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Supplementary Fig. S1. Functional analysis of module 18 ESCC-EAC-BE-heterozygous.

(A) Network-style display and the PLA result of module 18. In the network circles, diamonds and hexagons stand for lncRNAs, PCGs and subpathways, respectively. LncRNAs and PCGs annotated by us are marked by an orange border. The greater the node size, the larger the node degree. Blue, red and green edges represent lncRNA-PCG pairs that belong to the ESCC/normal, EAC/normal and BE/normal groups, respectively. Depth of the purple hexagons represents the significance (*p*-value) of every subpathway; the darker the hexagon, the more significant the subpathway (smaller *p*-value). Notably, the white node labels on a black background indicate the corresponding genes were not annotated as mutated in the COSMIC database.

(B) Magnified array-style display of module 18.

(C) GO BP enrichment analysis of module 18. In the histogram, the bar length is proportional to the *p*-value of the corresponding GO BP. Gold rectangles mark validated cancer-risk GO BPs.



Supplementary Fig. S2. Functional analysis of module 19 (EAC-BE-specific).

(A) Network-style display and PLA results of module 19. In the network, circles, diamonds and hexagons stand for lncRNAs, PCGs and subpathways, respectively. LncRNAs and PCGs annotated by us are marked with an orange border. The greater the node size, the larger node degree. Red and green edges represent lncRNA-PCG pairs that belong to the EAC/normal and BE/normal groups, respectively. Depth of the purple hexagons represents the significance (*p*-value) of every subpathway; the darker the hexagon, the more significant the subpathway (smaller *p*-value). Pink lines emphasize validated cancer-risk lncRNAs, PCGs and subpathways. Pink bordered figures are the genomic positions of the corresponding lncRNAs. Notably, the white node labels on a black background indicate the corresponding genes were not annotated as mutated in the COSMIC database, and those on a red background indicate the corresponding genes were annotated as mutated in the COSMIC Cancer census.

(B) Magnified array-style display of module 19.

(C) GO BP enrichment analysis of module 19. In the histogram, bar length is proportional to the p-value of the corresponding GO BP. Gold rectangles mark validated cancer-risk GO BPs.



Supplementary Fig. S3. Functional analysis of module 20 (EAC-BE specific).

(A) Network-style display and PLA results of module 20. In the network, circles, diamonds and hexagons stand for lncRNAs, PCGs and subpathways, respectively. LncRNAs and PCGs annotated by us are marked with an orange border. The greater the node size, the larger node degree. Red and green edges represent lncRNA-PCG pairs belonging to the EAC/normal and BE/normal groups, respectively. Depth of the purple

hexagons represents the significance (*p*-value) of every subpathway; the darker the hexagon, the more significant the subpathway (smaller *p*-value). Pink lines emphasize validated cancer-risk lncRNAs, PCGs and subpathways. Pink bordered figures are the genomic positions of the corresponding lncRNAs. Notably, the white node labels on a black background indicate the corresponding genes were not annotated as mutated in the COSMIC database.

(B) Magnified array-style display of module 20.

(C) GO BP enrichment analysis of module 19. In the histogram, bar length is proportional to the *p*-value of the corresponding GO BP. Gold rectangles mark validated cancer-risk GO BPs.



Supplementary Fig. 4. Genomic distribution of lncRNAs obtained by EPR and DE selection.

The four pie charts interpret the distribution of differentially-expressed lncRNAs on the genome in the four tissue-specific groups (ESCC/normal, EAC/normal, BE/normal and EAC/BE), respectively. Six different colors are used to distinguish the different kinds of lncRNAs regarding their individual genome location character.