Comprehensive cancer-gene panels can be used to estimate mutational load and predict clinical benefit to PD-1 blockade in clinical practice

Supplementary Material

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Table S1. FM-CGP genes.

GeneSymbol – FM-CGP

ABL1
ABL2
ACVR1B
AKT1
AKT2
AKT3
ALK
APC
AR
ARAF
ARFRP1
ARID1A
ARID1B
ARID2
ASXL1
ATM
ATR
ATRX
AURKA
AURKB
AXIN1
AXL
BAP1
BARD1
BCL2
BCL2L1
BCL2L2
BCL6
BCOR
BCORL1
BLM
BRAF
BRCA1
BRCA2
BRD4
BRIP1
BTG1
BTK
EMSY
CARD11
CBFB
CBL
CCND1
CCND2
CCND3
CCNE1
CD274
CD79A
CD79B
CDC73
CDH1
CDK12
CDK4
CDK6
CDK8
CDKN1A
CDKN1B
CDKN2A
CDKN2B
CDKN2C
CEBPA
CHD2
CHD4
CHEK1
CHEK2
CIC
CREBBP
CRKL
CRLF2
CSF1R
CTCF
CTNNA1
CTNNB1
CUL3
CYLD
DAXX
DDR2
DICER1
DNMT3A
DOT1L
EGFR
EP300
EPHA3
EPHA5
EPHA7
EPHB1
ERBB2
ERBB3
ERBB4
ERG
ERRFI1
ESR1
EZH2
AMER1
FAM46C
FANCA
FANCC
FANCD2
FANCE
FANCF
FANCG
FANCL
FAS
FAT1
FBXW7
FGF10
FGF14
FGF19
FGF23
FGF3
FGF4
FGF6
FGFR1
FGFR2
FGFR3
FGFR4
FH
FLCN
FLT1
FLT3
FLT4
FOXL2
FOXP1
FRS2
FUBP1
GABRA6
GATA1
GATA2
GATA3
GATA4
GATA6
c17orf39
GLi1
GNA11
GNA13
GNAQ
GNAS
GPR124
GRIN2A
GRM3
GSK3B
H3F3A
HGF
HNF1A
HRAS
HSD3B1
HSP90AA1
IDH1
IDH2
IGF1R
IGF2
IKBKE
IKZF1
IL7R
INHBA
INPP4B
IRF2
IRF4
IRS2
JAK1
JAK2
JAK3
JUN
KAT6A
KDM5A
KDM5C
KDM6A
KDR
KEAP1
KEL
KIT
KLHL6
KMT2A
KMT2C
KMT2D
KRAS
LMO1
LRP1B
LYN
LZTR1
MAGI2
MAP2K1
MAP2K2
MAP2K4
MAP3K1
MCL1
MDM2
MDM4
MED12
MEF2B
MEN1
MET
MITF
MLH1
MPL
MRE11A
MSH2
MSH6
MTOR
MUTYH
MYC
MYCL
MYCN
MYD88
NF1
NF2
NFE2L2
NFKBIA
NKX2-1
NOTCH1
NOTCH2
NOTCH3
NPM1
NRAS
NSD1
NTRK1
NTRK2
NTRK3
NUP93
PAK3
PALB2
PARK2
PAX5
PBRM1
PDCD1LG2
PDGFRA
PDGFRB
PDK1
PIK3C2B
PIK3CA
PIK3CB
PIK3CG
PIK3R1
PIK3R2
PLCG2
PMS2
POLD1
POLE
PPP2R1A
PRDM1
PREX2
PRKAR1A
PRKCI
PRKDC
PRSS8
PTCH1
PTEN
PTPN11
QKI
RAC1
RAD50
RAD51
RAF1
RANBP2
RARA
RB1
RBM10
RET
RICTOR
RNF43
ROS1
RPTOR
RUNX1
RUNX1T1
SDHA
SDHB
SDHC
SDHD
SETD2
SF3B1
SLIT2
SMAD2
SMAD3
SMAD4
SMARCA4
SMARCB1
SMO
SNCAIP
SOCS1
SOX10
SOX2
SOX9
SPEN
SPOP
SPTA1
SRC
STAG2
STAT3
STAT4
STK11
SUFU
SYK
TAF1
TBX3
TERC
TERT
TET2
TGFBR2
TNFAIP3
TNFRSF14
TOP1
TOP2A
TP53
TSC1
TSC2
TSHR
U2AF1
VEGFA
VHL
WISP3
WT1
XPO1
ZBTB2
ZNF217
ZNF703

Table S2. HSL-CGP genes.

GeneSymbol – HSL-CGP

AARS2
ABCB1
ABCC1
ABL1
ABL2
ACO1
ACVR1B
ACVR2B
ADAM10
ADCY1
ADNP
ADORA2A
AHNAK2
AJUBA
AKAP9
AKD1
AKT1
AKT2
AKT3
ALK
ALKBH6
ALPK2
AMPH
ANAPC1
ANK3
ANKRD12
APAF1
APC
APOL2
AR
ARAF
ARFRP1
ARHGAP32
ARHGAP35
ARHGEF6
ARID1A
ARID1B
ARID2
ARID5B
ASPM
ASXL1
ASXL2
ATG13
ATM
ATP5B
ATR
ATRX
AURKA
AURKB
AXIN1
AXIN2
AXL
AZGP1
B2M
BAP1
BARD1
BCL2
BCL2L1
BCL2L2
BCL6
BCLAF1
BCOR
BCORL1
BHMT2
BLM
BRAF
BRCA1
BRCA2
BRD4
BRE
BRIP1
BTG1
BTK
BUB1B
C11orf30
C3orf70
CAD
CAP2
CARD11
CARM1
CASP8
CAST
CBFB
CBL
CCAR1
CCDC120
CCDC6
CCND1
CCND2
CCND3
CCNE1
CD1D
CD274
CD70
CD79A
CD79B
CDC27
CDC73
CDH1
CDK12
CDK4
CDK6
CDK8
CDKN1A
CDKN1B
CDKN2A
CDKN2B
CDKN2C
CEBPA
CEP76
CFH
CHD2
CHD4
CHD8
CHEK1
CHEK2
CIC
CLIP1
CLTC
CLTCL1
CNBD1
CNKSR1
COL18A1
COL5A1
COL5A3
CREB1
CREBBP
CRKL
CRLF2
CRTC1
CRTC3
CSDE1
CSF1R
CTCF
CTNNA1
CTNNB1
CTNND1
CTSL1
CTTN
CUL1
CUL3
CUL4B
CUX1
CYLD
DAXX
DDR2
DDX3X
DDX5
DHX9
DIAPH1
DICER1
DIS3
DMD
DNAH12
DNER
DNMT1
DNMT3A
DOCK2
DOT1L
EEF1A1
EGFR
EIF2S2
EIF4A2
ELF3
EP300
EPHA2
EPHA3
EPHA5
EPHA7
EPHB1
ERBB2
ERBB2IP
ERBB3
ERBB4
ERCC2
ERG
ERRFI1
ESR1
EWSR1
EZH1
EZH2
EZR
FAM123B
FAM166A
FAM46C
FANCA
FANCC
FANCD2
FANCE
FANCF
FANCG
FANCL
FAS
FAT1
FBN2
FBXO11
FBXW7
FES
FGF10
FGF14
FGF19
FGF23
FGF3
FGF4
FGF6
FGFBP1
FGFR1
FGFR2
FGFR3
FGFR4
FH
FIGF
FKBP9
FLCN
FLG
FLT1
FLT3
FLT4
FN1
FOXA1
FOXA2
FOXL2
FOXP1
FOXQ1
FRG1B
FRMD7
FRS2
FUBP1
GABRA6
GATA1
GATA2
GATA3
GATA4
GATA6
GID4
GLi1
GNA11
GNA13
GNAI1
GNAQ
GNAS
GNB1
GNPTAB
GOLGA5
GOT1
GOT2
GPHN
GPR124
GPS2
GRIN2A
GRM3
GSK3B
GTF2H1
GUSB
H3F3A
H3F3C
HDAC4
HGF
HIST1H1E
HIST1H3B
HIST1H4E
HLA-A
HLA-B
HMGXB4
HNF1A
HRAS
HSD3B1
HSP90AA1
HSP90B1
HSPA8
HUWE1
IDH1
IDH2
IGF1R
IGF2
IGF2R
IKBKE
IKZF1
IL7R
ING1
INHBA
INPP4B
INPPL1
INTS12
IPO7
IRF2
IRF4
IRF6
IRS2
ITGA6
ITGB7
ITPKB
JAK1
JAK2
JAK3
JUN
KALRN
KAT6A
KDM5A
KDM5C
KDM6A
KDR
KEAP1
KEL
KIAA1109
KIFC3
KIT
KLF4
KLHL6
KLHL8
KRAS
LCP1
LCTL
LEPR
LIFR

GeneSymbol – HSL-CGP (cont.)

LMO1
LPP
LRP1B
LRRK2
LUM
LYN
LZTR1
MAGI2
MALAT1
MAP2K1
MAP2K2
MAP2K4
MAP3K1
MAP3K3
MAP3K4
MAP4K3
MAPK8IP1
MAST2
MATK
MAX
MBD1
MCL1
MDC1
MDM2
MDM4
MECOM
MED12
MED13
MED17
MED23
MEF2A
MEF2B
MEN1
MET
METTL14
MGA
MICALCL
MITF
MLH1
MLL
MLL2
MLL3
MLL4
MLLT10
MLLT3
MLLT4
MMP2
MN1
MORC4
MPL
MPO
MRE11A
MSH2
MSH6
MSN
MST1
MTOR
MUC17
MUTYH
MXRA5
MYB
MYC
MYCL
MYCN
MYD88
MYH9
MYOCD
NAV3
NBPF1
NBPF10
NCOA3
NCOA4
NCOR1
NCOR2
NEB
NEDD4L
NF1
NF2
NFE2L2
NFKBIA
NIN
NKX2-1
NLRP3
NONO
NOS1
NOTCH1
NOTCH2
NOTCH3
NPM1
NR1H2
NR4A2
NRAS
NSD1
NTN3
NTN4
NTRK1
NTRK2
NTRK3
NUMA1
NUP210L
NUP214
NUP93
NUP98
ODAM
OMA1
OR4A16
OR52N1
OTUD7A
PABPC1
PAK3
PALB2
PAPD5
PARK2
PARP1
PARP4
PAX5
PBRM1
PCBP1
PCM1
PDAP1
PDCD1LG2
PDCD2L
PDGFRA
PDGFRB
PDK1
PDSS2
PHF6
PHLDA1
PIK3C2A
PIK3C2B
PIK3CA
PIK3CB
PIK3CG
PIK3R1
PIK3R2
PIK3R5
PIP5K1A
PLCG1
PLCG2
PLEC
PMS2
POLD1
POLE
POLR3A
POTEF
POU2AF1
POU2F2
PPM1D
PPP2R1A
PPP6C
PRDM1
PREX2
PRKAR1A
PRKCD
PRKCE
PRKCI
PRKDC
PRPF8
PRSS8
PSEN1
PTCH1
PTEN
PTGS2
PTPN11
PTPRC
QKI
RAB40A
RAC1
RAD21
RAD50
RAD51
RAF1
RANBP2
RANBP3
RARA
RASA1
RB1
RBM10
RBMX
RET
RHEB
RHOA
RICTOR
RIT1
RNF213
RNF43
ROS1
RPGR
RPL22
RPL5
RPS15
RPS2
RPSAP58
RPTOR
RSBN1L
RUNX1
RUNX1T1
RXRA
SACS
SDHA
SDHB
SDHC
SDHD
SELP
SEPT12
SERPINB13
SETD2
SETDB1
SF3B1
SFRS2
SGK1
SIN3A
SIRT4
SLC1A3
SLC26A3
SLC44A3
SLC4A5
SLIT2
SMAD2
SMAD3
SMAD4
SMARCA4
SMARCB1
SMC1A
SMC3
SMO
SNCAIP
SNX25
SOCS1
SOS1
SOX10
SOX17
SOX2
SOX9
SPATA6
SPEN
SPOP
SPTA1
SRC
SRSF2
STAG2
STAT3
STAT4
STK11
STK19
STX2
SUFU
SUZ12
SYK
SYNE1
TAF1
TAP1
TBC1D12
TBL1XR1
TBX3
TCEB1
TCF12
TCF7
TCF7L2
TCP11L2
TDRD10
TERC
TERT
TET2
TFDP1
TGFBR2
TGIF1
TIMM17A
TJP2
TNF
TNFAIP3
TNFRSF10C
TNFRSF14
TNKS
TOM1
TOP1
TOP2A
TOP3A
TP53
TP53BP1
TPR
TPX2
TRAF3
TRAF7
TRIM23
TRIM7
TRIO
TRIP11
TRRAP
TSC1
TSC2
TSHR
TTLL9
TUBA1A
TXNDC8
TXNIP
U2AF1
UHRF1BP1L
VEGFA
VHL
WASF3
WHSC1
WHSC1L1
WISP3
WRN
WT1
XIRP2
XPO1
ZBTB2
ZFHX3
ZFP36L1
ZFP36L2
ZMYM2
ZNF132
ZNF180
ZNF217
ZNF300
ZNF471
ZNF483
ZNF620
ZNF703
ZNF750
ZNF814
ZNF844
ZNF91
ZRANB3

Table S3. NSCLC Data (Rizvi et al. 2014) – FM-CGP.

Durable Clinical Benefit (DCB)		No Durable Benefit (NDB)	
Patient_ID	**Mutation_Count**	**Patient_ID**	**Mutation_Count**
SA9755	32	**TU0428**	20
HE3202	29	**ZA6505**	19
Y2087	14	**MA7027**	9
RI1933	23	**JB112852**	6
M4945	22	**SR070761**	5
CA9903	11	**GR4788**	5
KA3947	5	**BL3403**	5
SC0899	7	**DM123062**	4
AL4602	7	**WA7899**	9
DI6359	8	**R7495**	2
RH090935	10	**LO3793**	9
SB010944	2	**RO3338**	5
SC6470	7	**LO5004**	4
GR0134	1	**NI9507**	4
		AU5884	2
		VA1330	3
		VA7859	0

Table S4. NSCLC Data (Rizvi et al. 2014) – HSL-CGP.

Durable Clinical Benefit (DCB)		No Durable Benefit (NDB)	
Patient_ID	**Mutation_Count**	**Patient_ID**	**Mutation_Count**
SA9755	81	**TU0428**	41
HE3202	60	**ZA6505**	26
Y2087	20	**MA7027**	22
RI1933	28	**JB112852**	10
M4945	35	**SR070761**	8
CA9903	19	**GR4788**	11
KA3947	13	**BL3403**	6
SC0899	26	**DM123062**	5
AL4602	13	**WA7899**	15
DI6359	18	**R7495**	7
RH090935	13	**LO3793**	13
SB010944	8	**RO3338**	7
SC6470	10	**LO5004**	8
GR0134	3	**NI9507**	4
		AU5884	4
		VA1330	4
		VA7859	2

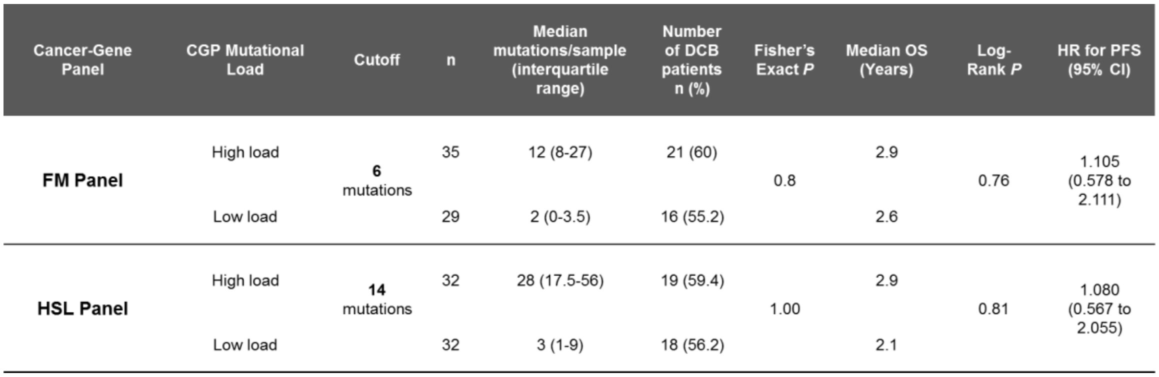
Table S5. Melanoma Data (Snyder et al. 2014) – FM-CGP.

Durable Clinical Benefit (DCB)		No Durable Benefit (NDB)	
Patient_ID	**Mutation_Count**	**Patient_ID**	**Mutation_Count**
CR1509	8	**SD2051**	3
CR9306	32	**SD5038**	10
CR0095	9	**SD5934**	4
CR4880	20	**SD5118**	1
CR7623	5	**SD6494**	10
CR3665	5	**SD7357**	30
CR9699	25	**NR3156**	0
SD0346	13	**NR5784**	0
SD6336	5	**NR8727**	0
SD1494	27	**NR4949**	9
SD2056	3	**NR1867**	2
CR04885	41	**NR3549**	12
CR06670	4	**NR9341**	0
CR22640	3	**NR4810**	8
CR6126	9	**NR2137**	17
CR6161	21	**NR4018**	2
CRNR0244	6	**NR4045**	14
CRNR2472	0	**NR4083**	6
CRNR4941	1	**NR4631**	20
LSD0167	4	**NR6689**	0
LSD2057	1	**NR6721**	3
LSD3484	14	**NR6842**	0
LSD4691	0	**NR8815**	37
LSD4744	33	**NR9445**	6
LSD6819	6	**NR9449**	12
LSDNR1120	7	**NR9521**	28
LSDNR1650	2	**NR9765**	2
LSDNR3086	2		
LSDNR9298	7		
NR9705	4		
PR03803	1		
PR11217	0		
PR4035	11		
PR4046	6		
PR4077	34		
PR4091	7		
PR4092	28		

Table S6. Melanoma Data (Snyder et al. 2014) – HSL-CGP.

Durable Clinical Benefit (DCB)		No Durable Benefit (NDB)	
Patient_ID	**Mutation_Count**	**Patient_ID**	**Mutation_Count**
CR1509	17	**SD2051**	4
CR9306	74	**SD5038**	15
CR0095	13	**SD5934**	8
CR4880	29	**SD5118**	2
CR7623	9	**SD6494**	32
CR3665	8	**SD7357**	52
CR9699	57	**NR3156**	0
SD0346	25	**NR5784**	0
SD6336	9	**NR8727**	0
SD1494	59	**NR4949**	23
SD2056	6	**NR1867**	2
CR04885	93	**NR3549**	24
CR06670	19	**NR9341**	1
CR22640	9	**NR4810**	16
CR6126	24	**NR2137**	31
CR6161	44	**NR4018**	9
CRNR0244	15	**NR4045**	19
CRNR2472	3	**NR4083**	8
CRNR4941	3	**NR4631**	49
LSD0167	10	**NR6689**	0
LSD2057	2	**NR6721**	6
LSD3484	28	**NR6842**	0
LSD4691	0	**NR8815**	81
LSD4744	63	**NR9445**	16
LSD6819	16	**NR9449**	17
LSDNR1120	15	**NR9521**	56
LSDNR1650	2	**NR9765**	3
LSDNR3086	2		
LSDNR9298	22		
NR9705	31		
PR03803	1		
PR11217	0		
PR4035	28		
PR4046	9		
PR4077	82		
PR4091	12		
PR4092	55		

Table S7. CGP-mutational load is not associated with clinical benefit to CTLA-4 blockade in melanoma patients.



Cancer-Gene Panel	CGP Mutational Load	Cutoff	n	Median mutations/sample (interquartile range)	Number of DCB patients n (%)	Fisher's Exact *P*	Median OS (Years)	Log-Rank *P*	HR for PFS (95% CI)
FM Panel	High load	**6** mutations	35	12 (8-27)	21 (60)	0.8	2.9	0.76	1.105 (0.578 to 2.111)
	Low load		29	2 (0-3.5)	16 (55.2)		2.6		
HSL Panel	High load	**14** mutations	32	28 (17.5-56)	19 (59.4)	1.00	2.9	0.81	1.080 (0.567 to 2.055)
	Low load		32	3 (1-9)	18 (56.2)		2.1		

Table S8. NSCLC Data (Rizvi et al. 2014) – Cancer SelectR 88-CGP.

Durable Clinical Benefit (DCB)		No Durable Benefit (NDB)	
Patient_ID	Mutation_Count	Patient_ID	Mutation_Count
SA9755	7	**TU0428**	9
HE3202	11	**ZA6505**	6
Y2087	4	**MA7027**	0
RI1933	4	**JB112852**	2
M4945	5	**SR070761**	1
CA9903	7	**GR4788**	3
KA3947	2	**BL3403**	1
SC0899	5	**DM123062**	2
AL4602	4	**WA7899**	0
DI6359	2	**R7495**	2
RH090935	3	**LO3793**	5
SB010944	1	**RO3338**	3
SC6470	2	**LO5004**	2
GR0134	1	**NI9507**	3
		AU5884	2
		VA1330	2
		VA7859	0

Table S9. NSCLC Data (Rizvi et al. 2014) – Cancer SelectR 203-CGP.

Durable Clinical Benefit (DCB)		No Durable Benefit (NDB)	
Patient_ID	**Mutation_Count**	**Patient_ID**	**Mutation_Count**
SA9755	20	**TU0428**	14
HE3202	18	**ZA6505**	12
Y2087	7	**MA7027**	2
RI1933	13	**JB112852**	3
M4945	13	**SR070761**	5
CA9903	7	**GR4788**	4
KA3947	2	**BL3403**	4
SC0899	9	**DM123062**	4
AL4602	5	**WA7899**	2
DI6359	2	**R7495**	2
RH090935	5	**LO3793**	7
SB010944	1	**RO3338**	5
SC6470	3	**LO5004**	2
GR0134	1	**NI9507**	3
		AU5884	2
		VA1330	2
		VA7859	0

Table S10. NSCLC Data (Rizvi et al. 2014) – Qiagen-CGP.

Durable Clinical Benefit (DCB)		No Durable Benefit (NDB)	
Patient_ID	Mutation_Count	Patient_ID	Mutation_Count
SA9755	17	TU0428	14
HE3202	17	ZA6505	12
Y2087	7	MA7027	4
RI1933	7	JB112852	3
M4945	12	SR070761	5
CA9903	7	GR4788	3
KA3947	4	BL3403	3
SC0899	6	DM123062	2
AL4602	6	WA7899	3
DI6359	2	R7495	2
RH090935	6	LO3793	7
SB010944	1	RO3338	5
SC6470	4	LO5004	2
GR0134	0	NI9507	3
		AU5884	2
		VA1330	1
		VA7859	0

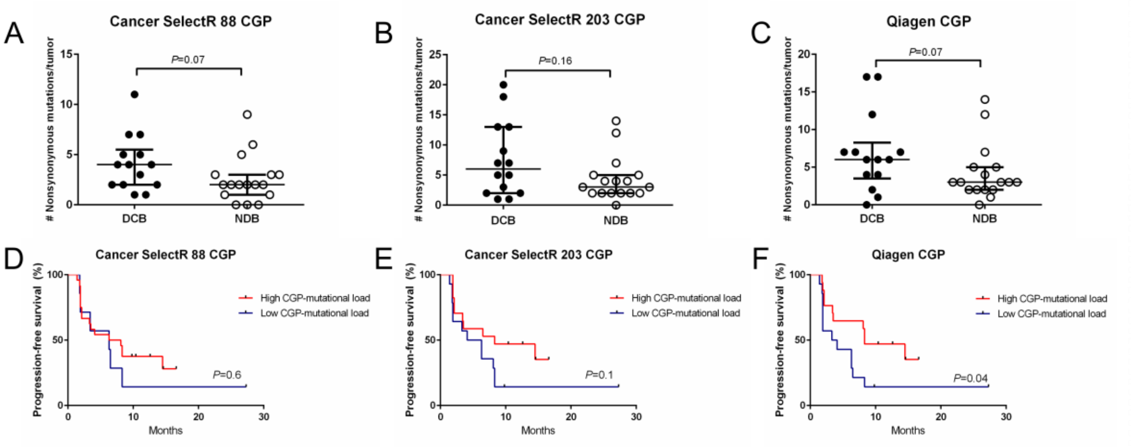


Figure S1. Smaller CGPs are not as accurate to determine clinical benefit of anti-PD-1 therapy in NSCLCs. (A) Cancer SelectR 88-CGP (76 cancer-genes, from PGDx) mutational load in patients with DCB (n=14) compared to those with NDB (n=17) (median 4 versus 2, Mann-Whitney *P*=0.07). **(B)** Cancer SelectR 203-CGP (195 cancer-genes, from PGDx) mutational load in in patients with DCB (n=14) compared to those with NDB (n=17) (median 6 versus 3, Mann-Whitney *P*=0.16). **(C)** Human Comprehensive Cancer GeneRead Targeted CGP (with 160 cancer-genes, from Qiagen) mutational load in patients with DCB (n=14) compared to those with NDB (n=17) (median 6 versus 3, Mann-Whitney *P*=0.07). **(D)** PFS in tumors with high CGP-mutational load compared to those with low CGP mutational load (Cutoff≥2) in Cancer SelectR 88-CGP (HR 0.71, 95% CI 0.25-2.04, Log-rank *P*=0.5). **(E)** PFS in tumors with high CGP-mutational load compared to those with low CGP mutational load (Cutoff≥4) in Cancer SelectR 203-CGP (HR 0.47, 95% CI 0.19-1.15, Log-rank *P*=0.1). **(F)** PFS in tumors with high CGP-mutational load compared to those with low CGP mutational load (Cutoff≥4) in Qiagen-CGP (HR 0.39, 95% CI 0.15-0.98, Log-rank *P*=0.04).