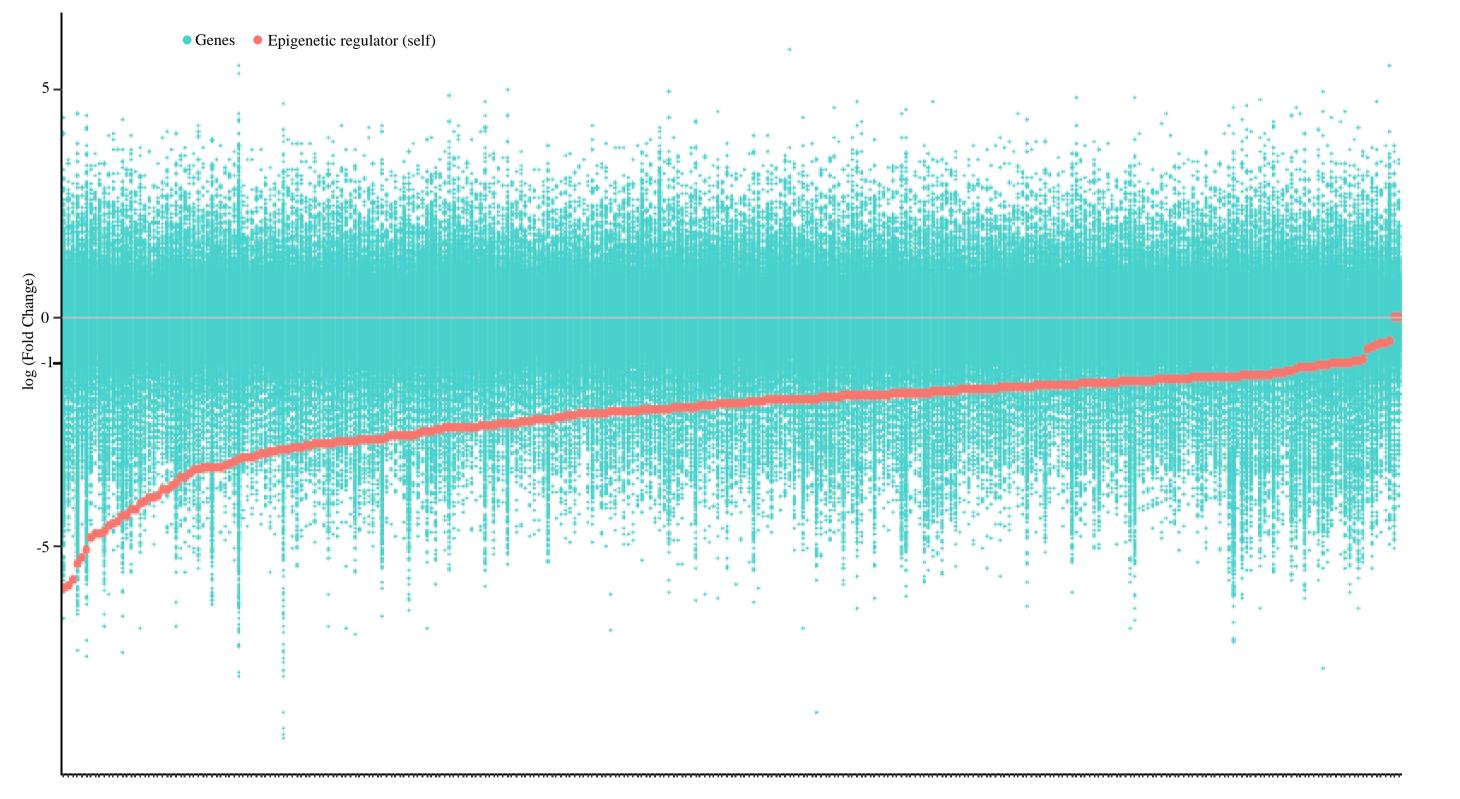


Figure S1. The workflow of HTS²

PCR products (161nt)



Epigenetic regulator knocking down

Figuer S2. Log(fold change) of gene after epigenetic regulator knocking down. The x axis is the epigenetic regulator

knocking down. The y axis is the log(fold change) of gene after epigenetic regulators knocking down. The red node represents the knocking down epigenetic regulator. The green node represents another 2,985 genes.

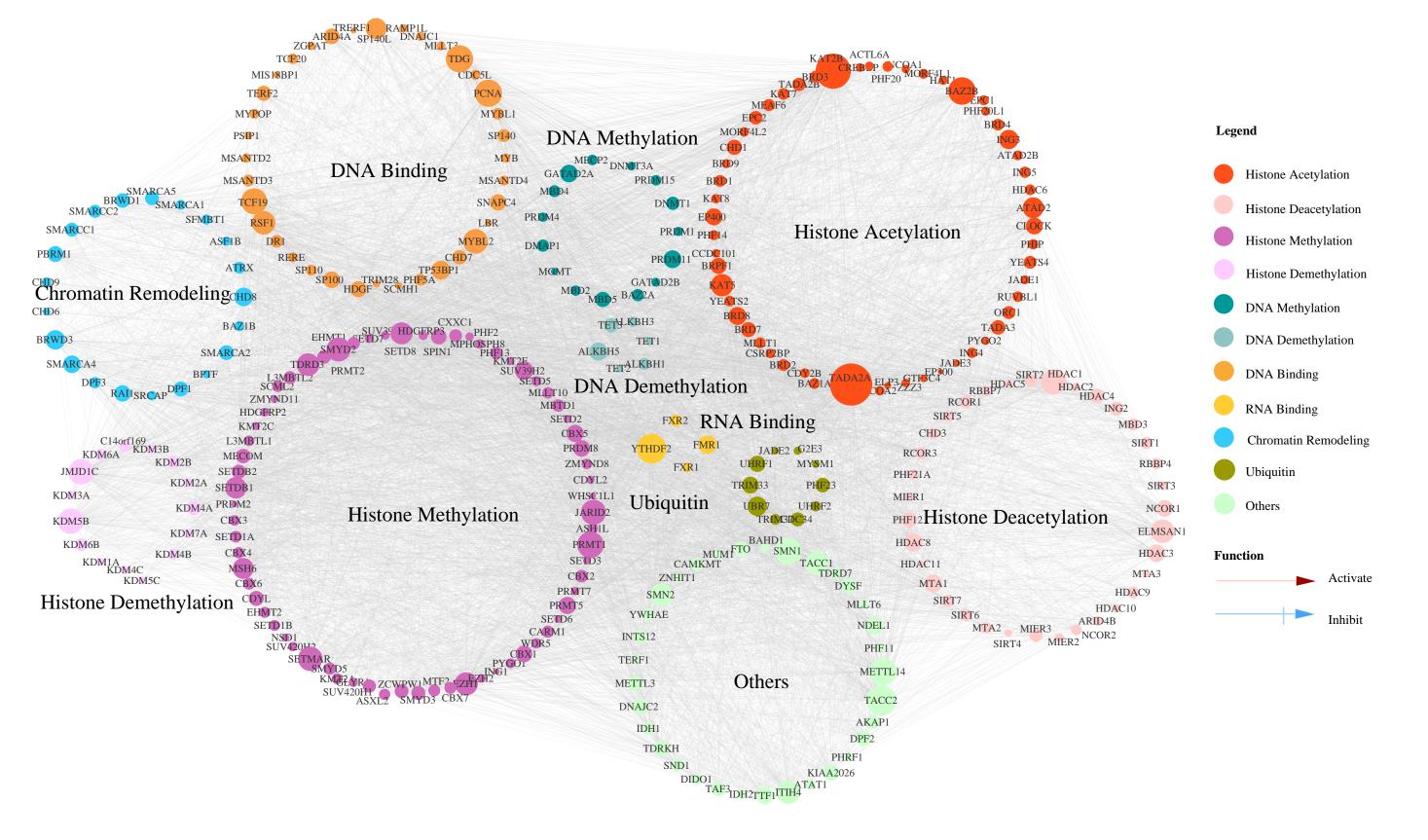
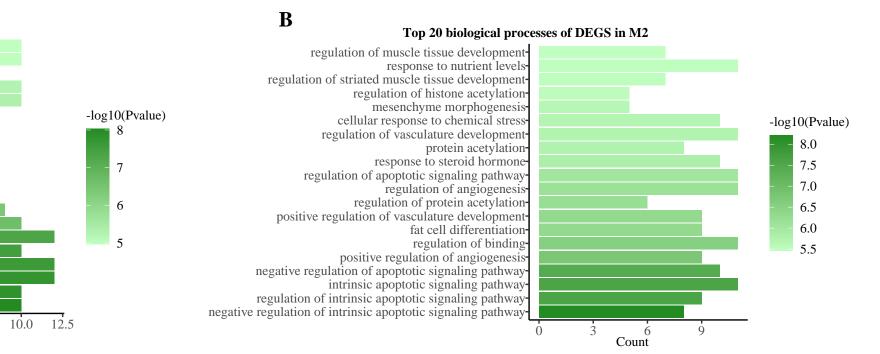


Figure S3. The regulatory network of 299 epigenetic regulators. Each node represents an epigenetic regulator and different color represents different function. The edge represents a regulatory interaction between two epigenetic regulators. The red arrow means activation, and the blue cross delta means inhibition.



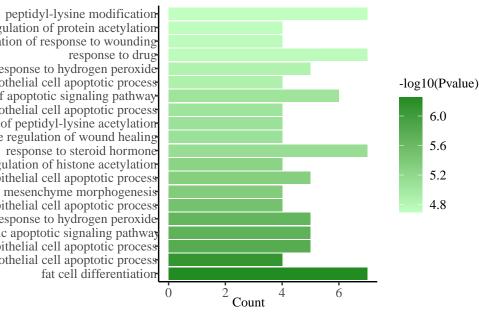
positive regulation of cytokine productionregulation of vasculature development-

regulation of apoptotic signaling pathway

positive regulation of vasculature development

Α Top 20 biological processes of DEGS in M1 positive regulation of cytokine productionregulation of vasculature development neuron cellular homeostasis regulation of apoptotic signaling pathway peptidyl-lysine modification regulation of peptidyl-lysine acetylation cellular response to hydrogen peroxide myeloid cell homeostasis negative regulation of intrinsic apoptotic signaling pathway positive regulation of angiogenesis signal transduction in response to DNA damage regulation of protein acetylation positive regulation of vasculature development intrinsic apoptotic signaling pathway response to oxygen levels cellular response to oxygen levels response to decreased oxygen levels response to hypoxia cellular response to decreased oxygen levels cellular response to hypoxia-5.0 Count 0.0 2.5 7.5

Top 20 biological processes of DEGS in M3



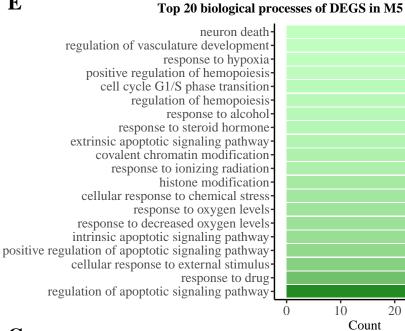
30

40

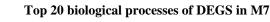
regulation of protein acetylation positive regulation of response to wounding response to drug response to hydrogen peroxide endothelial cell apoptotic process negative regulation of apoptotic signaling pathway regulation of endothelial cell apoptotic process regulation of peptidyl-lysine acetylation positive regulation of wound healing response to steroid hormone regulation of histone acetylation epithelial cell apoptotic process mesenchyme morphogenesis negative regulation of epithelial cell apoptotic process cellular response to hydrogen peroxide negative regulation of intrinsic apoptotic signaling pathway regulation of epithelial cell apoptotic process negative regulation of endothelial cell apoptotic process fat cell differentiation

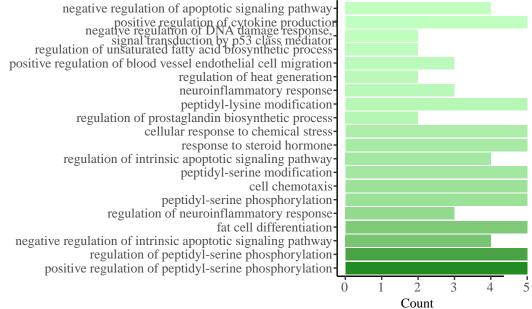
E

С



G





positive regulation of hemostasis positive regulation of blood coagulation positive regulation of angiogenesis

muscle cell migration regulation of angiogenesis

prostanoid biosynthetic process

prostaglandin biosynthetic process

positive regulation of coagulation

cellular response to hydrogen peroxide

cellular response to chemical stress positive regulation of blood vessel endothelial cell migrationpositive regulation of response to wounding regulation of intrinsic apoptotic signaling pathway positive regulation of wound healing negative regulation of apoptotic signaling pathway negative regulation of intrinsic apoptotic signaling pathway-

D

F

Η

-log10(Pvalue)

16

14

12

-log10(Pvalue)

6

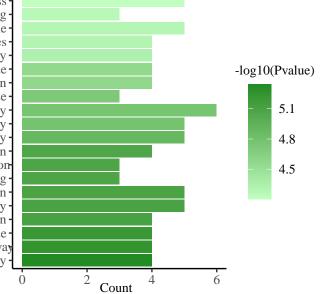
5

Top 20 biological processes of DEGS in M6

2

Count

Top 20 biological processes of DEGS in M4



-log10(Pvalue)

6.5

6.0

5.5

5.0

cellular response to chemical stresspositive regulation of wound healing response to steroid hormone. cellular response to reactive oxygen speciesregulation of intrinsic apoptotic signaling pathway response to hydrogen peroxide regulation of peptidyl-serine phosphorylation regulation of neuroinflammatory response. negative regulation of hydrolase activity negative regulation of peptidase activity. negative regulation of endopeptidase activity. positive regulation of peptidyl-serine phosphorylation negative regulation of protein maturation negative regulation of protein processing. fat cell differentiation. negative regulation of apoptotic signaling pathway muscle cell migration. cellular response to hydrogen peroxide. negative regulation of intrinsic apoptotic signaling pathway negative regulation of cysteine-type endopeptidase activity -

Top 20 biological processes of DEGS in M8

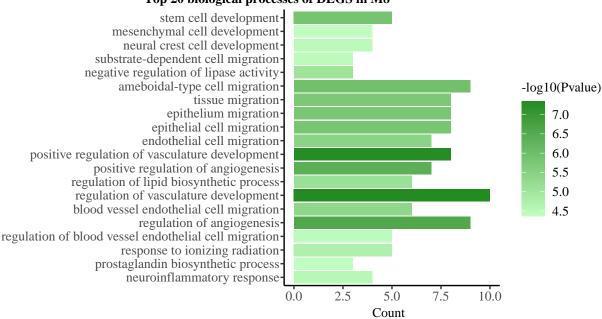


Figure S4. The functions of 8 modules. (A-H) The top 20 biological process term enriched by the DEGs regulated by 8 modules, respectively.

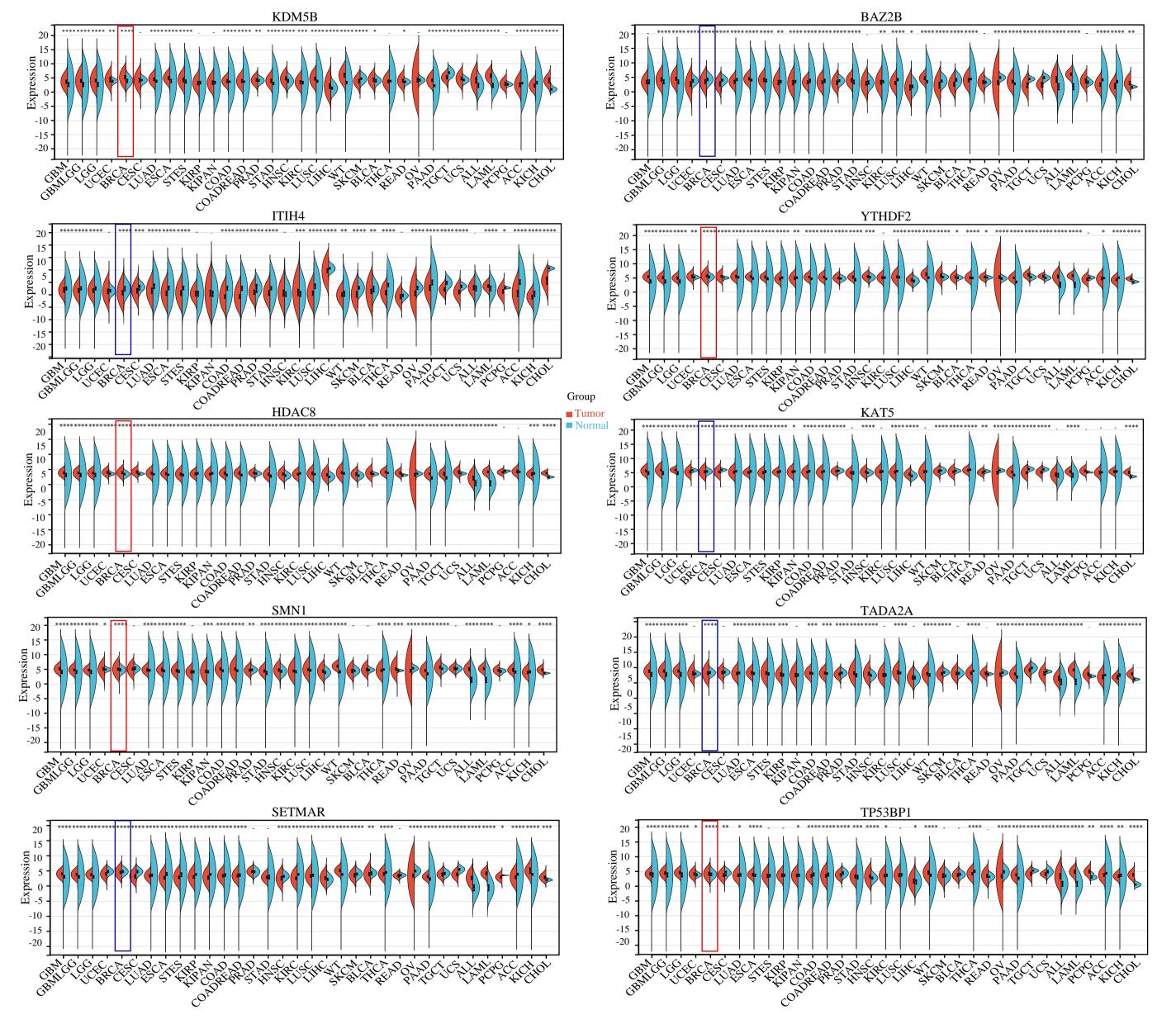


Figure S5. Differentially expression of 10 master epigenetic regulators in pan-cancers. The red is tumor sample, and the blue is normal sample. The differentially expression of 10 master epigenetic regulators in BRCA was highlighted by red box or blue box. The red box means that the master regulator was up-regulated in BRCA. And the blue box means that the master regulator was down-regulated in BRCA

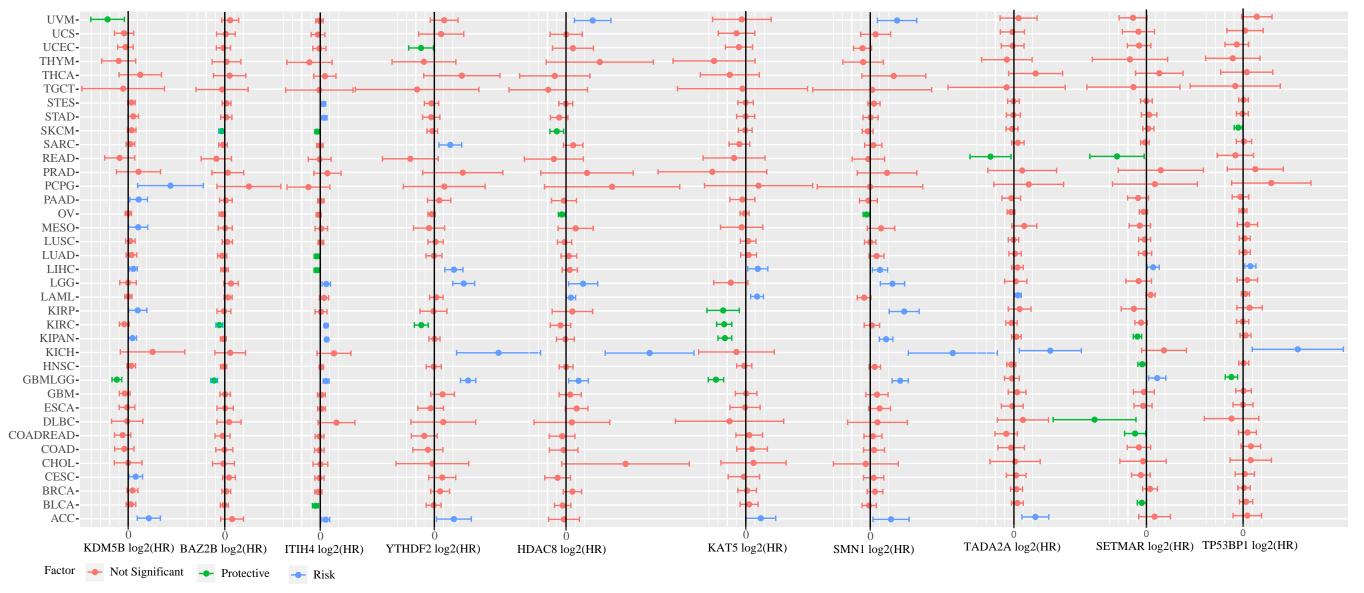


Figure S6. Survival analysis for 10 master epigenetic regulators in pan-cancers. The forest plots for 10 master epigenetic regulators in pan-cancer. The red means the epigenetic regulator has no significance for the survival of this cancer. The green means the epigenetic regulator is a protective factor for this cancer. And the bule means the epigenetic regulator for this cancer.