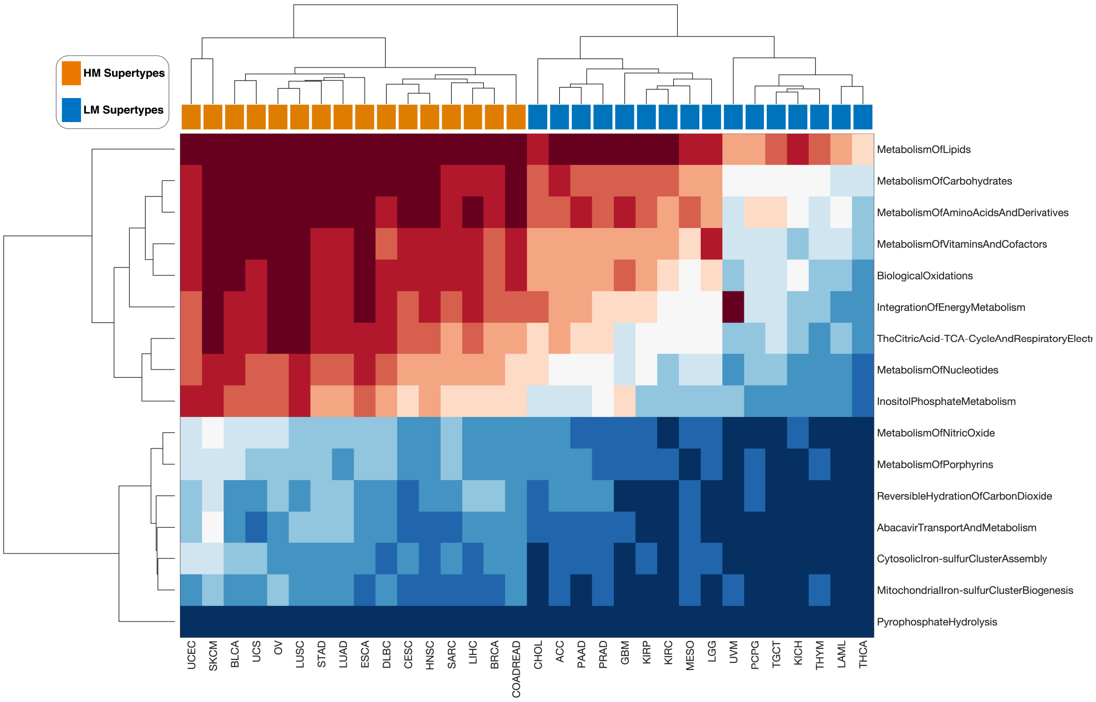
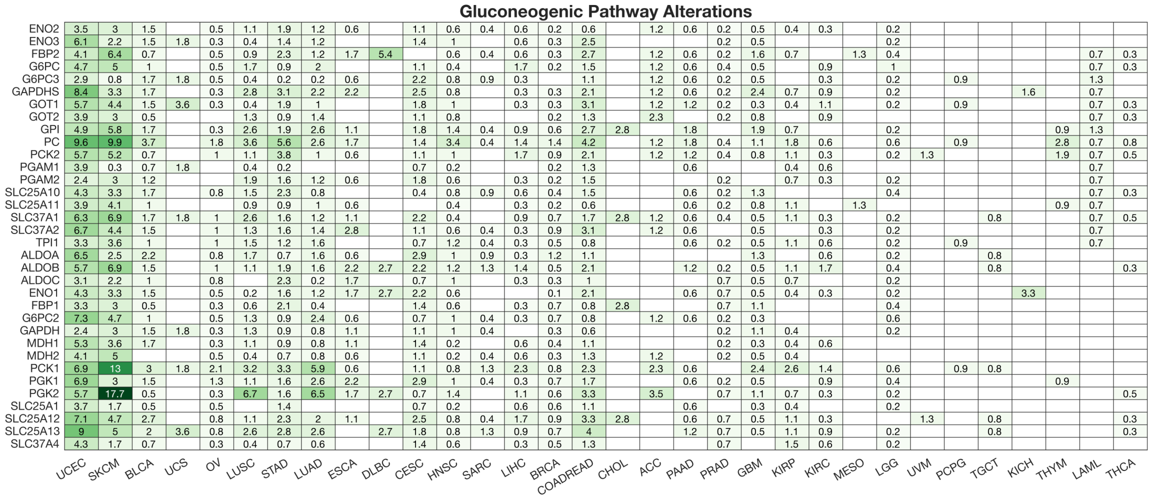
Supplementary Information



Supplementary Figure 1: Unsupervised hierarchical clustergram of tumours assigned to the two metabolic supertypes of human cancers. The fractions of tumours with altered genes that are involved in each of the 16 first-tier metabolic pathways were used for clustering. The clustergram was produced using the Spearman correlation distance metric with complete linkage.

	UCEC	SKCM	BLCA	UCS	OV	LUSC	STAD	LUAD	ESCA	DLBC	CESC	HNSC	SARC	LIHC	BRCA	COADREAD	CHOL	ACC	PAAD	PRAD	GBM	KIRP	KIRC	MESO	LGG	UVM	PCPG	TGCT	KICH	THYM	LAML	THCA
ADPGK	5.7	1.9	1	1.8	0.5		0.9	0.4	0.6		1.4	0.8	1.8		0.6	1			1.2	0.2	0.8			1.3	0.2			0.8			0.7	0.3
ENO2	3.5	3	1.5		0.5	1.1	1.9	1.2	0.6		1.1	0.6	0.4	0.6	0.2	0.6		1.2	0.6	0.2	0.5	0.4	0.3		0.2							
ENO3	6.1	2.2	1.5	1.8	0.3	0.4	1.4	1.2			1.4	1		0.6	0.3	2.5				0.2	0.5				0.2							
GAPDHS	8.4	3.3	1.7		0.3	2.8	3.1	2.2	2.2		2.5	0.8		0.3	0.3	2.1		1.2	0.6	0.2	2.4	0.7	0.9		0.2				1.6		0.7	
GCK	4.9	8	2.2	1.8	0.8	2.6	3.5	2.8	1.1		0.4	2	0.4	0.3	1	5			0.6	0.7	1.1	0.4	0.9	1.3	0.2							
GPI	4.9	5.8	1.7		0.3	2.6	1.9	2.6	1.1		1.8	1.4	0.4	0.9	0.6	2.7	2.8		1.8		1.9	0.7			0.2					0.9	1.3	
HK1	8.8	7.7	4.4		0.5	2.4	5.2	4.2	0.6		2.9	1.2	0.9	1.1	0.9	3.6			0.6	0.4	0.8	1.8	0.3	1.3	0.6	1.3					1.3	0.3
NUP107	7.1	6.1	3.2	1.8	0.5	2.4	4.7	2.4	2.2		0.7	1	2.6		1.2	4			1.2	0.9	0.8				0.8						0.7	
NUP153	11.4	5.8	4.2	3.6	0.5	4.5	4.5	2.6	4.4	5.4	2.9	1.8	0.4	2.3	1.3	4.2	2.8		1.8	0.4	1.3	0.4	1.4		0.6					0.9	1.3	
NUP155	7.5	7.5	4.9	1.8	2.1	4.7	4.2	3.4			4	3.2	0.9	1.7	1.3	3.6		2.3	1.2		0.8	0.7	0.3	2.6	1.2						0.7	0.3
NUP188	8.6	9.7	6.4		1.8	1.7	5.2	3.4	2.2	2.7	2.9	1.2	2.2	1.1	1.6	4.4			0.6	0.4	0.8	1.5	0.3		1					1.9	1.3	0.3
NUP205	11.8	9.4	8.4	3.6	2.3	5.8	7.3	5.1	0.6		2.9	2.6	1.3	1.1	1.2	8.4		2.3	1.8	0.7	2.1	1.5	2		0.6				1.6		1.3	
NUP210	13.8	20.7	6.7	3.6	1.3	4.1	7.5	5.3	4.4	5.4	1.8	1.8	0.9	1.7	1.1	5.9	2.8	1.2	1.8	0.9	1.9	2.6	0.6		0.8	1.3				0.9	0.7	
NUP214	12.4	13.3	4.9		2.3	3.4	6.8	5.1	0.6	2.7	2.5	2.4	0.9	2.6	1.4	5.2			0.6	0.9	0.8	2.9	0.6		0.4				1.6		1.3	0.8
NUP50	8.3	4.1	1		0.5	1.1	1.9	0.8	1.1		1.1	1	0.4	0.3	0.5	1.9		1.2	1.2	0.4		0.7	0.3								0.7	0.3
NUP62	6.5	3.3	1.5	1.8	0.8	1.7	2.8	1.2	1.1	2.7	2.9	1.2	0.4	0.9	0.8	2.3			1.2	0.2	0.5	0.7	0.6			1.3			1.6		0.7	
NUP85	5.1	4.4	3.2		0.8	0.6	1.9	1.4	0.6		2.2	0.8	1.3	0.3	0.3	2.1			0.6	0.4	0.5		0.6		0.2						1.3	
NUP88	6.9	4.4	3		0.5	1.1	3.3	0.4	1.1		1.4	1.2	0.4	0.9	0.4	2.5			0.6	0.2	0.8	0.7	0.9	1.3	0.4			0.8				
NUP93	8.4	5	2.7	1.8	0.5	1.9	3.1	1	2.2		1.4	2.2	1.3	0.9	0.7	2.7		1.2	0.6		0.5	0.7			0.4						0.7	1.1
NUP98	12.2	11.9	5.2	1.8	2.1	3.6	8	3.6	2.8	2.7	3.2	1.4	0.9	1.4	1.8	5.2	2.8	1.2	1.8	0.4	1.6	1.8	1.4		0.6		0.9				1.3	
PFKFB1	7.5	6.4	1.5	1.8	1.3	3	2.3	1.6	1.1		1.8	0.6	0.9	1.4	0.7	3.6			0.6	0.4	1.3	0.4	0.9		0.2						0.7	
PFKFB3	9	4.7	3		1.3	1.3	3.1	1.8	1.7		0.7	1	0.4	1.7	0.5	2.5			0.6		0.5	0.7	0.6		0.4					0.9	0.7	
PFKM	8.3	3.3	3.5		1	1.9	1.4	1.6	1.1		2.2	1.6	1.8		1	1	2.8		0.6	0.7	1.3	0.7	0.3		0.2		0.9			0.9	1.3	
PFKP	10.2	3.9	2.5	1.8	0.3	1.9	4.9	1.4			0.7	1	0.9	0.9	0.9	4.2	2.8		1.2	0.7	0.5	0.4	0.3		0.4					0.9	0.7	0.3
PGAM1	3.9	0.3	0.7	1.8		0.4	0.2				0.7	0.2			0.2	1.3			0.6			0.4	0.6								0.7	
PGAM2	2.4	3	1.2			1.9	1.6	1.2	0.6		1.8	0.6		0.3	0.2	1.5				0.2		0.7	0.3		0.2						0.7	
PGM2L1	7.3	2.5	1.7		1	2.4	0.9	1.4	0.6		1.4	1	0.9	0.6	0.7	1.9			0.6	0.2		0.4	0.3		0.2					0.9		
PKM	7.3	4.1	1	3.6	0.3	1.7	3.1	2	0.6		2.9	1.2			0.5	1.9		1.2	0.6		0.8	0.7	0.3	1.3					1.6		1.3	0.5
POM121C	12.2	7.2	2.2		0.5	2.1	4.7	2	0.6		2.2	1	1.3	0.6	0.6	5.4		1.2	0.6	0.9	1.9	2.6	0.9		0.6						0.7	0.3
PPP2R1B	6.5	5	2.2		0.3	1.5	3.1	0.8	0.6	5.4	1.8	1	0.9	1.4	0.4	1.9			1.8	0.4	1.3	0.4	0.9		0.2	1.3						
RAE1	8.3	3	1.2		0.8	1.3	2.1	0.6			1.1	0.4	0.4		0.5	1.9		1.2		0.2	0.8	0.7	0.6								0.7	
RANBP2	17.9	14.1	7.9	3.6	2.3	8.4	9.4	7.5	5	2.7	5.8	4	1.8	3.7	2.3	6.5		3.5	1.8	0.9	1.3	4	2.3	1.3	1.4		0.9	0.8			2.7	0.3
SEH1L	4.5	4.1	1			0.2	1.4	0.6	0.6		0.7	0.2			0.6	1		1.2	0.6	0.4	0.5				0.2		0.9				0.7	
TPI1	3.3	3.6	1		1	1.5	1.2	1.6			0.7	1.2	0.4	0.3	0.5	0.8			0.6	0.2	0.5	1.1	0.6		0.2		0.9				0.7	
TPR	14.9	10.8	8.6	1.8	1.8	10.1	8	7.1	2.2	5.4	4.7	2.8	0.9	1.7	3.4	6.9	2.8		1.2	1.3	2.4	1.8	3.4		0.8		0.9	1.5	3.3	1.9	2	0.3
AAAS	5.7	5.2	1.2		0.3	1.1	1.9	1			1.4	1			0.4	1.7			0.6		0.3	0.4	1.1		0.2		0.9	0.8				0.3
ALDOA	6.5	2.5	2.2		0.8	1.7	0.7	1.6	0.6		2.9	1	0.9	0.3	1.2	1.1					1.3		0.6		0.2			0.8				
ALDOB	5.7	6.9	1.5		1	1.1	1.9	1.6	2.2	2.7	2.2	1.2	1.3	1.4	0.5	2.1			1.2	0.2	0.5	1.1	1.7		0.4			0.8				0.3
ALDOC	3.1	2.2	1		0.8		2.3	0.2	1.7		0.7	1		0.3	0.3	1				0.7	0.5	0.7			0.2							
BPGM	5.7	2.5	0.5		0.3	0.9	1.9	1.2	0.6		0.4	0.4		0.3	0.6	1.1			0.6		1.1	0.7								0.9		
ENO1	4.3	3.3	1.5		0.5	0.2	1.6	1.2	1.7	2.7	2.2	0.6			0.1	2.1			0.6	0.7	0.5	0.4	0.3		0.2				3.3			
GAPDH	2.4	3	1.5	1.8	0.3	1.3	0.9	0.8	1.1		1.1	1	0.4		0.3	0.6				0.2	1.1	0.4			0.2							
GCKR	6.5	9.7	3.2	1.8	0.5	2.8	1.2	2.8			1.1	0.6	0.9	0.6	0.5	2.3			1.2	0.2	1.1		0.3		0.2		0.9	0.8		0.9		
GNPDA1	2.6	2.8	1.2			0.4	1.4	0.4	0.6		1.1	0.4		0.3	0.3	1		1.2	0.6	0.2	0.3				0.4							
GNPDA2	6.1	2.5	1.2		0.5	1.3	2.6	0.6	1.7		0.4	0.4		0.3	0.2	1.3			0.6		0.3		0.3							0.9		0.5
HK2	7.7	6.9	3	1.8	1.3	2.6	3.3	2.8	2.2		3.2	1.2	1.3	2.6	0.9	2.9	5.6	3.5	0.6	0.4	1.1		0.3		0.8							0.3
HK3	8.3	10.8	3		1.3	3.2	3.5	4.6	1.1		1.8	1.8	0.4	2	0.6	5.4		2.3	1.8	0.7	1.6	0.4	0.3	1.3	0.6			0.8				0.5
NDC1	6.3	4.1	1.5		0.5	1.5	1.4	1.4			2.5	1		0.6	0.3	2.7			1.2	0.2		0.7	0.3		0.4			0.8				
NUP133	8.4	6.4	2.7		1.5	4.1	4.2	3	1.7		1.4	1.2	0.4	3.7	0.9	4.4				0.9	1.1	2.6	1.4		0.4							0.5
NUP160	8.8	6.6	4.7		2.6	3.9	3.8	1.8	1.1		3.2	1.4		0.6	1.8	3.1		2.3	1.2	0.9	1.1	1.8	2		0.8					0.9		
NUP35	4.7	4.7	1.5		0.8	0.9	1.9	1.4	0.6	2.7	0.7	0.2		0.3	0.2	1.1					0.5	0.4	0.3		0.2							0.3
NUP37	3.9	2.2	1	1.8	0.3	1.5	1.2	0.4			0.7	0.8		0.9		1			0.6	0.4	0.3	0.4	0.6		0.2							0.3
NUP43	2.6	3	2.5	1.8	0.5	0.4	1.6	1.8	0.6			0.4			0.6	1.3				0.4	0.3	0.4	0.3		0.2					0.9		
NUPL2	3.1	3.9	4.9		0.3	2.1	2.3	1				0.4	0.9		0.3	1.5		1.2	1.2	0.2	0.5	0.7	0.3		0.2							
PFKFB2	6.7	4.4	1	1.8	0.8	0.9	1.6	1.2	1.7		1.4	1.4	0.4	0.9	1	2.7			0.6		0.8				0.8							0.3
PFKFB4	5.1	6.4	0.7		0.5	0.4	1.4	1	0.6			0.8	1.3		0.4	1.3			1.2	0.7	1.3	1.1	0.3	1.3	0.2							0.3
PFKL	7.5	4.4	1.7	1.8	0.3	2.6	2.6	2.6	0.6		1.1	2	1.3	0.3	0.6	2.3	2.8	2.3	0.6	0.2	1.3	2.2	0.9		1							
PGK1	6.9	3	1.5		1.3	1.1	1.6	2.6	2.2		2.9	1	0.4	0.3	0.7	1.7			0.6	0.2	0.5		0.9		0.4					0.9		
PGK2	5.7	17.7	0.5		0.3	6.7	1.6	6.5	1.7	2.7	0.7	1.4		1.1	0.6	3.3		3.5		0.7	1.1	0.7	0.3		0.2							0.5
PGP	1.6	0.8	0.7				0.9	0.4	0.6		0.7	0.2		0.6	0.2	0.2			0.6		0.3											
PKLR	6.9	7.5	3		1.5	3.4	5.2	3	2.2		1.8	0.6	0.9	1.1	1	3.6			0.6	0.2	0.8				0.4					0.9		0.5
POM121	14.3	11.6	6.2	1.8	2.8	3.2	5.9	2.2	3.9		4.7	3	2.2	2.3	2.3	6.5	5.6	2.3	0.6	1.3	2.1	2.6	0.9		0.2			1.5				0.5
PPP2CA	5.3	2.2	0.7		0.5	1.1	1.9	0.4	0.6	5.4	1.8	0.2		0.9	0.5	1			1.2	0.4	1.1		0.3		0.2							
PPP2CB	4.7	1.9	0.5			0.2	0.9	0.8			0.4	0.4		0.6	0.6	1.1			0.6	0.2	0.3	0.7	0.3		0.2							
PPP2R1A	18.5	5.2	1.7	28.6	1.3	2.8	3.5	2.8	2.2		3.6	1.4	0.9	0.9	0.8	3.6			1.2	0.2	0.8	1.1				2.5				0.9		0.5
PPP2R5D	6.7	2.8	2.5		1	0.9	1.6	1.8			1.8	1.4	0.4	1.7	0.9	2.3	2.8	1.2	0.6	0.2	0.8	0.4			0.6	1.3		1.5				0.3
PRKACA	6.3	3	2		0.5	0.4	1.9	1	1.7	2.7	1.4	1	0.9	1.1	0.6	1.3			0.6	0.7	1.6	0.7	0.6				0.9					
PRKACB	7.7	1.9	2.2		1	1.1	2.8	2.4	2.2		2.2	1.2	0.4	0.9	0.6	1.3		1.2	1.2		0.3	0.7	1.1				0.9			0.9		
PRKACG	5.1	9.9	0.2		0.5	1.7	2.6	1.2	1.1		1.8	1.2	0.9	1.1	0.8	3.4		1.2	0.6	0.4	0.5	1.1	0.9	1.3	0.4			3.8				0.3
SEC13	4.3	4.7	1.7		0.8	0.9	1.4	0.6	1.1		0.7	0.4	0.4	0.3	0.5	2.1			0.6		0.5	0.7	0.6		0.2							

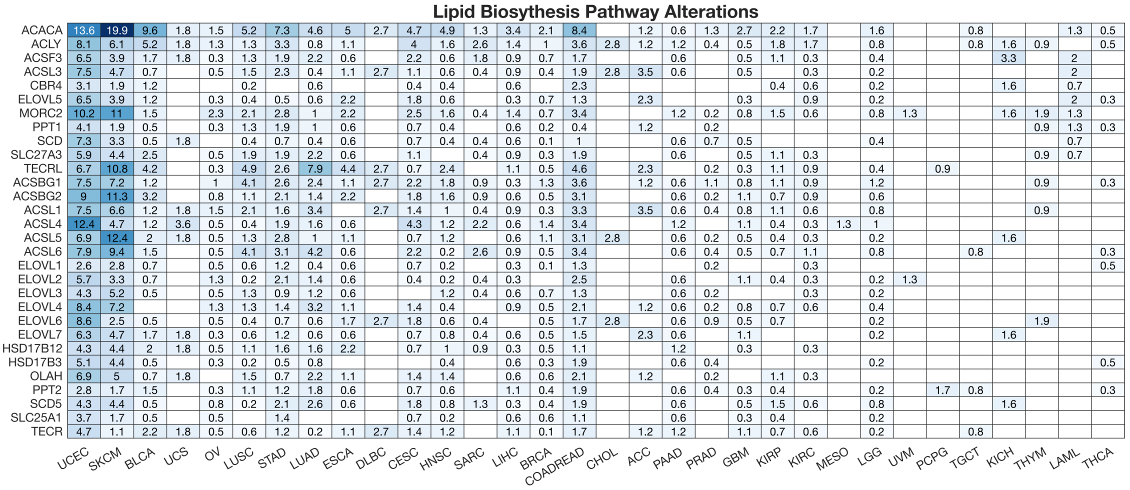
Supplementary Figure 2: Highlight table showing the fractions of tumours with alterations in glycolytic pathway genes across all human cancers. The increasing colour intensities denote higher percentages of altered genes.



Gluconeogenic Pathway Alterations

	UCEC	SKCM	BLCA	UCS	OV	LUSC	STAD	LUAD	ESCA	DLBC	CESC	HNSC	SARC	LIHC	BRCA	COADREAD	CHOL	ACC	PAAD	PRAD	GBM	KIRP	KIRC	MESO	LGG	UVM	PCPG	TGCT	KICH	THYM	LAML	THCA
ENO2	3.5	3	1.5		0.5	1.1	1.9	1.2	0.6		1.1	0.6	0.4	0.6	0.2	0.6		1.2	0.6	0.2	0.5	0.4	0.3		0.2							
ENO3	6.1	2.2	1.5	1.8	0.3	0.4	1.4	1.2			1.4	1		0.6	0.3	2.5				0.2	0.5				0.2							
FBP2	4.1	6.4	0.7		0.5	0.9	2.3	1.2	1.7	5.4		0.6	0.4	0.6	0.3	2.7		1.2	0.6	0.2	1.6	0.7		1.3	0.4						0.7	0.3
G6PC	4.7	5	1		0.5	1.7	0.9	2			1.1	0.4		1.7	0.2	1.5		1.2	0.6	0.4	0.5		0.9		1						0.7	0.3
G6PC3	2.9	0.8	1.7	1.8	0.5	0.4	0.2	0.2	0.6		2.2	0.8	0.9	0.3		1.1		1.2	0.6	0.2	0.5		0.3		0.2		0.9				1.3	
GAPDHS	8.4	3.3	1.7		0.3	2.8	3.1	2.2	2.2		2.5	0.8		0.3	0.3	2.1		1.2	0.6	0.2	2.4	0.7	0.9		0.2				1.6		0.7	
GOT1	5.7	4.4	1.5	3.6	0.3	0.4	1.9	1			1.8	1		0.3	0.3	3.1		1.2	1.2	0.2	0.3	0.4	1.1		0.2		0.9				0.7	0.3
GOT2	3.9	3	0.5			1.3	0.9	1.4			1.1	0.8			0.2	1.3		2.3		0.2	0.8		0.9								0.7	0.3
GPI	4.9	5.8	1.7		0.3	2.6	1.9	2.6	1.1		1.8	1.4	0.4	0.9	0.6	2.7	2.8		1.8		1.9	0.7			0.2					0.9	1.3	
PC	9.6	9.9	3.7		1.8	3.6	5.6	2.6	1.7		1.4	3.4	0.4	1.4	1.4	4.2		1.2	1.8	0.4	1.1	1.8	0.6		0.6		0.9			2.8	0.7	0.8
PCK2	5.7	5.2	0.7		1	1.1	3.8	1	0.6		1.1	1		1.7	0.9	2.1		1.2	1.2	0.4	0.8	1.1	0.3		0.2	1.3				1.9	0.7	0.5
PGAM1	3.9	0.3	0.7	1.8		0.4	0.2				0.7	0.2			0.2	1.3			0.6			0.4	0.6								0.7	
PGAM2	2.4	3	1.2			1.9	1.6	1.2	0.6		1.8	0.6		0.3	0.2	1.5				0.2		0.7	0.3		0.2						0.7	
SLC25A10	4.3	3.3	1.7		0.8	1.5	2.3	0.8			0.4	0.8	0.9	0.6	0.4	1.5			0.6	0.2	1.3				0.4						0.7	0.3
SLC25A11	3.9	4.1	1			0.9	0.9	1	0.6			0.4		0.3	0.2	0.6			0.6	0.2	0.8	1.1		1.3						0.9	0.7	
SLC37A1	6.3	6.9	1.7	1.8	1	2.6	1.6	1.2	1.1		2.2	0.4		0.9	0.7	1.7	2.8	1.2	0.6	0.4	0.5	1.1	0.3		0.2			0.8			0.7	0.5
SLC37A2	6.7	4.4	1.5		1	1.3	1.6	1.4	2.8		1.1	0.6	0.4	0.3	0.9	3.1		1.2	0.6		0.5		0.3		0.2						0.7	
TPI1	3.3	3.6	1		1	1.5	1.2	1.6			0.7	1.2	0.4	0.3	0.5	0.8			0.6	0.2	0.5	1.1	0.6		0.2		0.9				0.7	
ALDOA	6.5	2.5	2.2		0.8	1.7	0.7	1.6	0.6		2.9	1	0.9	0.3	1.2	1.1					1.3		0.6		0.2			0.8				
ALDOB	5.7	6.9	1.5		1	1.1	1.9	1.6	2.2	2.7	2.2	1.2	1.3	1.4	0.5	2.1			1.2	0.2	0.5	1.1	1.7		0.4			0.8				0.3
ALDOC	3.1	2.2	1		0.8		2.3	0.2	1.7		0.7	1		0.3	0.3	1				0.7	0.5	0.7			0.2							
ENO1	4.3	3.3	1.5		0.5	0.2	1.6	1.2	1.7	2.7	2.2	0.6			0.1	2.1			0.6	0.7	0.5	0.4	0.3		0.2				3.3			
FBP1	3.3	3	0.5		0.3	0.6	2.1	0.4			1.4	0.6		0.3	0.7	0.8	2.8			0.7	1.1				0.4							
G6PC2	7.3	4.7	1		0.5	1.3	0.9	2.4	0.6		0.7	1	0.4	0.3	0.7	0.8		1.2	0.6	0.2	0.3				0.6							
GAPDH	2.4	3	1.5	1.8	0.3	1.3	0.9	0.8	1.1		1.1	1	0.4		0.3	0.6				0.2	1.1	0.4			0.2							
MDH1	5.3	3.6	1.7		0.3	1.1	0.9	0.8	1.1		1.4	0.2		0.6	0.4	1.1				0.2	0.3	0.4	0.6									
MDH2	4.1	5			0.5	0.4	0.7	0.8	0.6		1.1	0.2	0.4	0.6	0.3	1.3		1.2		0.2	0.5	0.4										
PCK1	6.9	13	3	1.8	2.1	3.2	3.3	5.9	0.6		1.1	0.8	1.3	2.3	0.8	2.3		2.3	0.6		2.4	2.6	1.4		0.6		0.9	0.8				
PGK1	6.9	3	1.5		1.3	1.1	1.6	2.6	2.2		2.9	1	0.4	0.3	0.7	1.7			0.6	0.2	0.5		0.9		0.4					0.9		
PGK2	5.7	17.7	0.5		0.3	6.7	1.6	6.5	1.7	2.7	0.7	1.4		1.1	0.6	3.3		3.5		0.7	1.1	0.7	0.3		0.2							0.5
SLC25A1	3.7	1.7	0.5		0.5		1.4				0.7	0.2		0.6	0.6	1.1			0.6		0.3	0.4			0.2							
SLC25A12	7.1	4.7	2.7		0.8	1.1	2.3	2	1.1		2.5	0.8	0.4	1.7	0.9	3.3	2.8		0.6	0.7	0.5	1.1	0.3			1.3		0.8				0.3
SLC25A13	9	5	2	3.6	0.8	2.6	2.8	2.6		2.7	1.8	0.8	1.3	0.9	0.7	4			1.2	0.7	0.5	1.1	0.9		0.2			0.8				0.3
SLC37A4	4.3	1.7	0.7		0.3	0.4	0.7	0.6			1.4	0.6		0.3	0.5	1.3				0.7		1.5	0.6		0.2							

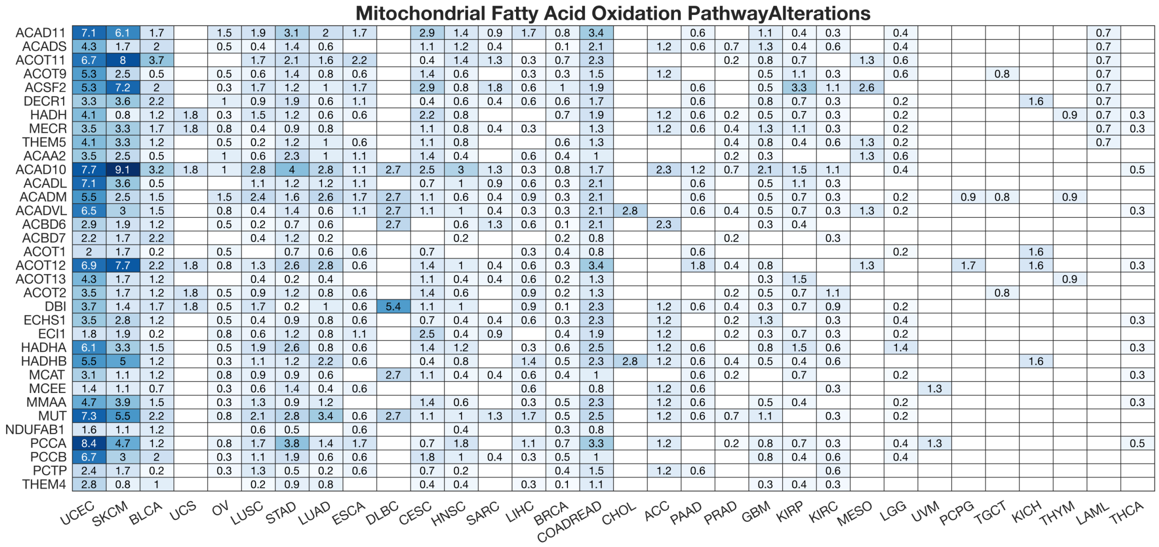
Supplementary Figure 3: Highlight table showing the fractions of tumours with alterations in gluconeogenic pathway genes across all human cancers. Increasing colour intensities denote higher percentages of altered genes.



Lipid Biosythesis Pathway Alterations

	UCEC	SKCM	BLCA	UCS	OV	LUSC	STAD	LUAD	ESCA	DLBC	CESC	HNSC	SARC	LIHC	BRCA	COADREAD	CHOL	ACC	PAAD	PRAD	GBM	KIRP	KIRC	MESO	LGG	UVM	PCPG	TGCT	KICH	THYM	LAML	THCA
ACACA	13.6	19.9	9.6	1.8	1.5	5.2	7.3	4.6	5	2.7	4.7	4.9	1.3	3.4	2.1	8.4		1.2	0.6	1.3	2.7	2.2	1.7		1.6			0.8			1.3	0.5
ACLY	8.1	6.1	5.2	1.8	1.3	1.3	3.3	0.8	1.1		4	1.6	2.6	1.4	1	3.6	2.8	1.2	1.2	0.4	0.5	1.8	1.7		0.8			0.8	1.6	0.9		0.5
ACSF3	6.5	3.9	1.7	1.8	0.3	1.3	1.9	2.2	0.6		2.2	0.6	1.8	0.9	0.7	1.7			0.6		0.5	1.1	0.3		0.4				3.3		2	
ACSL3	7.5	4.7	0.7		0.5	1.5	2.3	0.4	1.1	2.7	1.1	0.6	0.4	0.9	0.4	1.9	2.8	3.5	0.6		0.5		0.3		0.2						2	
CBR4	3.1	1.9	1.2			0.2		0.6			0.4	0.4		0.6		2.3						0.4	0.6		0.2				1.6		0.7	
ELOVL5	6.5	3.9	1.2		0.3	0.4	0.5	0.6	2.2		1.8	0.6		0.3	0.7	1.3		2.3			0.3		0.9		0.2						2	0.3
MORC2	10.2	11	1.5		2.3	2.1	2.8	1	2.2		2.5	1.6	0.4	1.4	0.7	3.4			1.2	0.2	0.8	1.5	0.6		0.8	1.3			1.6	1.9	1.3	
PPT1	4.1	1.9	0.5		0.3	1.3	1.9	1	0.6		0.7	0.4		0.6	0.2	0.4		1.2		0.2										0.9	1.3	0.3
SCD	7.3	3.3	0.5	1.8		0.4	0.7	0.4	0.6		0.7	0.4	0.4	0.6	0.1	1			0.6	0.7	0.5				0.4						0.7	
SLC27A3	5.9	4.4	2.5		0.5	1.9	1.9	2.2	0.6		1.1		0.4	0.9	0.3	1.9			0.6		0.5	1.1	0.3							0.9	0.7	
TECRL	6.7	10.8	4.2		0.3	4.9	2.6	7.9	4.4	2.7	0.7	2.4		1.1	0.5	4.6		2.3		0.2	0.3	1.1	0.9		0.4		0.9					
ACSBG1	7.5	7.2	1.2		1	4.1	2.6	2.4	1.1	2.7	2.2	1.8	0.9	0.3	1.3	3.6		1.2	0.6	1.1	0.8	1.1	0.9		1.2					0.9		0.3
ACSBG2	9	11.3	3.2		0.8	1.1	2.1	1.4	2.2		1.8	1.6	0.9	0.6	0.5	3.1			0.6	0.2	1.1	0.7	0.9		0.6							
ACSL1	7.5	6.6	1.2	1.8	1.5	2.1	1.6	3.4		2.7	1.4	1	0.4	0.9	0.3	3.3		3.5	0.6	0.4	0.8	1.1	0.6		0.8					0.9		
ACSL4	12.4	4.7	1.2	3.6	0.5	0.4	1.9	1.6	0.6		4.3	1.2	2.2	0.6	1.4	3.4			1.2		1.1	0.4	0.3	1.3	1							
ACSL5	6.9	12.4	2	1.8	0.5	1.3	2.8	1	1.1		0.7	1.2		0.6	1.1	3.1	2.8		0.6	0.2	0.5	0.4	0.3		0.2				1.6			
ACSL6	7.9	9.4	1.5		0.5	4.1	3.1	4.2	0.6		2.2	0.2	2.6	0.9	0.5	3.4			0.6	0.4	0.5	0.7	1.1		0.8			0.8				0.3
ELOVL1	2.6	2.8	0.7		0.5	0.6	1.2	0.4	0.6		0.7	0.2		0.3	0.1	1.3				0.2			0.3									0.5
ELOVL2	5.7	3.3	0.7		1.3	0.2	2.1	1.4	0.6		0.4	0.2	0.4	0.3		2.5			0.6		1.1	0.4	0.3		0.2	1.3						
ELOVL3	4.3	5.2	0.5		0.5	1.3	0.9	1.2	0.6			1.2	0.4	0.6	0.7	1.3			0.6	0.2			0.3		0.2							
ELOVL4	8.4	7.2			1.3	1.3	1.4	3.2	1.1		1.4	0.4		0.9	0.5	2.1		1.2	0.6	0.2	0.8	0.7	0.6		0.4							
ELOVL6	8.6	2.5	0.5		0.5	0.4	0.7	0.6	1.7	2.7	1.8	0.6	0.4		0.5	1.7	2.8		0.6	0.9	0.5	0.7			0.2					1.9		
ELOVL7	6.3	4.7	1.7	1.8	0.3	0.6	1.2	0.6	0.6		0.7	0.8	0.4	0.6	0.5	1.5		2.3	0.6		1.1				0.2				1.6			
HSD17B12	4.3	4.4	2	1.8	0.5	1.1	1.6	1.6	2.2		0.7	1	0.9	0.3	0.5	1.1			1.2		0.3		0.3									
HSD17B3	5.1	4.4	0.5		0.3	0.2	0.5	0.8				0.4		0.6	0.3	1.9			0.6	0.4					0.2							0.5
OLAH	6.9	5	0.7	1.8		1.5	0.7	2.2	1.1		1.4	1.4		0.6	0.6	2.1		1.2		0.2		1.1	0.3									
PPT2	2.8	1.7	1.5		0.3	1.1	1.2	1.8	0.6		0.7	0.6		1.1	0.4	1.9			0.6	0.4	0.3	0.4			0.2		1.7	0.8				0.3
SCD5	4.3	4.4	0.5		0.8	0.2	2.1	2.6	0.6		1.8	0.8	1.3	0.3	0.4	1.9			0.6		0.5	1.5	0.6		0.8				1.6			
SLC25A1	3.7	1.7	0.5		0.5		1.4				0.7	0.2		0.6	0.6	1.1			0.6		0.3	0.4			0.2							
TECR	4.7	1.1	2.2	1.8	0.5	0.6	1.2	0.2	1.1	2.7	1.4	1.2		1.1	0.1	1.7		1.2	1.2		1.1	0.7	0.6		0.2			0.8				

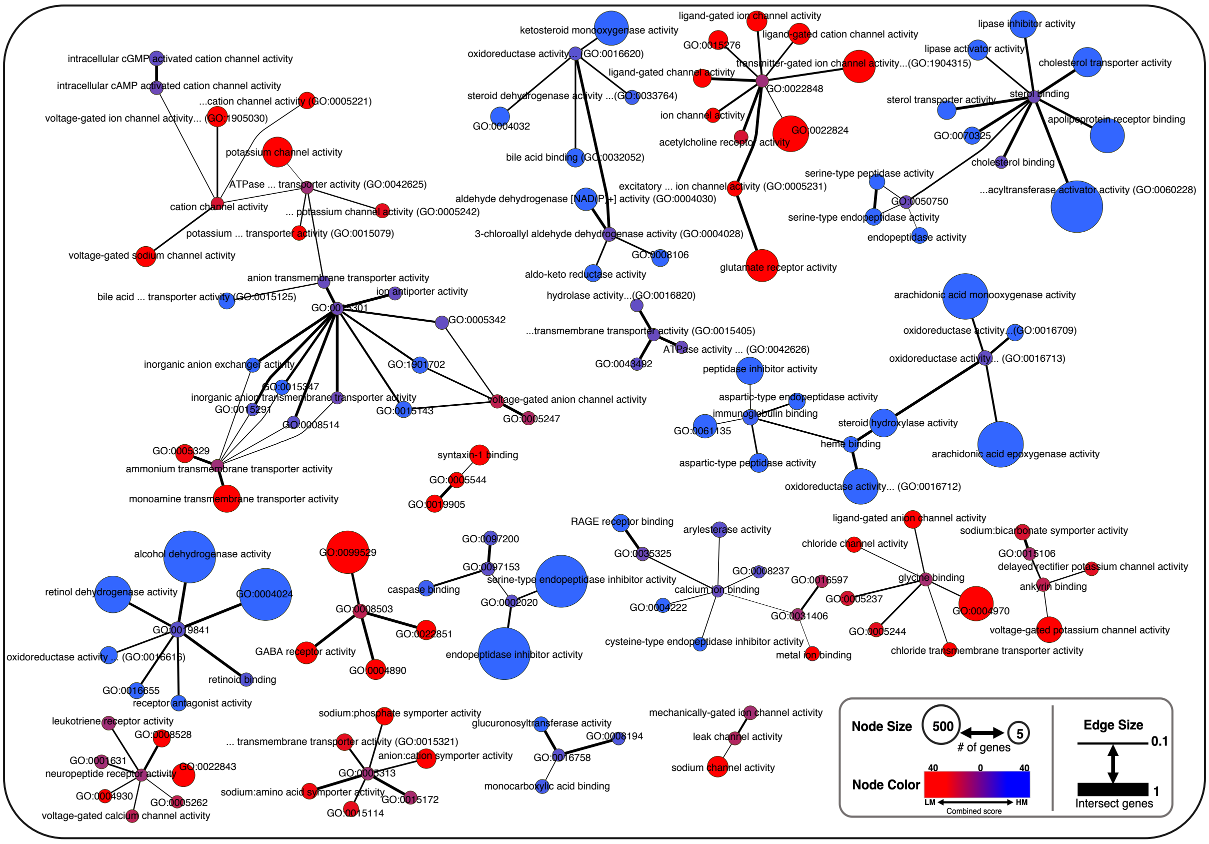
Supplementary Figure 4: Highlight table showing the fractions of tumours with alterations in mitochondrial fatty acid oxidation pathway genes across all human cancers. Increasing colour intensities denote higher percentages of altered genes.



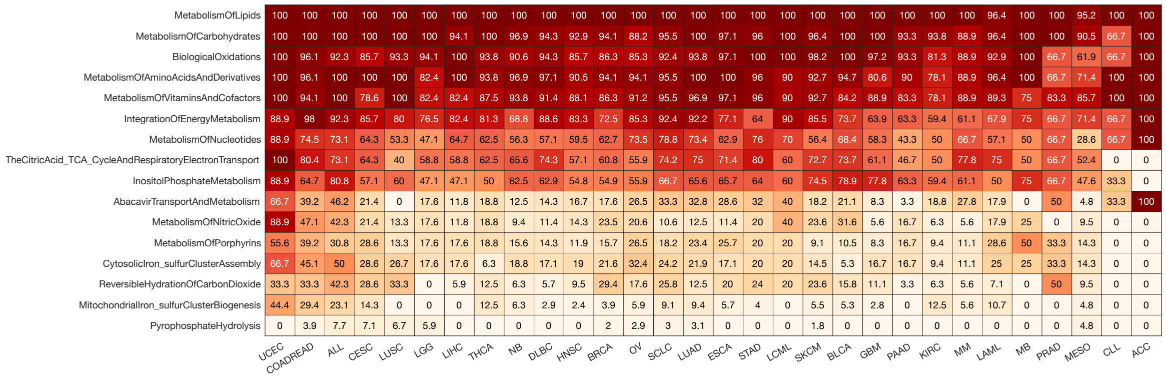
Mitochondrial Fatty Acid Oxidation PathwayAlterations

	UCEC	SKCM	BLCA	UCS	OV	LUSC	STAD	LUAD	ESCA	DLBC	CESC	HNSC	SARC	LIHC	BRCA	COADREAD	CHOL	ACC	PAAD	PRAD	GBM	KIRP	KIRC	MESO	LGG	UVM	PCPG	TGCT	KICH	THYM	LAML	THCA
ACAD11	7.1	6.1	1.7		1.5	1.9	3.1	2	1.7		2.9	1.4	0.9	1.7	0.8	3.4			0.6		1.1	0.4	0.3		0.4						0.7	
ACADS	4.3	1.7	2		0.5	0.4	1.4	0.6			1.1	1.2	0.4		0.1	2.1		1.2	0.6	0.7	1.3	0.4	0.6		0.4						0.7	
ACOT11	6.7	8	3.7			1.7	2.1	1.6	2.2		0.4	1.4	1.3	0.3	0.7	2.3				0.2	0.8	0.7		1.3	0.6						0.7	
ACOT9	5.3	2.5	0.5		0.5	0.6	1.4	0.8	0.6		1.4	0.6		0.3	0.3	1.5		1.2			0.5	1.1	0.3		0.6			0.8			0.7	
ACSF2	5.3	7.2	2		0.3	1.7	1.2	1	1.7		2.9	0.8	1.8	0.6	1	1.9			0.6		0.5	3.3	1.1	2.6							0.7	
DECR1	3.3	3.6	2.2		1	0.9	1.9	0.6	1.1		0.4	0.6	0.4	0.6	0.6	1.7			0.6		0.8	0.7	0.3		0.2				1.6		0.7	
HADH	4.1	0.8	1.2	1.8	0.3	1.5	1.2	0.6	0.6		2.2	0.8			0.7	1.9		1.2	0.6	0.2	0.5	0.7	0.3		0.2					0.9	0.7	0.3
MECR	3.5	3.3	1.7	1.8	0.8	0.4	0.9	0.8			1.1	0.8	0.4	0.3		1.3		1.2	0.6	0.4	1.3	1.1	0.3		0.2						0.7	0.3
THEM5	4.1	3.3	1.2		0.5	0.2	1.2	1	0.6		1.1	0.8			0.6	1.3				0.4	0.8	0.4	0.6	1.3	0.2						0.7	
ACAA2	3.5	2.5	0.5		1	0.6	2.3	1	1.1		1.4	0.4		0.6	0.4	1				0.2	0.3			1.3	0.6							
ACAD10	7.7	9.1	3.2	1.8	1	2.8	4	2.8	1.1	2.7	2.5	3	1.3	0.3	0.8	1.7		2.3	1.2	0.7	2.1	1.5	1.1		0.4							0.5
ACADL	7.1	3.6	0.5			1.1	1.2	1.2	1.1		0.7	1	0.9	0.6	0.3	2.1			0.6		0.5	1.1	0.3									
ACADM	5.5	2.5	1.5		1.5	2.4	1.6	2.6	1.7	2.7	1.1	0.6	0.4	0.9	0.3	2.1			0.6		0.5	0.7	0.3		0.2		0.9	0.8		0.9		
ACADVL	6.5	3	1.5		0.8	0.4	1.4	0.6	1.1	2.7	1.1	1	0.4	0.3	0.3	2.1	2.8		0.6	0.4	0.5	0.7	0.3	1.3	0.2							0.3
ACBD6	2.9	1.9	1.2		0.5	0.2	0.7	0.6		2.7		0.6	1.3	0.6	0.1	2.1		2.3			0.3	0.4										
ACBD7	2.2	1.7	2.2			0.4	1.2	0.2				0.2			0.2	0.8				0.2			0.3									
ACOT1	2	1.7	0.2		0.5		0.7	0.6	0.6		0.7			0.3	0.4	0.8			0.6						0.2				1.6			
ACOT12	6.9	7.7	2.2	1.8	0.8	1.3	2.6	2.8	0.6		1.4	1	0.4	0.6	0.3	3.4			1.8	0.4	0.8			1.3			1.7		1.6			0.3
ACOT13	4.3	1.7	1.2			0.4	0.2	0.4			1.1	0.4	0.4	0.6	0.2	1.3					0.3	1.5								0.9		
ACOT2	3.5	1.7	1.2	1.8	0.5	0.9	1.2	0.8	0.6		1.4	0.6		0.9	0.2	1.3				0.2	0.5	0.7	1.1					0.8				
DBI	3.7	1.4	1.7	1.8	0.5	1.7	0.2	1	0.6	5.4	1.1	1		0.9	0.1	2.3		1.2	0.6	0.4	0.3	0.7	0.9		0.2							
ECHS1	3.5	2.8	1.2		0.5	0.4	0.9	0.8	0.6		0.7	0.4	0.4	0.6	0.3	2.3		1.2		0.2	1.3		0.3		0.4							0.3
ECI1	1.8	1.9	0.2		0.8	0.6	1.2	0.8	1.1		2.5	0.4	0.9		0.4	1.9		1.2		0.2	0.3	0.7	0.3		0.2							
HADHA	6.1	3.3	1.5		0.5	1.9	2.6	0.8	0.6		1.4	1.2		0.3	0.6	2.5		1.2	0.6		0.8	1.5	0.6		1.4							0.3
HADHB	5.5	5	1.2		0.3	1.1	1.2	2.2	0.6		0.4	0.8		1.4	0.5	2.3	2.8	1.2	0.6	0.4	0.5	0.4	0.6						1.6			
MCAT	3.1	1.1	1.2		0.8	0.9	0.9	0.6		2.7	1.1	0.4	0.4	0.6	0.4	1			0.6	0.2		0.7			0.2							0.3
MCEE	1.4	1.1	0.7		0.3	0.6	1.4	0.4	0.6					0.6		0.8		1.2	0.6				0.3			1.3						
MMAA	4.7	3.9	1.5		0.3	1.3	0.9	1.2			1.4	0.6		0.3	0.5	2.3		1.2	0.6		0.5	0.4			0.2							0.3
MUT	7.3	5.5	2.2		0.8	2.1	2.8	3.4	0.6	2.7	1.1	1	1.3	1.7	0.5	2.5		1.2	0.6	0.7	1.1		0.3		0.2							
NDUFAB1	1.6	1.1	1.2			0.6	0.5		0.6			0.4			0.3	0.8																
PCCA	8.4	4.7	1.2		0.8	1.7	3.8	1.4	1.7		0.7	1.8		1.1	0.7	3.3		1.2		0.2	0.8	0.7	0.3		0.4	1.3						0.5
PCCB	6.7	3	2		0.3	1.1	1.9	0.6	0.6		1.8	1	0.4	0.3	0.5	1					0.8	0.4	0.6		0.4							
PCTP	2.4	1.7	0.2		0.3	1.3	0.5	0.2	0.6		0.7	0.2			0.4	1.5		1.2	0.6				0.6									
THEM4	2.8	0.8	1			0.2	0.9	0.8			0.4	0.4		0.3	0.1	1.1					0.3	0.4	0.3									

Supplementary Figure 5: Highlight table showing the fractions of tumours with alterations in lipid biosynthesis pathway genes across all human cancers. Increasing colour intensities denote higher percentages of altered genes.

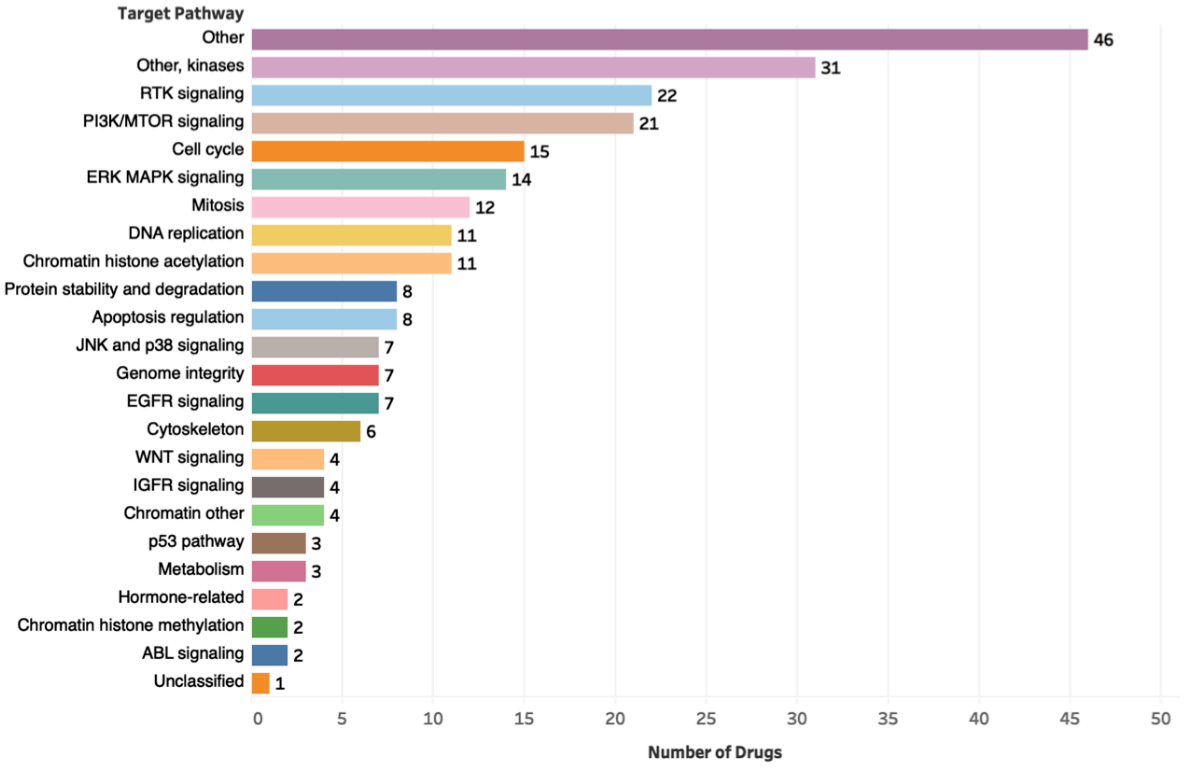


Supplementary Figure 6: Network of Gene Ontology (GO) molecular functions found to be enriched between the HM (high metabolic gene alteration frequencies) and LM (low metabolic gene alteration frequencies) supertypes [1]. Enrichr was used to obtain enriched GO-terms that were visualised in yEd (refer to the methods section; [2]). Each node represents a GO-term with similar nodes clustered together and connected by edges with the number of shared genes between the nodes being represented by the thickness of the edges. The size of each node denotes the gene set size of the represented GO-term. The colour of each node represents the magnitude of the combined enrichment score: red represents enrichment in LM supertype tumours and blue represents enrichment in HM supertypes tumours.

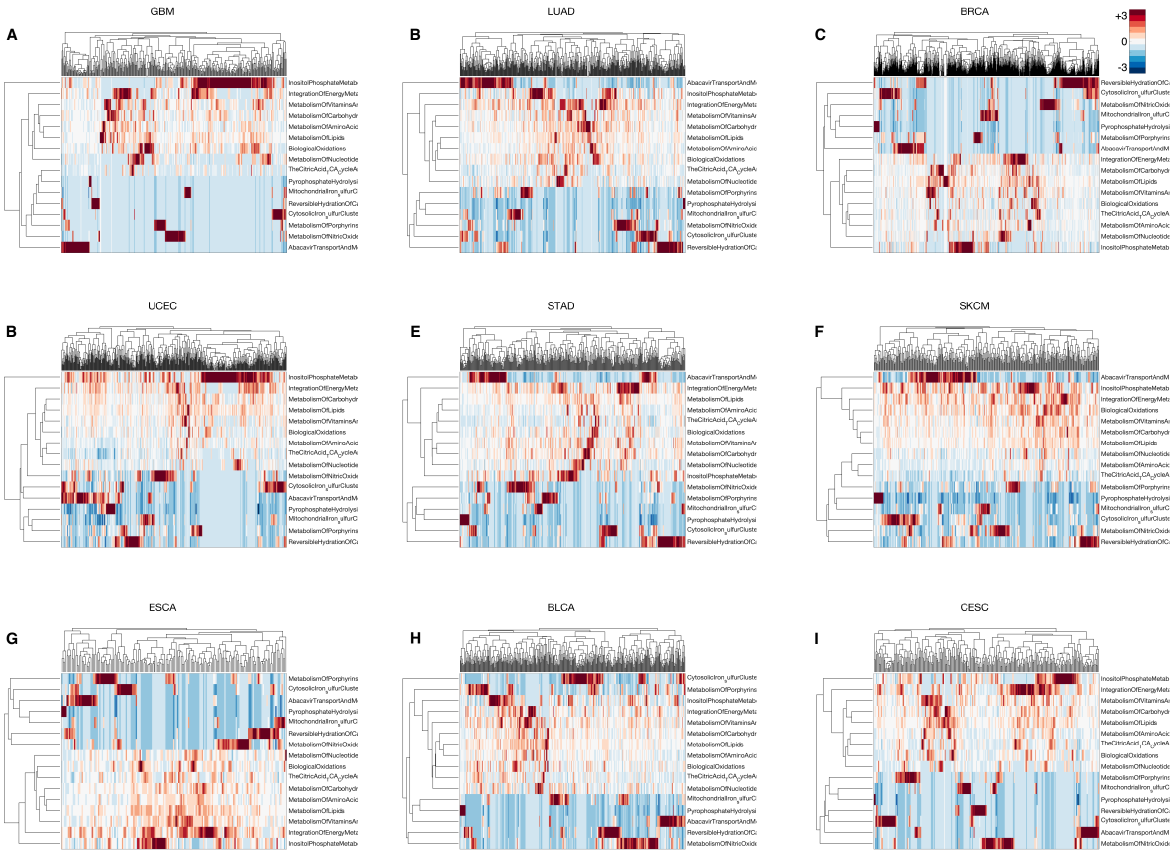


	UCEC	COADREAD	ALL	CESC	LUSC	LGG	LIHC	THCA	NB	DLBC	HNSC	BRCA	OV	SCLC	LUAD	ESCA	STAD	LCML	SKCM	BLCA	GBM	PAAD	KIRC	MM	LAML	MB	PRAD	MESO	CLL	ACC
MetabolismOfLipids	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	96.4	100	100	95.2	100	100
MetabolismOfCarbohydrates	100	100	100	100	100	100	94.1	100	96.9	94.3	92.9	94.1	88.2	95.5	100	97.1	96	100	96.4	100	100	93.3	93.8	88.9	96.4	100	100	90.5	66.7	100
BiologicalOxidations	100	96.1	92.3	85.7	93.3	94.1	100	93.8	90.6	94.3	85.7	86.3	85.3	92.4	93.8	97.1	100	100	98.2	100	97.2	93.3	81.3	88.9	92.9	100	66.7	61.9	66.7	100
MetabolismOfAminoAcidsAndDerivatives	100	96.1	100	100	100	82.4	100	93.8	96.9	97.1	90.5	94.1	94.1	95.5	100	100	96	90	92.7	94.7	80.6	90	78.1	88.9	96.4	100	66.7	71.4	100	100
MetabolismOfVitaminsAndCofactors	100	94.1	100	78.6	100	82.4	82.4	87.5	93.8	91.4	88.1	86.3	91.2	95.5	96.9	97.1	96	90	92.7	84.2	88.9	83.3	78.1	88.9	89.3	75	83.3	85.7	100	100
IntegrationOfEnergyMetabolism	88.9	98	92.3	85.7	80	76.5	82.4	81.3	68.8	88.6	83.3	72.5	85.3	92.4	92.2	77.1	64	90	85.5	73.7	63.9	63.3	59.4	61.1	67.9	75	66.7	71.4	66.7	100
MetabolismOfNucleotides	88.9	74.5	73.1	64.3	53.3	47.1	64.7	62.5	56.3	57.1	59.5	62.7	73.5	78.8	73.4	62.9	76	70	56.4	68.4	58.3	43.3	50	66.7	57.1	50	66.7	28.6	66.7	100
TheCitricAcid_TCA_CycleAndRespiratoryElectronTransport	100	80.4	73.1	64.3	40	58.8	58.8	62.5	65.6	74.3	57.1	60.8	55.9	74.2	75	71.4	80	60	72.7	73.7	61.1	46.7	50	77.8	75	50	66.7	52.4	0	0
InositolPhosphateMetabolism	88.9	64.7	80.8	57.1	60	47.1	47.1	50	62.5	62.9	54.8	54.9	55.9	66.7	65.6	65.7	64	60	74.5	78.9	77.8	63.3	59.4	61.1	50	75	66.7	47.6	33.3	0
AbacavirTransportAndMetabolism	66.7	39.2	46.2	21.4	0	17.6	11.8	18.8	12.5	14.3	16.7	17.6	26.5	33.3	32.8	28.6	32	40	18.2	21.1	8.3	3.3	18.8	27.8	17.9	0	50	4.8	33.3	100
MetabolismOfNitricOxide	88.9	47.1	42.3	21.4	13.3	17.6	11.8	18.8	9.4	11.4	14.3	23.5	20.6	10.6	12.5	11.4	20	40	23.6	31.6	5.6	16.7	6.3	5.6	17.9	25	0	9.5	0	0
MetabolismOfPorphyrins	55.6	39.2	30.8	28.6	13.3	17.6	17.6	18.8	15.6	14.3	11.9	15.7	26.5	18.2	23.4	25.7	20	20	9.1	10.5	8.3	16.7	9.4	11.1	28.6	50	33.3	14.3	0	0
CytosolicIron_sulfurClusterAssembly	66.7	45.1	50	28.6	26.7	17.6	17.6	6.3	18.8	17.1	19	21.6	32.4	24.2	21.9	17.1	20	20	14.5	5.3	16.7	16.7	9.4	11.1	25	25	33.3	14.3	0	0
ReversibleHydrationOfCarbonDioxide	33.3	33.3	42.3	28.6	33.3	0	5.9	12.5	6.3	5.7	9.5	29.4	17.6	25.8	12.5	20	24	20	23.6	15.8	11.1	3.3	6.3	5.6	7.1	0	50	9.5	0	0
MitochondrialIron_sulfurClusterBiogenesis	44.4	29.4	23.1	14.3	0	0	0	12.5	6.3	2.9	2.4	3.9	5.9	9.1	9.4	5.7	4	0	5.5	5.3	2.8	0	12.5	5.6	10.7	0	0	4.8	0	0
PyrophosphateHydrolysis	0	3.9	7.7	7.1	6.7	5.9	0	0	0	0	0	2	2.9	3	3.1	0	0	0	1.8	0	0	0	0	0	0	0	0	4.8	0	0

Supplementary Figure 7: Heatmap of Genomics of Drug Sensitivity in Cancer (GDSC) cancer lines showing the percentages of cell lines with alterations to genes involved in each of the 16 first-tier metabolic pathways [3]. Pathways are ordered by decreasing frequencies of gene alterations. Increasing colour intensities denote higher percentages of cell lines with gene alterations.



Supplementary Figure 8: The number of anticancer drugs that target 24 signalling pathways and/or biological process that were used by the GDSC to treat cancer cell lines. Colours indicate the targeted pathways.



Supplementary Figure 9: Metabolic pathway gene alterations within cancer types. The clustergrams of gene alterations in various human cancer types. Only nine examples of cancer types are shown. The clustergrams show the percentage of tumours with alterations to genes involved in each of the 16 first-tier metabolic pathways.

Supplementary References

1. Gene Ontology Consortium: going forward. *Nucleic Acids Res.* **43**, D1049–D1056 (2015).
2. Chen, E. Y. *et al.* Enrichr: interactive and collaborative HTML5 gene list enrichment analysis tool. *BMC Bioinformatics* **14**, 128 (2013).
3. Yang, W. *et al.* Genomics of Drug Sensitivity in Cancer (GDSC): a resource for therapeutic biomarker discovery in cancer cells. *Nucleic Acids Res.* **41**, D955–D961 (2012).