

Supplementary Table S6

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Supplementary Table S6: Comparative analysis of the mutational frequencies in genes affecting selected functional pathways in metastatic breast cancers and triple-negative invasive ductal carcinomas of no special type and correlations of mutational status with clinicopathologic parameters. $p<0.05$ are highlighted in bold. ^a: Fisher's exact test. ^b: Mann-Whitney U-test.

List of genes for functional annotation.					
Name	Source	Accession		Genes	
KEGG: PI3K/Akt/mTOR	KEGG	hsa04150 - mTOR signaling pathway; hsa04151 - PI3K-Akt signaling pathway; hsa04012 - Erbb signaling pathway	AKT1, AKT2, AKT3, CDKN1A, CDKN1B, ERBB2, ERBB3, ERBB4, FGFR1, FGFR2, FGFR3, FGFR4, GRB2, HIF1A, HRAS, IGF1R, IRS1, KIT, MTOR, NRAS, PDGFR, PDGFRB, PIK3CA, PIK3CB, PIK3R1, PRKCA, PRKCB, PRKG1, PTEN, RICTOR, RPS6KB1, RPTOR, SOS1, TSC1, TSC2		
GO: PI3K signaling	Gene Ontology	GO_0014065 - phosphatidylinositol 3-kinase signaling	C1QBP, EDN1, ERBB2, ERBB3, GATA3, HTR2A, HTR2B, IGF1, IGF1R, IRS1, LTK, NF1, NYAP1, NYAP2, PIK3C2A, PIK3C2B, PIK3C2G, PIK3CA, PIK3CB, PIK3CD, PIK3CG, PIK3R1, PIK3R2, PIK3R5, PLEKHA1, PREX2, SIRT2, TSC2, TYRO3, XBP1		
KEGG: canonical WNT signaling	KEGG	hsa04310 - WNT signaling pathway (canonical portion)	APC, APC2, AXIN1, AXIN2, BAMBI, CCND1, CCND2, CCND3, CER1, CHD8, CREBBP, CSNK1A1, CSNK1A1L, CSNK1E, CSNK1E1, CSNK2A1, CSNK2A2, CSNK2B, CTBP1, CTBP2, CTNNB1, CTNNBIP1, CUL1, CX3C4, DKK1, DKK2, DKK4, DVL1, DVL2, DVL3, EP300, FOSL1, FRAT1, FRAT2, FZD1, FZD2, FZD3, FZD4, FZD6, FZD7, FZD8, GSX3, JUN, LEF1, LOC400271, CSNK1E, LRP5, LRP6, MMP7, MYC, NKD1, NKD2, PORCN, PPARD, RUVBL1, SENP2, SERPINF1, SFRP1, SFRP2, SFRP4, SFRP5, SMAD3, SMAD4, SOST, SOX17, TCF7, TCF7L1, TCF7L2, WIF1, WNT1, WNT10A, WNT10B, WNT11, WNT16, WNT2, WNT2B, WNT3, WNT3A, WNT4, WNT5A, WNT6, WNT7A, WNT7B, WNT8A, WNT8B, WNT9A, WNT9B		
GO: canonical WNT signaling	Gene Ontology	GO_0006070 - canonical WNT signaling pathway	APC, AXIN1, BCL9L, BCL9L1, CCND1, CDC42, CDH15, CHD8, CTNNB1, DISC1, DIX01, DVL1, DVL1P1, DVL2, DVL3, EGF, FGFR, FZD1, FZD10, FZD2, FZD3, FZD4, FZD5, FZD7, FZD8, FZD9, GLU1, GSK3B, HOXB9, KDM6A, KLF4, LEF1, LRIP5, LRIP5L, LRP6, LRRK2, MED12, MYC, MYH6, NDRG1, NDRG2, NAA20, ITLN1, PORCN, PROBP1, PSEN1, PTEN, PTK7, PTPRU, PWTG, QAR2, RYK, RYR2, SC1, SFRP1, SHH, SMO, SNAI2, SOX17, SOX4, STK11, T, TBL1XR1, TCF7, TCF7L1, TCF7L2, UBE2B, WNT1, WNT10B, WNT11, WNT2, WNT2B, WNT3, WNT3A, WNT4, WNT5A, WNT7A, WNT7B, WNT8A, WNT9A, WNT9B, ZNRF3		
Homologous recombination (Supplementary Fig. 4)	Curated from literature	NA	ATM, ATR, ATRIP, ATRX, BABAM1, BARD1, BLM, BRCA1, BRCA2, BRCC3, BRE, BRIP1, C17orf70, C19orf40, C1orf86, CHEK1, CHEK2, DMCI, DN2A, EME1, EME2, ERCC4, EXO1, FAM175A, FAN1, FANCA, FANCB, FANCC, FANCI, FANCF, FANCG, FANCI, FANCL, FANCM, FIGN1L, GEN1, H2AFX, HELO, KATS, MDC1, MRE11A, MUS81, NBN, NONO, PALB2, PIAS1, PIAS4, POLN, RAD1, RAD17, RAD50, RAD51, RAD51AP1, RAD51B, RAD51C, RAD51D, RAD52, RAD54B, RAD54L, RAD9A, RBBP8, RECQL, REV1L, RMI1, RPL22, RNF169, RNF169, RNF4, RPA1, RPA2, RPA3, RTE1, SEL1, SFOP, SFRP1, SHFM1, SLX1A, SLX1B, SLX4, SMC1, SMC3, SPIDR, TIMELESS, TIPIN, TP53BP1, UMC1, USP1, USP1, WRN, XRC2, XRC3		

Comparative analysis of the mutational frequencies of genes affecting selected functional pathways between metaplastic breast cancers and triple-negative IDC-NSTSs

	Metaplastic breast cancers (n=35)		Triple-negative IDC-NSTs (n=69)		Fisher's exact test comparing metaplastic breast cancers to triple-negative IDC-NSTs		
Pathway	Number of cases with non-synonymous mutation	% of cases with non-synonymous mutation	Number of cases with non-synonymous mutation	% of cases with non-synonymous mutation	p-value	Odds ratio (95% confidence interval)	
KEGG: PI3K/Akt/mTOR	20	57%	15	22%	0.0004	4.717 (1.827-11.79)	MET439, PIK3CA:p.Glu542lys, MET542, KIT:p.Glu198Gly, META57, PIK3CA:p.His1047Arg, META61, PIK3R1:p.Phe456, Glu457dup, PIK3R1:p.Leu130fs, MP1, PIK3R1:p.Ser62fs, MP15, PIK3R1:c.174G>C>C, IFRTR:p.Arg85Gly, MP17, PIK3CA:p.His1047Arg, MP7, PIK3CA:p.His1047Arg, MTC01, PIK3CA:p.His1047Arg, MTC08, IFR1:p.Tyr43Asn, MTC11, 45R6K81:p.Glu45Asp, MTC12, PIK3R1:p.Asp281Val, PTEN:p.Leu112Gln, MTC13, ERBB4:p.Met226le, MTC14, PIK3CA:p.Gln286Glu, MTC15, PIK3CA:p.His1047Arg, MTC16, PIK3CA:p.Cys120Arg, PTEN:c.209+2T>C, PTEN:c.1027+1G>A, MTC17, PIK3CA:p.His1047Arg, MTC18, PIK3CA:p.His1047Arg, MTC20, PTEN:c.209+2G>A, MTC21, PIK3CA:p.Glu542lys
GO: PI3K signaling	16	46%	18	26%	0.0500	2.365 (1-5.736)	META39, PIK3CA:p.Asn158Val, PIK3CA:p.Glu542lys, META57, PIK3CA:p.His1047Arg, META61, PIK3R1:p.Phe456, Glu457dup, PIK3R1:p.Leu130fs, MP1, PIK3R1:p.Ser62fs, MP15, PIK3R1:c.174G>A>C, MP17, PIK3CA:p.His1047Arg, MP7, PIK3CA:p.His1047Arg, MTC01, PIK3CA:p.Glu172Gln, MTC06, IFR1:p.Tyr43Asn, TYRO3:p.Gln48His, MTC12, PIK3R1:p.Asp281Val, MTC13, PIK3CA:p.His1047Arg, PIK3CG:p.Ala676Thr, MTC14, PIK3CA:p.Gln240Arg, MTC20, PIK3CA:p.His1047Arg, MTC17, PIK3CA:p.Gln372Lys
KEGG: canonical WNT signaling	12	34%	13	19%	0.0939	2.229 (0.8653-5.739)	META31, EP300:p.Pro870Ser, META39, CUL1:p.Tyr50Asp, FZD7:p.Ile532Val, MYC:p.Gln52His, META40, PORCN:p.Trp305Cys, META42, LRP5:p.Thr236Leu, LRP5:p.Thr236Leu, SMAD2:p.Gly103Asp, META57, APC:p.Thr183Ser, WNT5A:p.Ala31Pro, MP1, AXIN1:p.Ser57Leu, MTC03, CHD8:p.Glu171Lys, MTC04, CX4C:p.Ser189Trp, MTC07, WNT5A:p.Ala167Thr, MTC17, FZD2:p.Ala73Thr, GLI1:p.Asp87His, MTC21, DDX10:p.Cys162Arg
GO: canonical WNT signaling	16	46%	18	26%	0.0500	2.365 (1-5.736)	META31, MYH6:p.Ala189Val, TBL1XR1:p.Thr322Leu, META39, FZD7:p.Ile532Val, MYC:p.Gln52His, META40, PORCN:p.Trp305Cys, META42, LRP5:p.Thr236Leu, LRP5:p.Thr236Leu, SMAD2:p.Gly103Asp, META57, APC:p.Thr183Ser, WNT5A:p.Ala31Pro, MP1, KDM6A:p.Arg717fs, MED12:p.Gly141Asp, MP11, AXIN1:p.Ser359Arg, MP18, BCL9L:p.Leu199Val, PTFE:p.Leu199Val, MP12, KDM6B:p.Arg717fs, MP13, AXIN1:p.Ser57Leu, MTC03, CHD8:p.Glu171Lys, MTC06, BCL9L:p.Leu199Val, RYR2:p.Leu308Val, MTC07, LRRK2:p.Tyr308Arg, WNT5A:p.Ala167Thr, MTC13, RYR2:p.Lys282Gln, MTC17, FZD2:p.Ala73Thr, GLI1:p.Asp87His, MTC21, DDX10:p.Cys162Arg
KEGG: canonical WNT signaling (including FAT1)	14	40%	14	20%	0.0381	2.593 (1.01-6.958)	META31, EP300:p.Pro870Ser, FAT1:p.Met168Ile, META39, CUL1:p.Tyr50Asp, FZD7:p.Ile532Val, MYC:p.Gln52His, META40, PORCN:p.Trp305Cys, META42, LRP5:p.Thr236Leu, SMAD2:p.Gly103Asp, META57, APC:p.Thr183Ser, PIK3CA:p.Thr183Ser, WNT5A:p.Ala31Pro, MP11, AXIN1:p.Ser359Arg, MP15, FAT1:p.Ser168Phe, MTC01, AXIN1:p.Ser57Leu, MTC03, CHD8:p.Glu171Lys, MTC04, CX4C:p.Ser189Trp, MTC07, WNT5A:p.Ala167Thr, MTC15, FAT1:p.Val216Iufs, MTC17, FAT1:p.Glu243Gln, FZD2:p.Ala473Thr
GO: canonical WNT signaling (including FAT1)	18	51%	19	28%	0.0189	2.757 (1.103-6.673)	META31, FAT1:p.Met168Ile, MYH6:p.Ala189Val, TBL1XR1:p.Thr322Leu, META39, FZD7:p.Ile532Val, MYC:p.Gln52His, META40, PORCN:p.Trp305Cys, META42, LRP5:p.Thr236Leu, SMAD2:p.Gly103Asp, META57, KDM6A:p.Arg717fs, MP1, AXIN1:p.Ser359Arg, MP15, FAT1:p.Ser568Arg, MP18, BCL9L:p.Phe149Val, MP1, KDM6B:p.Arg717fs, MP11, AXIN1:p.Ser57Leu, MTC03, CHD8:p.Glu171Lys, MTC06, BCL9L:p.Leu31Val, RYR2:p.Leu308Val, MTC07, LRRK2:p.Tyr308Arg, FZD2:p.Ala73Thr, GLI1:p.Asp87His, MTC21, DDX10:p.Cys162Arg

Comparative analysis of the mutational frequencies of genes affecting selected functional pathways between metaplastic breast cancers of triple-negative phenotype and triple-negative IDC-NSTs.

	Metaplastic breast cancers of triple-negative phenotype (n=33)		Triple-negative IDC-NSTs (n=69)		Fisher's exact test comparing metaplastic breast cancers of triple-negative phenotype to triple-negative IDC-NSTs		
Pathway	Number of cases with non-synonymous mutation	% of cases with non-synonymous mutation	Number of cases with non-synonymous mutation	% of cases with non-synonymous mutation	p-value	Odds ratio (95% confidence interval)	
KEGG: PI3K/Akt/mTOR	18	55%	15	22%	0.0014	4.249 (1.741-10.64)	META39, PIK3CA:p.Glu542Lys, META52, KIT:p.Glu198Gly, META57, PIK3CA:p.His1047Arg, META61, PIK3R1:p.Phe456_Gln457dup, PIK3R1:p.Leu103fs, MP1, PIK3R1:p.Ser626fs, MP15, PIK3R1:c.746+2>c-, RPTOR:p.Arg855Gly, MP17, PIK3CA:p.His1047Arg, MP7, PIK3CA:p.His1047Arg, MTC01, PIK3CA:p.His1047Arg, MTC06, IGF1R:p.Tyr43Asn, MTC11, PR56Kb1:p.Glu45Asp, MTC12, PIK3R1:p.Asp281Val, PTEN:p.Leu112Gln, MTC13, ERBB4:p.Met522Leu, MTC14, PTEN:p.Asp286Glu, MTC15, PIK3CA:p.His1047Leu, RICTOR:p.Glu40Asp, MTC20, PIK3CA:p.Cys420Arg, PTEN:c.209+2T>C, PTEN:c.1027+1G>A, MTC17, PIK3CA:p.His1047Leu, RICTOR:p.Glu40Asp, MTC20, PTEN:c.209+1_209+4delGTTAA

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	Metaplastic breast cancers of triple-negative phenotype (n=33)		Triple-negative IDC-NSTS (n=69)		Fisher's exact test comparing metaplastic breast cancers of triple negative phenotype to triple-negative IDC-NSTS with likely pathogenic mutations		
Pathway	Number of cases with likely pathogenic mutation	% of cases with likely pathogenic mutation	Number of cases with likely pathogenic mutation	% of cases with likely pathogenic mutation	p-value	Odds ratio (95% confidence interval)	Metaplastic breast cancers of triple-negative phenotype with likely pathogenic mutations
KEGG: PI3K/Akt/mTOR	15	45%	14	20%	0.0108	3.231 (1.265-8.233)	META39, PIK3Ca:p.Glu542lys, META57, PIK3Ca:p.His1047Arg, META61, PIK3R1:p.Leu193s, PIK3R1:p.Phe457dup, MP1, PIK3R1:p.Ser652s, MP15, PIK3R1:c.174-2A>C, MP17, PIK3Ca:p.His1047Arg, MP7, PIK3Ca:p.His1047Arg, MTC01, PIK3Ca:p.His1047Arg, MTC12, PTEN:p.Leu112Gm, PIK3R1:p.Asp281Val, MTC13, ERBB4:p.Met522Ile, MTC14, PTEN:p.Asp280Glu, MTC15, PIK3Ca:p.His1047Arg, MTC16, PTEN:c.209+1>A, PTEN:c.209+2>C, PIK3Ca:p.Cys420Arg, MTC17, PIK3Ca:p.His1047Leu, MTC20, PTEN:c.209+1_209+4delGTAA
GO: PI3K signaling	12	36%	13	19%	0.0835	2.438 (0.9453-6.253)	META39, PIK3Ca:p.Glu542lys, PIK3Ca:p.Asp1158Val, META57, PIK3Ca:p.His1047Arg, META61, PIK3R1:p.Leu193s, PIK3R1:p.Phe456, Glu457dup, MP1, PIK3R1:p.Ser652s, MP15, PIK3R1:c.174-2A>C, MP17, PIK3Ca:p.His1047Arg, MP7, PIK3Ca:p.His1047Arg, MTC01, PIK3Ca:p.His1047Arg, MTC12, PIK3R1:p.Asp281Val, MTC15, PIK3Ca:p.His1047Arg, PIK3Cg:p.Ala676Thr, MTC16, PIK3Ca:p.Cys420Arg, MTC17, PIK3Ca:p.His1047Leu
KEGG: canonical WNT signaling	5	15%	2	3%	0.0345	5.865 (1.141-43.83)	META31, EP300:p.Pre870Ser, META57, APC:p.Phe1838fs, MP1, AXIN1:p.Ser359Arg, MTC01, AXIN1:p.Ser57Leu, MTC03, CHD8:p.Glu171lys
GO: canonical WNT signaling	10	30%	5	7%	0.0051	5.456 (1.697-18.2)	META31, TBL1XR1:p.Phe322Leu, META42, SMO:p.Pro560Ala, META52, LRRK2:p.Val1903Glu, META57, APC:p.Phe1838fs, MP1, KDM6A:p.Arg571fs, MED12:p.Gln415Lys, MP11, AXIN1:p.Ser359Arg, MP18, KDM6B:p.Ile1022fs, MTC01, AXIN1:p.Ser57Leu, MTC03, CHD8:p.Glu171lys, MTC19, DIXDC1:p.Pro401Arg
KEGG: canonical WNT signaling (including FAT1)	8	24%	3	4%	0.0046	6.885 (1.663-32.41)	META31, FAT1:p.Met1688Ile, EP300:p.Pre870Ser, META57, APC:p.Phe1838fs, MP11, AXIN1:p.Ser359Arg, MP15, FAT1:p.Ser1568Phe, MTC01, AXIN1:p.Ser57Leu, MTC03, CHD8:p.Glu171lys, MTC15, FAT1:p.Val2168s, MTC17, FAT1:p.Glu4283Gln
GO: canonical WNT signaling (including FAT1)	13	39%	6	9%	0.0006	6.67 (2.192-20.92)	META31, FAT1:p.Met1688Ile, TBL1XR1:p.Phe322Leu, META42, SMO:p.Pro560Ala, META52, LRRK2:p.Val1903Glu, META57, APC:p.Phe1838fs, MP1, KDM6A:p.Arg571fs, MED12:p.Gln415Lys, MP11, AXIN1:p.Ser359Arg, MP15, FAT1:p.Ser1568Phe, MP18, KDM6B:p.Ile1022fs, MTC01, AXIN1:p.Ser57Leu, MTC03, CHD8:p.Glu171lys, MTC15, FAT1:p.Val2168s, MTC17, FAT1:p.Glu4283Gln, MTC19, DIXDC1:p.Pro401Arg

Comparative analysis of the mutational frequency of genes affecting selected functional pathways between metaplastic breast cancers with different histologic features

	Metaplastic breast cancers with chondroid metaplasia (n=16)		Metaplastic breast cancers with spindle metaplasia (n=10)		Metaplastic breast cancer with squamous metaplasia (n=9)		Fisher's exact test comparing metaplastic breast cancers with different histologic features			
Pathway	Number of cases with non-synonymous mutation	% of cases with non-synonymous mutation	Number of cases with non-synonymous mutation	% of cases with non-synonymous mutation	Number of cases with non-synonymous mutation	% of cases with non-synonymous mutation	p-value	Metaplastic breast cancers with chondroid metaplasia with non-synonymous mutations	Metaplastic breast cancers with spindle metaplasia with non-synonymous mutations	Metaplastic breast cancers with squamous metaplasia with non-synonymous mutations
KEGG: PI3K/Akt/mTOR	7	44%	7	70%	6	67%	0.3479	META52, K1Tp.Glu188Gly, MP1, PIK3R1.p.Ser620s, MP15, PIK3R1.c.1746-2A-C, RPTOR.p.Arg485Gly, MTC06, IGF1R.p.Tyr1185Asn, MTC11, RPS8B.p.Glu40Asp, MTC13, ERBB4.p.Met222Leu, MTC14, PTEN.p.Asp289Glu	META39, PIK3CA.p.Glu542Lys, META57, PIK3CA.p.His1047Arg, META61, PIK3R1.p.Lys1037Asn, PIK3R1.p.Leu193s, MP17, PIK3CA.p.His1047Arg, MP7, PIK3CA.p.His1047Arg, MTC01, PIK3CA.p.His1047Arg, MTC15, PIK3CA.p.His1047Arg	MTC12, PIK3R1.p.Asp281Val, PTEN.p.Leu112Gln, MTC16, PIK3CA.p.Cys420Arg, PTEN.p.Thr234Ile, PIK3CA.p.Ile1027-G-A, MTC17, PIK3CA.p.His1047Arg, RICTOR.p.Glu40Asp, MTC18, PIK3CA.p.His1047Arg, MTC20, PTEN.c.209+1_209+4delCTAA, MTC23, PIK3CA.p.Glu542Lys
GO: PI3K signaling	3	19%	8	80%	5	56%	0.0065	MP1, PIK3R1.p.Ser620s, MP15, PIK3R1.c.1746-2A-C, MTC06, IGF1R.p.Tyr643Asn, TYRO3.p.Gln84His	META39, PIK3C2B.p.Asp1158Vol, PIK3CA.p.Glu542Lys, META57, PIK3CA.p.His1047Arg, META61, PIK3R1.p.Cys575Asp, MTC07, PIK3CA.p.Lys1037Asn, PIK3CA.p.His1047Arg, MP7, PIK3CA.p.His1047Arg, MTC01, PIK3CA.p.His1047Arg, MTC03, PIK3C2B.p.Lys1268s, MTC15, PIK3CA.p.His1047Arg, PIK3CA.p.Ala876Thr	MTC12, PIK3R1.p.Asp281Val, MTC16, PIK3CA.p.Cys420Arg, MTC17, PIK3CA.p.His1047Leu, MTC18, PIK3CA.p.Ile1027Lys, PIK3CA.p.His1047Arg, MTC23, PIK3CA.p.Glu542Lys
KEGG: canonical WNT signaling	4	25%	4	40%	4	44%	0.6000	META31, EP300.p.Pro870Ser, META52, NKD1.p.Glu299Ala, MTC04, CXXC4.p.Ser189Trp, MTC07, WNT5A.p.Ala167Thr	META39, CUL1.p.Tyr50Asp, FZD7.p.Ile523Val, MYC.p.Gln52Ils, META57, APC.p.Tyr838fs, WNT5A.p.Ala167Pro, MTC01, AXIN1.p.Ser57Leu, MTC03, CHD8.p.Glu1718lys	META40, PORCN.p.Trp305Cys, META42, LRP5.p.Pro1236Leu, MP11, AXIN1.p.Ser359Arg, MTC17, FZD2.p.Ala473Thr
GO: canonical WNT signaling	8	50%	4	40%	4	44%	0.9105	META31, MYH9.p.Ala469Val, TBL1XR1.p.Phe322Leu, META52, LRRK2.p.Val1903Glu, MP1, KDM6A.p.Arg571fs, MED12.p.Gln415Lys, MP18, BCL8L.p.Phe149Leu, WIF1.p.Tyr108Asp, C6CBL1.p.Ile3Val, RYR2.p.Leu308Val, MTC07, LRRK2.p.Ser1036Arg, WNT5A.p.Ala167Thr, MTC13, RYR2.p.Lys3282Gln, MTC19, DDXDC1.p.Pro401Arg	META39, FZD7.p.Ile523Val, MYC.p.Gln52Ils, META57, APC.p.Tyr838s, WNT5A.p.Ala167Pro, MTC01, AXIN1.p.Ser57Leu, MTC03, CHD8.p.Glu1718lys	META40, PORCN.p.Trp305Oys, META42, LRP5.p.Pro1236Leu, SMO.p.Pro560A, MP11, AXIN1.p.Ser359Arg, MTC17, FZD2.p.Ala473Thr, GL11.p.Asp871His

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KEGG: canonical WNT signaling (including FAT1)	5	31%	5	50%	4	44%	0.6741	META31, EP300.p.Pro707Ser, FAT1.p.Met1688ile, META52, TBL1X.p.Glu229Ala, META52, LRRK2.p.Val1903Glu, MP1, KDM6A.p.Arg571fs, META31, FAT1.p.Ser189Trp, MTC04, CXXC4.p.Ser189Trp, MTC07, WNT5A.p.Ala167Thr	META30, CUL1.p.Tyr504Asp, FZD7.p.Lys395Val, MTC01, MP1, META57, APC.p.Phe1838fs, WNT5A.p.Ala31Pro, MTC01, AXIN1.p.Ser57Leu, MTC03, CHD8.p.Glu1718Lys, MTC15, FAT1.p.Val2168fs	META40, PORCN.p.Trp305Cys, META42, LRP5.p.Trp236Leu, MP11, AXIN1.p.Ser59Asn, MTC01, FAT1.p.Glu4283Gln, FZD2.p.Ala473Thr
GO: canonical WNT signaling (including FAT1)	9	56%	5	50%	4	44%	0.9099	META31, FAT1.p.Met1688ile, MYH6.p.Ala1887Val, TBL1X.p.Glu229Ala, META52, LRRK2.p.Val1903Glu, MP1, KDM6A.p.Arg571fs, META31, FAT1.p.Ser189Trp, MTC04, PCLM.p.Phe1498Leu, KDM6A.p.Ile1022fs, MTC06, BCL11.p.Ile3VAl, RYR2.p.Leu308Val, MTC07, LRRK2.p.Ser64Arg, AXIN1.p.Ser57Leu, MTC13, RYR2.p.Lys3282Gln, MTC19, DIXDC1.p.Pro401Arg	META39, FZD7.p.Ile532Val, MED12.p.Gln195Lys, META51, APC.p.Ser1417Phe, MTC01, MP1, AXIN1.p.Ser57Leu, MTC03, CHD8.p.Glu1718Lys, MTC15, FAT1.p.Val2168fs	META40, PORCN.p.Trp305Cys, META42, LRP5.p.Trp236Leu, SMO.p.Phe104Leu, MP11, AXIN1.p.Ser59Asn, MTC01, RYR2.p.Lys3282Gln, FZD2.p.Ala473Thr, GLI1.p.Asp871His

	Metaplastic breast cancers with chondroid metaplasia (n=16)		Metaplastic breast cancers with spindle metaplasia (n=10)		Metaplastic breast cancer with squamous metaplasia (n=9)		Fisher's exact test comparing metaplastic breast cancers with different histologic features with likely pathogenic mutations	Metaplastic breast cancers with chondroid metaplasia with likely pathogenic mutations	Metaplastic breast cancers with spindle metaplasia with likely pathogenic mutations	Metaplastic breast cancers with squamous metaplasia with likely pathogenic mutations	
Pathway	Number of cases with likely pathogenic mutation	% of cases with likely pathogenic mutation	Number of cases with likely pathogenic mutation	% of cases with likely pathogenic mutation	Number of cases with likely pathogenic mutation	% of cases with likely pathogenic mutation	p-value				
KEGG: PI3K/Akt/mTOR	4	25%	7	70%	6	67%	0.0383	MP1, PIK3R1:c.p.Ser652fs, MP15, PIK3R1:c.T174>A>C, MTC13, ERBB4:p.Met322Ile, MTC14, PTEN:p.Asp268Glu	META39, PIK3CA:p.His1047Arg, META61, PIK3R1:p.Leu1039s, PIK3R1:p.Phe456_Gln457dup, MP17, PIK3CA:p.His1047Arg, MP7, PIK3CA:p.His1047Arg, MTC01, PIK3CA:p.His1047Arg, MTC15, PIK3CA:p.His1047Arg	MTC12, PTEN:p.Lys120Ile, PIK3R1:p.Arg231Val, MTC16, PTEN:-1027_1G>A, PTEN:-209>2TC, PIK3CA:p.Cys420Arg, MTC17, PIK3CA:p.His1047Leu, MTC18, PIK3CA:p.His1047Arg, MTC20, PTEN:-209+1_209_4deGTTAA, MTC23, PIK3CA:p.Glu542Lys	
GO: PI3K signaling	2	13%	7	70%	5	56%	0.0088	MP1, PIK3R1:c.p.Ser652fs, MP15, PIK3R1:c.T174>A>C	META39, PIK3CA:p.Glu542Iys, PIK3C2B:p.Asp1158Val, META57, PIK3CA:p.His1047Arg, META61, PIK3R1:p.Leu1039s, PIK3R1:p.Phe456_Gln457dup, MP17, PIK3CA:p.His1047Arg, MP7, PIK3CA:p.His1047Arg, MTC01, PIK3CA:p.His1047Arg, MTC15, PIK3CA:p.His1047Arg, PIK3CG:p.Ala676Thr	MTC12, PIK3R1:p.Asp281Val, MTC16, PIK3C2B:p.Asp1158Arg, MTC17, PIK3CA:p.His1047Arg, MTC18, PIK3CA:p.His1047Arg, PIK3CA:p.Gln372Iys, MTC23, PIK3CA:p.Glu542Lys	
KEGG: canonical WNT signaling	1	6%	3	30%	1	11%	0.2863	META31, EP300:p.Pro870Ser	META37, APC:p.Phe1838fs, MTC01, AXIN1:p.Ser57Leu, MTC03, CHD8:p.Glu1718Lys	MP11, AXIN1:p.Ser359Arg	
GO: canonical WNT signaling	5	31%	3	30%	2	22%	1.0000		META21, TBL1XR1:p.Phe222Leu, META52, LRRK2:p.Val1903Glu, MP1, KDM6A:p.Arg571fs, MED12:p.Gln415Lys, MP18, KDM6A:p.Ile1022fs, MTC19, DIXDC1:p.Pro401Arg	META57, APC:p.Phe1838fs, MTC01, AXIN1:p.Ser57Leu, MTC03, CHD8:p.Glu1718Lys	META42, SMO:p.Pro560Ala, MP11, AXIN1:p.Ser359Arg
KEGG: canonical WNT signaling (including FAT1)	2	13%	4	40%	2	22%	0.2952	META31, FAT1:p.Met1688ile, EP300:p.Pro870Ser, MP15, FAT1:p.Ser1566Phe	META37, APC:p.Phe1838fs, MTC01, AXIN1:p.Ser57Leu, MTC03, CHD8:p.Glu1718Lys, MTC15, FAT1:p.Val2168fs	MP11, AXIN1:p.Ser359Arg, MTC17, FAT1:p.Glu4283Gln	
GO: canonical WNT signaling (including FAT1)	6	38%	4	40%	3	33%	1.0000	TBL1XR1:p.Phe322Leu, META52, LRRK2:p.Val1903Glu, MP1, KDM6A:p.Arg571fs, MED12:p.Gln415Lys, MP15, FAT1:p.Ser1566Phe, MP18, KDM6A:p.Ile1022fs, MTC19, DIXDC1:p.Pro401Arg	META57, APC:p.Phe1838fs, MTC01, AXIN1:p.Ser57Leu, MTC03, CHD8:p.Glu1718Lys, MTC15, FAT1:p.Val2168fs	META42, SMO:p.Pro560Ala, MP11, AXIN1:p.Ser359Arg, MTC17, FAT1:p.Glu4283Gln	

Comparative analysis of clinical and molecular features between MBCs and IDC-NSTs with and without mutations in the PI3K/AKT/mTOR and WNT pathways

	No non-synonymous mutation in PI3K/AKT/mTOR (MBC)	Non-synonymous mutation in PI3K/AKT/mTOR (MBC)	No non-synonymous mutation in PI3K/AKT/mTOR (triple-negative IDC-NST)	Non-synonymous mutation in PI3K/AKT/mTOR (triple-negative IDC-NST)	P-value between MBCs with and without non-synonymous mutation in PI3K/AKT/mTOR	P-value between triple-negative IDC-NSTs with and without non-synonymous mutation in PI3K/AKT/mTOR	P-value between MBCs and triple-negative with non-synonymous mutation in PI3K/AKT/mTOR	P-value between MBCs and triple-negative without non-synonymous mutation in PI3K/AKT/mTOR
pT stage*	T1	5	3	14	2	0.2152	0.4994	0.3894
	T2	9	12	33	11			
	T3	1	5	5	1			
	T4	0	0	1	1			
pN stage*	N0	14	14	35	9	0.6128	0.5396	0.7680
	N1	1	2	14	3			
	N2	0	1	3	2			
	N3	0	2	2	1			
M stage*	M0	14	15	53	15	0.2072	1.0000	0.0570
	M1	1	5	1	0			
Age at diagnosis [median and range]**	48 (34-64)	60.5 (35-82)	51.5 (29-82)	52 (26-82)	0.0048	0.4491	0.2496	0.2655
Tumor size [cm, median and range]**	2.25 (1.1-3.2)	3.55 (1-14)	NA	NA	0.0858	NA	NA	NA

		No likely pathogenic mutation in PI3K/AKT/mTOR (MBC)	Likely pathogenic mutation in PI3K/AKT/mTOR (MBC)	No likely pathogenic mutation in PI3K/AKT/mTOR (triple-negative IDC-NST)	Likely pathogenic mutation in PI3K/AKT/mTOR (triple-negative IDC-NST)	P-value between MBCs with and without likely pathogenic mutation in PI3K/AKT/mTOR	P-value between triple-negative IDC-NSTs with and without likely pathogenic mutation in PI3K/AKT/mTOR	P-value between MBCs and triple-negative with likely pathogenic mutation in PI3K/AKT/mTOR	P-value between MBCs and triple-negative without likely pathogenic mutation in PI3K/AKT/mTOR
pT stage*	T1	6	2	15	1	0.1102	0.2012	0.3396	0.9378
	T2	11	10	33	11				
	T3	1	5	5	1				
	T4	0	0	1	1				
N0		16	12	36	8				
N1		1	2	14	3	0.6000	0.1780	0.3060	0.1531

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M stage*	N2	0	1	3	2				
	N3	1	1	2	1				
M0	16	13	54	14		0.4018	1.0000	0.1075	0.1484
M1	2	4	1	0					
Age at diagnosis (median and range)**	49 (34-64)	62 (35-82)	51 (29-82)	54.5 (26-82)	0.0199	0.3664	0.3929	0.5819	
Tumor size (cm, median and range)**	2.25 (1-4)	3.55 (1.4-14)	NA	NA	0.1021	NA	NA	NA	

	No non-synonymous mutation in WNT (MBC)	Non-synonymous mutation in WNT (MBC)	No non-synonymous mutation in WNT (triple-negative IDC-NST)	No non-synonymous mutation in WNT (triple-negative IDC-NST)	P-value between MBCs with and without non-synonymous mutation in WNT	P-value between triple-negative IDC-NSTs with and without non-synonymous mutation in WNT	P-value between MBCs and triple-negative with non-synonymous mutation in WNT	P-value between MBCs and triple-negative without non-synonymous mutation in WNT
pT stage*	T1	4	4	13	3	0.6499	0.1466	0.2914
	T2	9	12	33	11			
	T3	4	2	4	2			
	T4	0	0	0	2			
pN stage*	N0	12	16	29	15	0.6869	0.3816	0.6868
	N1	2	1	13	4			
	N2	1	0	5	0			
	N3	1	1	3	0			
M stage*	M0	11	18	49	19	0.0076	1.0000	0.0007
	M1	6	0	1	0			
Age at diagnosis (median and range)**	52 (34-78)	54.5 (37-82)	51.5 (26-82)	54 (35-82)	0.8429	0.2853	0.9515	0.5117
Tumor size (cm, median and range)**	3.05 (1.1-14)	2.85 (1.7-8)	NA	NA	0.4984			

	No likely pathogenic mutation in WNT (MBC)	Likely pathogenic mutation in WNT (MBC)	No likely pathogenic mutation in WNT (triple-negative IDC-NST)	Likely pathogenic mutation in WNT (triple-negative IDC-NST)	P-value between MBCs with and without likely pathogenic mutation in WNT	P-value between triple-negative IDC-NSTs with and without likely pathogenic mutation in WNT	P-value between MBCs and triple-negative with likely pathogenic mutation in WNT	P-value between MBCs and triple-negative without likely pathogenic mutation in WNT
pT stage*	T1	5	3	14	2	0.5525	0.2548	0.4405
	T2	12	9	41	3			
	T3	5	1	6	0			
	T4	0	0	1	1			
pN stage*	N0	17	11	39	5	1.0000	1.0000	0.3858
	N1	2	1	16	1			
	N2	1	0	5	0			
	N3	1	1	3	0			
M stage*	M0	16	13	62	6	0.0645	1.0000	0.0010
	M1	6	0	1	0			
Age at diagnosis (median and range)**	51.5 (34-78)	50 (37-82)	51 (26-82)	62 (45-82)	0.3219	0.0232	0.3125	0.6370
Tumor size (cm, median and range)**	3 (1-14)	3 (1.4-7.8)	NA	NA	0.8376			

Comparative analysis of pathologic parameters between MBCs with and without mutations in the PI3K/AKT/mTOR and WNT pathways													
	No non-synonymous mutation in PI3K/AKT/mTOR	Non-synonymous mutation in PI3K/AKT/mTOR	P-value between cases with and without non-synonymous mutation in PI3K/AKT/mTOR	No likely pathogenic mutation in PI3K/AKT/mTOR	Likely pathogenic mutation in PI3K/AKT/mTOR	P-value between cases with and without likely pathogenic mutation in PI3K/AKT/mTOR	No non-synonymous mutation in WNT	Non-synonymous mutation in WNT	P-value between cases with and without non-synonymous mutation in WNT	No likely pathogenic mutation in WNT	Likely pathogenic mutation in WNT	P-value between cases with and without likely pathogenic mutation in WNT	
Histologic grade (n=35)*	2	1	4	0.3650	2	3	0.6581	2	3	1.0000	4	1	0.6300
	3	14	16		16	14		15	15	18	12		
Tubule formation (n=34)*	2	2	1	0.5555	3	0	0.2273	1	2	2	3	1.0000	
	3	12	19		14	17		15	16	19	12		
Nuclear grade (n=34)*	2	0	2	0.5009	1	1	1.0000	2	0	2	0	0.5134	
	3	14	18		16	16		14	18	19	13		
Mitotic index (n=34)*	1-2	3	10	0.1529	5	8	0.4813	6	7	8	5	1.0000	
	3	11	10		12	9		10	11	13	8		
Borders (n=33)*	Infiltrating	6	11		8	9		9	8	11	6	0.8282	
	Pushing	3	4	0.9002	4	3	1.0000	2	5	4	3	0.9002	
	Mixed	4	5		4	5		5	4	5	4		
Necrosis (n=34)*	Absent	4	7	1.0000	6	5	1.0000	5	6	7	4	1.0000	
	Present	10	13		11	12		11	12	14	9		
Necrosis (n=34)**	(%)	7.5 (0-60)	17.5 (0-60)	0.7344	5 (0-60)	20 (0-60)	0.3425	10 (0-60)	7.5 (0-60)	0.9159	10 (0-60)	10 (0-40)	0.8282
Lymphocyte infiltration (n=34)*	None	0	3		0	3		2	1	3	0		
	Mild	7	13		10	10		11	9	14	6	0.0768	
	Moderate	6	3	0.1699	6	3	0.2681	3	6	4	5		
Stromal TILs (n=34, median and range)**	Intense	1	1		1	1		0	2	0	2		
	(%)	15 (0-40)	5 (0-50)	0.1658	10 (0-40)	5 (0-50)	0.5063	5 (0-30)	10 (0-50)	0.3013	5 (0-30)	20 (1-50)	0.0175
% metaplastic element (n=34, median and range)**	Chondroid	30 (0-95)	0 (0-60)	0.0380	30 (0-95)	0 (0-60)	0.0206	0 (0-95)	15 (0-80)	0.5226	15 (0-95)	0 (0-80)	0.6798
	Osteos	0 (0-20)	0 (0-35)	0.9638	0 (0-20)	0 (0-35)	1.0000	0 (0-9)	0 (0-35)	0.1898	0 (0-35)	0 (0-20)	0.7944
	Spindle	0 (0-100)	2.5 (0-100)	0.6084	0 (0-100)	5 (0-100)	0.5377	0 (0-95)	5 (0-100)	0.5370	0 (0-95)	10 (0-100)	0.2819
	Squamous	0 (0-85)	2.5 (0-100)	0.0817	0 (0-85)	5 (0-100)	0.0425	2.5 (0-100)	0 (0-100)	0.1612	0 (0-100)	0 (0-100)	0.9032
	Epithelioid	17.5 (0-70)	2.5 (0-85)	0.2091	20 (0-70)	0 (0-85)	0.0968	10 (0-85)	12.5 (0-70)	0.9295	20 (0-85)	10 (0-70)	0.4135
	Rhabdoid	0 (0-0)	0 (0-10)	0.4372	0 (0-0)	0 (0-10)	0.3466	0 (0-10)	0 (0-0)	0.3165	0 (0-10)	0 (0-0)	0.4677