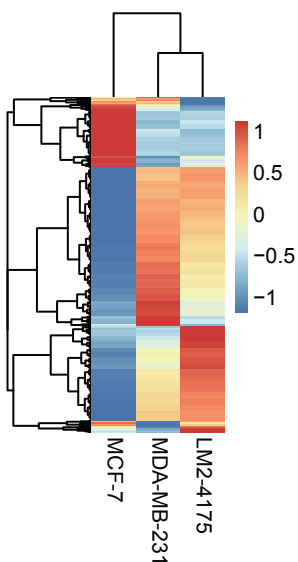
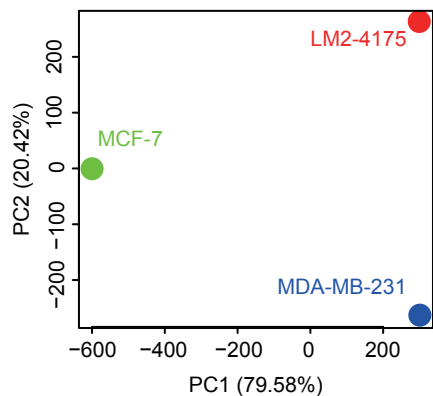


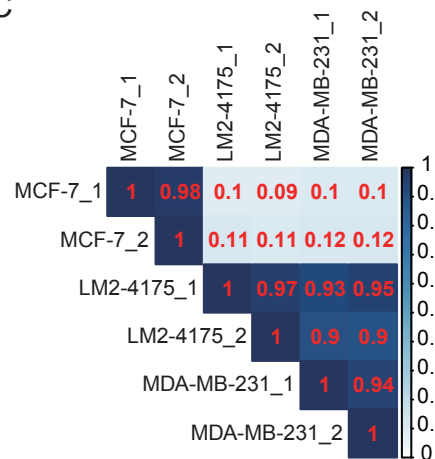
A



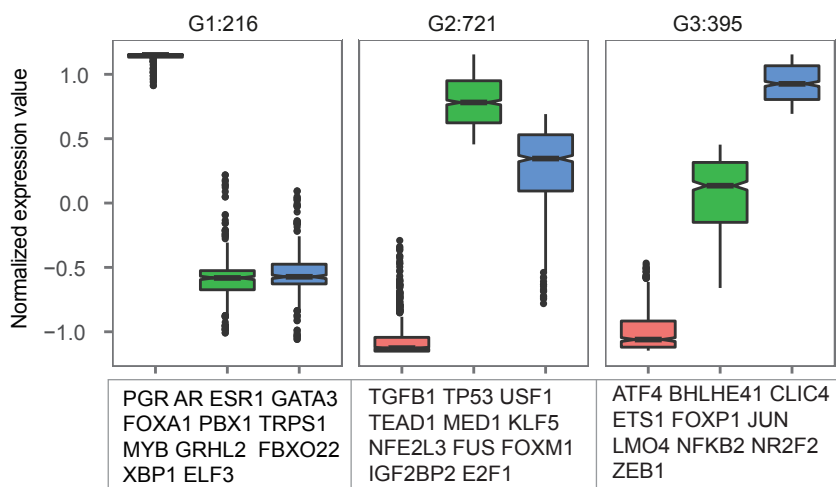
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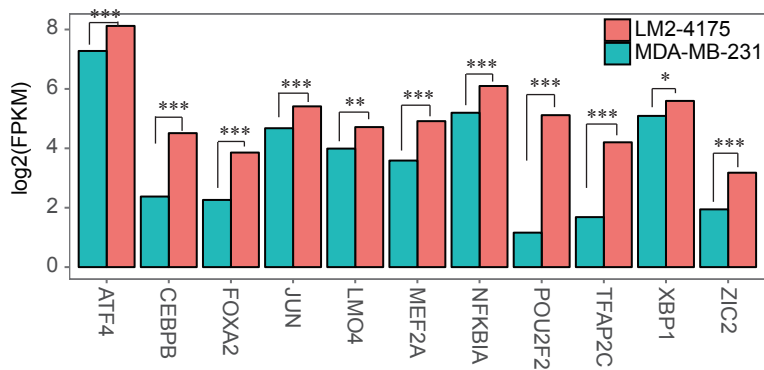
C



D



E



F

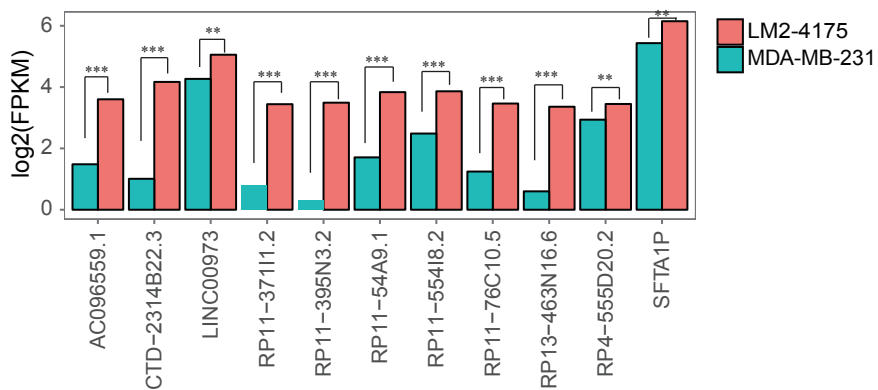
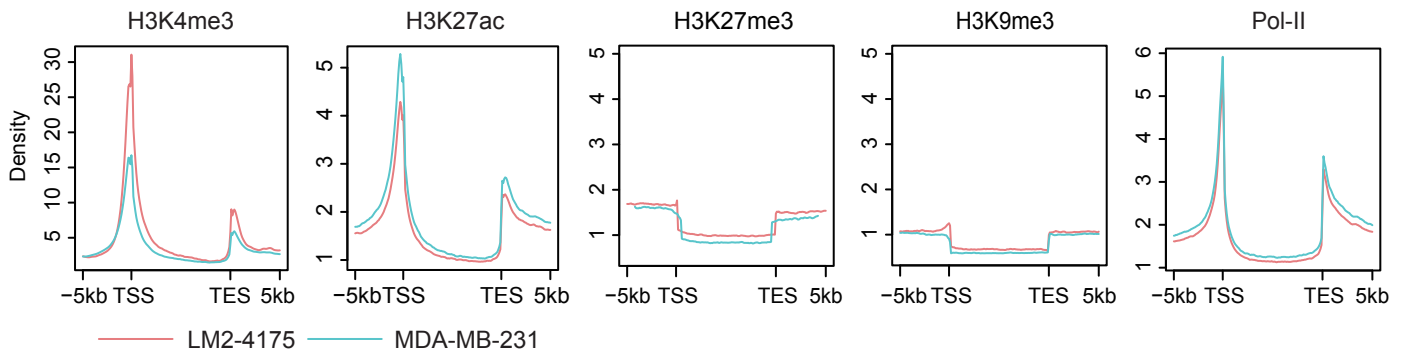
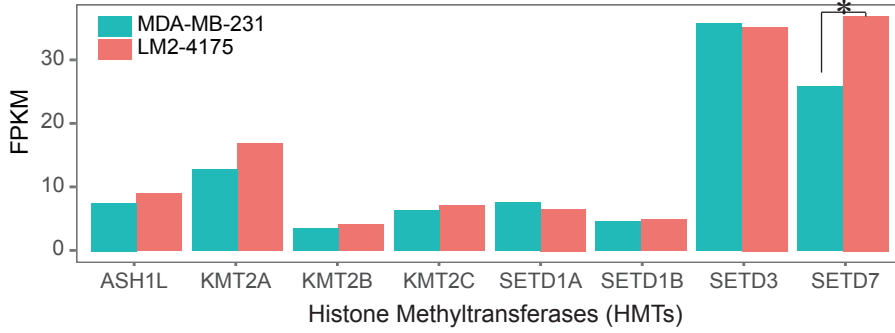


Figure S1. Transcriptome analysis of cell lines. (A) Heatmap for differentially expressed genes of non-metastasis, moderate-metastasis and high-metastasis-to-lung breast cancer cell lines. (B) Principal component analysis (PCA) of whole transcriptome data (RNA-Seq) of MCF-7, MDA-MB-231 and LM2-4175. (C) Correlation coefficient matrix for the whole transcriptome (RNA-Seq) data of different cell lines. Each cell line has two replicates. (D) Differentially expressed transcription factors were classified into three groups with different expression pattern in breast cancer cell lines. Examples of each group were shown. (E) Examples for significantly up-regulated TFs in lung-metastatic cell line LM2-4175 compared with MDA-MB-231. * indicates $p < 0.05$, ** indicates $p < 0.01$ and *** indicates $p < 0.001$. (F) Examples for significantly up-regulated lincRNAs in lung-metastatic cell line LM2-4175 compared with MDA-MB-231. * indicates $p < 0.05$, ** indicates $p < 0.01$ and *** indicates $p < 0.001$.

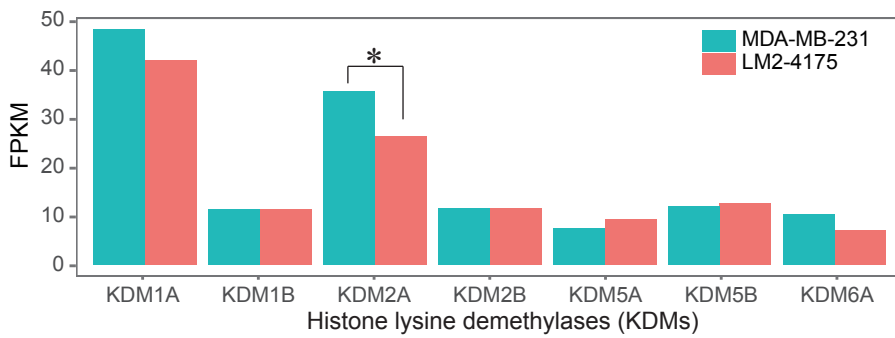
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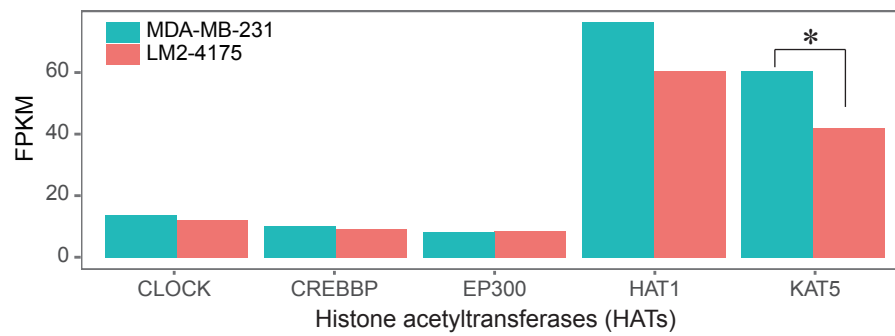
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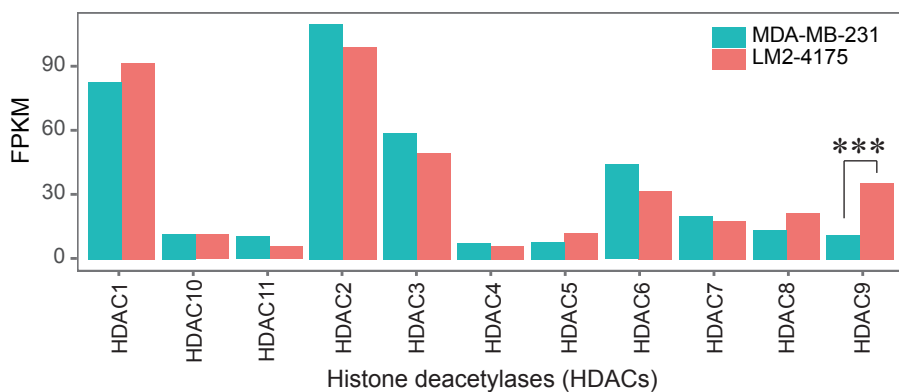


Figure S2. Changes of histone modification enrichment and epigenetic enzyme expressions from MDA-MB-231 to LM2-4175. (A) The average normalized ChIP-seq signal of H3K4me3, H3K27ac, H3K27me3, H3K9me3 and Pol-II enrichment on all genes in MDA-MB-231 and LM2-4175. Gene body, 5kb upstream and downstream regions were shown. (B) Expression changes of histone methyltransferases (HMTs). * indicates $p < 0.05$. (C) Expression changes of histone lysine demethylases (KDMs). * indicates $p < 0.05$. (D) Expression changes of histone acetyltransferases (HATs). * indicates $p < 0.05$. (E) Expression changes of histone deacetylases (HDACs). *** indicates $p < 0.001$.

A

Promoter State	Definition	LM2-4175-Count	MDA-MB-231-Count
Active	H3K4me3 > 10% & H3K27ac > 10% & H3K27me3 < 10%	18458	17516
Repressive	H3K4me3 < 10% & H3K27ac < 10% & H3K27me3 > 10%	2721	6902
Poised	H3K4me3 > 10% H3K27ac > 10% & H3K27me3 > 10%	426	1372
None	H3K4me3 < 10% & H3K27ac < 10% & H3K27me3 < 10%	41646	37488

B

LM2-4175

	Active	Poised	Repressive	None
MDA-MB-231 Active	29718	50	0	1256
MDA-MB-231 Poised	676	590	280	973
MDA-MB-231 Repressive	12	15	2230	4314
MDA-MB-231 None	2338	43	129	20654

C

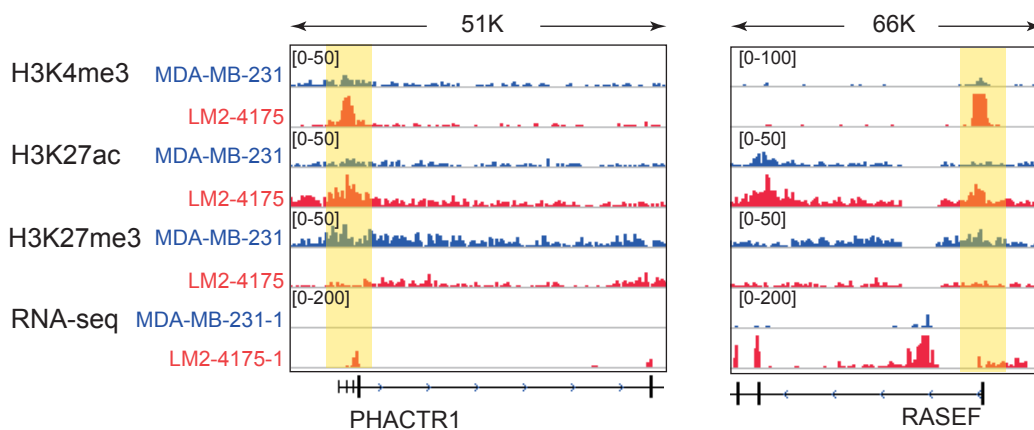
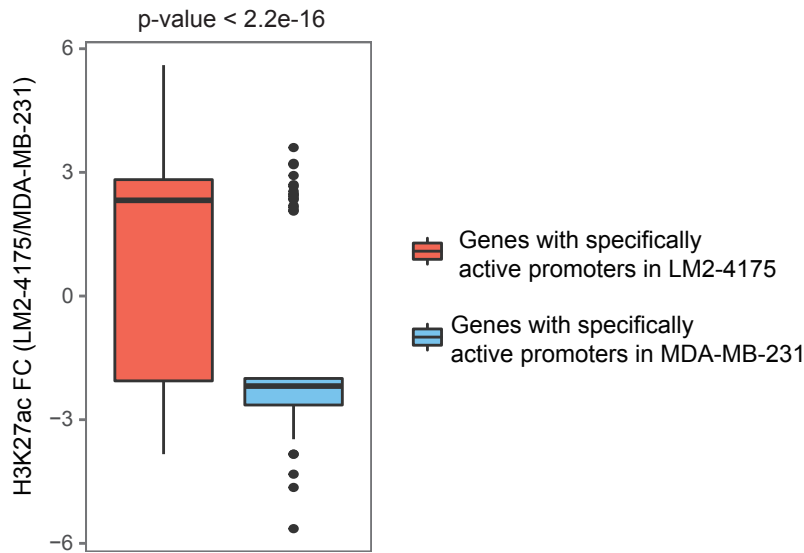


Figure S3. Promoter state transformation from MDA-MB-231 to LM2-4175. (A) Definition of promoter state using H3K4me3, H3K27ac and H3K27me3 enrichment percentage on promoter regions (TSS±2kb). & indicates “and”, | indicates “or”. The number of promoters of each state in MDA-MB-231 and LM2-4175 cell lines was also shown. (B) The number of transformed promoters. Row indicates promoters in MDA-MB-231, and column indicates promoters in LM2-4175. (C) Promoter state transformation of PHACTR1 and RASEF. The regions covered by yellow box represent promoters.

A



B

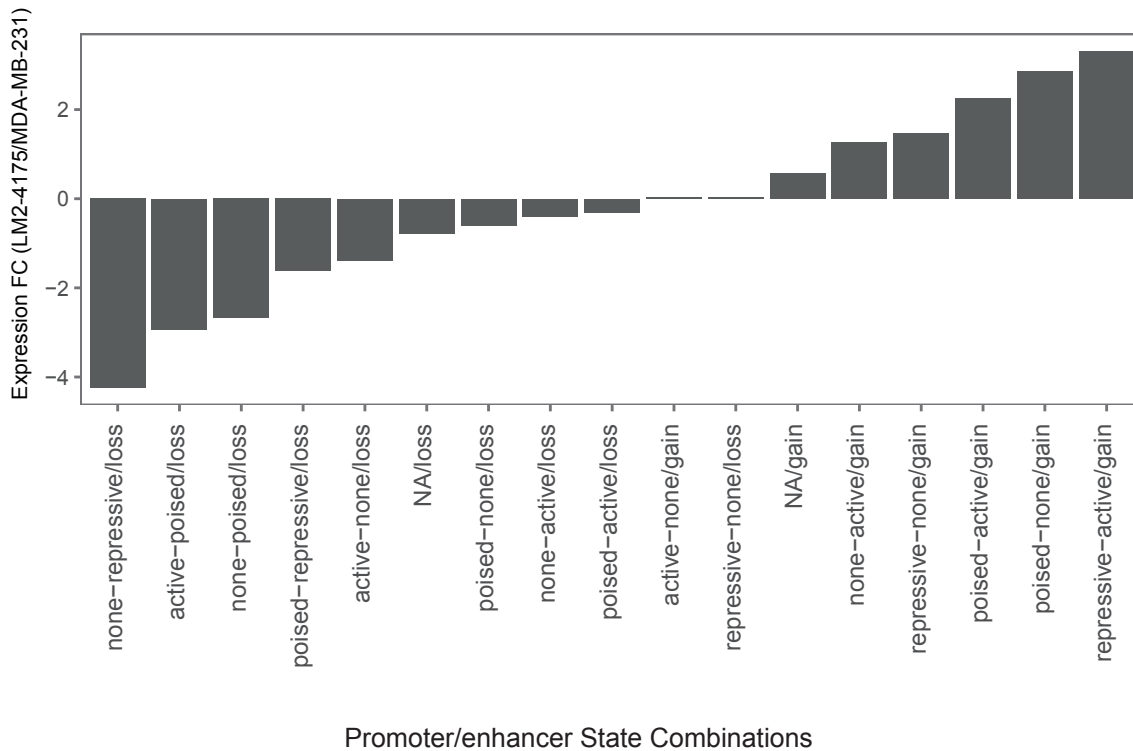
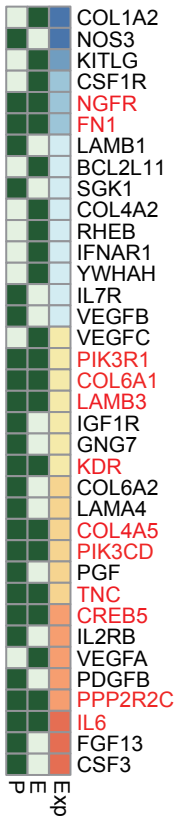
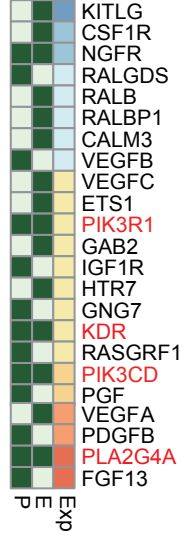


Figure S4. Analysis of promoter and enhancer interaction. (A) Promoter-distal H3K27ac enrichment fold-changes (LM2-4175/MDA-MB-231) of genes associated with activated promoters in LM2-4175 (red) and MDA-MB-231 (blue). (B) Expression fold-changes (LM2-4175/MDA-MB-231) of genes associated with different promoter/enhancer reprogramming combinations. The horizontal axis represents the various combinations of promoter state transformation and enhancer reprogramming, in which changes of promoter states (from MDA-MB-231 to LM2-4175) are shown before the slash, and changes of enhancers are shown after the slash. The events with less than 2 genes were not shown.

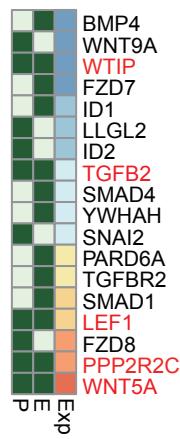
hsa04151:PI3K-Akt signaling pathway



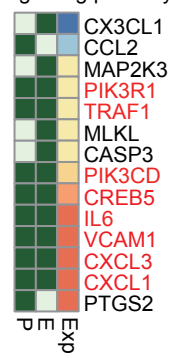
hsa04014:Ras signaling pathway



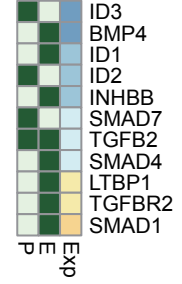
hsa04390:Hippo signaling pathway



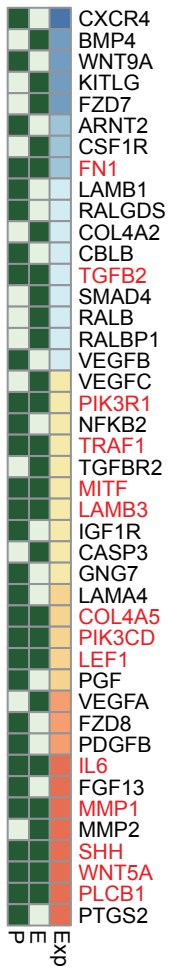
hsa04668:TNF signaling pathway



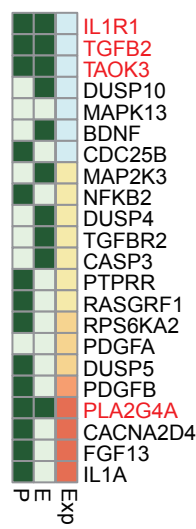
hsa04350:TGF-beta signaling pathway



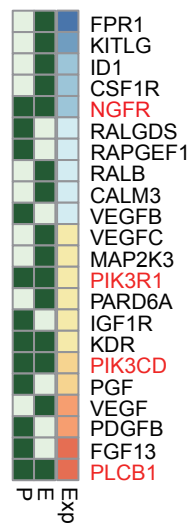
hsa05200:Pathways in cancer



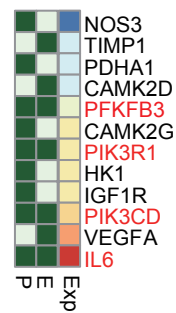
hsa04010:MAPK signaling pathway



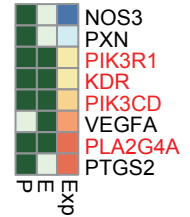
hsa04015:Rap1 signaling pathway



hsa04066:HIF-1 signaling pathway



hsa04370:VEGF signaling pathway



Differential
None-differential

Expression FC

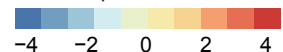


Figure S5. Significant KEGG pathways affected by reprogramming of promoters or enhancers. P indicates promoter, E indicates enhancer and Exp indicates expression fold-changes. Genes marked in red were differentially expressed, and had both promoter and enhancer changes.

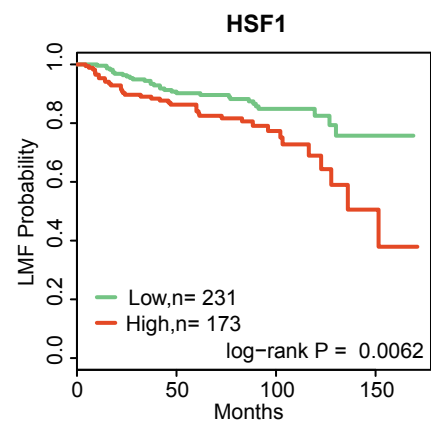
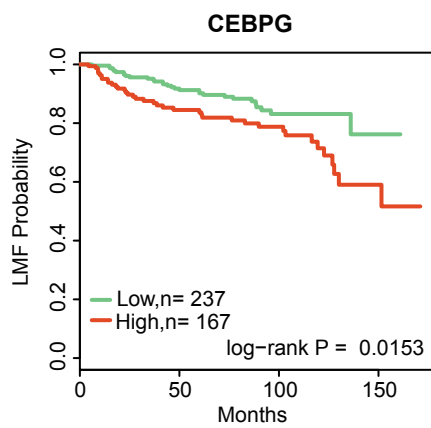
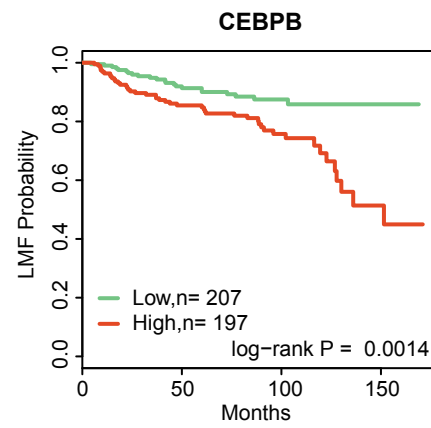
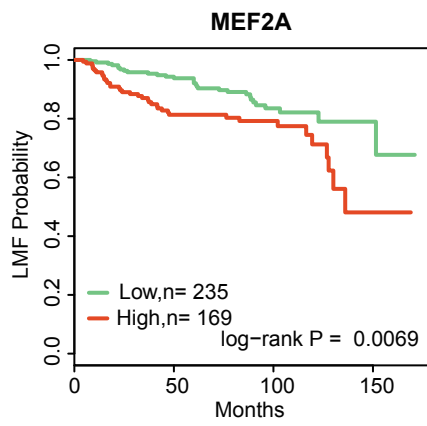


Figure S6. Significant regulators that had predictive power for LMF survival of breast cancer.