

Supplementary Table S6: Comparative analysis of the mutational frequencies in genes affecting selected functional pathways in metaplastic 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. *: Fisher's exact test. **: 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, FGF1, FGF2, FGF3, FGF4, GRB2, HIF1A, HRAS, IGF1R, IRS1, KIT, MTOC, NRAS, PDGFR, PDGFRB, PIK3CA, PIK3CB, PIK3R1, PRKCA, PRKCB, PRKCG, PTEN, RICTOR, RPS6KB1, RPTOR, SOS1, TSC1, TSC2
GO: PI3K signaling	Gene Ontology	GO:0014065 - phosphatidylinositol 3-kinase signaling	C1QB, EDN1, ERBB2, ERBB3, GATA3, HTR2A, HTR2B, IGF1, IGF1R, IRS1, LTK, NFK1, NYAP1, NYAP2, PIK3CA, PIK3CB, 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, CSNK2A1, CSNK2A2, CSNK2B, CTBP1, CTBP2, CTNBB1, CTNNB1P1, CUL1, CXXC4, DKR1, DKK2, DKK4, DVL1, DVL2, DVL3, EP300, FOSL1, FRAT1, FRAT2, FZD1, FZD10, FZD2, FZD3, FZD4, FZD5, FZD6, FZD7, FZD8, FZD9, GSK3B, JUN, LEF1, LOC400927-CSNK1E, LRP5, LRP6, MMP7, MYC, NDK1, NDC2, PORCN, PPAR, 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, WNT5B, WNT5, WNT7A, WNT7B, WNT8A, WNT8B, WNT9A, WNT9B
GO: canonical WNT signaling	Gene Ontology	GO:0060070 - canonical WNT signaling pathway	APC, AXIN1, BCL9, BCL9L, CCND1, CDC42, CDH15, CHD8, CTNNB1, DISC1, DIXDC1, DVL1, DVL1P1, DVL2, DVL3, EGF, FGF8, FZD1, FZD10, FZD2, FZD3, FZD4, FZD5, FZD7, FZD8, FZD9, GLI1, GSK3B, HOXB8, KDM6A, KLF4, LEF1, LRP5, LRP6, LRP6, LRRK2, MED12, MYC, MYH6, NDR, NKX2-5, NR4A2, OTULIN, PORCN, PRCOF1, PSEN1, PTK7, PTPFRJ, PYGO2, RARG, RYK, RYR2, SDC1, SFRP1, SHH, SMO, SNAI2, SOX17, SOX4, STK11, T, TBL1X, TBL1X1, TCF7, TCF7L1, TCF7L2, UBE2B, WNT1, WNT10B, WNT11, WNT2, WNT2B, WNT3, WNT3A, WNT4, WNT5A, WNT7A, WNT7B, WNT8A, WNT8B, WNT9A, WNT9B
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, DMC1, DNA2, EME1, EME2, ERCC4, EXO1, FAM175A, FAN1, FANCA, FANCB, FANCC, FANCD2, FANCF, FANCG, FANCI, FANCL, FANCLM, FIGL1, GEN1, H2AFX, HELQ, KAT5, MDC1, MRE11A, MUS81, NBN, NBN, PALB2, PASH1, PASHA, POLN, RADI1, RADI7, RADS5, RADS1, RADS1AP1, RAD51B, RAD51C, RAD51D, RAD52, RAD54L, RAD54, RBBP8, RECQL, REV1, RIF1, RMI1, RMI2, RNF168, RNF169, RNF4, RNF41, RPA2, RPA3, RTEL1, SETMAR, TOPBP1, TSG1, SFP1, SHFM1, SLX1A, SLX1B, SLX4, SMC1A, SMC3, SMC5, SMDR, TIMELESS, TIPIN, TOPBP1, TP53BP1, UIMC1, USP1, USP11, WRN, XRCC2, XRCC3

Comparative analysis of the mutational frequencies of genes affecting selected functional pathways between metaplastic breast cancers and triple-negative IDC-NSTs.						
Pathway	Metaplastic breast cancers (n=35)		Triple-negative IDC-NSTs (n=69)		Fisher's exact test comparing metaplastic breast cancers to triple-negative IDC-NSTs	
	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)
GO: PI3K signaling	16	46%	18	26%	0.0500	2.365 (1-5.736)
KEGG: canonical WNT signaling	12	34%	13	19%	0.0939	2.229 (0.8653-5.739)
GO: canonical WNT signaling	16	46%	18	26%	0.0500	2.365 (1-5.736)
KEGG: canonical WNT signaling (including FAT1)	14	40%	14	20%	0.0381	2.593 (1.01-6.958)
GO: canonical WNT signaling (including FAT1)	18	51%	19	28%	0.0189	2.757 (1.103-6.673)

Comparative analysis of the mutational frequencies of genes affecting selected functional pathways between metaplastic breast cancers with likely pathogenic mutations and triple-negative IDC-NSTs.						
Pathway	Metaplastic breast cancers with likely pathogenic mutations (n=35)		Triple-negative IDC-NSTs with likely pathogenic mutations (n=69)		Fisher's exact test comparing metaplastic breast cancers with likely pathogenic mutations to triple-negative IDC-NSTs with likely pathogenic mutations	
	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)
KEGG: PI3K/Akt/mTOR	17	49%	14	20%	0.0058	3.658 (1.508-9.337)
GO: PI3K signaling	14	40%	13	19%	0.0320	2.84 (1.088-7.22)
KEGG: canonical WNT signaling	5	14%	2	3%	0.0414	5.482 (1.071-40.87)
GO: canonical WNT signaling	10	29%	5	7%	0.0064	5.028 (1.567-16.68)
KEGG: canonical WNT signaling (including FAT1)	8	23%	3	4%	0.0063	6.387 (1.541-29.95)
GO: canonical WNT signaling (including FAT1)	13	37%	6	9%	0.0008	6.077 (2.026-18.76)

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.						
Pathway	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	
	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)

GO: PI3K signaling	14	42%	18	26%	0.1136	2.072 (0.8306-5.181)	META39, PIK3C2B.p.Asp1158Val, PIK3CA.p.Glu542Lys, META57, PIK3CA.p.His1047Arg, META61, PIK3R1.p.Phe456_Gln457dup, PIK3R1.p.Leu193fs, MP1, PIK3R1.p.Ser652fs, MP15, PIK3R1.c.1746-2A-C, MP17, PIK3CA.p.His1047Arg, MP7, PIK3CA.p.His1047Arg, MTC01, PIK3CA.p.His1047Arg, MTC03, PIK3C2G.p.Glu172Gln, META57, PIK3R1.p.Tyr643Asn, TYR03.p.Gln84His, MTC12, PIK3R1.p.Asp281Val, MTC15, PIK3CA.p.His1047Arg, PIK3C2C.p.Ala676Thr, MTC16, PIK3CA.p.Cys420Arg, MTC17, PIK3CA.p.His1047Arg
KEGG: canonical WNT signaling	12	36%	13	19%	0.0835	2.438 (0.9453-6.253)	META31, EP300.p.Pro870Ser, META39, CUL1.p.Tyr50Asp, FZD7.p.Ile532Val, MYC.p.Gln52His, META40, PORCN.p.Trp305Cys, META42, LRP5.p.Pro1236Leu, META52, NKD1.p.Glu299Ala, META57, APC.p.Phe1838fs, WNT5A.p.Ala31Pro, MP11, AXIN1.p.Ser57Leu, MTC03, CHD8.p.Glu1718Lys, MTC04, CXXC4.p.Ser189Trp, MTC07, WNT5A.p.Ala167Thr, MTC17, FZD2.p.Ala473Thr
GO: canonical WNT signaling	16	48%	18	26%	0.0422	2.639 (1.101-6.654)	META31, MYH6.p.Ala1887Val, TBL1XR1.p.Phe322Leu, META39, FZD7.p.Ile532Val, MYC.p.Gln52His, META40, PORCN.p.Trp305Cys, META42, LRP5.p.Pro1236Leu, META52, NKD1.p.Glu299Ala, META57, APC.p.Phe1838fs, WNT5A.p.Ala31Pro, MP11, AXIN1.p.Ser57Leu, MTC03, CHD8.p.Glu1718Lys, MTC06, BCL9L.p.Ile3Val, RYR2.p.Leu308Val, MTC07, LRRK2.p.Ser1036Arg, WNT5A.p.Ala167Thr, MTC13, RYR2.p.Lys3282Gln, MTC17, FZD2.p.Ala473Thr, GLI1.p.Asp87His, MTC19, DIXDC1.p.Pro401Arg
KEGG: canonical WNT signaling (including FAT1)	14	42%	14	20%	0.0315	2.862 (1.095-7.362)	META31, EP300.p.Pro870Ser, FAT1.p.Met1688Ile, META39, CUL1.p.Tyr50Asp, FZD7.p.Ile532Val, MYC.p.Gln52His, META40, PORCN.p.Trp305Cys, META42, LRP5.p.Pro1236Leu, META52, NKD1.p.Glu299Ala, META57, APC.p.Phe1838fs, WNT5A.p.Ala31Pro, MP11, AXIN1.p.Ser57Leu, MTC03, CHD8.p.Glu1718Lys, MTC04, CXXC4.p.Ser189Trp, MTC07, WNT5A.p.Ala167Thr, MTC15, FAT1.p.Val2168fs, MTC17, FAT1.p.Glu4283Gln, FZD2.p.Ala473Thr
GO: canonical WNT signaling (including FAT1)	18	55%	19	28%	0.0147	3.119 (1.272-7.954)	META31, FAT1.p.Met1688Ile, MYH6.p.Ala1887Val, TBL1XR1.p.Phe322Leu, META39, FZD7.p.Ile532Val, MYC.p.Gln52His, META40, PORCN.p.Trp305Cys, META42, LRP5.p.Pro1236Leu, META52, NKD1.p.Glu299Ala, META57, APC.p.Phe1838fs, WNT5A.p.Ala31Pro, MP11, AXIN1.p.Ser57Leu, MTC03, CHD8.p.Glu1718Lys, MTC06, BCL9L.p.Ile3Val, RYR2.p.Leu308Val, MTC07, LRRK2.p.Ser1036Arg, WNT5A.p.Ala167Thr, MTC13, RYR2.p.Lys3282Gln, MTC15, FAT1.p.Val2168fs, MTC17, FAT1.p.Glu4283Gln, FZD2.p.Ala473Thr, GLI1.p.Asp87His, MTC19, DIXDC1.p.Pro401Arg

Pathway	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		Metaplastic breast cancers of triple-negative phenotype with likely pathogenic mutations
	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)	
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.Leu193fs, PIK3R1.p.Phe456_Gln457dup, MP1, PIK3R1.p.Leu193fs, MP1, PIK3R1.c.1746-2A-C, MP17, PIK3CA.p.His1047Arg, MTC12, PTEN.p.Leu112Gln, PIK3R1.p.Asp281Val, MTC13, ERBB4.p.Met322Ile, MTC14, PTEN.p.Asp268Glu, MTC15, PIK3CA.p.His1047Arg, MTC16, PTEN.c.1027-1G>A, PTEN.c.209+2T>C, PIK3CA.p.Cys420Arg, MTC17, PIK3CA.p.His1047Arg, 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, PIK3C2B.p.Asp1158Val, META57, PIK3CA.p.His1047Arg, META61, PIK3R1.p.Leu193fs, PIK3R1.p.Phe456_Gln457dup, MP1, PIK3R1.p.Ser652fs, MP15, PIK3R1.c.1746-2A-C, MP17, PIK3CA.p.His1047Arg, MP7, PIK3CA.p.His1047Arg, MTC01, PIK3C2G.p.Glu172Gln, META57, PIK3R1.p.Tyr643Asn, TYR03.p.Gln84His, MTC12, PIK3R1.p.Asp281Val, MTC15, PIK3CA.p.His1047Arg, PIK3C2C.p.Ala676Thr, MTC16, PIK3CA.p.Cys420Arg, MTC17, PIK3CA.p.His1047Arg
KEGG: canonical WNT signaling	5	15%	2	3%	0.0345	5.865 (1.141-43.83)	META31, EP300.p.Pro870Ser, META57, APC.p.Phe1838fs, MP11, AXIN1.p.Ser359Arg, MTC01, AXIN1.p.Ser57Leu, MTC03, CHD8.p.Glu1718Lys
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.Arg57fs, MED12.p.Gln415Lys, MP11, AXIN1.p.Ser359Arg, MP18, KDM6A.p.Ile1022fs, MTC01, AXIN1.p.Ser57Leu, MTC03, CHD8.p.Glu1718Lys, 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.Pro870Ser, META57, APC.p.Phe1838fs, MP11, AXIN1.p.Ser359Arg, MP15, FAT1.p.Ser1566Phe, MTC01, AXIN1.p.Ser57Leu, MTC03, CHD8.p.Glu1718Lys, MTC15, FAT1.p.Val2168fs, 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.Arg57fs, MED12.p.Gln415Lys, MP11, AXIN1.p.Ser359Arg, MP15, FAT1.p.Ser1566Phe, MP18, KDM6A.p.Ile1022fs, MTC01, AXIN1.p.Ser57Leu, MTC03, CHD8.p.Glu1718Lys, MTC15, FAT1.p.Val2168fs, 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.										
Pathway	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	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
	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			
KEGG: PI3K/Akt/mTOR	7	44%	7	70%	6	67%	0.3479	META52, KIT.p.Glu198Gly, MP1, PIK3R1.p.Ser652fs, MP15, PIK3R1.c.1746-2A-C, RPTOR.p.Asp86Gly, MTC06, IGF1R.p.Tyr643Asn, MTC11, RPS8K81.p.Glu454Asp, MTC13, ERBB4.p.Met322Ile, MTC14, PTEN.p.Asp268Glu	META39, PIK3CA.p.Glu542Lys, META57, PIK3CA.p.His1047Arg, META61, PIK3R1.p.Phe456_Gln457dup, PIK3R1.p.Leu193fs, 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.c.209+2T>C, PTEN.c.1027-1G>A, MTC17, PIK3CA.p.His1047Arg, MP7, PIK3CA.p.His1047Arg, MTC20, PTEN.c.209+1_209+4delGTAA, MTC23, PIK3CA.p.Glu542Lys
GO: PI3K signaling	3	19%	8	80%	5	56%	0.0065	MP1, PIK3R1.p.Ser652fs, MP15, PIK3R1.c.1746-2A-C, MTC06, IGF1R.p.Tyr643Asn, TYR03.p.Gln84His	META39, PIK3C2B.p.Asp1158Val, PIK3CA.p.Glu542Lys, META57, PIK3CA.p.His1047Arg, META61, PIK3R1.p.Phe456_Gln457dup, PIK3R1.p.Leu193fs, MP17, PIK3CA.p.His1047Arg, MP7, PIK3CA.p.His1047Arg, MTC01, PIK3CA.p.His1047Arg, MTC03, PIK3C2G.p.Glu172Gln, MTC15, PIK3CA.p.His1047Arg, PIK3C2C.p.Ala676Thr	MTC12, PIK3R1.p.Asp281Val, MTC16, PIK3CA.p.Cys420Arg, MTC17, PIK3CA.p.His1047Arg, MTC18, PIK3CA.p.Gln72Lys, 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.Ile532Val, MYC.p.Gln52His, META57, APC.p.Phe1838fs, WNT5A.p.Ala31Pro, 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, MYH6.p.Ala1887Val, TBL1XR1.p.Phe322Leu, META52, LRRK2.p.Val1903Glu, MP1, KDM6A.p.Arg57fs, MP18, BCL9L.p.Ile1022fs, MTC06, KDM6A.p.Ile1022fs, MTC06, BCL9L.p.Ile3Val, RYR2.p.Leu308Val, MTC07, LRRK2.p.Ser1036Arg, WNT5A.p.Ala167Thr, MTC13, RYR2.p.Lys3282Gln, MTC19, DIXDC1.p.Pro401Arg	META39, FZD7.p.Ile532Val, MYC.p.Gln52His, META57, APC.p.Phe1838fs, WNT5A.p.Ala31Pro, MTC01, AXIN1.p.Ser57Leu, MTC03, CHD8.p.Glu1718Lys	META40, PORCN.p.Trp305Cys, META42, LRP5.p.Pro1236Leu, SMO.p.Pro560Ala, MP11, AXIN1.p.Ser359Arg, MTC17, FZD2.p.Ala473Thr, GLI1.p.Asp87His

KEGG: canonical WNT signaling (including FAT1)	5	31%	5	50%	4	44%	0.6741	META31, EP300.p.Pro870Ser, FAT1.p.Met1688Ile, META52, NCO1.p.Glu299Ala, MP15, FAT1.p.Ser1566Phe, MTC04, CXCKC4.p.Ser189Trp, MTC07, WNT5A.p.Ala167Thr	META39, CUL1.p.Tyr50Asp, FZD7.p.Ile532Val, MYC.p.Gln52His, 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.Pro1238Leu, MP11, AXIN1.p.Ser359Arg, MTC17, 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, TBL1XR1.p.Phe322Leu, META52, LRRK2.p.Val1903Glu, MP1, KDM6A.p.Arg571fs, MED12.p.Gln415Lys, MP15, FAT1.p.Ser1566Phe, MP18, BCL9L.p.Phe1498Leu, KDM6A.p.Ile1022fs, MTC06, BCL9L.p.Ile9Val, RYR2.p.Leu308Val, MTC07, LRRK2.p.Ser1098Arg, WNT5A.p.Ala167Thr, MTC13, RYR2.p.Lys3282Gln, MTC19, DDXDC1.p.Pro401Arg	META39, FZD7.p.Ile532Val, MYC.p.Gln52His, 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.Pro1238Leu, SMO.p.Pro560Ala, MP11, AXIN1.p.Ser359Arg, MTC17, FAT1.p.Glu4283Gln, FZD2.p.Ala473Thr, GLI1.p.Asp871His

Pathway	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
	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				
KEGG: PI3K/Akt/mTOR	4	25%	7	70%	6	67%	0.0383	MP1, PIK3R1.p.Ser652fs, MP15, PIK3R1.c.1746-2A>C, MTC13, ERBB4.p.Met322Ile, MTC14, PTEN.p.Asp268Glu	META39, PIK3CA.p.Glu542Lys, META57, PIK3CA.p.His1047Arg, META61, PIK3R1.p.Leu193fs, PIK3R1.p.Phe456_Gln457dup, MP17, PIK3CA.p.His1047Arg, MP7, PIK3CA.p.His1047Arg, MTC01, PIK3CA.p.His1047Arg, MTC15, PIK3CA.p.His1047Arg	MTC12, PTEN.p.Leu112Gln, PIK3R1.p.Asp281Val, MTC16, PTEN.c.1027-1G>A, PTEN.c.209+2T>C, PIK3CA.p.Cys420Arg, MTC17, PIK3CA.p.His1047Leu, MTC18, PIK3CA.p.His1047Arg, MTC20, PTEN.c.209+1_209+delGTA, MTC23, PIK3CA.p.Glu542Lys
GO: PI3K signalling	2	13%	7	70%	5	56%	0.0088	MP1, PIK3R1.p.Ser652fs, MP15, PIK3R1.c.1746-2A>C	META39, PIK3CA.p.Glu542Lys, PIK3C2B.p.Asp1158Val, META57, PIK3CA.p.His1047Arg, META61, PIK3R1.p.Leu193fs, 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, PIK3CA.p.Cys420Arg, MTC17, PIK3CA.p.His1047Leu, MTC18, PIK3CA.p.His1047Arg, MTC20, PIK3CA.p.Glu542Lys
KEGG: canonical WNT signaling	1	6%	3	30%	1	11%	0.2863	META31, EP300.p.Pro870Ser	META57, 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	META31, TBL1XR1.p.Phe322Leu, META52, LRRK2.p.Val1903Glu, MP1, KDM6A.p.Arg571fs, MED12.p.Gln415Lys, MP18, KDM6A.p.Ile1022fs, MTC19, DDXDC1.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	META57, APC.p.Phe1838fs, MTC01, AXIN1.p.Ser57Leu, MTC03, CHD8.p.Glu1718Lys, 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	META31, FAT1.p.Met1688Ile, TBL1XR1.p.Phe322Leu, META52, LRRK2.p.Val1903Glu, MP1, KDM6A.p.Arg571fs, MED12.p.Gln415Lys, MP15, FAT1.p.Ser1566Phe, MP18, KDM6A.p.Ile1022fs, MTC19, DDXDC1.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			
	N0	14	14	35	9			
pN stage*	N1	1	2	14	3	0.6128	0.5396	0.7680
	N2	0	1	3	2			
	N3	0	2	2	1			
N 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
	T2	11	10	33	11			
	T3	1	5	5	1			
	T4	0	0	1	1			
	N0	16	12	36	8			
pN stage*	N1	1	2	14	3	0.6860	0.4770	0.7863
	N2	0	1	3	2			

