# Supplementary materials

Metabolomics, transcriptomic and genetic - integrative analysis reveals important roles of adenosine diphosphate in haemostasis and platelet activation in non-small cell lung cancer

### Supplementary Table 1: Reactome Pathway Analysis of the Turquoise Module

D-41	Entities			Reactions		
Pathway name	found	ratio	p-value	FDR*	found	ratio
G2/M Checkpoints	88 / 154	0.011	1.11e-16	2.72e-14	24 / 24	0.002
Mitotic G1-G1/S phases	96 / 173	0.012	1.11e-16	2.72e-14	95 / 98	0.008
Cell Cycle, Mitotic	255 / 570	0.041	1.11e-16	2.72e-14	309 / 322	0.027
G1/S Transition	86 / 150	0.011	1.11e-16	2.72e-14	58 / 61	0.005
M Phase	158 / 390	0.028	1.11e-16	2.72e-14	62 / 66	0.006
Cell Cycle	294 / 682	0.049	1.11e-16	2.72e-14	379 / 411	0.035
Cell Cycle Checkpoints	151 / 279	0.02	1.11e-16	2.72e-14	40 / 57	0.005
DNA Replication	75 / 141	0.01	5.30e-14	1.05e-11	46 / 47	0.004
Separation of Sister Chromatids	92 / 194	0.014	5.53e-14	1.05e-11	8 / 8	6.79e-04
Mitotic Metaphase and Anaphase	97 / 211	0.015	6.93e-14	1.16e-11	12 / 12	0.001
Mitotic Anaphase	96 / 208	0.015	7.45e-14	1.16e-11	11 / 11	9.33e-04
Amplification of signal from unattached kinetochores via a MAD2 inhibitory signal	57 / 94	0.007	3.63e-13	4.80e-11	4 / 4	3.39e-04
Amplification of signal from the kinetochores	57 / 94	0.007	3.63e-13	4.80e-11	4 / 4	3.39e-04
DNA Replication Pre-Initiation	54 / 88	0.006	9.58e-13	1.17e-10	20 / 21	0.002
Synthesis of DNA	68 / 132	0.009	3.15e-12	3.37e-10	26 / 26	0.002
Mitotic Spindle Checkpoint	60 / 110	0.008	6.33e-12	6.39e-10	7 / 7	5.94e-04
S Phase	81 / 179	0.013	1.66e-11	1.57e-09	49 / 54	0.005
Chromosome Maintenance	57 / 105	0.008	2.51e-11	2.26e-09	27 / 27	0.002
Homology Directed Repair	63 / 130	0.009	2.13e-10	1.81e-08	48 / 50	0.004
Assembly of the pre-replicative complex	42 / 68	0.005	2.49e-10	2.02e-08	11 / 12	0.001
Resolution of Sister Chromatid Cohesion	64 / 134	0.01	2.72e-10	2.12e-08	8 / 8	6.79e-04
Nucleosome assembly	36 / 54	0.004	6.48e-10	4.60e-08	4 / 4	3.39e-04
Deposition of new CENPA-containing nucleosomes at the centromere	36 / 54	0.004	6.48e-10	4.60e-08	4 / 4	3 <b>.</b> 39e-04
Mitotic Prometaphase	84 / 207	0.015	1.18e-09	8.02e-08	15 / 15	0.001
G1/S-Specific Transcription	31 / 43	0.003	1.63e-09	1.03e-07	28 / 28	0.002

<sup>\*</sup> False Discovery Rate

Supplementary Table 2: Genes contained in the Agilent Gene Panel for targeted capture sequencing. The gene panel consists of 12129 probes with a total size of 266.937 kbp.

AKT1	EP300	MTAP	RIT1
ALK	ERBB2	MYC	ROBO1
ARID1A	ERBB4	MYCL	ROS1
ARID1B	FBBXW7	NF1	SETD2
ARID2	FGFR3	NFE2L2	SF3B1
BRAF	FHIT	NOTCH1	SMARCA4
CCND1	FOXP1	NRAS	SOX2
CCND3	HRAS	NTRK1	STK11
CDK4	KEAP1	PIK3CA	TERT
CDKN2A	KRAS	PTEN	TP53
CREBBP	MAP2K1	RB1	TSC1
CUL3	MDM2	RBM10	TSC2
EGFR	MET	RET	U2AF1

### Supplementary Figure 1

Α В Squamous cell - Normal Adenocarcinoma - Normal -2 0 2 -2 0 2 Squamous cell - Tumour Adenocarcinoma - Tumour Alanine and Aspartate Metabolism Alanine and Aspartate Metabolism Aminosugar Meatbolism Ascorbate and Aldarate Metabolism Carnitine Metabolism Dipeptide Drug Fatty Acid Fructose, Manose and Galactose Metabolism Fatty Acid Metabolism Glutamate Metabolism Glycine, Serine and Threonine Metabolism Glutamate Metabolism Glycolysis, Gluconeogenesis, and Pyruvate Metabolism Hemoglobin and Porphyrin Metabolism Inositol Metabolism Glycine, Serine and Threonine Metabolism Leucine, Isoleucine and Valine Metabolism Glycolysis, Gluconeogenesis, and Pyruvate Metabolism Long Chain Fatty Acid Hemoglobin and Porphyrin Metabolism Inositol Metabolism Leucine, Isoleucine and Valine Metabolism Long Chain Fatty Acid Lysine Metabolism Lysolipid Lysolipid Medium Chain Fatty Acid Methionine, Cysteine, SAM and Taurine Metabolism Methionine, Cysteine, SAM and Taurine Metabolism Monoacylglycerol Pentose Metabolism Pentose Metabolism Phenylalanine and Tyrosine Metabolism Phenylalanine and Tyrosine Metabolism Phospholipid Metabolism Phospholipid Metabolism Polyunsaturated Fatty Acid (n3 and n6) Polyunsaturated Fatty Acid (n3 and n6) Purine Metabolism, (Hypo)Xanthine/ Inosine Containing Purine Metabolism Purine Metabolism, Adenine containing Pyrimidine Metabolism, Uracil containing Steroid

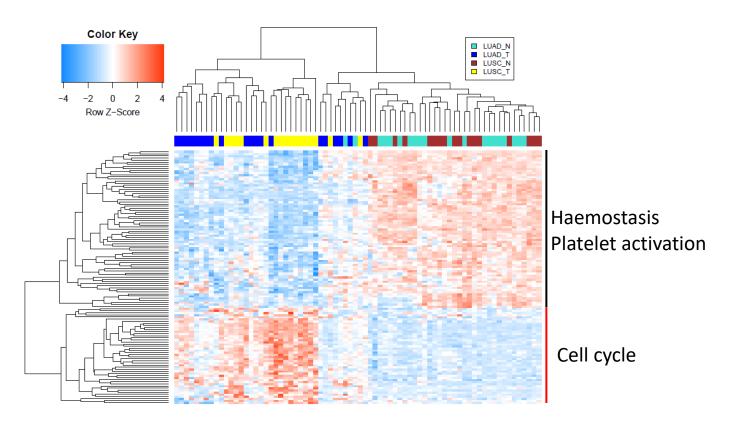
Urea Cycle, Arginine nad Proline Metabolism

I TCA cycle

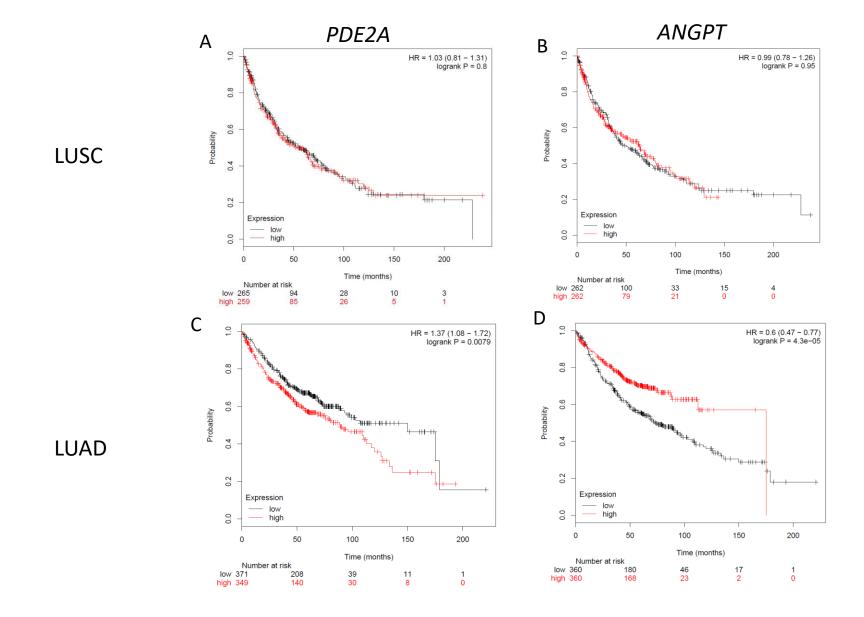
I Tryptophan Metabolism

Urea cycle, Arginine and Proline Metabolism

## Supplementary Figure 2



### Supplementary Figure 3



Supplementary Figure 1: Hierarchical clustering analysis of significant metabolites between tumour and matched normal control of LUSC (A) and LUAD (B). Metabolites with a higher level of expression in the tumours are shown in red or whilst those with a lower level of expression are indicated in blue.

Supplementary Figure 2: Hierarchical clustering analysis of transcripts that formed the metabolites – transcripts network in Figure 3A. Transcripts contributing to haemostasis and platelet activation were less abundant in both LUSC and LUAD tumours while those involving in cell cycle were more abundant. Transcripts with higher level in the tumours are shown in red or lower level in blue. LUAD-N: Normal tissue LUAD, LUAD-T: Tumour LUAD, LUSC-N: normal tissue LUSC, LUSC-T: Tumour LUSC

Supplementary Figure 3: Survival analysis (www.kmplot.com) using published expression data of *PED2A* and *ANGPT1* in lung cancer patients. The expression level of *PED2A* and *ANGPT1* was not associated with survival outcome in patients with LUSC (A and B). In contrast, in LUAD, high expression level of *PDE2A* was associated with poorer survival (C) while high expression of *ANGPT1* was associated with better survival outcome (D).