

Supplemental Table 4: Gene sequence panel and filtered results for BETRNet EACs and NDBEs.

A sequencing gene panel (n=243)

AKT1	BLM	CDKN2A	ERBB4	HLA-A	MAP2K1	NKX2-1
AKT2	BRAF	CDKN2B	ETV4	HLA-B	MAP2K2	NOTCH1
AKT3	BRCA1	CDKN2C	EYA4	ID1	MAP2K2	NOTCH2
ALK	BRCA2	CHL1	FAM190A	IDH1	MAP2K4	NOTCH3
ALPK2	BRD4	CHRD	FAT1	IDH2	MAP3K1	NOTCH4
APC	CA9	CIC	FAT2	IGF1R	MAP3K5	NR2F2
AR	CACNA2D3	CLDN18	FAT3	IGF2	MAP3K7	NRAS
ARAF	CASP3	CRIP1	FAT4	IGF2BP3	MAP3K8	PAK1
ARHGAP26	CASZ1	CRKL	FBXW7	IGF2R	MAP3K9	PALB2
ARHGAP6	CCND1	CSMD1	FGF19	IL8	MAPK1	PARD3B
ARID1A	CCND2	CTNNA1	FGF3	ING5	MAPK3	PARK2
ARID1B	CCND3	CTNNA3	FGF4	IRF2	MCL1	PAX9
ARID2	CCNE1	CTNNB1	FGFR1	JAK2	MDM2	PBRM1
ATM	CD274	CTSB	FGFR2	KDM6A	MECOM	PCGF6
AXL	CD44	CXCL10	FGFR3	KEAP1	MET	PDCD1LG2
B2M	CDH1	DOCK2	FGFR4	KIF13A	MLL3	PDE4D
BAK1	CDK1	E2F1	FHIT	KIT	MSH2	PDGFRA
BCL2	CDK12	E2F3	FRS2	KLF12	MSH6	PDGFRB
BCL2A1	CDK2	EGFR	GAB1	KLF5	MTOR	PGM5
BCL2L1	CDK4	ELF3	GAB2	KMT2D	MUTYH	PHLDA1
BCL2L12	CDK5	ELMO1	GATA4	KRAS	MYB	PIK3CA
BCL2L2	CDK6	EP300	GATA6	LARP4B	MYC	PIK3CG
BCL6	CDK8	EPHB3	GLI3	LRP1B	MYD88	PIK3R1
BCL9	CDK9	EPHB6	GLIPR1	LRP6	NEGR1	PLK2
BCOR	CDKN1A	ERBB2	GNAS	MACF1	NEIL2	POLB
BCORL1	CDKN1B	ERBB2IP	HES1	MACROD2	NF1	POU5F1B
BIRC5	CDKN1C	ERBB3	HGF	MAGI3	NFE2L2	PREX2

BETRNet EAC filtered alterations by sample.

Meth Group	<u>DX</u>	<u>SubjectID</u>	<u>analysis</u>	<u>chromosome</u>	<u>position</u>	<u>reference allele</u>
HM	EAC	9	MuTect	17	37868208	C
HM	EAC	9	GATK	17	7579540	AT

HM	EAC	11	MuTect	9	21971028	C
HM	EAC	11	MuTect	17	37868208	C
HM	EAC	11	MuTect	4	187532905	G
HM	EAC	11	MuTect	6	152464784	C
HM	EAC	11	MuTect	17	7578176	C
HM	EAC	13	GATK	2	141108388	C
HM	EAC	13	MuTect	2	141816482	G
HM	EAC	13	MuTect	18	48591918	C
HM	EAC	13	GATK	17	7577137	C
HM	EAC	38	MuTect	17	7577121	G
HM	EAC	37	GATK	1	27106385	T
HM	EAC	37	GATK	1	27106388	A
HM	EAC	37	MuTect	17	37868208	C
HM	EAC	37	GATK	16	79245873	G
HM	EAC	42	MuTect	5	39002707	G
HM	EAC	42	GATK	17	7573998	CTCTCGGAACA
IM	EAC	3	MuTect	5	142283145	C
IM	EAC	3	GATK	1	27092824	TC
IM	EAC	3	MuTect	6	29911240	T
IM	EAC	3	MuTect	7	151921114	A
IM	EAC	3	MuTect	17	29508451	A
IM	EAC	3	MuTect	17	7577559	G
IM	EAC	3	GATK	16	79245873	G
IM	EAC	8	MuTect	2	212495321	T
IM	EAC	8	MuTect	17	7578406	C
IM	EAC	24	GATK	2	141092106	CA
IM	EAC	24	GATK	12	49426021	TGG
IM	EAC	24	MuTect	2	178096196	C
IM	EAC	24	GATK	10	114710517	TGCC
IM	EAC	24	MuTect	17	7578406	C
IM	EAC	23	MuTect	17	37868208	C
IM	EAC	23	MuTect	18	48591919	G
IM	EAC	22	MuTect	17	7577559	G

LM	EAC	14	MuTect	1	27100207	C
LM	EAC	14	MuTect	9	21971120	G
LM	EAC	14	MuTect	6	29911240	T
LM	EAC	14	MuTect	18	48591918	C
LM	EAC	14	MuTect	17	7577548	C
LM	EAC	14	MuTect	17	7578406	C
LM	EAC	15	MuTect	6	29911240	T
LM	EAC	15	MuTect	1	120612013	G
LM	EAC	15	GATK	19	15281354	CA
LM	EAC	15	MuTect	17	7578263	G
LM	EAC	5	GATK	6	157469855	TGGACAAG
LM	EAC	5	MuTect	17	7577115	A
LM	EAC	21	MuTect	20	57484420	C
LM	EAC	21	MuTect	3	178952065	G
LM	EAC	21	GATK	12	57490754	GCAGGCCCTGC
LM	EAC	21	MuTect	17	7578475	G
LM	EAC	31	MuTect	1	27106536	G
LM	EAC	31	MuTect	17	7578212	G
LM	EAC	34	GATK	9	21974714	GGCAGCGCCCCCGCCTCCA
LM	EAC	34	GATK	7	81355331	TCCCTATTG
LM	EAC	34	MuTect	2	141128746	A
LM	EAC	34	MuTect	17	7577538	C
MM	EAC	1	MuTect	17	7577106	G
MM	EAC	106	GATK	6	29911318	CG
MM	EAC	106	MuTect	4	26426291	C
MM	EAC	106	MuTect	17	7577548	C
MM	EAC	41	MuTect	4	153247175	T
MM	EAC	41	GATK	13	49039201	TCATGCAGAGA

C

BETRNet NDBE filtered alterations by sample.

<u>Meth Group</u>	<u>DX</u>	<u>Subject</u>	<u>analysis</u>	<u>chromosome</u>	<u>position</u>	<u>reference allele</u>
HM	BE	53	GATK	9	21994170	CGCTG
HM	BE	53	GATK	7	151882659	TC

HM	BE	53	MuTect	7	151932961	G
HM	BE	64	MuTect	6	29911240	T
HM	BE	64	MuTect	17	29556136	C
IM	BE	55	GATK	6	157502295	AT
IM	BE	55	GATK	9	21971123	TGA
LM	BE	29	GATK	1	27106687	CA
LM	BE	29	GATK	9	21974726	GCCTCCAGCAGCGCCCGCA
LM	BE	29	GATK	6	29911318	CG
LM	BE	29	MuTect	17	7578389	G
LM	BE	58	GATK	1	27105855	AT
LM	BE	58	GATK	12	25368468	CA
LM	BE	58	MuTect	6	152831401	G

PRKCi	TERT
PTCH1	TGFBR2
PTCH2	TLN1
PTEN	TLR4
PTPN23	TP53
PTPRD	TP63
RASA1	TP73
RASSF7	TRAF2
RB1	TSC1
RBPJ	TSC2
RhoA	USP9X
RICTOR	VEGFA
RNF43	VPS13A
RPTOR	WT1
RUNX1	WWOX
RUNX1T1	YAP1
RUNX3	ZNF217
SFRP4	ZNF750
SMAD2	SOX9
SMAD3	SRC
SMAD4	STAT3
SMARCA4	STAT6
SMARCA5	STK11
SMO	SYNE1
SMURF1	TCF7L1
SOHLH2	TCF7L2
SOX2	TERC

<u>alternate allele</u>	<u>BestEffect Variant</u>	<u>BestEffect Hugo Symbol</u>	<u>BestEffect Annotation Transcript</u>	<u>BestEffect Refseq mRNA Id</u>
T	Missense_Mutation	ERBB2	uc002hso.2	NM_004448
A	Frame_Shift_Del	TP53	uc002gim.2	NM_001126112

T	Nonsense_Mutation	CDKN2A	uc003zpk.2	NM_000077
T	Missense_Mutation	ERBB2	uc002hso.2	NM_004448
T	Nonsense_Mutation	FAT1	uc003izf.2	NM_005245
A	Nonsense_Mutation	SYNE1	uc010kiw.2	NM_182961
T	Missense_Mutation	TP53	uc010vug.1	NM_001126114
CT	Frame_Shift_Ins	LRP1B	uc002tvj.1	NM_018557
A	Nonsense_Mutation	LRP1B	uc002tvj.1	NM_018557
T	Missense_Mutation	SMAD4	uc010xdp.1	NM_005359
CCGTCCCAGTAGATTA	In_Frame_Ins	TP53	uc002gim.2	NM_001126112
A	Missense_Mutation	TP53	uc002gim.2	NM_001126112
TTG	Frame_Shift_Ins	ARID1A	uc001bmv.1	NM_006015
AT	Frame_Shift_Ins	ARID1A	uc001bmv.1	NM_006015
T	Missense_Mutation	ERBB2	uc002hso.2	NM_004448
GGTAAA	Frame_Shift_Ins	WWOX	uc010che.2	
A	Nonsense_Mutation	RICTOR	uc003jlo.2	NM_152756
C	Frame_Shift_Del	TP53	uc002gim.2	NM_001126112
G	Nonsense_Mutation	ARHGAP26	uc011dbj.1	NM_015071
T	Frame_Shift_Del	ARID1A	uc001bmv.1	NM_006015
A	Nonsense_Mutation	HLA-A	uc003noo.2	
T	Nonsense_Mutation	MLL3	uc003wla.2	NM_170606
T	Nonsense_Mutation	NF1	uc002hgg.2	NM_001042492
A	Missense_Mutation	TP53	uc002gim.2	NM_001126112
GGTAAA	Frame_Shift_Ins	WWOX	uc010che.2	
C	Splice_Site	ERBB4	uc002veg.1	NM_005235
T	Missense_Mutation	TP53	uc002gim.2	NM_001126112
C	Frame_Shift_Del	LRP1B	uc002tvj.1	NM_018557
T	Frame_Shift_Del	MLL2	uc001rta.3	NM_003482
A	Nonsense_Mutation	NFE2L2	uc002ulh.3	NM_006164
T	In_Frame_Del	TCF7L2	uc001lae.3	NM_001146274
T	Missense_Mutation	TP53	uc002gim.2	NM_001126112
T	Missense_Mutation	ERBB2	uc002hso.2	NM_004448
A	Missense_Mutation	SMAD4	uc010xdp.1	NM_005359
A	Missense_Mutation	TP53	uc002gim.2	NM_001126112

T	Nonsense_Mutation	ARID1A	uc001bmv.1	NM_006015
A	Nonsense_Mutation	CDKN2A	uc003zpk.2	NM_000077
A	Nonsense_Mutation	HLA-A	uc003noo.2	
T	Missense_Mutation	SMAD4	uc010xdp.1	NM_005359
T	Missense_Mutation	TP53	uc002gim.2	NM_001126112
T	Missense_Mutation	TP53	uc002gim.2	NM_001126112
A	Nonsense_Mutation	HLA-A	uc003noo.2	
A	Missense_Mutation	NOTCH2	uc001eik.2	NM_024408
C	Frame_Shift_Del	NOTCH3	uc002nan.2	NM_000435
A	Nonsense_Mutation	TP53	uc002gim.2	NM_001126112
T	Frame_Shift_Del	ARID1B	uc003qqn.2	NM_017519
C	Missense_Mutation	TP53	uc002gim.2	NM_001126112
T	Missense_Mutation	GNAS	uc002xzw.2	NM_080425
A	Missense_Mutation	PIK3CA	uc003fjk.2	NM_006218
G	Splice_Site	STAT6	uc009zpg.2	NM_003153
A	Missense_Mutation	TP53	uc002gim.2	NM_001126112
A	Nonsense_Mutation	ARID1A	uc001bmv.1	NM_006015
A	Nonsense_Mutation	TP53	uc002gim.2	NM_001126112
G	In_Frame_Del	CDKN2A	uc003zpk.2	NM_000077
T	Splice_Site	HGF	uc003uhl.2	NM_000601
G	Splice_Site	LRP1B	uc002tvj.1	NM_018557
T	Missense_Mutation	TP53	uc002gim.2	NM_001126112
C	Missense_Mutation	TP53	uc002gim.2	NM_001126112
C	Frame_Shift_Del	HLA-A	uc003noo.2	
T	Nonsense_Mutation	RBPJ	uc003grx.1	NM_005349
T	Missense_Mutation	TP53	uc002gim.2	NM_001126112
A	Nonsense_Mutation	FBXW7	uc003ims.2	NM_033632
T	Frame_Shift_Del	RB1	uc001vcb.2	NM_000321

<u>alternate allele</u>	<u>BestEffect Variant</u>	<u>BestEffect Hugo S</u>	<u>BestEffect Annotation T</u>	<u>BestEffect Refseq</u>
C	Frame_Shift_Del	CDKN2A	uc003zpl.2	NM_058195
T	Frame_Shift_Del	MLL3	uc003wla.2	NM_170606

A	Nonsense_Mutation	MLL3	uc003wla.2	NM_170606
A	Nonsense_Mutation	HLA-A	uc003noo.2	
T	Nonsense_Mutation	NF1	uc002hgg.2	NM_001042492
A	Frame_Shift_Del	ARID1B	uc003qqn.2	NM_017519
T	Frame_Shift_Del	CDKN2A	uc003zpl.2	NM_058195
C	Frame_Shift_Del	ARID1A	uc001bmv.1	NM_006015
G	In_Frame_Del	CDKN2A	uc003zpk.2	NM_000077
C	Frame_Shift_Del	HLA-A	uc003noo.2	
A	Missense_Mutation	TP53	uc002gim.2	NM_001126112
A	Frame_Shift_Del	ARID1A	uc001bmv.1	NM_006015
C	Frame_Shift_Del	KRAS	uc001rgp.1	NM_033360
A	Missense_Mutation	SYNE1	uc010kiw.2	NM_182961

<u>BestEffect Protein Change</u>	<u>BestEffect cDNA Change</u>	<u>dbSNP site</u>	<u>tumor fraction</u>
p.S310F	c.929C>T	COSMIC	0.368421
p.D49fs	c.146_147AT>T		0.7037

p.W110*	c.330G>A	COSMIC	0.698925
p.S310F	c.929C>T	COSMIC	0.075188
p.S3163*	c.9488C>A	NOVEL	0.171429
p.E8365*	c.25093G>T	NOVEL	0.235955
p.V186I	c.556G>A	COSMIC	0.3125
p.R3957fs	c.11870_11870G>AG		0.4875
p.R460*	c.1378C>T	NOVEL	0.528302
p.R361C	c.1081C>T	COSMIC	0.530435
p.267_267R>RNLLGR	c.801_801G>TAATCTACTGGGACGG		0.1678
p.R273C	c.817C>T	COSMIC	0.692308
p.F1999fs	c.5996_5996T>TTG		0.2254
p.E2000fs	c.5999_5999A>AT		0.2347
p.S310F	c.929C>T	COSMIC	0.921842
p.G260fs	c.778_778G>GGTAAA		0.2556
p.R108*	c.322C>T	NOVEL	0.43
p.M340fs	c.1019_1029TGTTCCGAGAG>G		0.6526
p.S248*	c.743C>G	NOVEL	0.106838
p.S949fs	c.2845_2846TC>T		0.2541
p.L180*	c.539T>A	COSMIC	0.428571
p.C1103*	c.3309T>A	COSMIC	0.062147
p.K200*	c.598A>T	NOVEL	0.244444
p.S241F	c.722C>T	COSMIC	0.393939
p.G260fs	c.778_778G>GGTAAA		0.314
p.R649_splice	c.1947_splice	NOVEL	0.223684
p.R175H	c.524G>A	COSMIC	0.351351
p.V4046fs	c.12138_12139TG>G		0.3596
p.P4155fs	c.12465_12467CCA>A		0.05
p.E379*	c.1135G>T	NOVEL	0.121212
p.P2del	c.2_5TGCC>T		0.3377
p.R175H	c.524G>A	COSMIC	0.425339
p.S310F	c.929C>T	COSMIC	0.737226
p.R361H	c.1082G>A	COSMIC	0.6875
p.S241F	c.722C>T	COSMIC	0.604167

p.R1335*	c.4003C>T	COSMIC	0.448276
p.R80*	c.238C>T	COSMIC	0.66055
p.L180*	c.539T>A	COSMIC	1
p.R361C	c.1081C>T	COSMIC	0.296296
p.G245S	c.733G>A	COSMIC	0.149254
p.R175H	c.524G>A	COSMIC	0.436548
p.L180*	c.539T>A	COSMIC	0.138889
p.A3V	c.8C>T	COSMIC	0.085106
p.L1634fs	c.4901_4902TG>G		0.0776
p.R196*	c.586C>T	COSMIC	0.210256
p.H812fs	c.2436_2443TGGACAAG>T		0.1985
p.C275G	c.823T>G	COSMIC	0.663934
p.R844C	c.2530C>T	COSMIC	0.29703
p.M1040I	c.3120G>A	COSMIC	0.24772
p.Q791_splice	c.2373_splice		0.1293
p.P152L	c.455C>T	COSMIC	0.555944
p.W2049*	c.6147G>A	NOVEL	0.368071
p.R213*	c.637C>T	COSMIC	0.301471
p.LEAGAL32del	c.95_113TGGAGGCGGGGGCGCTGCC>C		0.5758
p.K347_splice	c.1041_splice		0.2222
p.E3625_splice	c.10875_splice	NOVEL	0.418182
p.R248Q	c.743G>A	COSMIC	0.532258
p.P278A	c.832C>G	COSMIC	0.822034
p.T206fs	c.617_618CG>C		0.1616
p.R238*	c.712C>T	DBSNP	0.107438
p.G245S	c.733G>A	COSMIC	0.411348
p.R543*	c.1627A>T	COSMIC	0.276596
p.F760fs	c.2279_2289TCATGCAGAGA>T		0.0531

<u>BestEffect Protein Change</u>	<u>BestEffect cDNA Change</u>	<u>tumor fraction</u>
p.Q94fs	c.280_284CAGCG>G	0.5263
p.E1689fs	c.5065_5066GA>A	0.0588

p.R904*	c.2710C>T	0.044665
p.L180*	c.539T>A	1
p.Q835*	c.2503C>T	0.082192
p.I1092fs	c.3274_3275AT>A	0.3247
p.S133fs	c.399_401TCA>A	0.5758
p.Q2100fs	c.6298_6299CA>C	0.202
p.VRALLE28del	c.83_101TGCGGGCGCTGCTGGAGGC>C	0.2114
p.T206fs	c.617_618CG>C	0.1
p.R181C	c.541C>T	0.236111
p.P1822fs	c.5466_5467AT>A	0.3862
p.L159fs	c.476_477TG>G	0.547
p.R170W	c.508C>T	0.315