69409 33	0.019 92	0.019 92	0.01
REACTOME_PYRUVATE_METABOLISM_AND_CITRIC_ACID_TCA_CYCLE	- 0.65357 37	- 1.93337 89	0.008 23	0.008 23	0.004
KEGG_CITRATE_CYCLE_TCA_CYCLE	- 0.75444 055	- 1.65578 47	0.032 692	0.032 692	0.017
GOBP_INOSINE_METABOLIC_PROCESS	- 0.71015 054	- 1.29903 54	0.184 265	0.184 265	0.089
KEGG_NICOTINATE_AND_NICOTINAMIDE_METABOLISM	- 0.56647 474	- 1.61305 09	0.022 133	0.022 133	0.011
GOBP_NAD_BIOSYNTHESIS_VIA_NICOTINAMIDE_RIBOSIDE_SALVAGE_PATHWAY	- 0.79406 12	- 1.80060 79	0.003 831	0.003 831	0.002

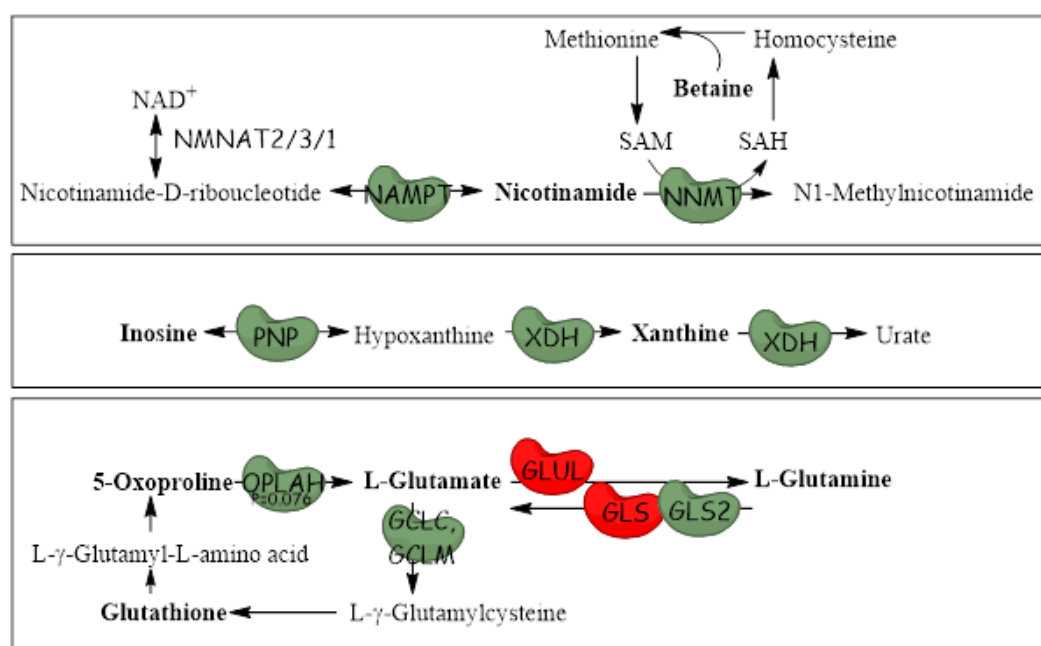


Figure S5: Aberrant metabolic pathways in HB compared to in healthy liver, according to untargeted metabolomics and transcriptomics analyses. Metabolites in bold are significantly decreased in abundance in HB, green genes are significantly decreased and red genes significantly increased in expression in HB.