Supplementary Material

Mutational landscape of cell-free DNA identifies distinct molecular features associated with therapeutic response to platinum based first-line chemotherapy in patients with advanced NSCLC

Tao Jiang, Xuefei Li, Jianfei Wang, Chunxia Su, Wenbo Han, Chao Zhao, Fengying Wu, Guanghui Gao, Wei Li, Jie Zhang, Xiaoxia Chen, Jiayu Li, Fei Zhou, Jing Zhao, Weijing Cai, Anwen Xiong, Henghui Zhang, Bo Du, Jun Zhang, Shengxiang Ren, Caicun Zhou, Hui Yu, Fred, R. Hirsch

Supplemental Figures

Supplemental Table S1. List of 1086 detected genes in the initial panel (in alphabetical order).

Supplementary Figure S1. Association between baseline cfDNA concentration and treatment response.
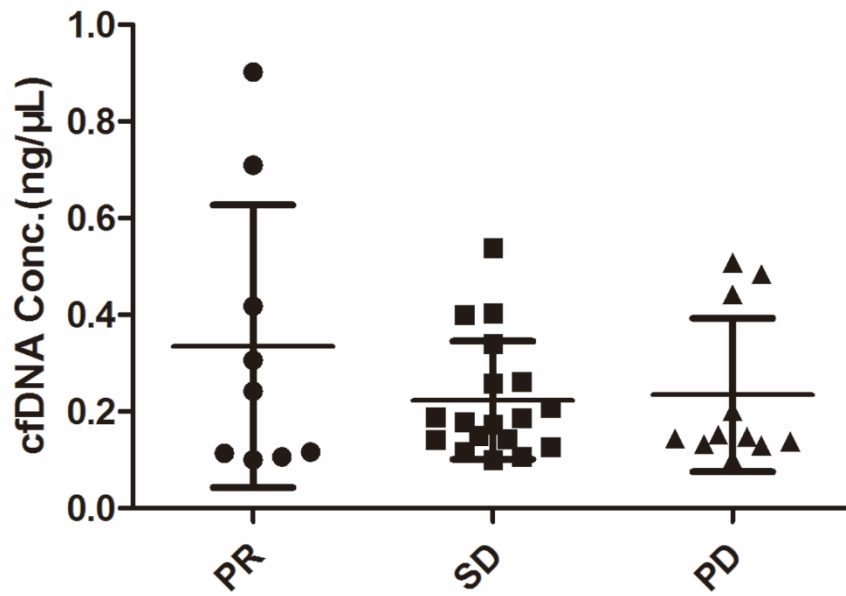
Supplemental Figure S2. Relationship between copy number variation (CNV) [#] from genomic DNA and response to treatment. **(A)** CNV profiles from genomic DNA was significantly different between patients with PR vs. SD/PD; **(B)** No segregation according to objective response was observed via hierarchical clustering of genomic DNA. [#] CNV here was calculated through the value of genomic DNA compared with the DNA value of the patient's blood cell pellets.
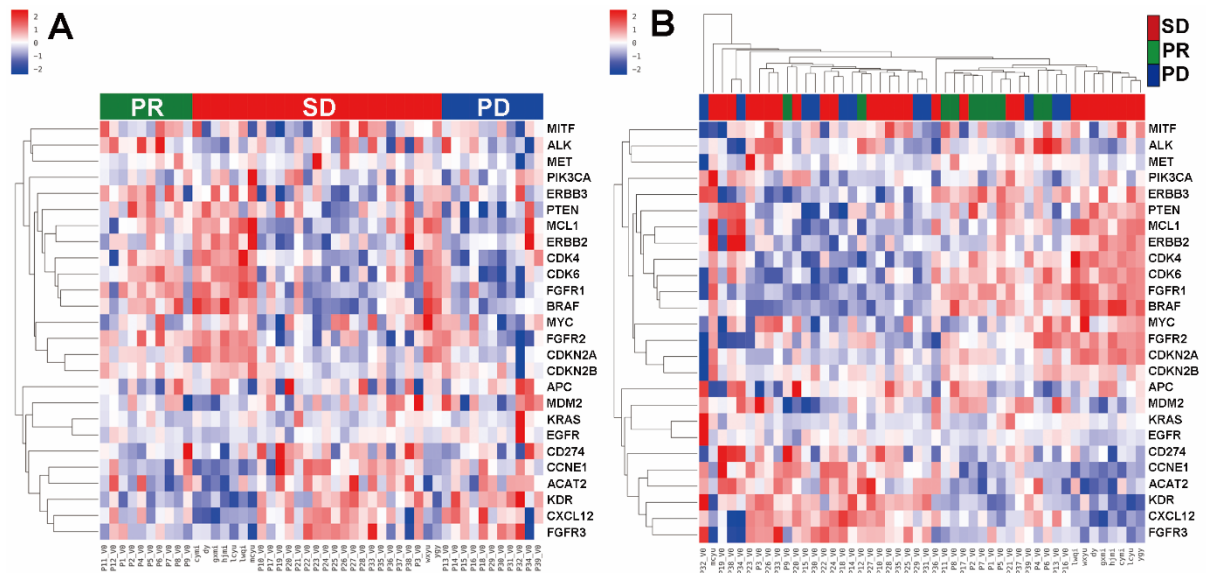
Supplemental Figure S3. Association between baseline *TP53* mutational burden and treatment response.

Supplemental Figure S4. *The association between molecular mutational burden of 8 genes (BCL2, CD74, GSTP1, MTHFR, MLH1, RRM1, XPC and XRCC1) and treatment response.*
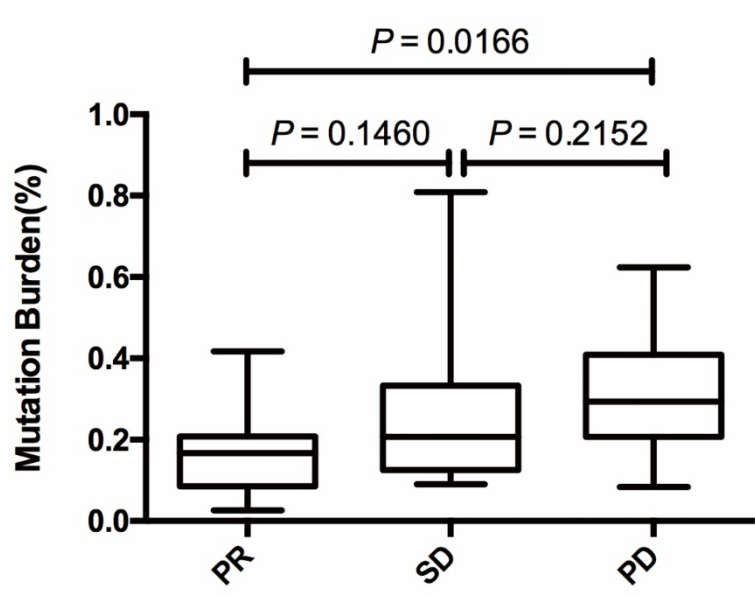
Supplemental Figure S5. *The association between molecular mutational burden of 8 genes (BCL2, CD74, GSTP1, MTHFR, MLH1, RRM1, XPC and XRCC1) and progression free survival.*

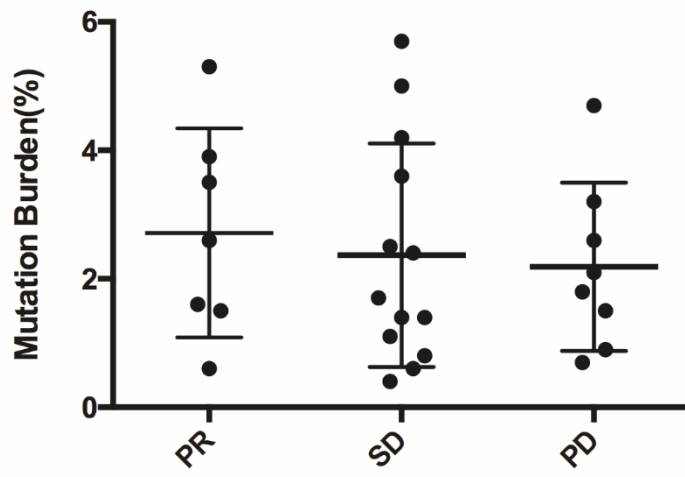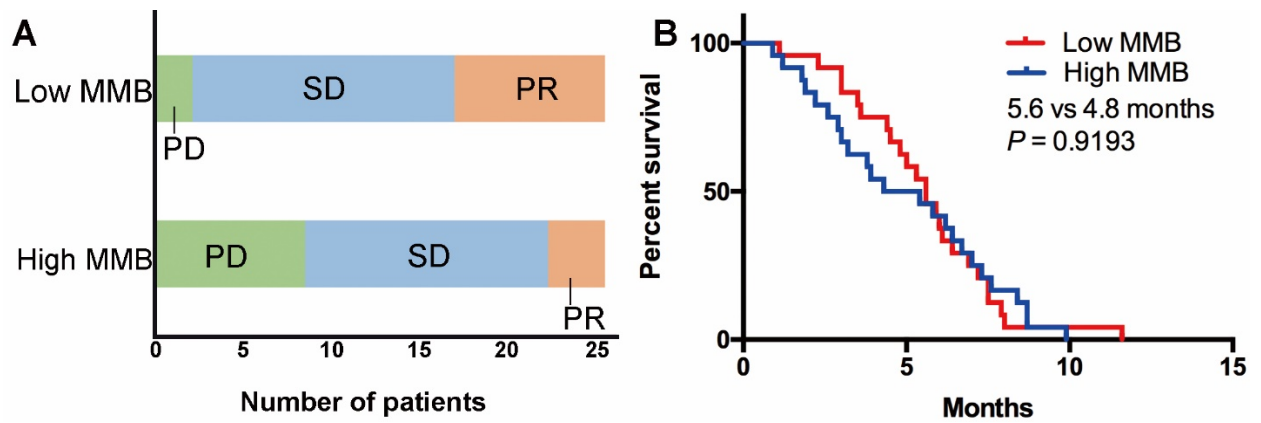**Supplemental Table S1.** List of 1086 detected genes in the initial panel (in alphabetical order).

A

ABCA1	ABCA3	ABCB1	ABCB11	ABCB4	ABCB6	ABCC1
ABCC11	ABCC2	ABCC3	ABCC4	ABCC5	ABCC5-AS1	ABCC6
ABCC9	ABCG1	ABCG2	ABL1	ACE	ACHE	ACO1
ACP5	ACPP	ACSM2A	ACSS2	ACTA2	ACTB	ACTG1
ACTR8	ACVR2B	ACYP2	ADAM22	ADAMTSL4-AS1	ADCY10	ADCY2
ADD1	ADGRB3	ADH1A	ADH1B	ADH1C	ADH7	ADIPOQ
ADIPOQ-AS1	ADRA2A	ADRA2B	ADRA2C	ADRB1	ADRB2	ADRB3
AFMID	AGO1	AGO2	AGT	AGTR1	AGTRAP	AGXT
AHR	AKAP9	AKNA	AKR1C2	AKR1C3	AKT1	AKT2
ALB	ALDH1A1	ALDH3A1	ALDH5A1	ALK	ALOX12	ANK1
ANKK1	ANTXR2	ANXA11	AOC1	AOX1	APC	APCS
APOA1	APOA1-AS	APOA4	APOA5	APOB	APOBEC2	APOC3
APOE	APOH	AQP2	AQP9	AR	ARAF	AREG
ARHGEF10	ARHGEF4	ARID1A	ARID5B	ARNT	ARRDC3	ARVCF
ASH1L	ASS1	ATG5	ATIC	ATM	ATP7A	ATP7B
ATR	ATXN2L	AURKA	AXIN2	AZGP1	AZU1	

B

B2M	BAIAP2L1	BAP1	BAZ2B	BCAT1	BCHE	BCL2
BCL2L1	BCL2L11	BCOR	BCR	BDNF-AS	BGLAP	BLMH
BMP7	BMX	BRAF	BRCA1	BRCA2	BRD2	BRD4
BRWD1	BTK	BTN3A1	BTRC	BZRAP1-AS1		

C

C10orf11	C20orf194	C2-AS1	C5orf22	C8orf34	CA1	CA12
CA13	CA14	CA3-AS1	CA4	CALM3	CAMK1	CAMK2A
CAMK4	CANT1	CAPG	CARD16	CARS	CARTPT	CASP1
CASP3	CASP7	CASP9	CAT	CBL	CBR1	CBR3
CBS	CCAT2	CCBL1	CCDC189	CCDC6	CCL1	CCND1
CCND2	CCND3	CCNE1	CCNH	CCNY	CD14	CD180
CD1D	CD274	CD28	CD3EAP	CD40LG	CD47	CD55
CD74	CDA	CDC5L	CDH1	CDK4	CDK6	CDK7
CDK8	CDKN1A	CDKN1B	CDKN2A	CDKN2A-AS1	CDKN2B	CDKN2B-AS1
CDKN2C	CEACAM22P	CEP89	CES2	CFTR	CHAT	CHEK2
CHRNA3	CHRNA5	CHST3	CLCN6	CLDN34	CLIC1	CLIP1
CLK3	CLTC	CMPK1	CMTR1	CNOT1	CNR1	COL1A1
COL1A2	COL4A1	COLEC10	COMT	CPA1	CPA2	CPA4
CPB2	CRABP2	CRAT	CREBBP	CRP	CRYZ	CSDE1
CSF1R	CSF2RB	CSF3R	CSNK2A1	CSNK2A3	CSPG4	CSTF1
CTLA4	CTNNB1	CTSL	CTSS	CXCL10	CXCL12	CXCL8
CXCR2	CXXC4	CYBA	CYP11B2	CYP19A1	CYP1A1	CYP1A2
CYP1B1	CYP24A1	CYP2A6	CYP2B6	CYP2C19	CYP2C8	CYP2D6
CYP2E1	CYP2R1	CYP3A4	CYP3A5	CYP46A1	CYP4B1	CYP4F2

D

DAPK1	DAZL	DBH	DCBLD1	DCK	DCP1B	DCTD
DCTN1	DCTN5	DDR1	DDR2	DDX20	DDX53	DDX6
DERL3	DGKI	DHFR	DKFZP434I0714	DLG4	DLG5	DLGAP1
DNMT3A	DOCK4	DOT1L	DPEP1	DPP4	DPYD	DPYS
DRD2	DROSHA	DSCAM	DTYMK			

E

E2F7	ECT2L	EFNB2	EGF	EGFR	EGLN3	EIF3A
EIF4E2	ELDR	EML4	ENOSF1	EP300	EPAS1	EPHA2
EPHA3	EPHA4	EPHA5	EPHA6	EPHX1	EPHX2	EPM2AIP1
EPRS	ERAP2	ERBB2	ERBB3	ERBB4	ERC1	ERCC1
ERCC2	ERCC3	ERCC4	ERCC5	ERCC6	EREG	ERG
ERP44	ESR1	ESR2	ESRP1	ETF1	ETV1	ETV4
ETV5	ETV6	EVI2A	EXO1	EZH2	EZR	

F

F10	F2	FAAH	FABP1	FAF1	FAM131B	FAM96B
FANCA	FANCC	FAP	FARS2	FASLG	FAT1	FBXW7
FCGR2A	FCGR3A	FCHSD1	FCN1	FCN2	FDPS	FECH
FGD4	FGF3	FGF4	FGFR1	FGFR2	FGFR3	FGFR4
FIBCD1	FKBP4	FKBP5	FLCN	FLT1	FLT3	FLT4
FMO2	FMO3	FN1	FNTA	FNTB	FOLH1	FOLR2
FOLR3	FOXA1	FRS2	FSTL5	FTO	FTSJ2	

G

GABBR1	GABBR2	GAK	GALE	GALNS	GALNT10	GALNT14
GAPDH	GARS	GATA3	GATA3-AS1	GATA4	GATM	GCKR
GDNF	GEMIN4	GGCT	GGH	GIPR	GLP1R	GLRB
GLRX	GLRX2	GNA11	GNAI1	GNAQ	GNAS	GNB3
GNL3	GOLGA5	GOPC	GP1BA	GPC1	GPX5	GRIK1-AS2
GRIN2B	GRK5	GSG2	GSR	GSS	GSTA1	GSTA2
GSTA3	GSTA5	GSTM3	GSTO1	GSTP1	GSTT1-AS1	GUSB

H

H19	HACL1	HADH	HAS3	HAT1	HCN4	HDAC1
HDAC2	HDAC8	HERPUD1	HEXB	HFE	HGF	HIF1A
HIP1	HLA-A	HLA-B	HLA-C	HLA-DOA	HLA-DOB	HLA-DPA1
HLA-DPB1	HLA-DQA1	HLA-DQB1	HLA-DRA	HLA-DRB1	HLA-G	HMGB1
HMGCR	HNF4A	HNMT	HNRNPUL1	HOOK1	HOOK3	HOTAIR
HOTTIP	HOXA13	HPGDS	HRAS	HSCB	HSP90AA1	HSPA5
HSPA8	HTR2A	HTR2C	HTR3B	HYKK		

I

IDH1	IDH2	IFNG	IFNL2	IFNL3	IFNL4	IGF1
IGF1R	IGF2	IGF2BP2	IGFBP3	IL12B	IL13	IL17A
IL17F	IL18	IL1B	IL1RL1	IL20RA	IL21R	IL23R
IL6	IL6R	IL6ST	IL7R	IMPDH1	INPP4B	INS-IGF2
Intergenic	IRS1	ITGA2B	ITGA4	ITGA5	ITGAV	ITGAX
ITGB1	ITGB2	ITGB5	ITPA			

J

JAG1	JAK1	JAK2	JAK3	JMJD6	JAG1	JAK1

K

KARS	KCNMB3	KCNQ1	KCNQ5	KDM4D	KDR	KEAP1
KIF5B	KIF9-AS1	KIT	KLC1	KLC3	KLHL12	KLLN
KMT5A	KMT5B	KRAS	KRT19P2	KSR2		

L

LAMP3	LANCL1	LARP1B	LDHA	LDHB	LDLR	LEP
LEPR	LGALS3BP	LGR5	LIG3	LIG4	LINC00441	LINC00673
LINC00704	LIPF	LMNA	LOC100128714	LOC100507053	LOC100996325	LOC101054525
LOC101927066	LOC101927318	LOC101927768	LOC101928100	LOC101928402	LOC101929532	LOC101929709
LOC102724050	LOC284454	LOC553103	LPAR6	LPL	LRIG3	LRP1B
LRP2	LRP5	LRP6	LRRC4C	LRRC56	LRTM1	LSM14A
LTA	LTA4H	LY86	LY96	LYRM5		

M

MAD1L1	MALAT1	MALT1	MAOB	MAP2K1	MAP2K2	MAP3K1
MAP3K5	MAP3K7	MAPK11	MAPK14	MC4R	MCL1	MDM2
MDM4	MECP2	MEG3	MEP1B	MET	METAP1	METTL1
METTL23	MFSD11	MGAM	MGAT4A	MGMT	MICB	MIEN1
MIR1206	MIR1307	MIR146A	MIR2053	MIR300	MIR323B	MIR423
MIR4288	MIR449B	MIR4673	MIR4713	MIR4728	MIR4733	MIR4761
MIR483	MIR5187	MIR577	MIR604	MIR618	MIR641	MIR675
MIR6759	MIR6891	MISP	MITD1	MITF	MKRN1	MKRN2
MLLT3	MMAB	MME	MMP13	MMP2	MMP8	MPL
MROH2A	MSH2	MSH3	MSH6	MSN	MST1R	MTAP
MTHFD1	MTHFR	MTOR	MTR	MTRNR2L2	MTRR	MUTYH
MVP	MYC	MYD88	MYLIP	MYO5A		

N

NAGA	NALCN	NAMPT	NAT2	NBR2	NCAM2	NCF4
NCOA1	NCOA4	NEDD4	NEU2	NEURL2	NF1	NF2
NFASC	NFATC2	NLGN1	NLGN4X	NMRAL1	NOD2	NOS3
NOTCH1	NOTCH2	NPC1	NPM1	NQO1	NQO2	NR1I2

NR1I3	NR3C1	NR3C2	NRAS	NRG1	NSD1	NT5C2
NT5C3A	NT5E	NTHL1	NTRK1	NTRK3	NUDC	NUDT15
NUDT2	NUP210L					

<p align="center">O</p>

OASL	OPRD1	OPRM1	OR4D6	OSGEP	OTOS	

<p align="center">P</p>

PACERR	PACSIN2	PAGR1	PAH	PAK1	PALB2	PAPD7
PARD3B	PARPBP	PAX5	PBRM1	PC	PCK1	PCM1
PDCD1	PDE10A	PDE4B	PDE5A	PDGFB	PDGFRA	PDGFRB
PDK3	PDPK1	PDXK	PDZRN3	PFKFB3	PGAP3	PGBD3
PGR	PHF7	PHF8	PHKG2	PIGF	PIK3CA	PIK3CB
PIK3R1	PIK3R2	PIKFYVE	PIM1	PINLYP	PKD1	PLA2G7
PLAU	PLCB1	PLCB3	PLCG2	PLG	PLPPR2	PLXNC1
PMEL	PMM2	PNMT	PNP	POFUT2	POLA2	POLE
POLK	PON1	POR	POU3F2	PPARA	PPARD	PPARG
PPFIBP1	PPIF	PPIP5K2	PPP1R13L	PRB2	PRCP	PRDX4
PREP	PRKAA2	PRKAR1A	PRKCH	PRKCI	PRKG1	PROM1
PSMA8	PTCH1	PTEN	PTGER4	PTGES	PTGR1	PTGS2
PTH	PTH1R	PTK2	PTPN1	PTPN23	PTPRG	PTPRK
PTPRM	PTRH2	PUS1	PWWP2A	PYGL	PYGM	

<p align="center">R</p>

RAB3D	RAC1	RAC2	RAD50	RAD51C	RAD52	RAF1
RALBP1	RANBP2	RAPGEF5	RARG	RARS	RAVER2	RB1
RBFOX1	RBP2	RBP4	REN	RET	REV1	REV3L
RFK	RGS5	RICTOR	RNASE2	RNF128	RNF130	RNF43
RORC	ROS1	RRAS2	RRM1	RRM2	RUNDC3B	RXRA

<p align="center">S</p>

SCARB1	SCN10A	SCN1A	SCO2	SDC4	SDCBP	SEC16A
SEC31A	SELE	SELL	SEMA3C	SERPINA3	SERPINA6	SERPINA7
SERPINE1	SERPING1	SETD2	SETD3	SETD6	SF3B1	SFXN4
SH2B3	SH2D5	SHTN1	SIGLEC7	SIRPA	SIRT2	SLC10A2
SLC15A1	SLC19A1	SLC1A1	SLC22A1	SLC22A12	SLC22A16	SLC22A17
SLC22A2	SLC22A4	SLC22A5	SLC22A7	SLC25A13	SLC28A1	SLC28A2
SLC28A3	SLC29A1	SLC2A1-AS1	SLC31A1	SLC34A2	SLC37A1	SLC3A2
SLC45A3	SLC6A4	SLC7A5	SLCO1A2	SLCO1B1	SLCO1B3	SLCO4C1
SMARCA1	SMARCA4	SMARCAD1	SMARCB1	SMCR8	SMO	SMS
SMYD2	SMYD3	SNAPC5	SND1	SNRNP200	SOCS1	SOD2
SOD3	SOS2	SOX10	SPARC	SPG7	SPIDR	SPON1
SPP1	SQSTM1	SRC	SRGAP3	SRXN1	SSBP2	ST14

STAG2	STIM1	STK11	STRADA	STRN	STS	SULT1A1
SULT1C4	SULT1E1	SULT2B1	SUPT4H1	SUV39H2	SUZ12	SVOP
SYK	SYN1	SYNE1				

T

TAB1	TACC3	TANC1	TAS2R16	TBC1D1	TBC1D20	TCL1A
TCN1	TDP1	TEK	TENM1	TF	TFG	TGFB1
TGM2	TH2LCRR	THRA	THRB	TKT	TLR2	TLR3
TLR4	TLR7	TLR9	TMPRSS2	TNF	TNFRSF10B	TNFRSF11A
TNFRSF11B	TNFRSF1A	TNFSF11	TNFSF14	TNIP1	TNNC1	TNRC6A
TNRC6B	TOMM40L	TOP1	TOP2A	TOP2B	TP53	TPBG
TPH2	TPM3	TPM4	TPMT	TPP1	TRIM24	TRIM27
TRIM33	TRMT61B	TRPV4	TSC1	TSC2	TSG1	TSHR
TSPAN31	TTK	TTR	TUBB1	TUBB2A	TXNRD2	TYMP
TYMS	TYW3					

U

U2AF1	UBASH3B	UBC	UBE2D1	UBE2I	UGT1A1	UGT1A3
UGT1A4	UGT1A6	UGT1A7	UGT1A8	UGT1A9	UGT2B7	ULBP3
ULK3	ULK4	UMPS	UPB1	UPP1	USP6	UTY

V

VAC14	VCL	VDR	VEGFA	VEGFC	VHL	VKORC1
VWF						

W

WAPL	WARS	WDR7	WNT5B	WWOX		

X

XBP1	XDH	XPA	XPC	XPO5	XRCC1	XRCC3
XRCC4	XRCC5					

Z

ZADH2	ZBTB17	ZC3H13	ZCCHC6	ZNF276	ZNF423	ZNRF3
ZPR1	ZSCAN30					