Supplementary Information

Functional proteomics outlines the complexity of breast cancer molecular subtypes

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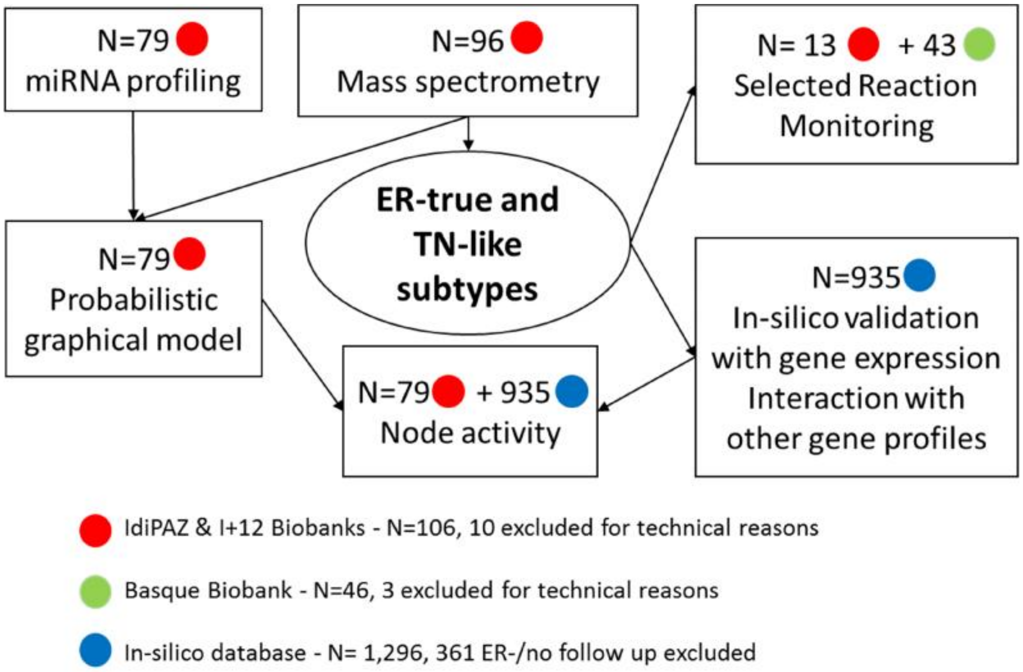
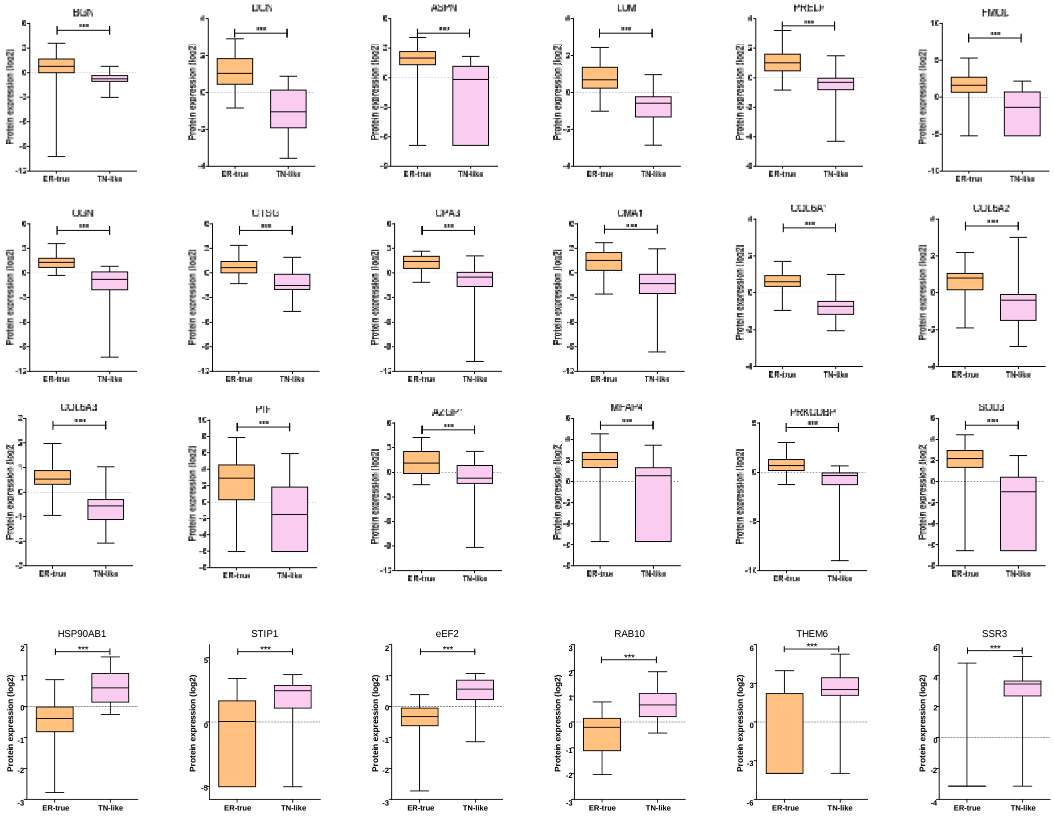
Supplementary Figure 1

Chart of samples used in each analysis.



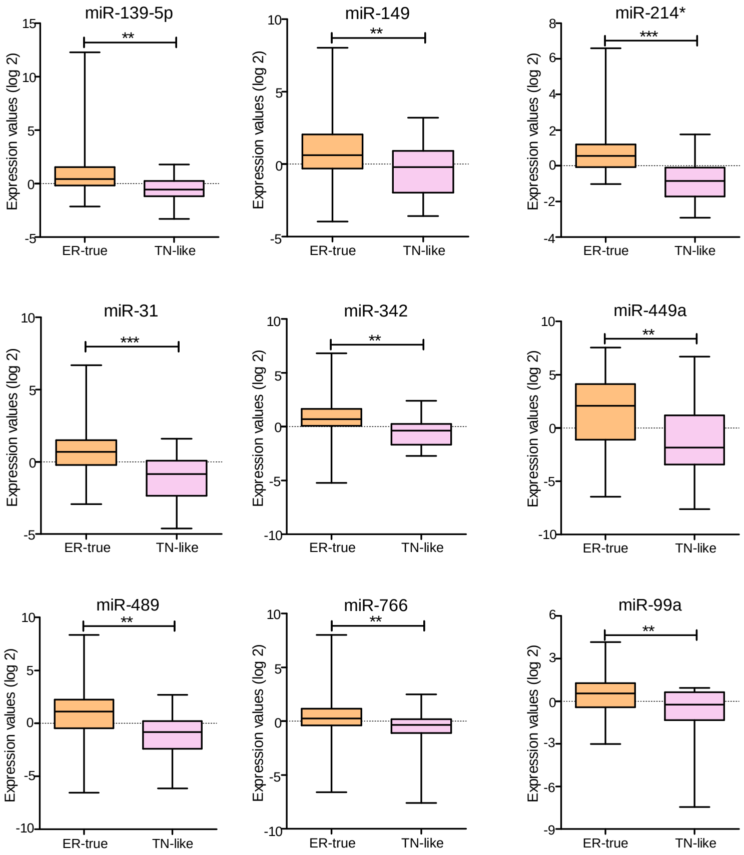
Supplementary Figure 2

Boxplots showing most relevant proteins differentially expressed between ER-true and TN-like tumors. In all cases, n(ER-true)=50, n(TN-like)=21, p< 0.0001.



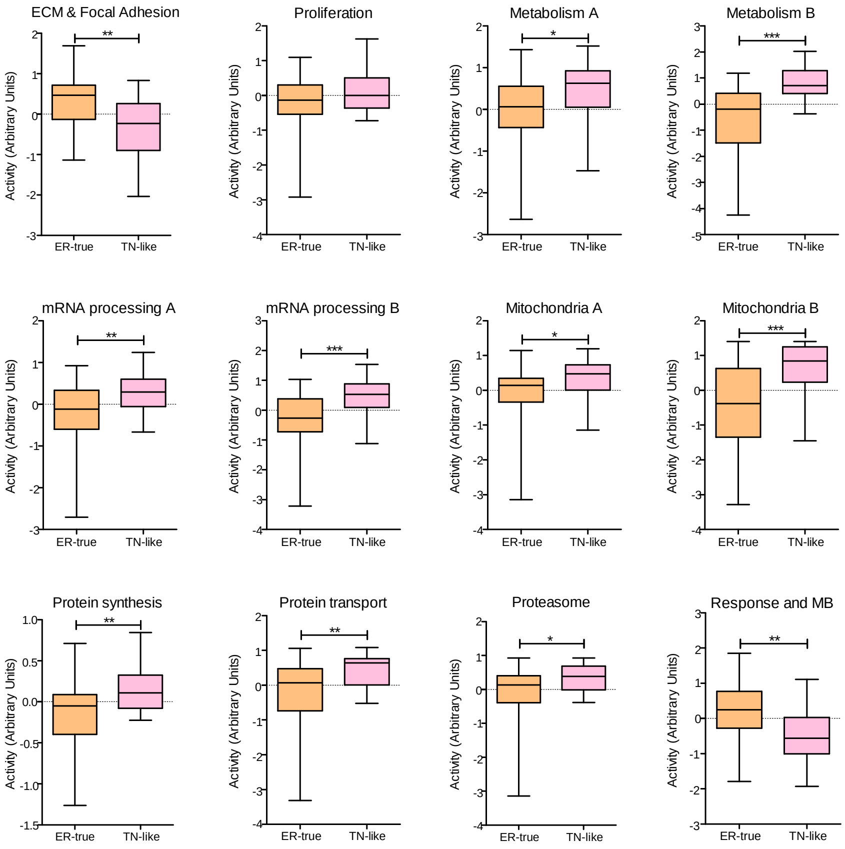
Supplementary figure 3

Boxplots showing miRNAs differentially expressed between ER-true and TN-like tumors. In all cases, n(ER-true)=50, n(TN-like)=21, ***p< 0.0001, **p<0.001.



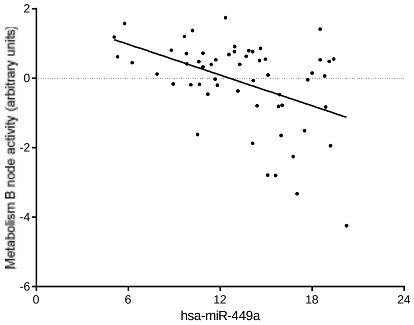
Supplementary figure 4

Boxplots comparing functional node activities between ER-true and TN-like tumors. In all cases, n(ER-true)=50, n(TN-like)=21, ***p< 0.0001, **p<0.001, *p<0.05.

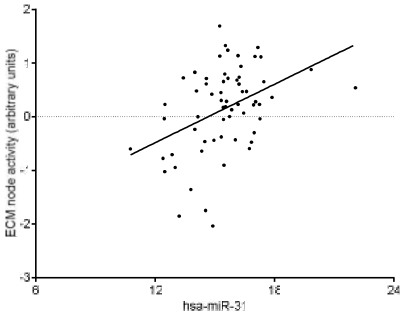


Supplementary figure 5

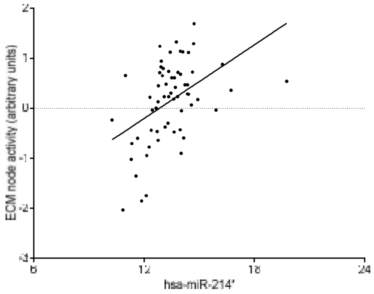
Correlation between miRNA expression values and functional node activity (n=71).



r	-0.4489
95% confidence interval	-0.6352 to -0.2133
R squared	0.2015
P value	
P (two-tailed)	0.0005



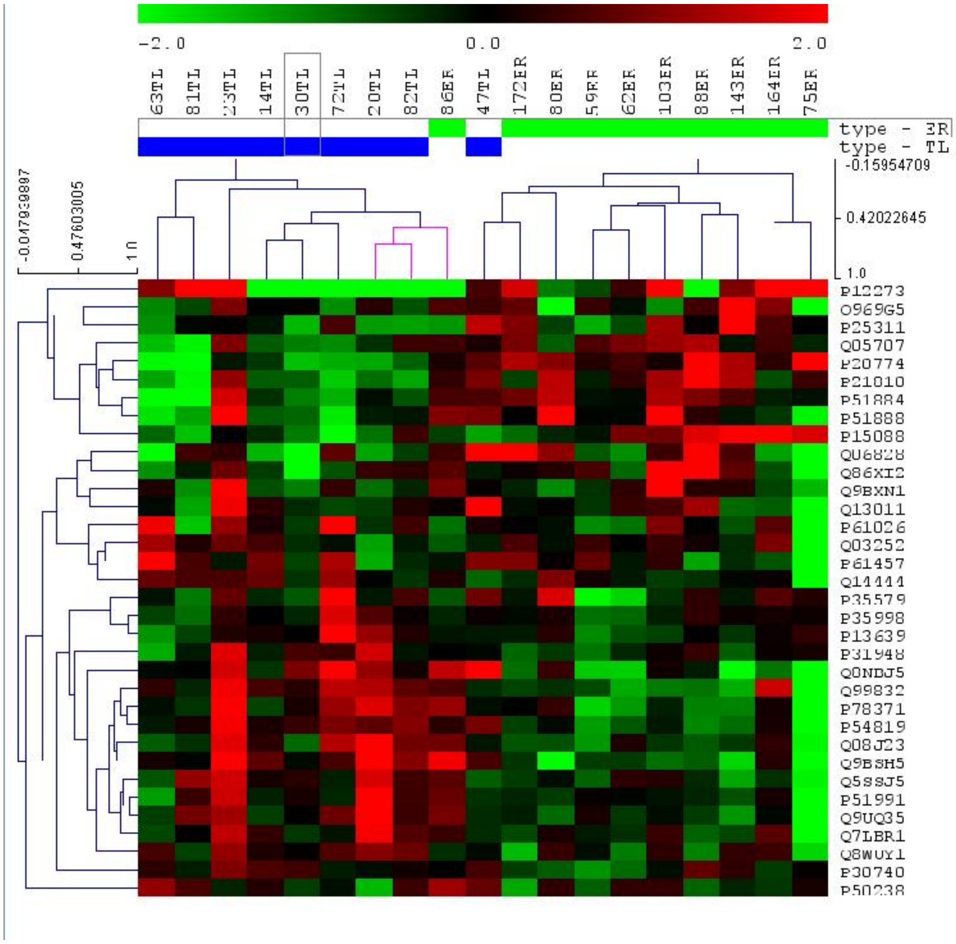
r	0.4124
95% confidence interval	0.1834 to 0.5990
R squared	0.1701
P value	
P (two-tailed)	0.0008



r	0.4538
95% confidence interval	0.2321 to 0.6307
R squared	0.2059
P value	
P (two-tailed)	0.0002

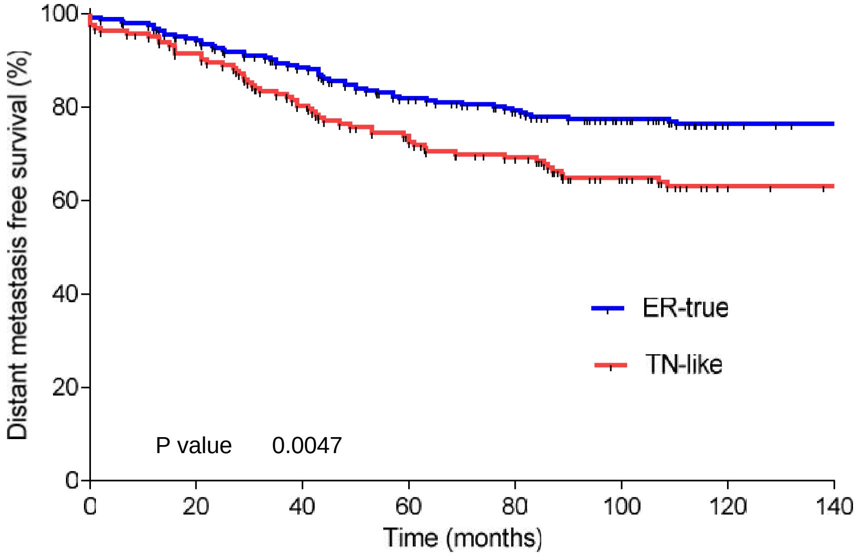
Supplementary figure 6

SRM data hierarchical cluster analysis shows differences between ER-true (ER) and TN-like (TL) tumors.



Supplementary figure 7

Kaplan-Meier analysis of 421 tumors with ER+/N+ characteristics from meta-genomics external dataset. DMFS at five years was81.8% and 72.5% for ER-true (n=246) and TN-like (n=164) groups respectively (p<0.005, HR= 0.5769).



Supplementary Table 1

Proteins differentially expressed between ER+ and TNBC tumors identified by SAM analysis with a FDR<5%.

(see supplementary_table1.xlsx)

Supplementary Table 2

Proteins differentially expressed between ER-true and TN-like tumors identified by SAM analysis with a FDR<5%.

Entry	UNIPROT_ID	Protein name	Gene name	Protein-to-gene
O14558	HSPB6_HUMAN	Heat shock protein beta-6	HSPB6	yes
O15355	PPM1G_HUMAN	Protein phosphatase 1G	PPM1G	
P02452	CO1A1_HUMAN	Collagen alpha-1(I) chain	COL1A1	yes
P02743	SAMP_HUMAN	Serum amyloid P-component	APCS PTX2	yes
P05023	AT1A1_HUMAN	Sodium/potassium-transporting ATPase subunit alpha-1	ATP1A1	
P07585	PGS2_HUMAN	Decorin (Bone proteoglycan II)	DCN	yes
P08238	HS90B_HUMAN	Heat shock protein HSP 90-beta	HSP90AB1	yes
P08294	SODE_HUMAN	Extracellular superoxide dismutase [Cu-Zn]	SOD3	yes
P08311	CATG_HUMAN	Cathepsin G	CTSG	yes
P12109	CO6A1_HUMAN	Collagen alpha-1(VI) chain	COL6A1	yes
P12110	CO6A2_HUMAN	Collagen alpha-2(VI) chain	COL6A2	yes
P12111	CO6A3_HUMAN	Collagen alpha-3(VI) chain	COL6A3	yes
P12273	PIP_HUMAN	Prolactin-inducible protein	PIP	yes
P13639	EF2_HUMAN	Elongation factor 2 (EF-2)	EEF2	yes
P15088	CBPA3_HUMAN	Mast cell carboxypeptidase A	CPA3	yes
P20774	MIME_HUMAN	Mimecan	OGN	yes
P21810	PGS1_HUMAN	Biglycan	BGN	yes
P23946	CMA1_HUMAN	Chymase	CMA1	yes
P25311	ZA2G_HUMAN	Zinc-alpha-2-glycoprotein	AZGP1	yes
P31948	STIP1_HUMAN	Stress-induced-phosphoprotein 1	STIP1	yes
P35998	PRS7_HUMAN	26S protease regulatory subunit 7	PSMC2	yes
P51884	LUM_HUMAN	Lumican	LUM	yes
P51888	PRELP_HUMAN	Prolargin	PRELP	yes
P55083	MFAP4_HUMAN	Microfibril-associated glycoprotein 4	MFAP4	
P61026	RAB10_HUMAN	Ras-related protein Rab-10	RAB10	yes
Q05707	COEA1_HUMAN	Collagen alpha-1(XIV) chain	COL14A1	yes
Q06828	FMOD_HUMAN	Fibromodulin	FMOD	yes
Q08J23	NSUN2_HUMAN	tRNA (cytosine(34)-C(5))-methyltransferase	NSUN2	yes
Q14444	CAPR1_HUMAN	Caprin-1	CAPRIN1	yes
Q15459	SF3A1_HUMAN	Splicing factor 3A subunit 1	SF3A1	yes
Q4G0X9	CCD40_HUMAN	Coiled-coil domain-containing protein 40	CCDC40	yes
Q86XI2	CNDG2_HUMAN	Condensin-2 complex subunit G2	NCAPG2	yes
Q8NBJ5	GT251_HUMAN	Procollagen galactosyltransferase 1	COLGALT1	yes
Q8WUY1	THEM6_HUMAN	Mesenchymal stem cell protein DSCD75	THEM6	yes
Q969G5	PRDBP_HUMAN	Protein kinase C delta-binding protein	PRKCDBP	yes
Q99832	TCPH_HUMAN	T-complex protein 1 subunit eta	CCT7	yes
Q9BXN1	ASPN_HUMAN	Asporin	ASPN	yes
Q9BY44	EIF2A_HUMAN	Eukaryotic translation initiation factor 2A	EIF2A	yes
Q9UNL2	SSRG_HUMAN	Translocon-associated protein subunit gamma	SSR3	
Q9UQ35	SRRM2_HUMAN	Serine/arginine repetitive matrix protein	SRRM2	yes

Supplementary Table 3

Gene ontology terms enriched in the protein list differentially expressed between ER-true and TN-like tumors.

Term	Term	p-value
GOTERM_CC_FAT	GO:0031012~extracellular matrix	1.79E-12
GOTERM_CC_FAT	GO:0005581~collagen	2.06E-06
GOTERM_BP_FAT	GO:0030198~extracellular matrix organization	8.84E-05
KEGG_PATHWAY	hsa04512:ECM-receptor interaction	8.59E-04
GOTERM_BP_FAT	GO:0007155~cell adhesion	0.0203
GOTERM_BP_FAT	GO:0022610~biological adhesion	0.0204
KEGG_PATHWAY	hsa04510:Focal adhesion	0.0102
PANTHER_PATHWAY	P00034:Integrin signaling pathway	0.0031

Supplementary table 4

Cox regression analysis of TN-like subtype in each risk category defined by prognostic signatures.

Prognostic test	Risk group	TN-like subtype	N	DMFS	HR	p-value
70-gene Signature	Low	ER-true	449	92.5%	2.1	0.0056
		TN-like	137	84.1%		
	High	ER-true	154	71.0%	1.1	0.58
		TN-like	195	67.1%		
Recurrence Score	Low	ER-true	358	93.7%	2.5	0.0037
		TN-like	114	84.5%		
	Intermediate	ER-true	120	83.7%	0.99	0.97
		TN-like	108	80.1%		
	high	ER-true	125	70.8%	1.22	0.31
		TN-like	143	65.8%		
8-gene Score	Low	ER-true	445	91.5%	2.1	0.0014
		TN-like	165	81.2%		
	High	ER-true	158	74.1	1.3	0.15
		TN-like	167	67.1		