

Supplementary Table 1. Mutated genes that contain protein domains identified through mutation enrichment analysis

A. Breast cancers

<u>InterPro ID</u>	<u>Mutated genes (number of mutations)</u>
IPR000219	ARHGEF4(2), ECT2(1), FARP1(1), FLJ20184(1), MCF2L2(1), NET1(1), OBSCN(5), RASGRF2(2), TRAD(1), VAV3(1)
IPR000225	APC2(2), JUP(1), KPNA5(2), SPAG6(1)
IPR000357	ARFGEF2(2), CMYA4(1), DRIM(2), JUP(1), KPNA5(2), PIK3R4(1), SPAG6(1)
IPR000533	AKAP9(2), C10orf39(1), C20orf23(1), CUTL1(1), HOOK1(1), HOOK3(1), KTN1(2), LRRFIP1(3), MYH1(3), MYH9(2), NEF3(1), NF2(1), RSN(1), TAX1BP1(1), TPM4(1)
IPR000694	ADAM12(3), ADAMTS19(1), APC2(2), APXL(1), ARID1B(1), BAT2(2), BAT3(1), BCAR1(1), BCL11A(2), BCORL1(1), C14orf155(3), C1orf2(1), C1QB(1), C6orf31(1), C7orf11(1), CD2(1), CENTD3(3), CHD5(3), CIC(3), CMYA1(2), COL11A1(3), COL19A1(2), COL7A1(3), DAZAP1(1), DBN1(3), DVL3(1), EIF5(1), FAM44A(1), FAM47B(1), FHOD1(1), FLJ20584(1), G3BP2(2), GAB1(2), GGA3(1), GLI1(3), GPNMB(2), GRIN2D(3), HCN3(1), HOXA3(2), HOXA4(1), IRS4(1), KCNA5(1), KCNC2(1), LIP8(1), LOC374955(1), MAGEE1(2), MICAL1(2), MICAL-L1(1), MLLT2(1), MMP15(1), N4BP2(1), NCOA6(2), NHS(1), NUP214(3), ODZ1(3), PER1(2), PER2(1), PHC1(1), PLXNB1(1), PPM1E(2), RAI17(2), RAPH1(2), RBAF600(2), SCARF2(1), SEMA4G(1), SLC16A2(1), SORBS1(1), SPEN(2), SPG4(1), TBX1(1), TCF1(2), TCF7L1(1), TESK1(1), THG-1(1), TP53(18), TRIF(1), ZBTB3(2), ZNF318(2)
IPR000909	CENTB1(2), PLCB1(1), PLCG1(1)
IPR000998	AEGP(3), EGFL6(2), PRSS7(1)
IPR001140	ABCB10(2), ABCB6(1), ABCB8(2)
IPR001164	ARFGAP3(1), CENTB1(2), CENTD3(3), CENTG1(2)
IPR001589	DMD(2), ELA1(1), FLNB(5), MACF1(4), PLS3(1)
IPR001715	DMD(2), EHBP1(1), FLNB(5), MACF1(4), MICAL1(2), MICAL-L1(1), PLS3(1), VAV3(1)
IPR001849	APPL(1), ARHGEF4(2), CENTB1(2), CENTD3(3), CENTG1(2), FARP1(1), GAB1(2), IRS4(1), MCF2L2(1), NET1(1), OBSCN(5), OSBPL11(1), PLCG1(1), PLD2(2), PLEKHA8(2), RAPH1(2), RASAL2(2), RASGRF2(2), TRAD(1), VAV3(1), VEPH1(3)
IPR002017	AKAP6(3), GOLGB1(2), HOOK1(1), KTN1(2), MACF1(4), MYH9(2), SPTAN1(5), SYNE2(3)
IPR002172	AEGP(3), PRSS7(1), SORL1(3), TMPRSS3(1), TMPRSS6(3)
IPR003439	ABCA3(3), ABCA4(1), ABCB10(2), ABCB6(1), ABCB8(2), CNTN6(2), RIF1(2), SMC4L1(1)
IPR003961	BOC(1), CDON(1), CNTN6(2), COL7A1(3), FN1(2), FNDC3B(1), IL7R(1), NRCAM(2), OBSCN(5), PTPRC(2), SORL1(3), TEK(1), TRAD(1), TRIM36(1)
IPR003962	BOC(1), CDON(1), CNTN6(2), COL7A1(3), FN1(2), FNDC3B(1), NRCAM(2), TRAD(1)
IPR005479	AKAP9(2), CPS1(1), DNAH9(3)
IPR013032	ATRN(1), BMP1(1), CUBN(4), EGFL6(2), EREG(1), FN1(2), ITGB2(1), LAMA2(1), NID2(2), ODZ1(3), SCARF2(1), SORL1(3), TECTA(4), TEK(1), THBS3(2), TLL1(1), TNFRSF25(1)
IPR013091	BMP1(1), CUBN(4), EGFL6(2), NID2(2), THBS3(2), TLL1(1)
IPR013111	ADAM12(3), ATRN(1), CUBN(4), EGFL6(2), ITGB2(1), ODZ1(3), SCARF2(1), TEK(1)
IPR013563	ABCA3(3), ABCA4(1), ABCB10(2), ABCB6(1), ABCB8(2)

B. Colorectal cancers

<u>InterPro ID</u>	<u>Genes Mutated (number of mutations)</u>
IPR000033	LRP1(2), LRP2(3), NID(1), SORL1(2)
IPR000152	C1QR1(2), CD248(2), CRB1(1), CUBN(1), LRP1(2), LRP2(3), NELL1(1), NID(1), PROS1(1)
IPR000219	ARHGEF1(1), DEPDC2(3), FLJ10521(1), HAPIP(1), MCF2L2(2), OBSCN(7), RASGRF2(2), TIAM1(2)
IPR000694	ACIN1(1), ADAM19(2), ADAM29(2), BCL11B(1), C15orf2(2), CAD(2), CBFA2T3(3), CD248(2), CENTD3(1), COL3A1(2), COL4A6(1), CTNND2(2), DCC(1), DSCAML1(2), EDA(1), EFS(1), EIF4G1(1), EN1(1), ERF(1), EVL(2), FIGN(1), FLJ34633(1), GLI3(3), GRM1(1), HIVEP3(1), IGSF9(1), IRS2(1), IRS4(2), KCNH4(1), KIAA0182(2), KLF5(1), MCM3AP(2), MGC13125(1), MLL3(6), MMP11(1), NFATC1(1), NOS3(2), NR3C2(1), ODZ1(2), PER1(1), PRIMA1(1), RALGDS(1), SALL3(1), SETBP1(1), SF3A1(1), SHANK1(2), SMTN(2), SYNPO(1), TBX1(1), TCERG1L(1), TCF7L2(3), TFG(1), TP53(18), UTX(1)
IPR000742	ADAM19(2), ADAM33(1), AMACO(1), C1QR1(2), CRB1(1), CUBN(1), LRP1(2), LRP2(3), NELL1(1), NID(1), ODZ1(2), PROS1(1)
IPR000977	LIG1(2), LIG3(1), LRP2(3), SORL1(2)
IPR001090	EPHA3(4), EPHA4(1), EPHA7(1), EPHB6(4)
IPR001132	SMAD2(3), SMAD3(2), SMAD4(4)
IPR001426	EPHA3(4), EPHA4(1), EPHA7(1), EPHB6(4)
IPR001590	ADAM19(2), ADAM29(2), ADAM33(1), ADAMTS15(2), ADAMTS18(3)
IPR001762	ADAM19(2), ADAM29(2), ADAM33(1)
IPR001849	ARHGEF1(1), CENTB1(1), CENTD3(1), CNKSR2(1), DDEFL1(1), DEPDC2(3), HAPIP(1), IRS2(1), IRS4(2), MCF2L2(2), OBSCN(7), OSBP(1), RASAL2(1), RASGRF2(2), SPTBN2(1), TIAM1(2)
IPR001881	C1QR1(2), CD248(2), CRB1(1), CUBN(1), LRP1(2), LRP2(3), NELL1(1), NID(1), PROS1(1)
IPR002126	CDH18(1), CDH6(1), CLSTN2(2), CLSTN3(1), DCHS1(1), PCDH11X(2), RET(3)
IPR002870	ADAM19(2), ADAM29(2), ADAM33(1), ADAMTS15(2), ADAMTS18(3)
IPR003619	SMAD2(3), SMAD3(2), SMAD4(4)
IPR003961	CHL1(2), CNTN1(1), CNTN4(2), DCC(1), DSCAML1(2), EPHA3(4), EPHA4(1), EPHA7(1), EPHB6(4), FN1(2), IGSF9(1), IL6ST(1), LIFR(1), OBSCN(7), PTPRD(3), PTPRU(3), SORL1(2)
IPR003962	CHL1(2), CNTN1(1), CNTN4(2), DCC(1), DSCAML1(2), EPHA3(4), EPHA4(1), EPHA7(1), EPHB6(4), FN1(2), IGSF9(1), PTPRD(3), PTPRU(3)
IPR003993	CBFA2T3(3), HIST1H1B(2), HIST1H1E(1), TCOF1(1)
IPR006209	AMACO(1), C1QR1(2), CD248(2), CRB1(1), CUBN(1), ITGB3(1), LRP1(2), LRP2(3), NELL1(1), NID(1), ODZ1(2), PROS1(1)
IPR006586	ADAM19(2), ADAM29(2), ADAM33(1)
IPR011510	CENTD3(1), CNKSR2(1), EPHA3(4), EPHA4(1), EPHA7(1), EPHB6(4), SHANK1(2)
IPR013032	ADAM19(2), ADAM33(1), C1QR1(2), CD248(2), CRB1(1), CUBN(1), EPHA3(4), EPHA7(1), EPHB6(4), FN1(2), ITGB3(1), LAMB3(1), LAMC1(1), LRP1(2), LRP2(3), NELL1(1), NID(1), ODZ1(2), PROS1(1), SORL1(2), TNFRSF9(1)
IPR013091	C1QR1(2), CD248(2), CRB1(1), CUBN(1), LRP1(2), LRP2(3), NELL1(1), NID(1), PROS1(1)
IPR013098	ADAMTSL3(4), CHL1(2), CNTN1(1), CNTN4(2), DCC(1), DSCAML1(2), FSTL5(1), IGSF9(1), ISLR(1), KDR(2), LRRC4(1), OBSCN(7), PTPRD(3), SIGLEC7(1), TTID(1)
IPR013106	ADAMTSL3(4), CHL1(2), CNTN1(1), CNTN4(2), DCC(1), DSCAML1(2), FSTL5(1), HAPLN1(2), IGSF9(1), IREM2(1), KDR(2), LRRC4(1), MGC15730(1), OBSCN(7), PTPRD(3), SCN3B(2), SIGLEC7(1), TTID(1)
IPR013111	ADAM19(2), ADAM33(1), CRB1(1), CUBN(1), ITGB3(1), LRP2(3), NELL1(1), ODZ1(2)
IPR013151	ADAMTSL3(4), C10orf72(1), CHL1(2), CNTN1(1), CNTN4(2), DCC(1), DSCAML1(2), FSTL5(1),

IGSF9(1), KDR(2), LRRC4(1), MGC15730(1), OBSCN(7), PTPRD(3), SIGLEC7(1), TTID(1)
IPR013585 CDH18(1), CDH6(1), CLSTN2(2), CLSTN3(1), DCHS1(1), PCDH11X(2), RET(3)

Supplementary Table 2. Mutated genes in Gene Ontology groups identified through mutation enrichment analysis

A. Breast cancers

<u>GO ID</u>	<u>Genes Mutated (number of mutations)</u>
GO:0003779	ABLIM1(1), CFL2(1), DBN1(3), DMD(2), FHOD1(1), FLNB(5), GSN(3), MYH1(3), MYH9(2), PLS3(1), SPTAN1(5), TNS(1), TPM4(1)
GO:0004722	MTMR3(3), PPM1E(2), PPM1F(1)
GO:0005089	ALS2CL(2), ARHGEF4(2), ECT2(1), FARP1(1), FLJ20184(1), MCF2L2(1), RASGRF2(2), TRAD(1), VAV3(1)
GO:0005096	CENTB1(2), ECT2(1), RANBP1(1), RAP1GA1(2), RASAL2(2), SIPA1L1(1), SRGAP3(1), STARD8(2), TBC1D19(1), VAV3(1)
GO:0005201	BGN(2), COL11A1(3), COL19A1(2), MFAP5(1), TECTA(4), WNT2(1)
GO:0005509	ANKRD5(1), APCS(1), ASGR1(1), ATP2A3(1), BMP1(1), CDH10(2), CDH20(3), CDH8(1), CSEN(2), CUBN(4), DGKG(1), DNAJA5(1), DNASE1L3(2), DTNA(1), EGFL6(2), ELA1(1), ENPEP(1), FLJ40342(1), GALNT5(2), GRIN2D(3), GSN(3), ITGA9(2), KIAA0676(1), LOC374955(1), MACF1(4), MCOLN1(1), MGC34837(1), MMP10(1), MMP15(1), NID2(2), NOS2A(1), PADI3(1), PCDH20(1), PCDH8(1), PCDHB15(2), PDCD6(1), PKDREJ(2), PLA2G4A(1), PLCB1(1), PLCG1(1), PLS3(1), PRRG1(1), SPTAN1(5), STAT1(1), STAT4(1), SYT3(1), THBS3(2), TLL1(1), TRPC4(1)
GO:0008017	APC2(2), HOOK1(1), HOOK3(1), MACF1(4), RSN(1)
GO:0016887	ABCA3(3), ABCA4(1), ABCB10(2), ABCB6(1), ABCB8(2), ATP8B1(4), DNAH5(1), DNAH9(3)
GO:0042626	ABCA3(3), ABCA4(1), ABCB10(2), ABCB6(1), ABCB8(2)
GO:0000050	EBF(2), NRIP1(1), PTPN14(1)
GO:0006526	ARPC5(1), EBF(2), PTPN14(1)
GO:0016337	CTNND2(2), FLJ23356(3), HRH4(3), MYO3A(1), SIRT2(1)
GO:0030198	DNAH5(2), FLJ23356(3), PROCR(3)
GO:0035023	BBS5(1), CSTA(2), HRAS(1), LOC203427(2), PRKCE(2), SCR3(1), SLC9A2(1), SLC05A1(1), TGFB2(1)

B. Colorectal cancers

<u>GO ID</u>	<u>Genes Mutated (number of mutations)</u>
GO:0004222	ADAM29(2), ADAM33(1), ADAMTS15(2), ADAMTS18(3), OMA1(1), UQCRC2(2)
GO:0004872	ADORA1(1), C1QR1(2), CMKOR1(1), CUBN(1), EPHA3(4), EPHA4(1), EPHA7(1), EPHB6(4), FZD4(1), GHRHR(1), GPR124(1), GPR8(1), GPR87(1), GRID2(1), GRIK3(1), GRM1(1), HRH1(1), HTR5A(1), IL6ST(1), IREM2(1), IRS4(2), ITGB3(1), KDR(2), LIFR(1), LRP1(2), LRP2(3), MS4A5(1), NCR1(1), OR1E2(1), P2RX7(2), P2RY14(2), PKHD1(5), PTPRN2(1), PTPRU(3), RET(3), SIGLEC7(1), TGFB2(3), TNFRSF9(1), UNC13B(1)
GO:0005003	EPHA3(4), EPHA4(1), EPHA7(1), EPHB6(4)
GO:0005158	IRS2(1), IRS4(2), PHIP(2)
GO:0051018	AKAP12(2), AKAP3(1), AKAP6(2)
GO:0006898	LGTM(3), PIGK(2), ZNF655(1)
GO:0007155	ARHGEF2(1), CHRN3(1), CISH(1), FBXO2(1), FLJ45949(1), G22P1(1), GGTLA1(1), GPR62(1), GRIN1(1), ISYNA1(1), JAK3(1), LOC112714(2), MCM2(31), NALP10(1), ODC1(2), PBX3(1), PDIR(2), PRKX(1), RANBP1(2), RASSF1(2), RGSL2(1), SYK(2), TERF1(1), TRIP4(1)
GO:0007156	CHRN3(1), GPR62(1), LOC112714(2), MAPKAPK3(1), PBX3(1), POLR2J3(3), RANBP1(2)

GO:0008202	KLF10(1), MBTPS2(2), PIGK(2), ZNF655(1)
GO:0008203	PIGK(2), YY2(2), ZNF498(1)
GO:0045786	38964(1), FASTK(1), MCM2(31), PSMC2(1), SCUBE2(1), SIGLEC9(1), ZFP36(1)

Supplementary Table 3. Mutated genes in cellular pathways identified through mutation enrichment analysis

iPath database - breast cancers

<u>Pathway Description</u>	<u>Genes Mutated (number of mutations)</u>
AKT signaling	GAB1(2), IKBKB(1), NFKB1(1), NFKBIA(1), PIK3R1(1), PIK3R1(1), TP53(18)
ATM/ATR regulation of G1/S checkpoint	CLSPN(1), MRE11A(2), NFKB1(1), NFKBIA(1), POU2F1(1), TP53(18)
Cell Cycle Regulation by Brca1	BRCA1(3), POLR2F(1), POU2F1(1), STAT1(1), TP53(18)
NGF signaling pathway	CENTG1(2), GAB1(2), PIK3R1(1), PIK3R1(1), PLCG1(1)
RAN regulation pathway	KPNA5(2), NUP133(2), NUP214(3), NUP98(2), RANBP1(1), UBE2I(1), UBE2I(1)
Role of Brca1 and Brca2 in DNA repair	BRCA1(3), BRCA2(1), MRE11A(2), POLR2F(1), TP53(18)

iPath database - colorectal cancers

<u>Pathway Description</u>	<u>Genes Mutated (number of mutations)</u>
A2B receptor: action via G-protein alpha s (map 1)	ADCY8(1), GNAS(3), HIST1H1B(2), HIST1H1E(1)
ATM/ATR regulation of G2/M checkpoint	CCNB3(1), FANCG(1), TP53(18), TP53BP1(1)
ATM-H2AX-NFBD1 DNA damage response	TP53(18), TP53BP1(1)
Caspases activation via nuclear import	ACIN1(1), ITGB3(1), TP53(18)
PKA signaling	ADCY8(1), ADD3(1), ADD3(1), ANAPC4(1), CACNB1(1), CACNB2(1), CACNB2(1), GNAS(3), PHKB(1)
Pleckstrin homology proteins interactions. Part VI	PRKD1(2), SPTBN2(1), TIAM1(2)
Putative integrins pathway. Part 2	IGFBP3(2), ITGB3(1), LEF1(1), RPS6KB1(1), TP53(18)
WNT signaling pathway. Part 2	APC(31), FZD4(1), LEF1(1), TCF7L2(3), VIM(1), WNT16(1), WNT16(1), WNT8B(1)

KEGG database - breast cancers

<u>Pathway Description</u>	<u>Genes Mutated (number of mutations)</u>
Urea cycle and metabolism of amino groups	ACY1(1), ASL(2), CPS1(1), OTC(1)
ABC transporters	ABCA3(3), ABCA4(1), ABCB10(2), ABCB6(1), ABCB8(2)
PPAR signaling pathway	ACADM(2), FABP4(1), AQP7(2), HMGCS1(1), APOA1(2), SCP2(1), SORBS1(1)
Regulation of autophagy	IFNA2(1), PIK3R4(1), PRKAA1(1), PRKAA2(2)
Pancreatic cancer	BRCA2(1), IKBKB(1), NFKB1(1), PIK3R1(1), RAC2(1), STAT1(1), TP53(18)

KEGG database - colorectal cancers

<u>Pathway Description</u>	<u>Genes Mutated (number of mutations)</u>
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Cell Communication	COL3A1(2), COL4A6(1), CX40.1(2), COL5A1(1), KRT73(2), LAMB3(1), LAMC1(1), LMNB2(1), VIM(1)
Wnt signaling pathway	APC(31), CSNK1A1L(1), FZD4(1), LEF1(1), NFATC1(1), SMAD2(3), SMAD3(2), SMAD4(4), TCF7L2(3), CAMK2A(1), TP53(18), WNT16(1), WNT8B(1)
Hedgehog signaling pathway	BMP6(2), CSNK1A1L(1), GLI3(3), LRP2(3), WNT16(1), WNT8B(1)
TGF-beta signaling pathway	BMP6(2), NODAL(1), RPS6KB1(1), SMAD2(3), SMAD3(2), SMAD4(4), TGFBR2(3)
Axon guidance	PAK3(1), DCC(1), DPYSL2(1), EPHA3(4), EPHA4(1), EPHA7(1), EPHB6(4), KRAS(16), NFATC1(1), PAK6(1)
Adherens junction	LEF1(1), LMO7(2), SMAD2(3), SMAD3(2), SMAD4(4), TCF7L2(3), TGFBR2(3)
Gap junction	ADCY8(1), CSNK1A1L(1), GNAS(3), GRM1(1), GUCY1A2(3), KRAS(16), TUBB2B(1), PDGFD(1)
Long-term depression	GNAS(3), GRID2(1), GRM1(1), GUCY1A2(3), KRAS(16), NOS3(2)
Taste transduction	ACCN1(1), ADCY8(1), GNAS(3), SCNN1B(1), SCNN1G(1)
Insulin signaling pathway	IRS2(1), IRS4(2), KRAS(16), PHKB(1), PIK3R5(1), PRKCZ(1), RHEB(1), RPS6KB1(1), SOCS6(1)
Type II diabetes mellitus	IRS2(1), IRS4(2), PIK3R5(1), PRKCE(1), PRKCZ(1), SOCS6(1)
Colorectal cancer	APC(31), DCC(1), FZD4(1), KRAS(16), LEF1(1), PIK3R5(1), RALGDS(1), SMAD2(3), SMAD3(2), SMAD4(4), TGFBR2(3), TP53(18)
Pancreatic cancer	KRAS(16), RALGDS(1), SMAD2(3), SMAD3(2), SMAD4(4), TGFBR2(3), TP53(18)

sigPathways database - breast cancers

<u>Pathway Description</u>	<u>Genes Mutated (number of mutations)</u>
Cancer Drug Resistance	ERCC3(1), BRCA2(1), NFKB1(1), TP53(18), CYP1A1(2), TOP1(1), BRCA1(3), CRR9(1)
Cancer Pathway Find	PIK3R1(1), BRCA2(1), NFKB1(1), NFKBIA(1), TP53(18), TNFRSF25(1), BRCA1(3)
Signal Transduction	MMP10(1), WNT2(1), NFKB1(1), NFKBIA(1), TRIM25(1), TP53(18), ATF2(1), BRCA1(3)

sigPathways database - colorectal cancers

<u>Pathway Description</u>	<u>Genes Mutated (number of mutations)</u>
Immunology Signaling	SMAD2(3), NFATC1(1), BRAF(1), PRKCZ(1), NOS3(2), RPS6KB1(1), TLR8(1), TP53(18), P2RX7(2), SMAD4(4), SOCS6(1), TLR9(2), STAM(1), KRAS(16), SMAD3(2), ENPP2(1)
Osteogenesis	SMAD2(3), MMP2(3), TGFBR2(3), SMAD4(4), BMP6(2), SMAD3(2), COL3A1(2)
TGF-beta BMP Signaling	SMAD2(3), TGFBR2(3), SMAD4(4), BMP6(2), NODAL(1), SMAD3(2), COL3A1(2)

BioCarta database - breast cancers

<u>Pathway Description</u>	<u>Genes Mutated (number of mutations)</u>
Apoptotic Signaling in Response to DNA Damage	PARP1(1), STAT1(1), TP53(18)
ATM Signaling Pathway	MRE11A(2), NFKB1(1), NFKBIA(1), BRCA1(3), TP53(18)
Chaperones modulate interferon Signaling Pathway	IKKB(1), NFKB1(1), NFKBIA(1), TP53(18), DNAJA3(1)
Double Stranded RNA Induced Gene Expression	NFKB1(1), NFKBIA(1), TP53(18)

HIV-I Nef: negative effector of Fas and TNF
Induction of apoptosis through DR3 and DR4/5
Death Receptors
Role of BRCA1, BRCA2 and ATR in Cancer
Susceptibility

PARP1(1), GSN(3), NFKB1(1), NFKBIA(1), SPTAN1(5)
NFKB1(1), NFKBIA(1), SPTAN1(5), TNFRSF25(1)
MRE11A(2), BRCA1(3), BRCA2(1), TP53(18)

BioCarta database - colon cancers

Pathway Description

Cell Cycle: G1/S Check Point
CTCF: First Multivalent Nuclear Factor
Inactivation of Gsk3 by AKT
Multi-step Regulation of Transcription by Pitx2
NFkB activation by Nontypeable Hemophilus influenzae
TGF beta signaling pathway

Genes Mutated (number of mutations)

SMAD3(2), SMAD4(4), TP53(18)
SMAD4(4), RPS6KB1(1), TP53(18)
CUTL1(1), APC(31), LEF1(1)
APC(31), LEF1(1), LDB1(1)
SMAD3(2), SMAD4(4), TGFBR2(3)
APC(31), SMAD2(3), SMAD3(2), SMAD4(4),
TGFBR2(3)

Supplementary Table 4A. Genes annotated through different mutation enrichment classification methods in colorectal cancer

Number of classification methods	Classification method					Number of mutated genes	Gene symbols
	Gene mutation enrichment	Gene group or pathway enrichment					
		Protein domain	Gene ontology	Protein interaction	Cellular pathways		
4	●	●		●	●	1	TP53
4	●	●	●		●	3	EPHA3, EPHB6, LRP2
4		●	●	●	●	1	IRS4
3	●		●		●	3	P2RX7, PRKD1, TGFBFR2
3	●		●	●		1	ERCC6
3	●	●	●			5	ADAM29, ADAMTS15, ADAMTS18, PTPRU, RET
3	●	●			●	5	HIST1H1B, SMAD2, SMAD3, SMAD4, TCF7L2
3		●	●		●	5	EPHA4, EPHA7, GRM1, IRS2, ITGB3
2	●		●			6	CD109, P2RY14, PHIP, PKHD1, TTL3, UQCRC2
2	●				●	7	APC, GNAS, GUCY1A2, K6IRS3, KRAS, LMO7, MMP2
2	●	●				11	ADAMTSL3, C15orf2, CD248, CHL1, CNTN4, EVL, HAPLN1, MLL3, OBSCN, PTPRD, SCN3B
2			●		●	4	FZD4, GRID2, PRKCZ, TLR8
2		●	●			13	ADAM33, C1QR1, CUBN, IL6ST, IREM2, KDR, LIFR, LIG1, LIG3, LRP1, PROS1, SIGLEC7, TNFRSF9
2		●			●	15	ACIN1, COL3A1, COL4A6, DCC, GLI3, HIST1H1E, LAMB3, LAMC1, LEF1, NFATC1, NOS3, RALGDS, SPTBN2, TCOF1, TIAM1
2				●	●	1	SCNN1B
2		●		●		2	PER1, SORL1
1	●					27	ABCA1, ACSL5, C10orf137, C6orf29, CSMD3, EYA4, FBXW7, GALNS, KCNQ5, KIAA1409, LGR6, LOC157697, MAP2, MCP, MGC33407, MKRN3, NF1, PKNOX1, RUNX1T1, SDBCAG84, SEC8L1, SFRS6, SLC29A1, SYNE1, TBX22, UHRF2, ZNF442
						64	ADAM19, AMACO, ARHGEF1, BCL11B, C10orf72, CAD, CBFA2T3, CDH18, CDH6, CENTB1, CENTD3, CLSTN2, CLSTN3, CNKSR2, CNTN1, CRB1, CTNND2, DCHS1, DDEFL1, DEPD2, DSCAMLL1, EDA, EFS, EIF4G1, EN1, ERF, FIGN, FLJ10521, FLJ34633, FN1, FSTL5, HAPIP, HIVEP3, IGSF9, ISLR, KCNH4, KIAA0182, KLF5, LRRC4, MCF2L2, MCM3AP, MGC13125, MGC15730, MMP11, NELL1, NID, NR3C2, ODZ1, OSBP, PCDH11X, PRIMA1, RASAL2, RASGRF2, SALL3, SETBP1, SF3A1, SHANK1, SMTN, SYNPO, TBX1, TCERG1L, TFG, TTID, UTX
1		●				71	38964, ADARB2, ADORA1, AKAP12, AKAP3, AKAP6, ARHGEF2, AUH, CHRN3, CISH, CMKOR1, EDG8, EDN3, FAM3B, FASTK, FBXO2, FLJ36119, FLJ45949, G22P1, GGT1A1, GHRHR, GPR124, GPR62, GPR8, GPR87, GRIK3, GRIN1, HRH1, HTR5A, HYDIN, ISYNA1, JAK3, KLF10, LGTN, LOC112714, MAPKAPK3, MBTPS2, MCM2, MS4A5, NALP10, NCR1, NUDT14, ODC1, OMA1, OR1E2, PBX3, PDIR, PHACTR3, PIGK, POLR2J, PRKX, PSMC2, PTPRN2, RANBP1, RASSF1, RGS16, RGS12, RPS19, SCUBE2, SIGLEC9, SYK, TERF1, TRIO, TRIP4, UNC13B, WRN, YY2, ZFP36, ZNF498, ZNF638, ZNF655
1			●			78	ADAM12, ANK1, ASL, ATF2, BAT3, BCAR1, BRCA1, BRCA2, CD2, CDS1, CENTG1, CGI-37, CPSF3, CSNK1D, DBN1, DDX18, DNAJA3, DRIM, DVL3, EIF5, ERCC3, FAAH, FUS, FXR1, GAB1, GGA1, GSN, HDLBP, IKBKAP, IKBKB, KIAA1012, LRRFIP1, LZTS2, MAGEA4, MAPK13, MGC27019, MYH9, NEDD4, NF2, NFKB1, NFKBIA, NIPBL, NUP133, OTC, PARP1, PDLIM7, PER2, PHC1, PHF7, PIK3R1, PLCG1, POU2F1, PP, PRKAA2, PRPF4B, PTD004, PTPRC, PUS1, RFC4, RHAG, RNU3IP2, RPL3, SFRS1, SH2D3A, SLC4A3, SLC9A2, SPTAN1, STAT1, STX5A, TCP1, TEK, THBS3, TIMELESS, TOP1, TRIM29, VAV3, WBP4, ZNF646
1				●		37	ACCN1, ADCY8, ADD3, ANAPC4, BMP6, BRAF, CACNB1, CACNB2, CAPN6, CCNB3, CSNK1A1L, CUTL1, CX40.1, DPYSL2, ENPP2, FANCG, FCN1, IGFBP3, LDB1, LMNB2, MGC8685, NODAL, PAK6, PDGFD, PHKB, PIK3R5, PRKCE, RHEB, RPS6KB1, SCNN1G, SOCS6, STAM, TLR9, TP53BP1, VIM, WNT16, WNT8B

Supplementary Table 4B. Genes annotated through different mutation enrichment classification methods in breast cancer

Number of classification methods	Classification method					Number of mutated genes	Gene symbols
	Gene mutation enrichment	Gene group or pathway enrichment					
		Protein domain	Gene ontology	Protein interaction	Cellular pathways		
5	●	●	●	●	●	2	SPTAN1, TP53
4	●		●	●	●	2	BRCA1, GSN
4	●	●	●		●	3	ABCA3, ABCB10, ABCB8,
4	●	●	●	●		4	CUBN, DBN1, RASAL2, THBS3
4	●	●		●	●	2	CENTG1, GAB1
4		●	●	●	●	1	PLCG1
3	●		●	●		1	SLC9A2
3	●	●	●			14	APC2, ARHGEF4, CENTB1, COL11A1, COL19A1, DNAH9, EGFL6, FLNB, GRIN2D, MACF1, MYH1, PPM1E, RASGRF2, TECTA
3	●			●	●	2	ASL, NUP133
3	●	●			●	2	KPNA5, NUP214
3	●	●		●		3	ADAM12, LRRFIP1, SORL1
3			●	●	●	1	STAT1
3		●	●		●	2	ABCA4, ABCB6
3		●	●	●		2	MYH9, VAV3
2	●		●			14	ALS2CL, ATP8B1, BGN, CDH10, CDH20, DNASE1L3, GALNT5, ITGA9, MTMR3, PCDHB15, PKDREJ, PTPN14, RAPIGA1, STARD8
2	●				●	4	ACADM, CYP11A1, KIAA0999, MRE11A
2	●			●		5	GGA1, HDLBP, PRPF4B, RNU3IP2, SCNN1B
2	●	●				23	AEGP, BCL11A, C14orf155, CHD5, CIC, CMYA1, CNTN6, COL7A1, GLI1, GPNMB, HOXA3, KTN1, MAGEE1, NCOA6, NRCAM, OBSCN, PLEKHA8, RAPH1, SYNE2, TCF1, TMPRSS6, VEPH1, ZNF318
2			●		●	3	MMP10, RANBP1, WNT2
2			●	●		2	ANK1, PRKCE
2		●	●			19	BMP1, DMD, ECT2, ELA1, FARP1, FHOD1, FLJ20184, HOOK1, HOOK3, LOC374955, MCF2L2, MMP15, NID2, PLCB1, PLS3, RSN, TLL1, TPM4, TRAD
2				●	●	14	ATF2, BRCA2, CDS1, DNAJA3, ERCC3, IKBKB, NFKB1, NFKBIA, OTC, PARP1, PIK3R1, POU2F1, PRKAA2, TOP1
2		●			●	5	CPS1, PIK3R4, SORBS1, SPEN, TNFRSF25
2		●		●		13	BAT3, BCAR1, CD2, DRIM, DVL3, EIF5, IRS4, NF2, PER1, PER2, PHC1, PTPRC, TEK
1	●					41	AMFR, C22orf19, CNM4, DDX10, EHMT1, FLJ10458, FLJ13479, FLJ40869, HDAC4, ICAM5, INHBE, IRTA2, KEAP1, KIAA0427, KIAA0934, KIAA1632, LOC283849, LRBA, MAP3K6, MGC24047, MYOD1, NALP8, NCB5OR, OTOF, PFC, PHACS, PRPS1, RFX2, RGL1, SBNO1, SEMA5B, SERPINB1, SIX4, SLC6A3, SP110, SULF2, XDH, ZCSSL3, ZFP64, ZFYVE26, ZNF569
1		●				72	ADAMTS19, AKAP6, AKAP9, APPL, APXL, ARFGAP3, ARHGEF2, ARID1B, ATRN, BAT2, BCORL1, BOC, C10orf39, C1orf2, C1QB, C20orf23, C6orf31, C7orf11, CDON, CENTD3, CMYA4, CUTL1, DAZAP1, EHBPI, EREG, FAM44A, FAM47B, FLJ20584, FN1, FNDC3B, G3BP2, GGA3, GOLGB1, HCN3, HOXA4, IL7R, ITGB2, JUP, KCNA5, KCNC2, LAMA2, LIP8, MICAL1, MICAL-L1, MLLT2, N4BP2, NEF3, NET1, NHS, ODZ1, OSBP1L1, PLD2, PLXNB1, PRSS7, RAI17, RBAF600, RIF1, SCARF2, SEMA4G, SLC16A2, SMC4L1, SPAG6, SPG4, TAX1BP1, TBX1, TCF7L1, TESK1, THG-1, TMPRSS3, TRIF, TRIM36, ZBTB3
1			●			49	ABUM1, ANKRD5, APC5, ARPC5, ASGR1, ATP2A3, BBS5, CDH8, CFL2, CSEN, CSTA, CTNND2, DGKG, DNAH5, DNAJA5, DTNA, EBF, ENPEP, FLJ23356, FLJ40342, HRAS, HRH4, KIAA0676, LOC203427, MCOLN1, MFAP5, MGC34837, MYO3A, NOS2A, NRIP1, PADI3, PCDH20, PCDH8, PDCD6, PLA2G4A, PPM1F, PROCR, PRRG1, SCRN3, SIPA1L1, SIRT2, SLC05A1, SRGAP3, STAT4, SYT3, TBC1D19, TGFBR2, TNS, TRPC4
1				●		84	ACSL4, ADORA1, APG5L, APOB, ARHGEF1, ARHGEF1, BRF1, C1QR1, C4BPA, CDH18, CDH6, CSH-37, CNTN1, COL4A6, CPSF3, CSE1L, CSNK1D, DDX18, DLG3, EIF2S2, ERCC6, FAAH, FBXO30, FLJ20729, FUS, FXR1, GLI3, GRM1, GUCY1A2, IKBKAP, IL6ST, ITGB3, KIAA1012, KRT20, LAMC1, LEF1, LIFR, LRP1, LRP2, LZTS2, MAGEA4, MAPK13, MCM3AP, MCRS1, MGC27019, NEDD4, NID, NIPBL, POLM7, PHF7, PP, PRKCZ, PRKD1, PROS1, PTDO04, PUS1, RAB38, RFC4, RHAG, RPL3, RUNX1T1, SCNN1G, SFRS1, SH2D3A, SLC4A3, SMAD2, SMAD3, SMAD4, STAM, STX5A, TCF3, TCP1, TGM2, TIAM1, TIMELESS, TP53BP1, TRIM29, VIM, VPS13A, VPS18, WBP4, WRN, ZFX1B, ZNF646
1					●	16	ACY1, CDC27, CLSPN, CRR9, FABP4, FCMD, FLJ32363, GTF2A1, IFNA2, NUP98, POLR2F, PRKAA1, RAC2, SCP2, TRIM25, UBE2I