Supplementary Figures



Supplementary Fig. S1. Quality Control (QC) Analysis of multi-omics data from TCGA. Illustrated is the example of a). IncRNA expression profile; b). gene expression profile and c). DNA methylation profile for breast cancer. Top panels of the plots are the scree plots which indicate the fractional variation of the total data variation accounted for by each of the top-ranked and significant singular vectors from the SVD analysis. The number of significantly variable singular vectors was determined by Random Matrix Theory (RMT). Lower panels depict heatmaps of P-values of association between each singular vector and biological and technical factors. Color Codes: Dark-red (P<1e-10), Red (P<1e-5), Orange (P<0.01), Pink (P<0.05), White (P> 0.05). As we can see, the top ranked singular vectors correlate strongly with hormone receptor status (PR status, ER status), which could have strong confounding effects. For other cancer types which the singular vector correlated unambiguously with normal/cancer status (for lncRNA, gene expression profiles and 450k DNA methylation) were directly used in this study.



Supplementary Fig. S2. LncRNA profiles across human cancers. a). Number of lncRNAs in each category, showing that 'lincRNA' and 'antisense' consists of the most. b). The number of lncRNAs in each cancer type, which ranges from ranges from 10438 to 14013. c). Expression level distribution of lncRNAs and protein coding genes, showing lower levels of lncRNAs compared with protein coding genes.



Supplementary Fig. S3. Global landscape of DNA methylation mediated lncRNA regulatory network across 18 cancer types. Blue nodes represent lncRNAs and red nodes represent target genes.



Supplementary Fig. S4. The percentage of protein coding genes and lncRNAs within networks across 18 types of cancer. a). Percentage of protein coding genes whose promoter methylation changes attribute to lncRNA regulation. b) Percentage of expressed lncRNAs in regulation of methylation change.



Supplementary Fig. S5. The Degree distribution of the DNA methylation mediated IncRNA regulatory networks. A power law distribution was observed across 18 cancer types.



Supplementary Fig. S6. The Degree distribution of the lncRNAs within networks across 18 cancer types.



Supplementary Fig. S7. The Degree distribution of the protein coding genes within networks across 18 cancer types.



Supplementary Fig. S8. The correlation between promoter of the targets and the total expression of lncRNAs is plotted as a function of the number of lncRNA targets across 18 cancer types.



Supplementary Fig. S9. The correlation between expression of the genes and the total expression of lncRNAs is plotted as a function of the number of lncRNA targets across 18 cancer types.



Supplementary Fig. S10. The correlation between promoter of the protein coding genes and the total expression of lncRNAs is plotted as a function of the number of lncRNA regulators across 18 cancer types.



Supplementary Fig. S11. The correlation between expression of the genes and the total expression of lncRNAs is plotted as a function of the number of lncRNA regulators across 18 cancer types.



Supplementary Fig. S12. Boxplots indicated that lncRNA-gene interaction pairs mainly occur *in Trans* **across cancers**. The percentage of distance distribution between lncRNAs and gene the interactions are mainly from different chromosomes or long range from the same chromosome.



Supplementary Fig. S13. Diagram for different types of lncRNA-gene interactions according to their expression status in both normal and cancer samples.



Supplementary Fig. S14. The proportion of cancer specific a). IncRNA targets and b). IncRNA-gene pairs in each cancer type.



Supplementary Fig. S15. Percentage of different type of lncRNA modulators across categories.



Supplementary Fig. S16. Boxplot of the degree distribution for three different types of the lncRNA modulators from 18 cancer types. For each cancer type presents the average degree for pan-cancer modulators are generally higher than Moderate and Cancer-specific modulators.





Supplementary Fig. S17. Boxplot of the Jaccard coefficient for pair-wise cancer type comparison to measure the similarity at the lncRNA, gene and lncRNA-gene pairs respectively. Significance P-values were calculated by using paired Wilcoxon rank sum test.



Supplementary Fig. S18. The functions of lncRNA targets derived from similar tissues, including a). LUSC and LUAD, b). KIRC and KIRP and c). LIHC and CHOL. Upper panels are Venn diagram indicated the number of shared lncRNA target genes and lower panels are biological processes enriched by these genes



Supplementary Fig. S19. Scatter plot of ENSG00000227036 expression and methylation of CpG sites within promoter region of *KRT15*. green points represent normal samples and red points are cancer samples. P-values from Pearson correlation analysis indicated 5/6 of the CpG sites present significant correlation between methylation and lncRNA expression.



Supplementary Fig. S20. Scatter plot of ENSG00000203499 expression and methylation of CpG sites within promoter region of *CDKN1A*. green points represent normal samples and red points are cancer samples. P-values from Pearson correlation analysis indicated all of the 9 CpG sites present significant correlation between methylation and lncRNA expression.



Supplementary Fig. S21. Scatter plot of ENSG00000203499 expression and average methylation of *CDKN1A* **promoter region across cancer types.** P-values from Pearson correlation analysis indicated 14 cancer types present significant correlation between methylation and lncRNA expression.



Supplementary Fig. S22. *ZEB2-AS1* associated module identified and Kaplan– Meier plot of survival for a). BLCA, b). LUSC and c). PAAD. The upper panels are the modules, the middle and lower panels are survival plots in Discovery and Validation Sets respectively.



Supplementary Fig. S23. Number of genes whose expression dysregulation driven by DNA methylation in each cancer type.