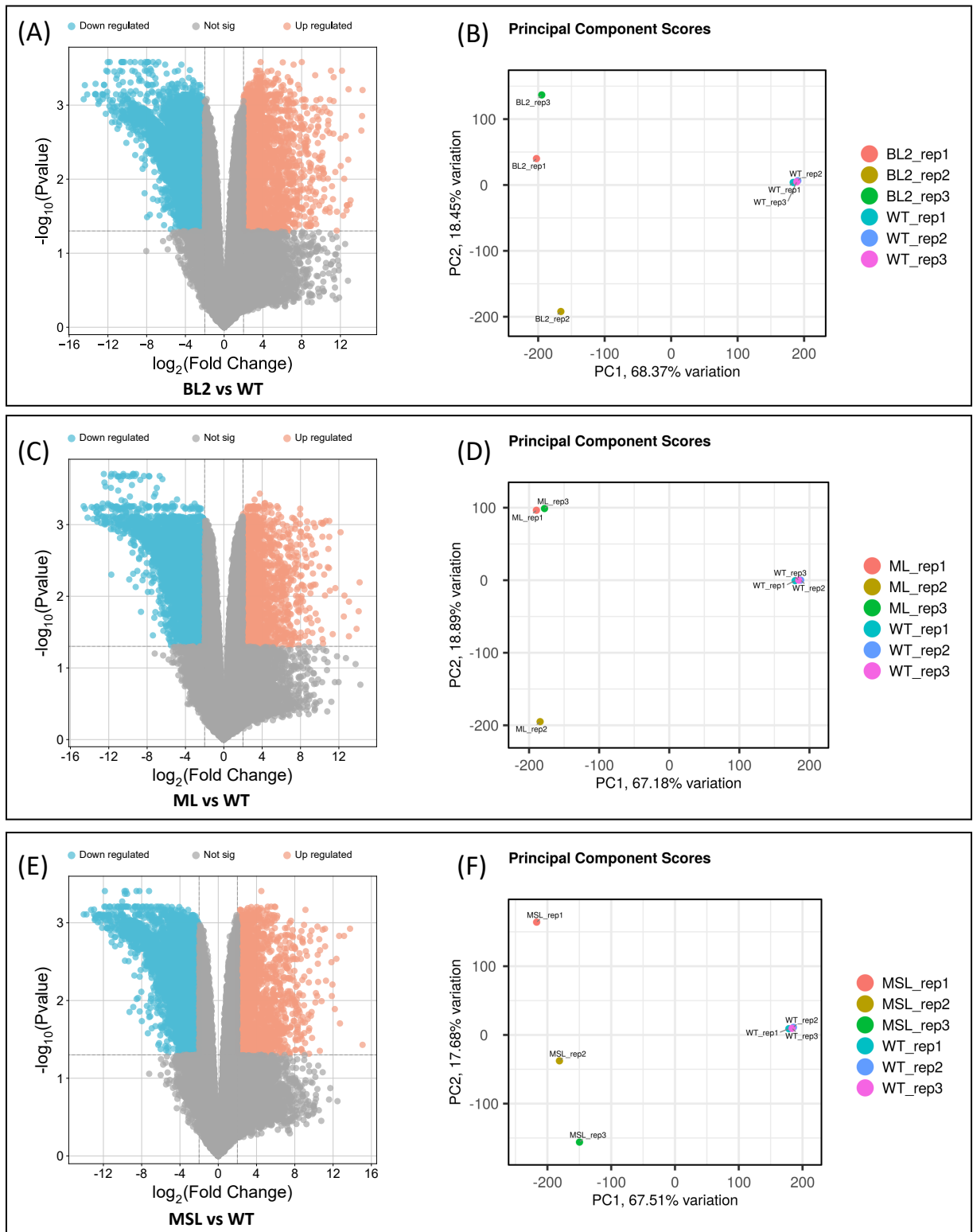
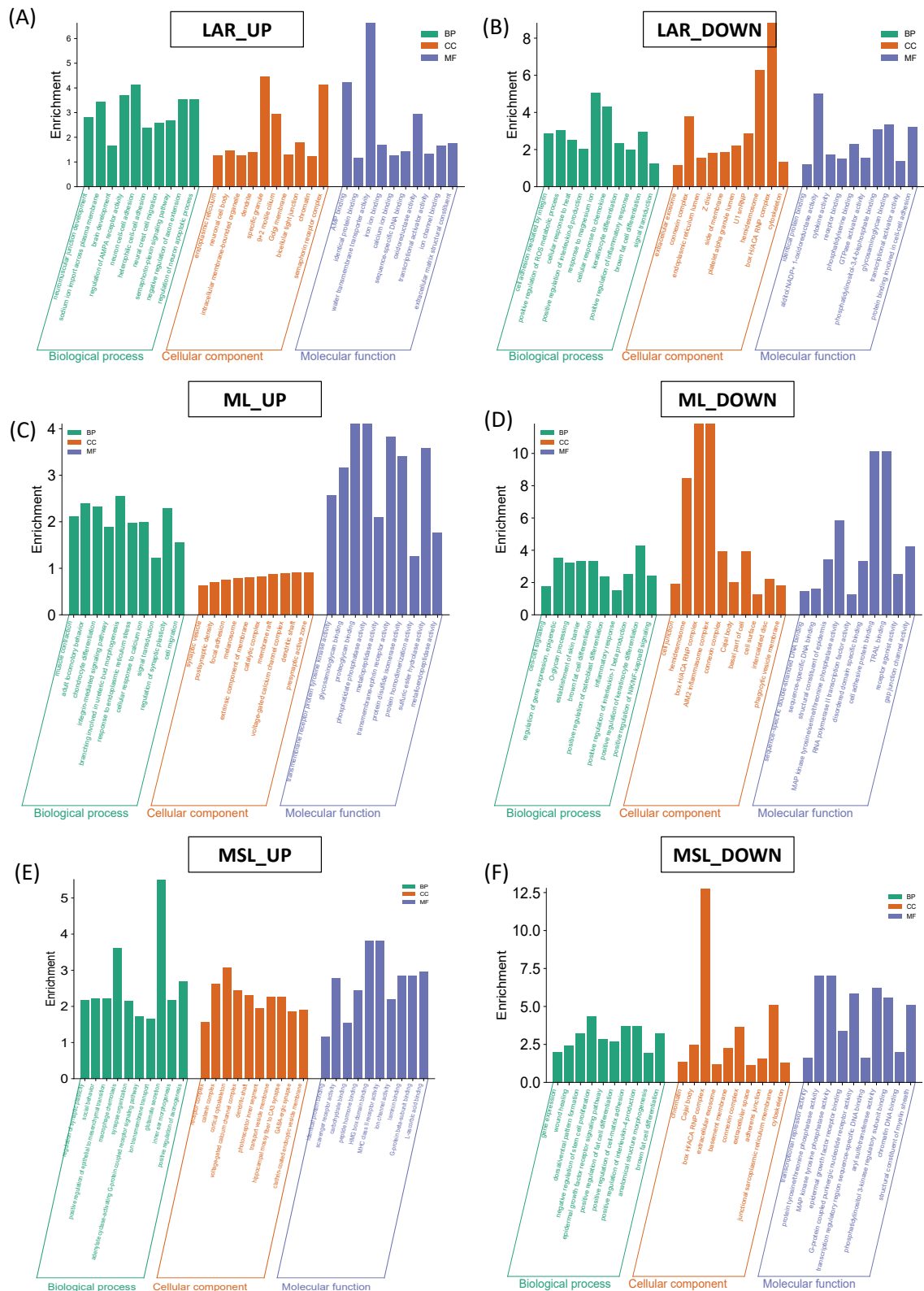
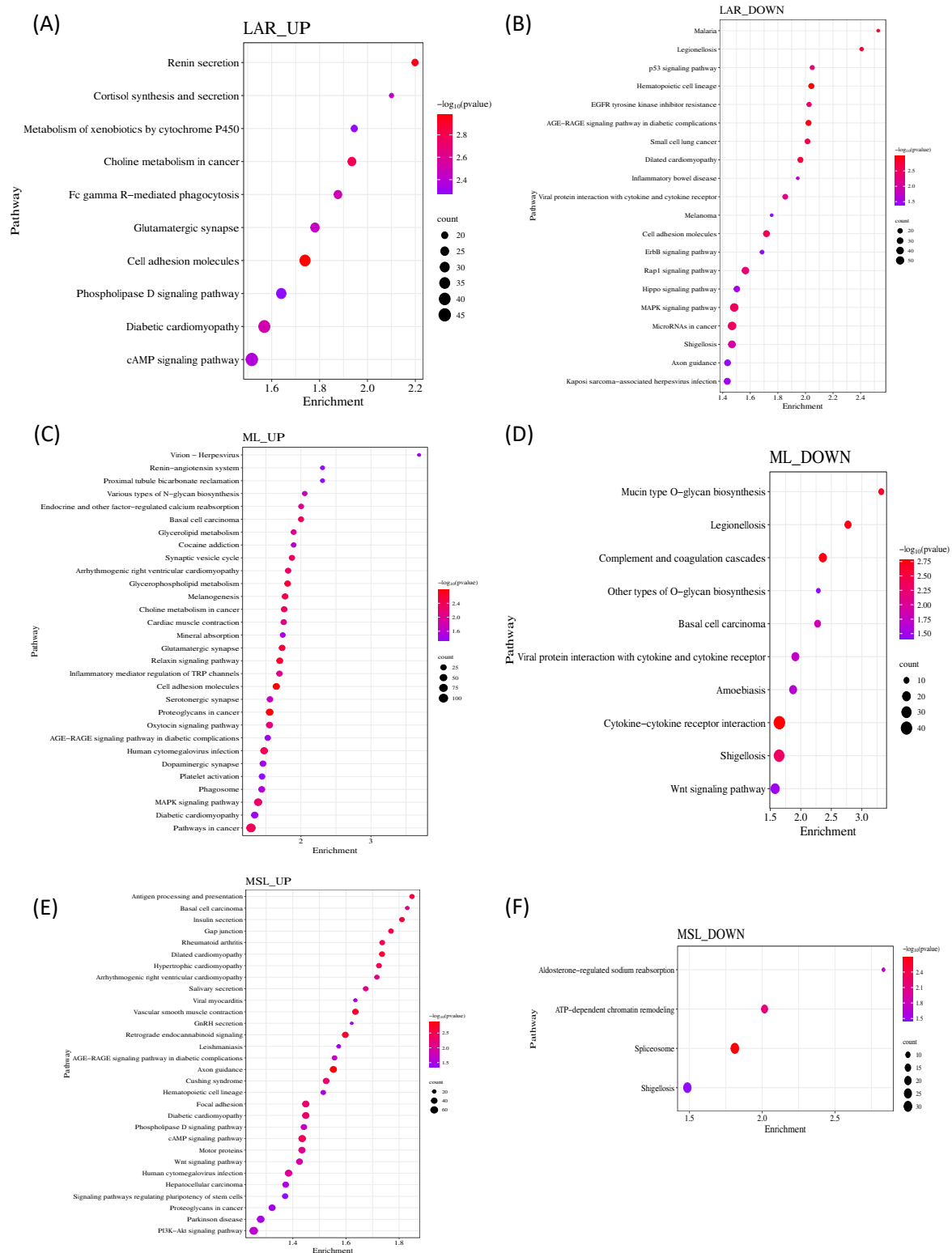




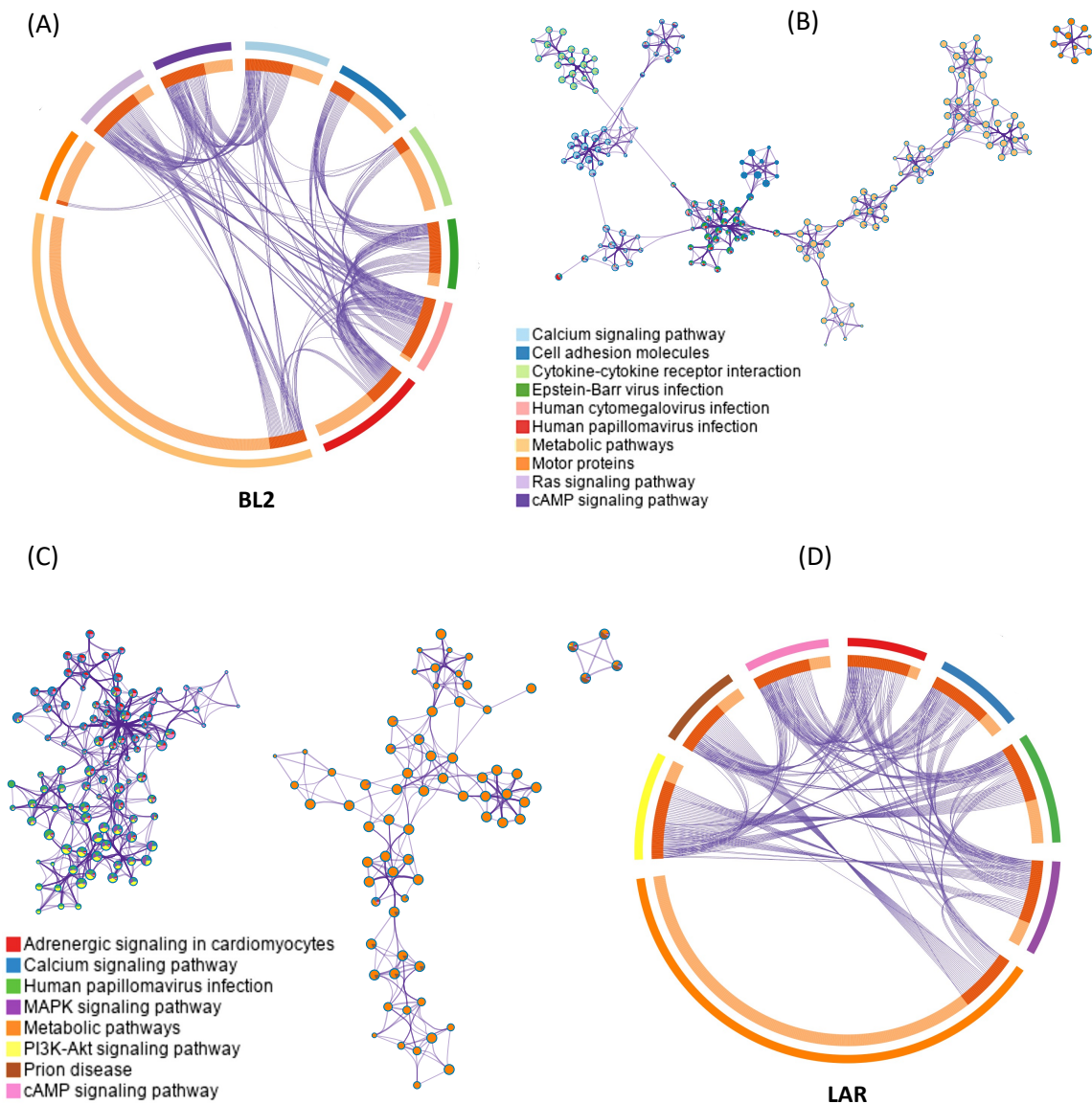
Supplementary Fig. S1 Volcano plots and PCA plots of differential expression between; (A and B) normal breast epithelia cell line and Basal like 2, (C and D) normal breast epithelia cell line and Mesenchymal like, (E and F) normal breast epithelia cell line and Mesenchymal stem like TNBC subtype.



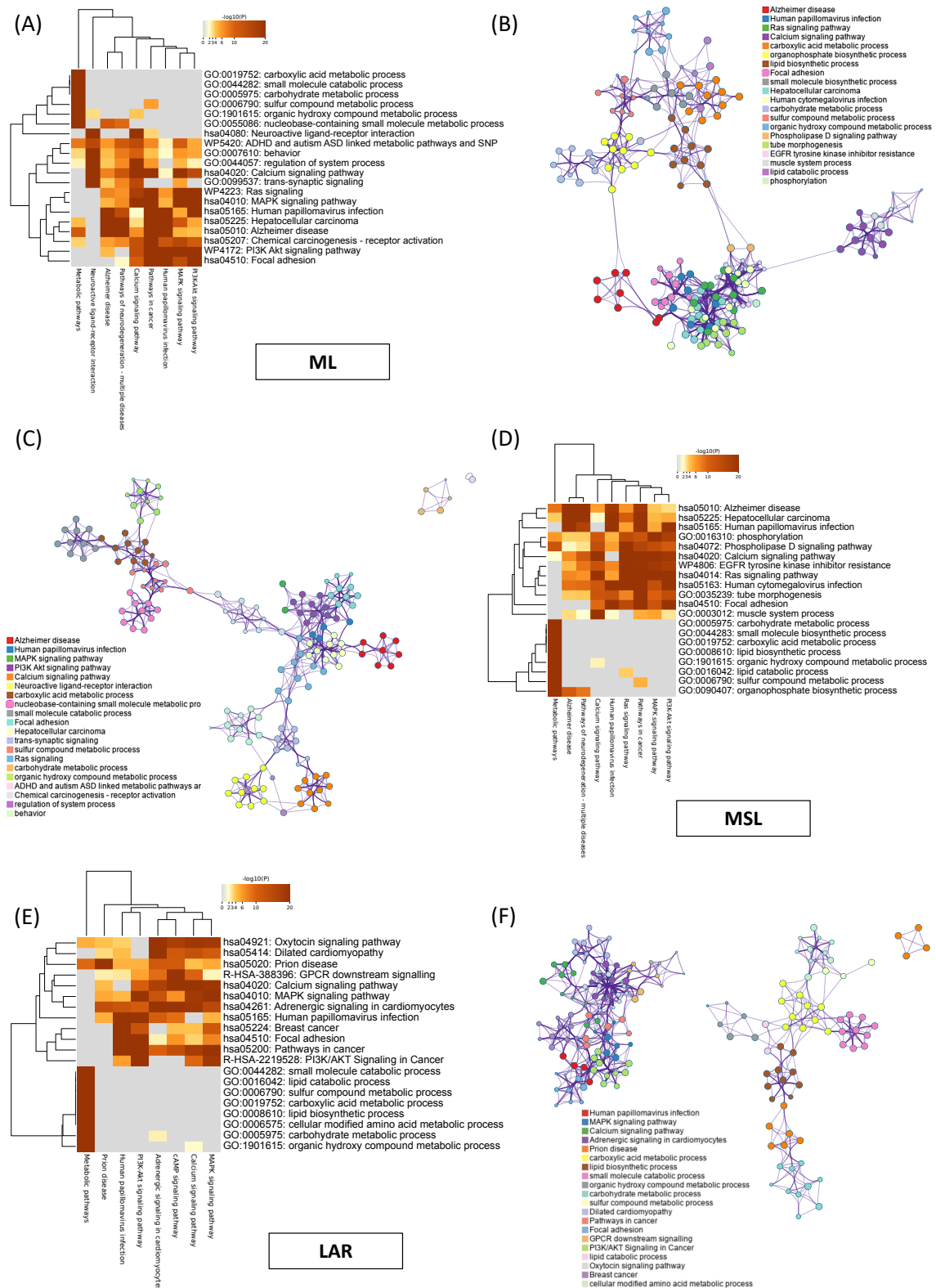
Supplementary Fig. S2 Gene ontology reports on differentially over expressed genes (DOEGs) and differentially under expressed genes (DUEGs) of (A and B) Luminal androgen receptor subtype, (C and D) Mesenchymal-like subtype, (E and F) Mesenchymal stem like subtype.



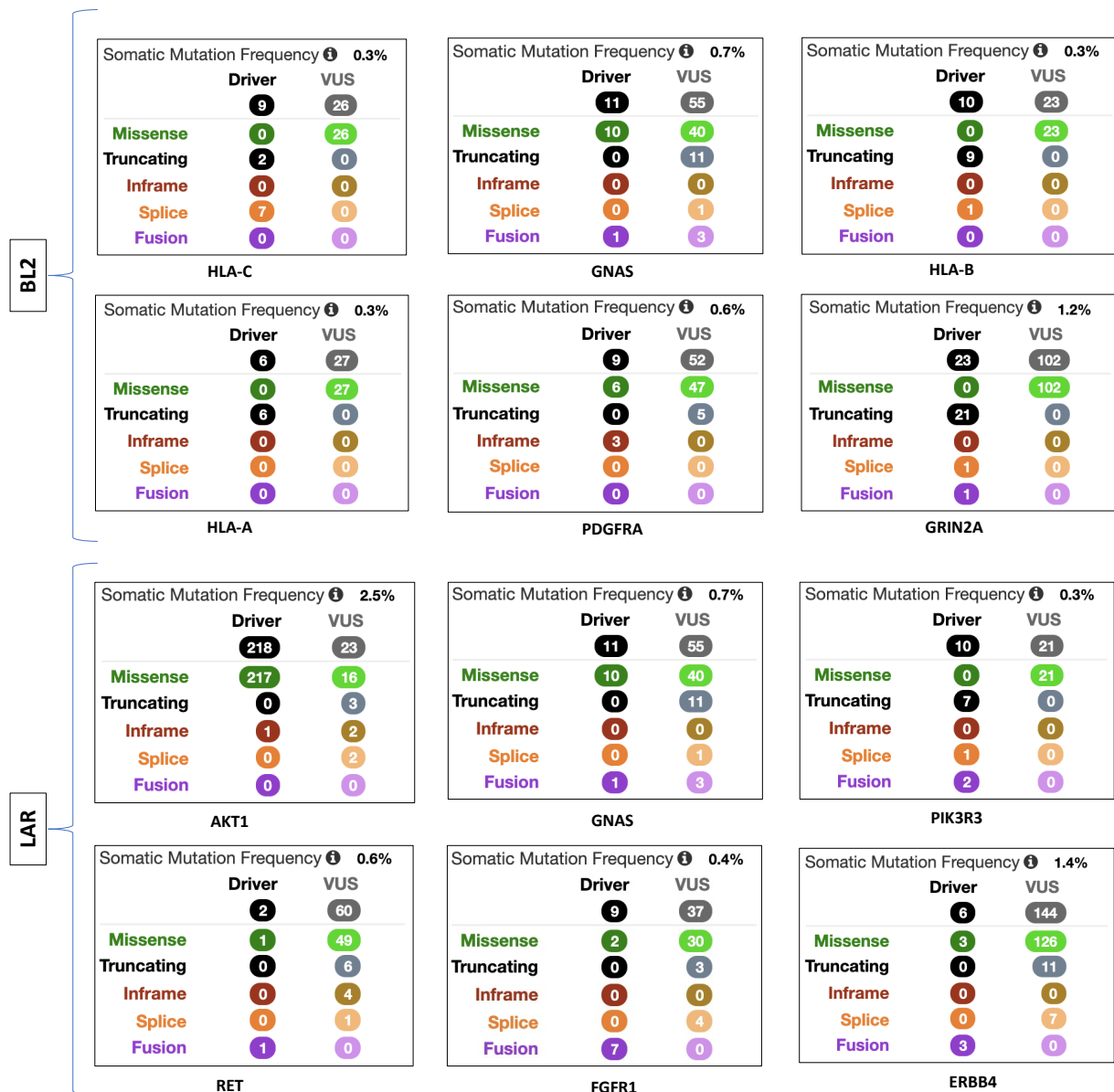
Supplementary Fig. S3 KEGG Pathway enrichment reports on differentially over expressed genes (DOEGs) and differentially under expressed genes (DUEGs) of (A and B) Luminal androgen receptor, (C and D) Mesenchymal like, (E and F) Mesenchymal stem like TNBC subtype.



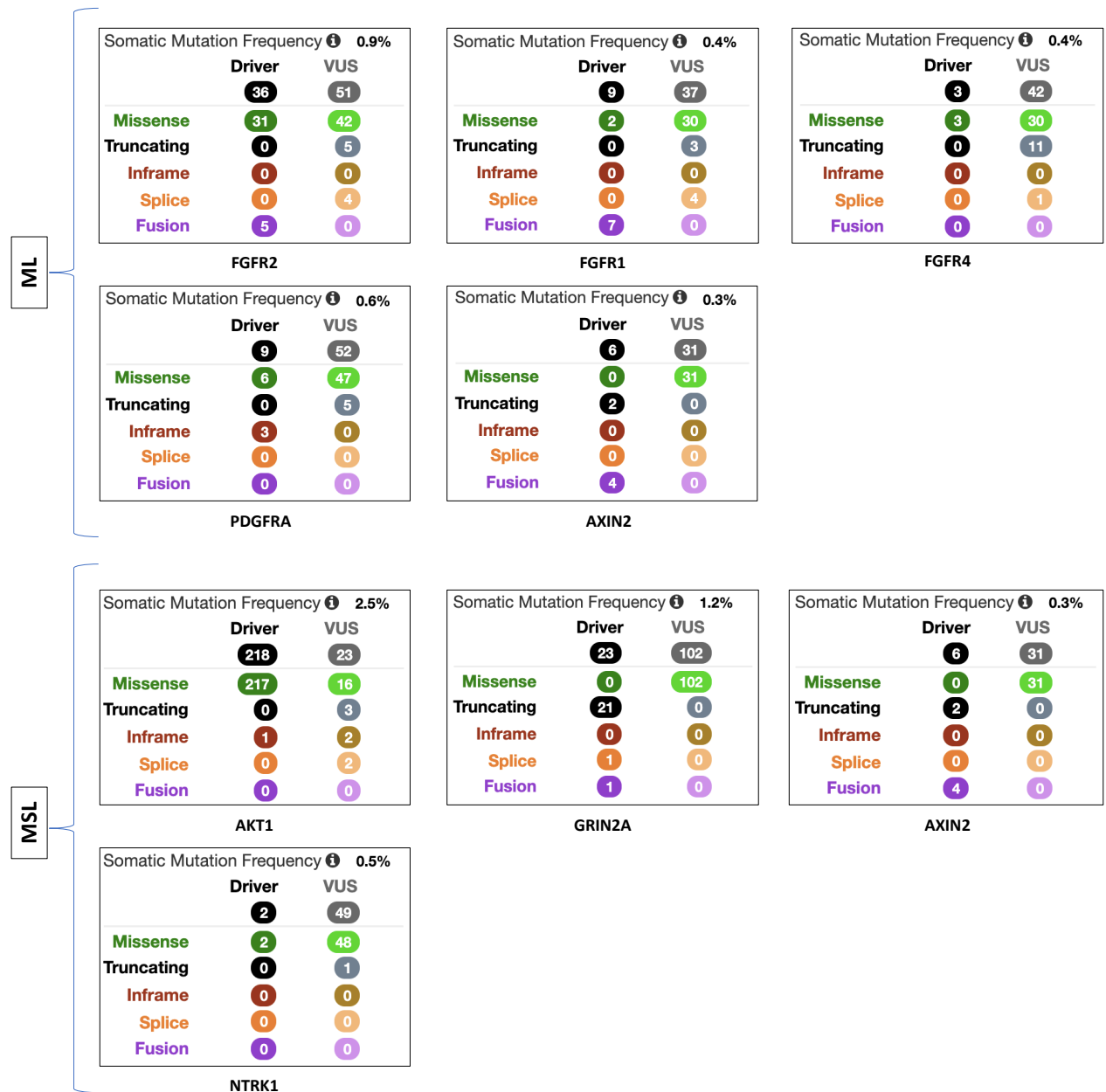
Supplementary Fig. S4 Identification of pathways connected with common set of genes and interconnected network clusters report: (A and D) Circos plot represent the upregulated pathways connected with common set of genes in the BL2 and LAR subtype respectively, (B and C) Enriched pathway network represented by small pie charts indicating their connection with each other where the color code represents the identities of pathways in BL2 and LAR subtype respectively.



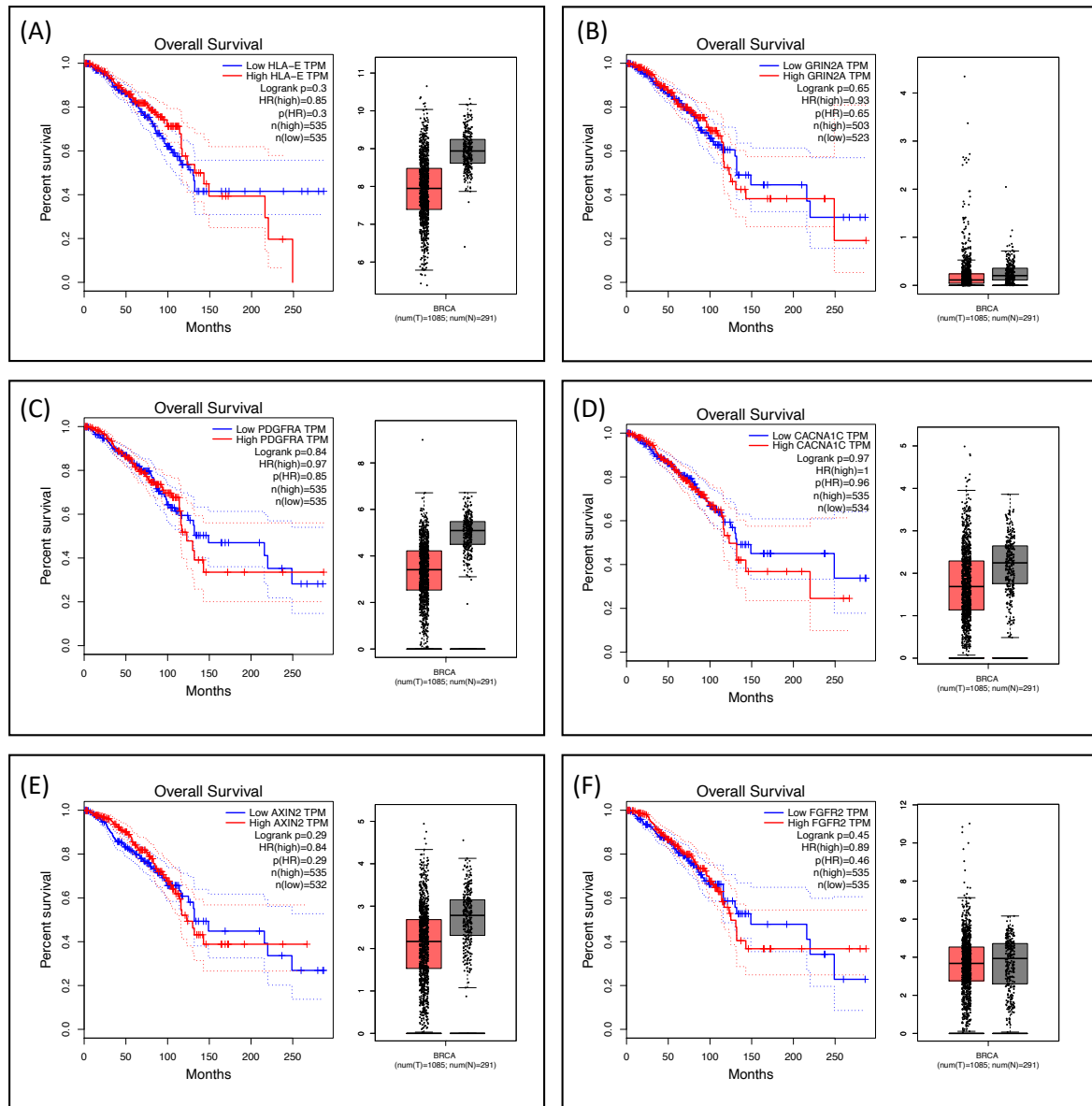
Supplementary Fig. S5 Identification of connected GOs and network clusters with top 10% pathways of (A and B) Mesenchymal like, (C and D) Mesenchymal stem like, and (E and F) Luminal androgen receptor TNBC subtypes respectively.



Supplementary Fig. S6 Alteration frequency of the candidate genes with somatic driver mutations in the BL2 and LAR TNBC subtype.



Supplementary Fig. S6 (continued) Alteration frequency of the candidate genes with somatic driver mutations in the ML and MSL TNBC subtype.



Supplementary Fig. S7 Survivability analysis and gene level expression report of driver mutated candidate genes; (A) HLA-E, (B) GRIN2A, (C) PDGFRA, (D) CACNA1C, (E) AXIN2, and (F) FGFR2.

Original id	Calcium Signaling pathway	Cell adhesion molecules	Cytokine cytokine receptor interaction	Human papillomavirus infection	MAPK signaling pathway	Metabolic pathways	Neuroactive ligand receptor interaction	PI3K Akt signaling pathway	Ras signaling pathway	cAMP signaling pathway	TOTAL
PIK3CD	0	0	0	1	0	1	0	1	1	1	5
MAPK3	0	0	0	1	1	0	0	1	1	1	5
PRKACA	1	0	0	1	1	0	0	0	1	1	5
MAP2K2	0	0	0	1	1	0	0	1	1	1	5
EGF	1	0	0	1	1	0	0	1	1	0	5
NGF	1	0	1	0	1	0	0	1	1	0	5
FLT4	1	0	0	0	1	0	0	1	1	0	4
NGFR	0	0	1	0	1	0	0	1	1	0	4
FGFR4	1	0	0	0	1	0	0	1	1	0	4
VEGFB	1	0	0	0	1	0	0	1	1	0	4
FGF17	1	0	0	0	1	0	0	1	1	0	4
FGF19	1	0	0	0	1	0	0	1	1	0	4
PDGFB	1	0	0	0	1	0	0	1	1	0	4
PDGFRA	1	0	0	0	1	0	0	1	1	0	4
IKBKG	0	0	0	1	1	0	0	1	1	0	4
FGF21	1	0	0	0	1	0	0	1	1	0	4
NTRK2	1	0	0	0	1	0	0	1	1	0	4
FGFR2	1	0	0	0	1	0	0	1	1	0	4
GRIN1	1	0	0	0	0	0	1	0	1	1	4
CALML6	1	0	0	0	0	0	0	0	1	1	3
EFNA2	0	0	0	0	1	0	0	1	1	0	3
TNF	0	0	1	1	1	0	0	0	0	0	3
NFATC1	1	0	0	0	1	0	0	0	0	1	3
CREB3L1	0	0	0	1	0	0	0	1	0	1	3
GRIN2D	1	0	0	0	0	0	1	0	0	1	3
RET	1	0	0	0	1	0	0	1	0	0	3
ERBB3	1	0	0	0	1	0	0	1	0	0	3
ERBB4	1	0	0	0	1	0	0	1	0	0	3
PLA2G4F	0	0	0	0	1	1	0	0	1	0	3
PRKCG	1	0	0	0	1	0	0	0	1	0	3
PLA2G4B	0	0	0	0	1	1	0	0	1	0	3

Supplementary Table. S1 List of top 5% of genes have been selected which appeared as a common set of genes (candidate genes) involved in the top 10% pathways in the BL1 TNBC subtype.

Names	total	elements
BL1 BL2 MSL	1	MYC
BL2 ML MSL	1	FLI1
BL1 BL2	2	RFXANK, HIVEP2
BL1 MSL	1	MYCN
BL2 MSL	1	NFKBIA
LAR MSL	1	TWIST1
BL1	1	IRF3
BL2	1	STAT1
LAR	6	STAT6, ETS1, CEBPB, AR, ETS2, MYB
ML	3	CEBPA, HOXB7, SATB1
MSL	1	TFAP2A

Supplementary Table. S2 List of common and unique pathway specific dysregulated transcription factors among the TNBC subtypes.

Target Genes	Antineoplastic Drugs	Repurposing Drugs	Uncategorized Drugs
ERBB4	LAPATINIB	PALIPERIDONE	AFATINIB DIMALEATE
	DACOMITINIB ANHYDROUS		ACALABRUTINIB
	GEFITINIB		CURCUMIN
	AFATINIB		
	DASATINIB ANHYDROUS		
	NERATINIB		
	TUCATINIB		
	IBRUTINIB		
	VANDETANIB		
	ERLOTINIB		
FGFR4	ERLOTINIB	METHOTREXATE	ERDAFITINIB
	PONATINIB	EVEROLIMUS	INFIGRATINIB PHOSPHATE
	NINTEDANIB ESYLATE		CYCLOPHOSPHAMID E ANHYDROUS
	PALIFERMIN		INFIGRATINIB
			FUTIBATINIB
			FLUOROURACIL
AKT1	RESVERATROL	EVEROLIMUS	NELFINAVIR
	VEMURAFENIB	DESIPRAMINE	CAPIVASERTIB
	TOPOTECAN HYDROCHLORIDE	CLOMIPRAMINE	
	DABRAFENIB	DOXEPIN HYDROCHLORIDE	
	FULVESTRANT	TRIMIPRAMINE	
	NINTEDANIB ESYLATE	LOVASTATIN	
		NORTRIPTYLINE	
		AMITRIPTYLINE HYDROCHLORIDE	
		TRIFLUOPERAZINE	
ERBB3	GEFITINIB		SELUMETINIB
	LAPATINIB		CURCUMIN
	CETUXIMAB		MOMELOTINIB
	TRAMETINIB DIMETHYL SULFOXIDE		CARBOPLATIN
	VANDETANIB		

	ERLOTINIB		
	PERTUZUMAB		
	TRASTUZUMAB		
	DOCETAXEL ANHYDROUS		
	MARGETUXIMAB		
	AFATINIB		
	DACOMITINIB ANHYDROUS		
HLA-B	THALIDOMIDE	ETANERCEPT	PEGINTERFERON ALFA-2B
	PEGINTERFERON ALFA-2A	METHAZOLAMIDE	STAVUDINE
	PAZOPANIB	FOSPHENYTOIN	MINOCYCLINE
	INTERFERON BETA-1A	CARBAMAZEPINE	FLOXACILLIN
	LAPATINIB	CARBIMAZOLE	ABACAVIR
		ACETAZOLAMIDE	PENICILLIN G POTASSIUM
		INFLIXIMAB	DAPSONE
		CLOZAPINE	ISONIAZID
		SULFASALAZINE	RIBAVIRIN
		CLAVULANIC ACID	PENICILLIN V
		PHENYTOIN SODIUM	AMOXICILLIN ANHYDROUS
		TICLOPIDINE	CLINDAMYCIN
		METHIMAZOLE	LAMIVUDINE
		OXCARBAZEPINE	
GNAS		AMITRIPTYLINE HYDROCHLORIDE	FLUOROURACIL
		MIFEPRISTONE	NICLOSAMIDE
			TRIACETIN
			CISPLATIN
PIK3R3			ALPELISIB
			COPANLISIB
			INFIGRATINIB
			QUERCETIN

Supplementary Table. S3 List of drugs inhibiting potential marker genes

MARKER GENE	DRUGS	Docking Score	Ligand rmsd (Å)	Number of H-bonds	Number of hydrophobic interactions
ERBB3	GEFITINIB	-156.89	30	3	
	CETUXIMAB	-322.66	65.24		
	LAPATINIB	-174.49	54.85	3	2
	AFATINIB	-170.89	45.99	6	2
	DACOMITINIB ANHYDROUS	-161.97	31.36	2	3
	DOCETAXEL ANHYDROUS	-240.4	29.33	4	5
	ERLOTINIB	-157.12	59.71	3	1
	TRAMETINIB DIMETHYL SULFOXIDE	-171.43	142.22	3	1
	VANDETANIB	-167.5	33.15	3	1
	PERTUZUMAB	-341.81	110.64		
	TRASTUZUMAB	-317.89	159.15		
ERBB4	LAPATINIB	-170.48	45.18	2	11
	DACOMITINIB ANHYDROUS	-154.91	46.76		2
	GEFITINIB	-145.46	45.43	3	3
	AFATINIB	-161.03	62.99	3	4
	DASATINIB ANHYDROUS	-149.26	47.41		2
	NERATINIB	-184.62	48.68	4	6
	TUCATINIB	-169.76	46.82	3	6
	IBRUTINIB	-154.18	47.88	1	2
	VANDETANIB	-151.36	49.15	4	2
	ERLOTINIB	-149.67	47.32	1	3
AKT1	RESVERATROL	-135.97	48.9	2	4
	VEMURAFENIB	-209.49	45.29	3	7
	TOPOTECAN HYDROCHLORIDE	-215.57	33.72	1	2
	DABRAFENIB	-211.67	59.53	3	3
	FULVESTRANT	-208.98	34.84	1	14
	NINTEDANIB ESYLATE	-225.47	37.86	3	5
EGFR4	ERLOTINIB	-136	31.83		4

	PONATINIB	-156.64	39.84	2	5
	NINTEDANIB ESYLATE	-152.84	21.35	2	2
	PALIFERMIN	-240.81	74.72		
HLA-B	THALIDOMIDE	-148.24	95.12	2	1
	PEGINTERFERON ALFA-2A	-278.86	157.72		
	PAZOPANIB	-181.97	136.4	3	7
	INTERFERON BETA-1A	-259.41	89.85		
	LAPATINIB	-194.42	102.27	1	4

Supplementary Table. S4 Docking score, Ligand RMSD and number of interacting bonds in protein-drug docking complex

Target gene	miRNA	Experiment(s)	Reference - PMID
ERBB3	hsa-miR-125a-5p	Luciferase reporter assay, Northern blot, qRT-PCR, Western blot	17110380
	hsa-miR-125a-5p	Luciferase reporter assay, Microarray, Western blot	20864407
	hsa-miR-125a-5p	Western blot, qRT-PCR	23519125
	hsa-miR-125b-5p	Luciferase reporter assay, Northern blot, qRT-PCR, Western blot	17110380
	hsa-miR-125b-5p	Immunoblot, Immunohistochemistry, Luciferase reporter assay, qRT-PCR	23146892
	hsa-miR-125b-5p	Western blot, qRT-PCR	23519125
	hsa-miR-143-5p	Luciferase reporter assay, qRT-PCR, Western blot	25248370
	hsa-miR-199a-5p	Immunoblot, Immunohistochemistry, Luciferase reporter assay, qRT-PCR	23146892
	hsa-miR-205-5p	Luciferase reporter assay, Reporter assay;Other	19238171
	hsa-miR-205-5p	Luciferase reporter assay	20065103
	hsa-miR-205-5p	Luciferase reporter assay, qRT-PCR, Western blot	19276373
	hsa-miR-205-5p	Luciferase reporter assay, Microarray, Western blot	20864407
	hsa-miR-205-5p	Western blot, qRT-PCR	23519125
	hsa-miR-22-3p	Luciferase reporter assay, qRT-PCR, Western blot	22484852

ERBB4	hsa-miR-146a-5p	Luciferase reporter assay, Microarray, Western blot	20864407
	hsa-miR-146a-5p	Luciferase reporter assay, Northern blot	23619365
	hsa-miR-146b-5p	Luciferase reporter assay	27400799
	hsa-miR-193a-3p	Luciferase reporter assay, qRT-PCR, Western blot	24469061
	hsa-miR-19a-3p	Luciferase reporter assay, Microarray	19885849
	hsa-miR-302b-3p	Luciferase reporter assay, qRT-PCR, Western blot	24438167
	hsa-miR-302d-3p	Luciferase reporter assay, Microarray	19885849
	hsa-miR-372-3p	Luciferase reporter assay, Microarray	19885849
PIK3R3	hsa-miR-132-3p	Luciferase reporter assay, qRT-PCR, Western blot	26252738
	hsa-miR-148b-3p	Western blot, Luciferase reporter assay,	24632606
	hsa-miR-152-3p	Luciferase reporter assay, qRT-PCR, Western blot	26820128
	hsa-miR-193a-5p	Luciferase reporter assay, qRT-PCR, Western blot	24469061
	hsa-miR-7-5p	ELISA, Luciferase reporter assay, qRT-PCR, Western blot	23135998
AKT1	hsa-miR-100-5p	Luciferase reporter assay, Microarray, qRT-PCR, Western blot	23724047
	hsa-miR-105-5p	Luciferase reporter assay, Western blot	25280563
	hsa-miR-10b-5p	qRT-PCR, Western blot	27347488
	hsa-miR-125a-5p	qRT-PCR, Western blot	26622553
	hsa-miR-125b-5p	qRT-PCR, Western blot	18649363
	hsa-miR-126-3p	qRT-PCR, Western blot	26659078
	hsa-miR-133b	Luciferase reporter assay, qRT-PCR, Western blot	25414595
	hsa-miR-138-5p	Immunohistochemistry, Luciferase reporter assay, Western blot	28122142
	hsa-miR-143-3p	Luciferase reporter assay, qRT-PCR, Western blot	23104321
	hsa-miR-149-3p	Luciferase reporter assay, qRT-PCR, Western blot, Reporter assay; Western blot; qRT-PCR; Other	20623644
	hsa-miR-184	Luciferase reporter assay	27666871
	hsa-miR-185-3p	Luciferase reporter assay MTT	26617940
	hsa-miR-192-5p	Western blot	26351877
	hsa-miR-196b-5p	Flow, qRT-PCR, Western blot	26998071
	hsa-miR-19a-3p	qRT-PCR, Western blot	25400827

	hsa-miR-19a-3p	qRT-PCR, Western blot	25914465
	hsa-miR-206	qRT-PCR, Western blot	28386239
	hsa-miR-22-3p	Luciferase reporter assay, Western blot	26364720
	hsa-miR-302a-3p	Luciferase reporter assay	23185040
	hsa-miR-302b-3p	Luciferase reporter assay	23185040
	hsa-miR-302c-3p	Luciferase reporter assay	23185040
	hsa-miR-302d-3p	Luciferase reporter assay	23185040
	hsa-miR-340-5p	Western blot	28057912
	hsa-miR-34a-5p	Flow, qRT-PCR, Western blot	27073535
	hsa-miR-374b-5p	Luciferase reporter assay, Microarray, qRT-PCR, Western blot	26100275
	hsa-miR-382-3p	qRT-PCR, Western blot, Immunostaining	26636539
	hsa-miR-409-3p	Luciferase reporter assay, qRT-PCR, Western blot	26631969
	hsa-miR-451a	qRT-PCR, Western blot	20816946
	hsa-miR-4689	Luciferase reporter assay, qRT-PCR	25756961
	hsa-miR-494-3p	Immunofluorescence, Immunohistochemistry, qRT-PCR, Western blot	25662849
	hsa-miR-495-3p	Luciferase reporter assay, qRT-PCR, Western blot	27323412
	hsa-miR-542-3p	Immunohistochemistry, Luciferase reporter assay, Western blot	26286747
	hsa-miR-637	Immunohistochemistry, In situ hybridization, Western blot, Luciferase reporter assay	25597410
	hsa-miR-708-5p	Flow, qRT-PCR, Western blot	23754151
	hsa-miR-99a-5p	Luciferase reporter assay	25187230
	hsa-miR-99a-5p	Luciferase reporter assay	27158364
AXIN2	hsa-miR-107	Luciferase reporter assay	21501592
	hsa-miR-1246	Immunofluorescence, Luciferase reporter assay, qRT-PCR	27639189
	hsa-miR-15b-5p	Luciferase reporter assay	21501592
	hsa-miR-16-5p	Luciferase reporter assay	21501592
	hsa-miR-34a-3p	Luciferase reporter assay, Western blot	22421157
	hsa-miR-34a-5p	Luciferase reporter assay	19336450
	hsa-miR-34b-5p	Luciferase reporter assay, Western blot	22421157
	hsa-miR-34c-3p	Luciferase reporter assay, Western blot	22421157
	hsa-miR-374a-3p	Luciferase reporter assay, qRT-PCR, Western blot	26617789

	hsa-miR-582-3p	Luciferase reporter assay, qRT-PCR, Western blot, RNA immunoprecipitation, TOP/FOP luciferase assay	26468775
--	----------------	--	----------

Supplementary Table. S5 List of miRNA regulating potential marker genes

TNBC subtypes	Previous studies	Focus of study	Data used	Key findings	Our findings relevant to previous studies
Basal Like 1	Green et al., 2016 (British journal of cancer)	The functional role of MYC and c-MYC between molecular subtypes of BCs.	Large-scale transcriptomic data (METABRIC RNA) (RNA from fresh frozen tumors (n ≈ 1980)) and protein expression (IHC in Nottingham cohort, n= 1106) data to study MYC gene and protein expression in breast cancer (ER+, HER2+, TNBC subtypes, and invasive BC).	Higher tumor grade and the basal-like phenotype were linked to elevated MYC expression.	Our analysis indicates that MYC was downregulated in both basal-like (BL1 and BL2) TNBC subtypes.
	Kim et al., 2016 (BMC cancer)	Determining the prognostic value of ERBB4 gene expression in patients with triple negative breast cancer	Retrospective clinical data with FFPE tissue-based IHC and NanoString gene expression profiling of HER-family/ESR1 genes in invasive breast cancer (Stage I–IIIC, including TNBC) to evaluate associations with prognosis.	Increased expression of ERBB4 is linked to a poor prognosis based on survival analysis, according to the investigation of the expression profiles of the HER family genes in TNBC tissue specimens. ERBB4 expression is found to be a predictor of long-term prognosis in TNBC patients.	From our study, we anticipate that the ERBB4/PDGFRα signalling axis may serve as a significant area of study in the future. ERBB4 might be used as a marker gene and an essential part of therapeutic applications for patients suffering from BL1 TNBC subtype.

	Lyu et al., 2023 (Cancer Cell International)	Identifying HER3 as an effective therapeutic target in triple negative breast cancer	Human breast cancer cell lines: SKBR3, MDA-MB-468, HCC70, HCC1806, MDA-MB-231, HCC1937, BT549, Hs578T, TNBC xenografts in athymic nude mice, and 125 TNBC patient tissue microarrays to test the efficacy of a novel anti-HER3 monoclonal antibody (4A7), alone and in combination with paclitaxel, against TNBC tumor growth, metastasis, and HER3-driven signaling.	The overall survival (OS) and relapse-free survival (RFS) of TNBC patients with high HER3 mRNA expression in their tumours were considerably worse than those with low HER3 expression, according to analyses of TCGA datasets. The levels of phosphorylated HER3, EGFR, Akt, and ERK1/2 in TNBC cells were significantly reduced by combinations of 4A7 and the EGFR-tyrosine kinase inhibitor (TKI) gefitinib, which also strongly inhibited proliferation and caused cell death.	We identified ERBB3 (HER3) as a marker gene for TNBC BL1 subtype. TWIST1 and TWIST2 are key transcription regulators of the ERBB3 gene, and both negatively regulate its expression. We found these two TFs to be significantly downregulated in the BL1 subtype. Therefore, ERBB3 can be considered a potential marker gene and therapeutic target.
	Wei et al., 2020 (Translational Cancer Research)	The association between FGFR4 and TNBC prognosis.	Clinical survival data and immunohistochemistry (IHC) on FGFR4, ER, PR, HER2, Ki67, and p53 from 282 TNBC invasive ductal carcinoma patients (Harbin Medical University cohort) to assess prognosis, especially the role of FGFR4 expression.	TNBC tissues had higher quantities of the FGFR4 protein, according to the study. Both p53 status and the existence of lymph node metastases were associated with high FGFR4 expression. Patients with high FGFR4 expression had a lower overall survival rate than those with low expression.	In our investigation, we discovered that FGFR4 was overexpressed and showed up as a potential risk gene in the BL1 subtype. Analysis of expression at the gene and protein levels revealed that FGFR4 might be a useful marker for the BL1 subtype.

Basal Like 2	Noblejas-López et al., 2019 (Oncoimmunology)	Assessment of antigen recognition markers in tumor immune state of basal-like breast cancer patients.	Transcriptomic (microarray and RNA-seq), mutation, neoantigen prediction, and survival/clinical outcome data from breast cancer patients (n ≈ 2000 across EGA and TCGA cohorts). The cancer type was breast cancer, including TNBC (basal-like), HER2-enriched, Luminal A, and Luminal B subtypes.	Breast cancer tumours that have elevated expression of the MHC-I molecules HLA-A and HLA-B are more likely to activate immunological T cells, which leads to a better prognosis.	While exploring subtype-specific molecular patterns, we observed that the BL2 subtype was associated with significantly increased HLA-A and HLA-B expression. HIVEP2 and MYC are two of the key transcription regulators of HLA-B, both of which were significantly downregulated in the BL2 subtype. However, according to the TRRUST database, regulatory role of HIVEP2 is unknown, whereas MYC is annotated as an activator. These contradictory findings suggest the need for further investigation.
	Limsakul et al., 2024 (<i>International journal of molecular medicine</i>)	Identifying BL2-specific tyrosine kinases with prognostic value.	RNA-seq TPM data (TCGA-BRCA, n = 183 TNBC samples, BL1 (64), BL2 (37), LAR (27), and M (55), with focus on BL1 & BL2 = 101 samples) plus clinical metadata to perform subtype-specific differential gene expression analysis in TNBC.	Identifying BL2-specific tyrosine kinases with prognostic value. High EGFR/PDGFR/PDGFRB expression is linked to poor survival outcomes.	We identified GNAS, and HLA-B as potential markers for BL2 subtype where PDGFRA has been identified as a risk gene. GLI1 is one of the key transcription regulators of PDGFRA, positively regulating its expression, and showed significant upregulation in BL2.

Luminal Androgen Receptor	Thompson et al., 2022	Molecular and clinical characterization of LAR TNBC subtype	Multi-cohort transcriptomic data (TCGA RNA-seq, microarray, RNA-seq from clinical trials), single-cell RNA-seq, and clinicopathological records from TNBC patients, to develop and benchmark the LAR-Sig signature, characterize the LAR subtype, and assess its prognostic and predictive value.	Identified AR expression and AR-driven luminal gene signatures as the defining feature of LAR TNBC. Study reported hormone-regulated and PI3K/AKT pathway enrichment in LAR TNBC, linking it to distinct biology.	We found AR upregulation and placed AR as a key transcription factor regulating LAR marker genes (e.g., AKT1, PIK3R3). Identified AKT1 and PIK3R3 as LAR-specific marker genes and confirmed PI3K/AKT signalling enrichment.
	Liu et al., 2015 (Cancer research)	Identifying the mechanisms of HOXB7-induced aggressive phenotypes in breast cancer	Human invasive ductal carcinoma tissues, breast cancer cell lines (human and mouse), and mouse xenograft models, along with molecular/cellular functional assays, to investigate how HOXB7 regulates TGFβ2 signaling and promotes tumor invasion, EMT, immune modulation, and metastasis in breast cancer.	HOXB7 promotes tumor progression in a cell-autonomous and non-cell-autonomous manner by activating TGFβ/SMAD3 signaling in breast tumor tissues.	We have also found HOXB7 to get upregulated with a log2FC of 8.72 and acting as a pathway-specific common TF regulating the DOEGs for TNBC LAR subtype progression.

	Gucalp A. et al., 2013	A proof-of-concept phase II clinical trial testing the anti-androgen bicalutamide in patients with AR-positive, ER/PR-negative metastatic breast cancer (a clinical surrogate for LAR/AR+ TNBC).	Clinical trial data from AR-positive, ER/PgR-negative metastatic breast cancer patients, with FFPE tissue tested for AR expression by IHC, to evaluate the efficacy and safety of bicalutamide therapy.	In a small subset of patients with ER/PgR-negative, AR-positive metastatic breast cancer, the study showed that the minimally toxic androgen blocker drug bicalutamide provides evidence of principle for the effectiveness of targeting the AR pathway. Patients with AR(+) ER/PgR(-) breast tumours have different clinical characteristics from those of TNBC. Since this AR-dependent subtype of breast cancer differs from the basal-like subtypes (BL1 and BL2), the lack of basal-like breast cancer IHC markers would indicate the response to antiandrogen therapy. Co-dependence on the PI3K/AKT pathway is frequently highlighted in the clinical justification of AR+ TNBC studies (and other publications). These results imply that in this subgroup of patients with breast cancer, AR expression might be a viable therapeutic target.	We identified GNAS as a risk gene linked to PI3K-AKT signaling through the PKA/PI3K/AKT/Snail1/E-cadherin axis in LAR and nominated ERBB4 / PIK3R3 as LAR-specific markers. We also predict that GNAS has a strong connection with these two markers. These molecular leads in our work suggest combination strategies (for example AR+PIK3R3/AKT pathway targeting) that go beyond single-agent antiandrogen therapy.
--	------------------------	--	---	--	--

	Jung et al., 2016 (Scientific reports)	The molecular processes that underlie statin-induced growth inhibition of TNBC include overexpressing the transcription factor ets proto-oncogene 1 (ets-1) and downregulating the expression of dual specialised protein phosphatase 4 (dusp4).	Breast cancer cell line transcriptomic data of 10 TNBC and 12 non-TNBC cell lines, protein assays, and simvastatin treatment experiments to study differential ETS gene expression and signaling pathway regulation in TNBC vs. non-TNBC cell lines.	TNBC cell lines overexpressed ETS1 and other members of the ETS family, including ETS2, ETV1, ETV5, ELK3, and FLI1, in contrast to other BC cell lines. Consequently, increased expression of ETS family members (such as ETS1) may be a factor in TNBC cell tumour expansion and aggressiveness in addition to chemotherapy resistance.	We have detected ETS1 and ETS2 to be significantly downregulated in the LAR TNBC subtype which is a contrasting report against results presented by Juan and colleagues.
Mesenchymal Like	Ahn & Jo., 2023 (in vivo)	The biological significance and mechanism of Axin2 in breast cancer using transcriptomic and molecular techniques.	TNBC Cell line (MDA-MB-231), TNBC xenograft mouse models using pLKO-Tet-shAXIN2-transfected TNBC cells, and clinical patient datasets (TCGA, KM plotter) to evaluate how AXIN2 regulates Snail1 and EMT, contributing to TNBC tumorigenesis and prognosis.	Axin2 may serve as an oncogene in breast cancer by mediating Snail1-induced EMT. Snail1 is thought to be a strong inducer of EMT in both cancerous and healthy cells. The MDA-MB-231 TNBC's capacity to cause tumours in vivo was reduced when Axin2 was knocked down.	We have also identified AXIN2 as a marker gene for ML and MSL TNBC. MYC is one of the key TFs regulating AXIN2. According to the TRRUST database, its mode of regulation is unknown. However, we observed contrasting results, with MYC showing significant down-regulation in our study suggesting involvement of other key TF in the process.

	Wei et al., 2020 (Translational Cancer Research)	The association between FGFR4 and TNBC prognosis.	Clinical survival data and immunohistochemistry (IHC) on FGFR4, ER, PR, HER2, Ki67, and p53 from 282 TNBC invasive ductal carcinoma patients (Harbin Medical University cohort) to assess prognosis, especially the role of FGFR4 expression.	TNBC tissues had higher quantities of the FGFR4 protein, according to the study. Both p53 status and the existence of lymph node metastases were associated with high FGFR4 expression. Patients with high FGFR4 expression had a lower overall survival rate than those with low expression.	In our study, we found that in ML subtype, FGFR4 was overexpressed and appeared as one of the candidate genes. FGFR4 emerged as a cancer risk gene, which eventually lowered the overall patient's survivability. Gene level and protein level expression analyses suggested that FGFR4 could serve as a potential marker for ML subtype.
	Yu et al., 2002 (Molecular Endocrinology)	Role of the Zinc-Finger Transcription Factor Ikaros Targeting Fibroblast Growth Factor Receptor 4 in the Pituitary	NIH 3T3 (fibroblast, non-endocrine control) and rat pituitary tumor-derived cell lines (PRL 235, GH4C1) as endocrine cancer models.	This research highlights a novel role for Ikaros outside the hematopoietic system, suggesting its involvement in the transcriptional regulation of FGFR4 in the pituitary gland. The findings propose a collaborative mechanism where Ikaros, Sp, and Ets transcription factors work together to regulate gene expression in endocrine cells.	We have found IKZF1 to be significantly upregulated in both BL2 and ML subtypes and is a key transcription regulator of the FGFR4 according to TRUST database. To date, there is no published research directly reporting that IKZF1 transcriptionally regulates FGFR4-mediated mesenchymal-like progression in triple-negative breast cancer (TNBC). While in pituitary IKZF1 acts as a key regulator of FGFR4, their potential interaction in TNBC progression remains unexplored. Therefore, we predict there might be some relation in between these two genes in TNBC progression

					especially in BL2 and ML subtypes.
Mesenchymal Stem Like	Bredel et al., 2013 (International Journal of Radiation Oncology, Biology, Physics)	Deletional effect of the tumour suppressor gene NFKBIA in TNBC	Large-scale genomic and expression data (>5000 breast cancers), functional cell culture assays (with NFKBIA genotypes), and clinical outcome data to study the tumor suppressor role of NFKBIA and its impact on NF-κB signaling in breast cancer.	Loss of NFKBIA exerts a haplo-insufficient effect on NFKBIA expression and the transactivation of several NFκB target genes with important roles in breast carcinogenesis, including chemokine (C-X-C motif) ligand 1 (CXCL1) significantly associated with TNBC progression.	We also found that NFKBIA gene expression was significantly downregulated in both BL2 and MSL subtypes suggesting loss of NFKBIA mediated tumour suppression.
	Zhang et al., 2021 (Breast Cancer Research)	Metastatic inhibition of TNBC via degradation of Twist1 and Notch1 oncoproteins	Human TNBC cell lines and TNBC xenograft mouse models, along with a range of functional, molecular, and histological assays, to investigate triptonide's effect on TNBC tumor growth, metastasis, and vasculogenic mimicry.	Triptonide drug mediated degradation of Twist1 and Notch1 oncoproteins and inhibited NF-κB signaling in TNBC, resulting in potent suppression of TNBC cell tumorigenesis and metastasis.	TWIST1 is a master EMT-inducing gene and plays a critical role in cancer metastasis in various malignant tumors. Overexpression of TWIST1 promotes TNBC metastasis and is associated with poor prognosis. However, we have found in both LAR and MSL subtypes, TWIST1 was significantly downregulated.
	Green, A. R et al., 2016 (British journal of cancer)	The functional role of MYC and c-MYC between molecular subtypes of BCs.	In this study they used large-scale transcriptomic data (METABRIC RNA) (RNA from fresh frozen tumors (n ≈ 1980)) and protein expression (IHC in Nottingham cohort, n= 1106)	Higher tumor grade and the basal-like phenotype were linked to elevated MYC expression.	In our study we have found MYC to be significantly downregulated in TNBC MSL subtype.

			data to study MYC gene and protein expression in breast cancer (ER+, HER2+, TNBC subtypes, and invasive BC).		
--	--	--	--	--	--

Supplementary Table. S6 Comparative study with previously published reports

References used in Supplementary Table. S6

1. Ahn, S. Y., & Jo, C. H. Implications of Axis Inhibition Protein 2 in Breast Cancer Progression. *in vivo*, 37(2), 634-643 (2023).
2. Bredel, M. et al. Deletion of the tumor suppressor NFKBIA in triple-negative breast cancer. *International Journal of Radiation Oncology, Biology, Physics*, 87(2), S98 (2013).
3. Green, A. R. et al. MYC functions are specific in biological subtypes of breast cancer and confers resistance to endocrine therapy in luminal tumours. *British journal of cancer*, 114(8), 917-928 (2016).
4. Gucalp, A., Tolane, S., Isakoff, S. J., Ingle, J. N., Liu, M. C., Carey, L. A., ... & Traina, T. A. (2013). Phase II trial of bicalutamide in patients with androgen receptor-positive, estrogen receptor-negative metastatic breast cancer. *Clinical cancer research*, 19(19), 5505-5512.
5. Jung, H. H. et al. Statins affect ETS1-overexpressing triple-negative breast cancer cells by restoring DUSP4 deficiency. *Scientific reports*, 6(1), 33035 (2016).
6. Kim, J. Y. et al. Prognostic value of ERBB4 expression in patients with triple negative breast cancer. *BMC cancer*, 16, 1-12 (2016).
7. Lehmann, B. D., Bauer, J. A., Schafer, J. M., Pendleton, C. S., Tang, L., Johnson, K. C., ... & Pietenpol, J. A. (2014). PIK3CA mutations in androgen receptor-positive triple negative breast cancer confer sensitivity to the combination of PI3K and androgen receptor inhibitors. *Breast Cancer Research*, 16(4), 406.
8. Limsakul, P., Choochuen, P., Jungrungrueang, T., & Charupanit, K. (2024). Prognostic Markers in Tyrosine Kinases Specific to Basal-like 2 Subtype of Triple-Negative Breast Cancer. *International Journal of Molecular Sciences*, 25(3), 1405.
9. Liu, S., Jin, K., Hui, Y., Fu, J., Jie, C., Feng, S., ... & Chen, H. (2015). HOXB7 promotes malignant progression by activating the TGFβ signaling pathway. *Cancer research*, 75(4), 709-719.
10. Lyu, H. et al. HER3 functions as an effective therapeutic target in triple negative breast cancer to potentiate the antitumor activity of gefitinib and paclitaxel. *Cancer Cell International*, 23(1), 204 (2023).
11. Noblejas-López, M. D. M. et al. Expression of MHC class I, HLA-A and HLA-B identifies immune-activated breast tumors with favorable outcome. *Oncoimmunology*, 8(10), e1629780 (2019).
12. Thompson, K. J., Leon-Ferre, R. A., Sinnwell, J. P., Zahrieh, D. M., Suman, V. J., Metzger, F. O., ... & Sikov, W. M. Luminal androgen receptor breast cancer subtype and investigation of the microenvironment and neoadjuvant chemotherapy response., 2022, 4, p. zcac018. DOI: <https://doi.org/10.1093/narcan/zcac018>. PMID: <https://www.ncbi.nlm.nih.gov/pubmed/35734391>.

13. Wei, W., Cao, S., Liu, J., Wang, Y., Song, Q., Sun, S., ... & Jiang, Y. (2020). Fibroblast growth factor receptor 4 as a prognostic indicator in triple-negative breast cancer. *Translational Cancer Research*, 9(11), 6881.
14. Yu, S., Asa, S. L., & Ezzat, S. (2002). Fibroblast growth factor receptor 4 is a target for the zinc-finger transcription factor Ikaros in the pituitary. *Molecular Endocrinology*, 16(5), 1069-1078.
15. Zhang, M. et al. Triptonide effectively inhibits triple-negative breast cancer metastasis through concurrent degradation of Twist1 and Notch1 oncoproteins. *Breast Cancer Research*, 23, 1-16 (2021).