Supplementary Information

Candidate Markers of Olaparib Response from Genomic Data Analyses of Human Cancer Cell Lines

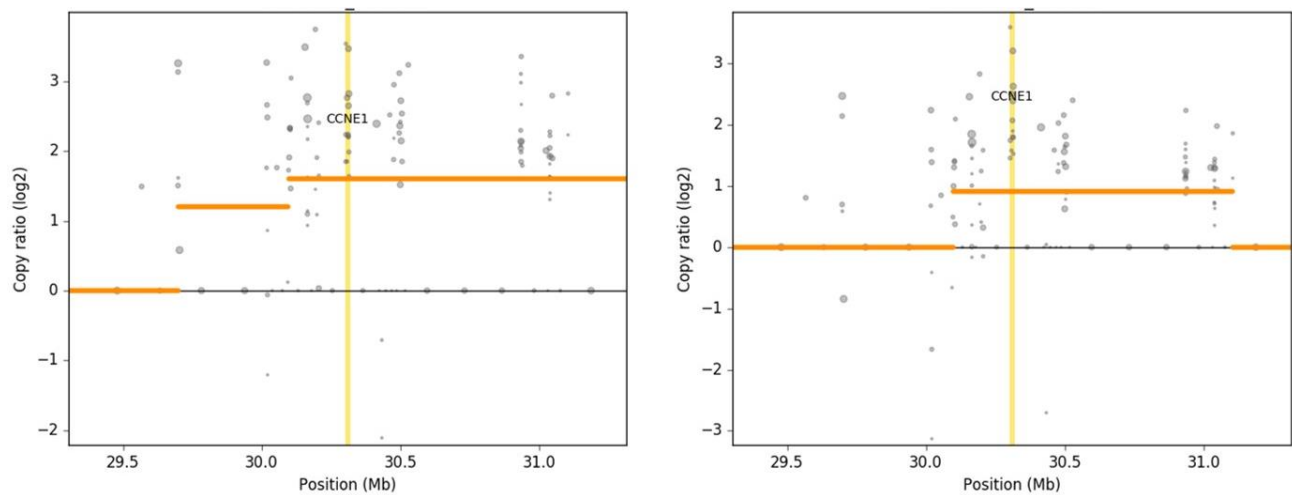Setor Amuzu, Euridice Carmona, Anne-Marie Mes-Masson, Celia M.T. Greenwood, Patricia N. Tonin, Ioannis Ragoussis

Figure S1. Amplification of *CCNE1* locus in resistant OV866(2) (left) and intermediate TOV3291G (right) cell lines.
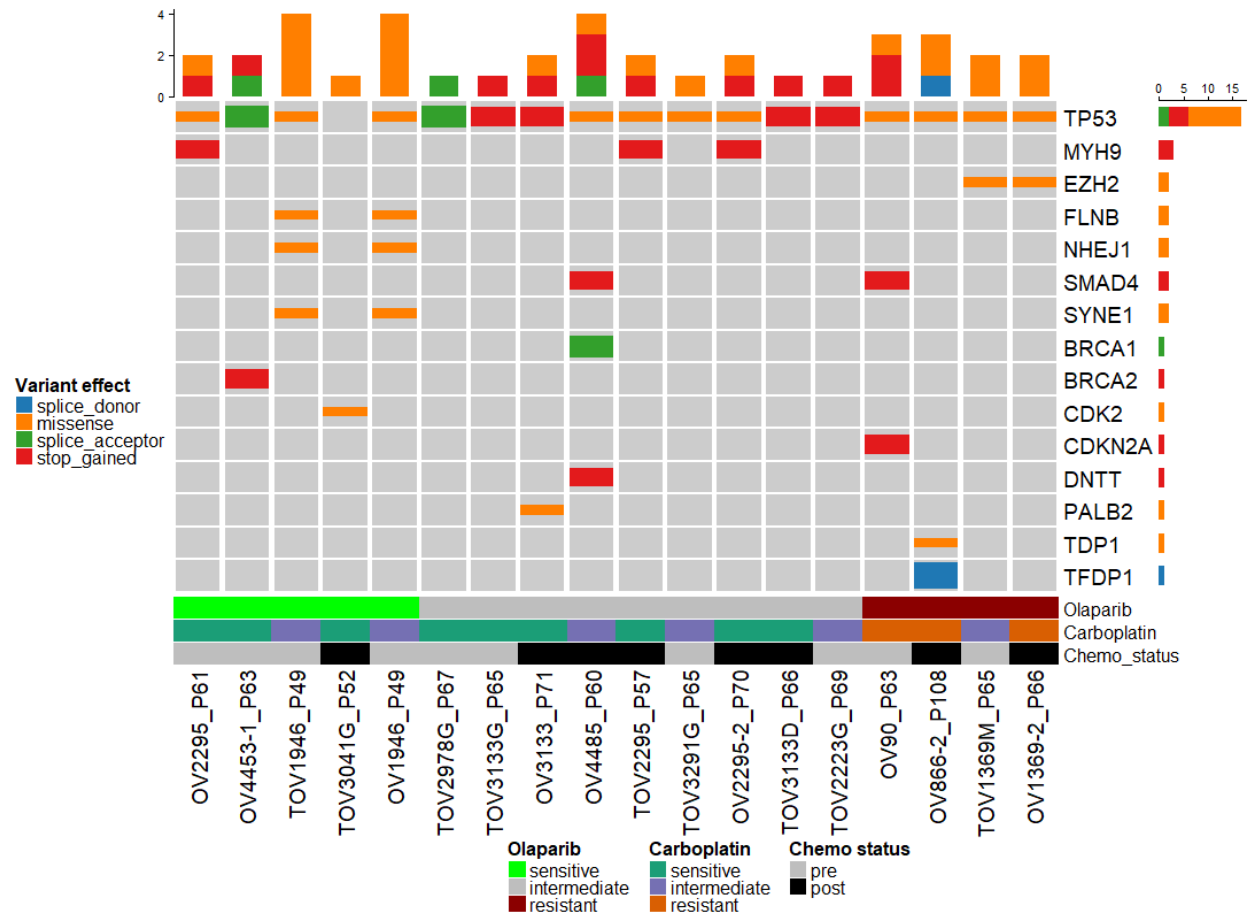
Figure S2. Rare, potentially deleterious, homozygous variants in DNA repair and cell cycle genes for 18 HGSOC cell lines. Cell lines arranged, left to right, in order of increasing resistance. OV2295 and OV1369(R2) are most sensitive and resistant cell lines respectively.
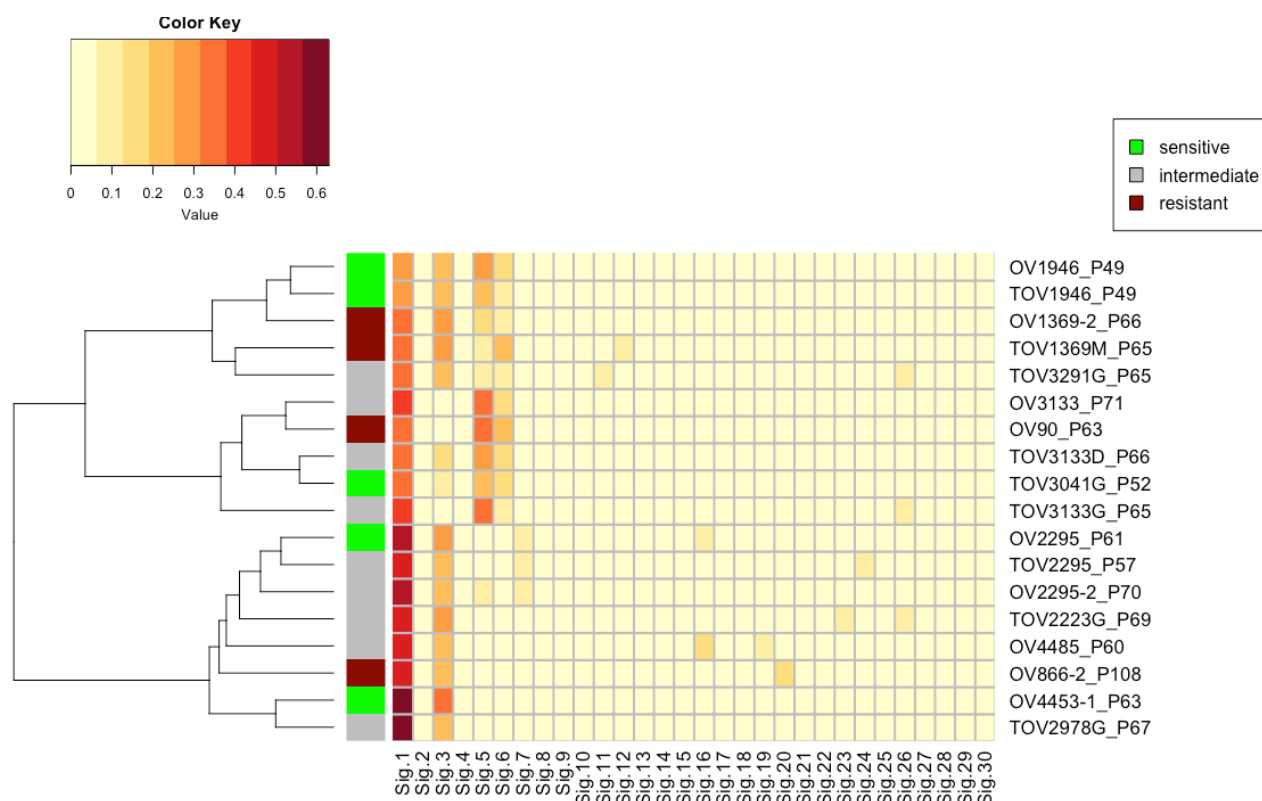
Figure S3. Hierarchical clustering of cell lines by COSMIC single base substitution mutational signatures based on Euclidean distance and complete linkage. Signature 1 is observed in all 18 cell lines while signature 3 is seen in 15 cell lines including *BRCA1/2*-mutated OV4485 and OV4453.
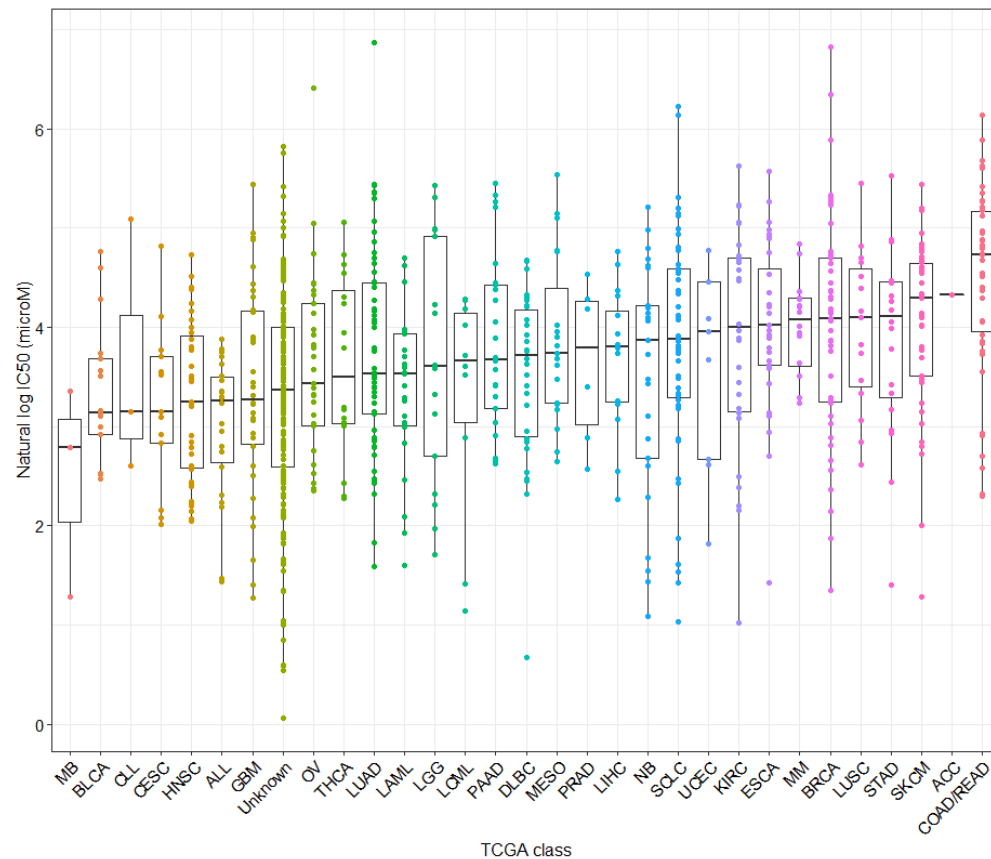
Figure S4. Distribution of *in vitro* olaparib response (IC$_{50}$) across cell lines of multiple cancer types using TCGA classifications. Dots represent individual cell lines. Boxplots represent cell lines in TCGA classes. Boxplots are ordered according to median IC$_{50}$.
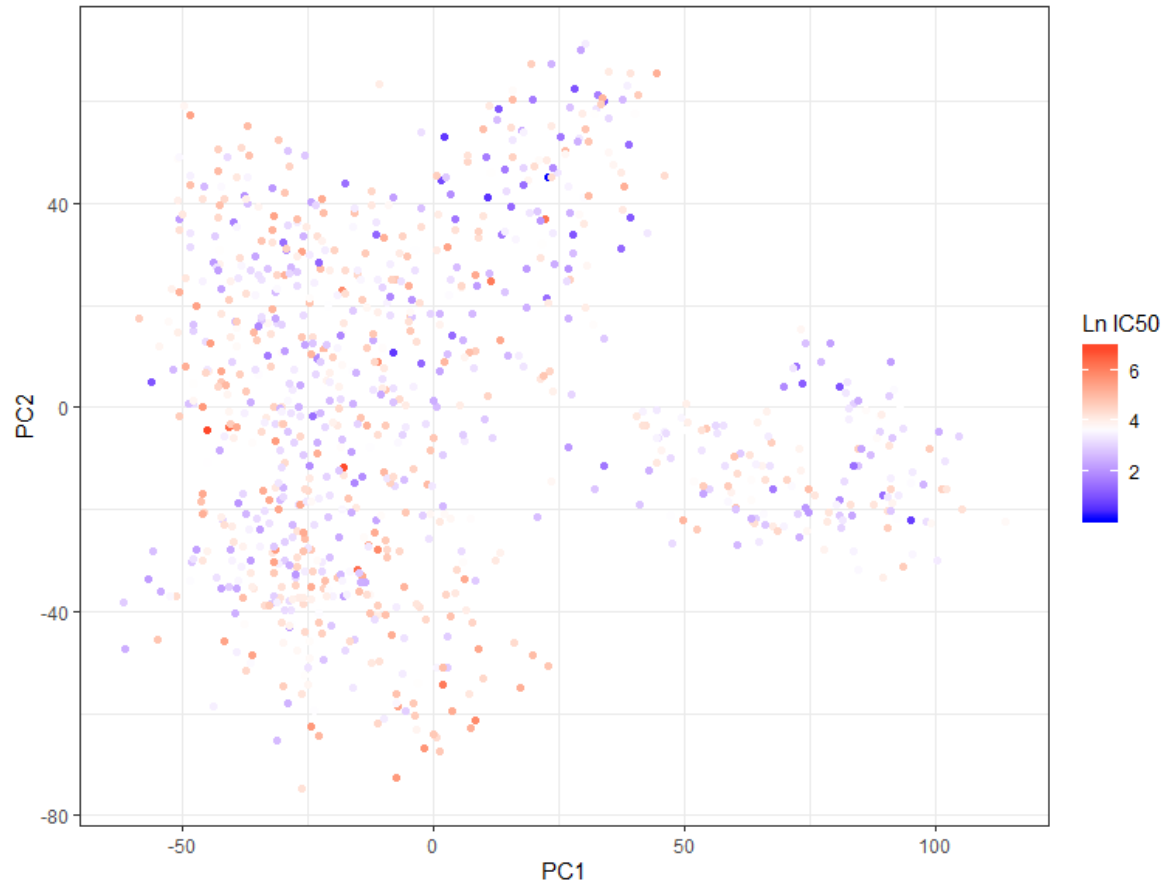
Figure S5. Principal component analysis plot of GDSC cell lines based on gene expression. First two principal components (PC1 and PC2) are shown. Each dot represents a cell line. PC1 and PC2 capture 16.7% of variation in cell lines. Dots are colored by natural log of olaparib IC_{50}.
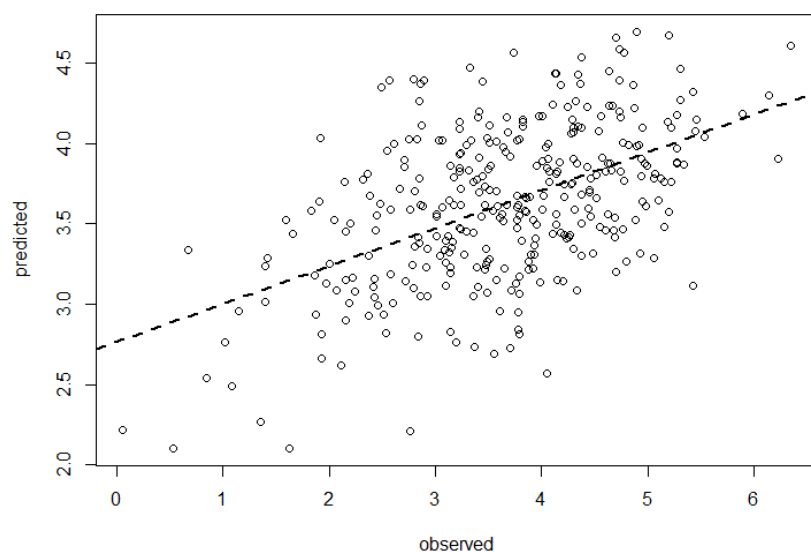
Figure S6. Performance of elastic net multivariate linear regression model on prediction of IC_{50} in test data. Observed IC_{50} values (horizontal axis) in test dataset plotted against predicted IC_{50} values (vertical axis) using elastic net model developed from training dataset. Points along the dashed line show agreement between observed and predicted values.

Tables S1–S3 in a separate file.

Table S4. List of DNA repair and cell cycle control genes investigated for genomic variations in HGSOC cell lines

Genes (n = 533)				
ABL1	CENPF	HES1	PAICS	SCARA3
ACAT2	CENPH	HEY1	PALB2	SETMAR
AEN	CENPK	HIST2H3C	PARG	SFN
ALKBH1	CENPM	HJURP	PARP1	SFRP1
ANAPC1	CENPN	HLTF	PARP2	SKP1
ANAPC10	CEP55	HMGA2	PARP3	SKP2
ANAPC11	CETN1	HMGB1	PARP4	SLC25A5
ANAPC13	CETN2	HMGB2	PARPBP	SLC38A2
ANAPC2	CETN3	HMGN2	PAXIP1	SLIRP
ANAPC4	CFL1	HMMR	PBK	SLX1A
ANAPC5	CFL2	HPRT1	PCNA	SLX1B
ANAPC7	CHAF1A	HSPD1	PER1	SMAD2
ANLN	CHAF1B	HUS1	PFN1	SMAD3
ANP32E	CHEK1	ID1	PFN2	SMAD4
APC2	CHEK2	IDH1	PKMYT1	SMARCA4
APEX1	CHFR	INCENP	PLK1	SMARCC1
APEX2	CIT	INF2	PLK3	SMC1A

APTX	*CKAP2*	*IPO7*	*PMS1*	*SMC1B*
ASCC3	*CKAP5*	*ITGA6*	*PMS2*	*SMC2*
ASPM	*CKS1B*	*KAT5*	*PNKP*	*SMC3*
ATAD2	*CKS2*	*KIAA0101*	*POLA1*	*SMC5*
ATM	*CLK2*	*KIAA1524*	*POLB*	*SMC6*
ATR	*CREBBP*	*KIF11*	*POLD1*	*SMUG1*
ATRIP	*CSE1L*	*KIF15*	*POLD2*	*SNRPA1*
ATRX	*CTNNAL1*	*KIF18A*	*POLD3*	*SNRPD1*
AURKA	*CUL1*	*KIF20A*	*POLD4*	*SNRPD3*
AURKB	*CUL3*	*KIF22*	*POLE*	*SNRPG*
BABAM1	*CUL4A*	*KIF23*	*POLE2*	*SOX4*
BARD1	*CUL5*	*KIF3B*	*POLE3*	*SPAG5*
BCAS2	*DBF4*	*KIF4A*	*POLG*	*SPC24*
BCCIP	*DBI*	*KIFC1*	*POLH*	*SPC25*
BIRC5	*DCLRE1A*	*KNTC1*	*POLI*	*SPO11*
BLM	*DCLRE1B*	*KRT18*	*POLL*	*SSBP1*
BORA	*DCLRE1C*	*LIG1*	*POLM*	*STAG1*
BRCA1	*DCUN1D1*	*LIG3*	*POLQ*	*STAG2*
BRCA2	*DDB1*	*LIG4*	*PPP1CC*	*STK38L*
BRCC3	*DDB2*	*LIMK1*	*PPP1R12A*	*STK4*
BRIP1	*DERA*	*LLGL1*	*PPP2R1B*	*SYNE1*
BUB1	*DMC1*	*LLGL2*	*PPP2R2B*	*SYNE2*
BUB1B	*DNA2*	*MAD1L1*	*PPP2R5D*	*TCEA1*
BUB3	*DNTT*	*MAD2L1*	*PPP4C*	*TDG*
C17orf70	*DTL*	*MAD2L2*	*PPP4R1*	*TDP1*
C19orf40	*DTYMK*	*MAPK14*	*PPP4R4*	*TDP2*
C1orf86	*DUT*	*MAPRE1*	*PRDX4*	*TELO2*
CALM1	*E2F1*	*MAPRE2*	*PRDX6*	*TFDP1*
CCDC86	*E2F2*	*MASTL*	*PRIM1*	*TFDP2*
CCNA1	*E2F3*	*MBD4*	*PRKCA*	*TGFB1*
CCNA2	*E2F4*	*MCM2*	*PRKDC*	*TGFB2*
CCNB1	*E2F5*	*MCM3*	*PRPF19*	*TGFB3*
CCNB2	*E2F8*	*MCM4*	*PSMB3*	*TIPIN*
CCNB3	*EBP*	*MCM5*	*PSMB6*	*TK1*
CCNC	*ECT2*	*MCM6*	*PSMC3IP*	*TKT*
CCND1	*EEF1E1*	*MCM7*	*PTEN*	*TOP2A*
CCND2	*ENO1*	*MDC1*	*PTTG1*	*TOP3A*
CCND3	*EP300*	*MDM2*	*PTTG2*	*TOP3B*
CCNE1	*ERC1*	*MELK*	*RAB6A*	*TOPBP1*
CCNE2	*ERCC1*	*MGMT*	*RAB6C*	*TP53*
CCNF	*ERCC2*	*MKI67*	*RACGAP1*	*TP53BP1*
CCNG1	*ERCC3*	*MLH1*	*RAD1*	*TP73*
CCNG2	*ERCC4*	*MLH3*	*RAD17*	*TREX1*
CCNH	*ERCC5*	*MMS19*	*RAD21*	*TREX2*
CCNK	*ERCC6*	*MNAT1*	*RAD23A*	*TRIP13*
CCNL1	*ERCC8*	*MND1*	*RAD23B*	*TTK*
CCNL2	*ESPL1*	*MORF4L1*	*RAD50*	*TUBA1C*

CCNT1	EXO1	MPG	RAD51	TUBA4A
CCNT2	EXO5	MRPL23	RAD51AP1	TUBG2
CCT5	EZH2	MRPL35	RAD51B	TUBGCP2
CD320	FAM64A	MRPL40	RAD51C	TUBGCP3
CD9	FAN1	MRPS17	RAD51D	TYMS
CDC14A	FANCA	MRPS28	RAD52	UBE2A
CDC14B	FANCC	MRTO4	RAD54B	UBE2B
CDC16	FANCE	MSH2	RAD54L	UBE2C
CDC20	FANCF	MSH3	RAD9A	UBE2N
CDC20B	FANCG	MSH6	RASSF1	UBE2S
CDC23	FANCI	MTHFD1	RB1	UBE2T
CDC25A	FANCL	MUS81	RBBP4	UBE2V2
CDC25B	FBL	MUTYH	RBBP8	UCK2
CDC25C	FBXO5	MYC	RBL1	UIMC1
CDC26	FDPS	MYH10	RBL2	UNG
CDC27	FEN1	MYH9	RBX1	UQCRH
CDC45	FLNA	MYL6	RECQL	USP1
CDC5L	FLNB	MYL7	RECQL4	VAMP8
CDC6	FMN1	MYLK	RECQL5	WDHD1
CDC7	FMN2	NABP2	REV1	WDR48
CDCA5	FOXN3	NBN	REV3L	WEE1
CDCA8	FXYD5	NCAPG	RFC1	WEE2
CDH1	FZR1	NDC80	RFC2	WRN
CDK1	GADD45A	NEIL1	RFC3	XAB2
CDK10	GADD45B	NEIL3	RFC4	XPA
CDK2	GADD45G	NEK2	RFC5	XPC
CDK3	GAPDH	NFATC2IP	RHOA	XRCC1
CDK4	GINS2	NHEJ1	RIF1	XRCC2
CDK5	GMNN	NSMCE4A	RIT1	XRCC3
CDK6	GSK3B	NTHL1	RMI1	XRCC4
CDK7	GSTO1	NUDT1	RNF4	XRCC5
CDK8	GTF2H1	NUDT15	RNF8	XRCC6
CDK9	GTF2H2	NUDT18	RNMT	YWHAB
CDKL1	GTF2H3	NUDT4	ROCK1	YWHAE
CDKN1A	GTF2H4	NUF2	ROCK2	YWHAG
CDKN1B	GTF2H5	OGG1	RPA1	YWHAH
CDKN1C	GTSE1	ORC1	RPA2	YWHAQ
CDKN2A	H2AFV	ORC2	RPA3	YWHAZ
CDKN2B	H2AFX	ORC3	RPA4	ZBTB17
CDKN2C	H2AFZ	ORC4	RRM1	ZRANB2
CDKN2D	HDAC1	ORC5	RRM2	ZW10
CDKN3	HDAC2	ORC6	RTEL1	ZWINT
CENPE	HERC2	PA2G4		