

**Figure-S1. The human core essential lncRNAs and genes.**

A, The number of essential genes identified in different number of cell lines for three independent studies. Left for Hart et al., middle for Blomen et al., and right for Wang et al.

B, The overlap of essential lncRNAs across cancer cell lines. The up panel shows the number of lncRNAs for different combinations shown in the middle panel. Black dots represent the occurrence while the gray dots represent absent. The right panel shows the number of lncRNA in each cell line.

C, The Venn plot shows the overlap of core essential genes in three studies.



**Figure-S2. The miRNA regulation of human essential lncRNAs.**

A-E, The number of miRNA regulators for essential lncRNAs and other lncRNAs in five cell lines. A, MCF-7; B, MDA-MB-231; C, K562; D, Hela and E, U87.

F, The computational pipeline for identification ceRNA regulation in cancer.

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**Figure-S3. The cancer mutations for ceRNAs in five types of cancer.**

A, The mutation frequency of ceRNAs and other genes.

B, The frequency of mutations in ceRNAs and other genes of five cancer types.

C, The CADD score for mutations in ceRNAs and randomly selected mutations in five cancer types.

D, The conservation score for mutations in ceRNAs and randomly selected mutations in five cancer types. P-values were calculated by Wilcoxon rank sum test.

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**Figure-S4.** **Functional characteristic of essential coding genes.**

A, The average expression level of essential genes and other genes across normal tissues in human protein atlas.

B and C, The distribution of degree (B) and betweenness (C) for essential genes and other genes in human protein-protein interaction network.

D, The average number of interacting partners for essential genes and other genes across human tissue specific interaction network.

E, The frequency of mutations in essential genes and randomly selected mutations.

F, The CADD score for mutations in essential genes and randomly selected mutations.

G, The conservation score for mutations in essential genes and randomly selected mutations. P-values were calculated by Wilcoxon rank sum test. Green, essential genes from Blomen et al. study. Light green, essential genes from Wang et al. study, blue, essential genes from Hart et al. study.

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**Figure-S5. Network-based essentiality prediction.**

A, The distribution of degree for ceRNA regulatory network in five cancer types.

B, The distribution of AUCs based on different essential gene sets as seed. Up, essential genes from Hart et al. study, middle, essential genes from Blomen et al. study, bottom, essential genes from Wang et al. study.

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**Figure-S6. Functional characteristic of essential coding genes.**

A, GSEA enriched pathways by genes with higher essential scores.

B, The cell cycle pathways enriched by both essential lncRNA and protein coding genes. Genes were colored by essential lncRNA regulated genes (light blue), essential protein coding genes (green) and overlapping genes (red).

C, The number of interactions among human essentialome. Red dot, the number of observed interactions among human essential lncRNA regulated genes and essential coding genes. The grey line indicated the distribution for the same number of randomly selected genes in human interaction network.

D, The cell cycle module in human interaction network. The size of genes corresponds to the number of interactions and the color is same as B.



**Figure S7. Cancer hallmarks related ceRNA regulation and drug targets.**

A, The lncRNA-hallmark network in cancer. Green, essential lncRNAs; orange, ceRNAs of essential lncRNAs; blue, cancer hallmarks. The lncRNA-gene links were ceRNA regulation and genes were linked to their associated hallmarks based on functional annotation.

B, Two representative lncRNAs (*TUG1* and *PVT1*) related subnetworks.