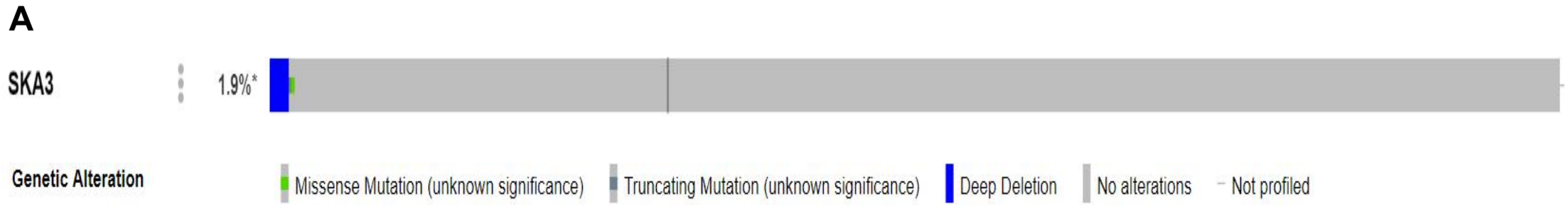
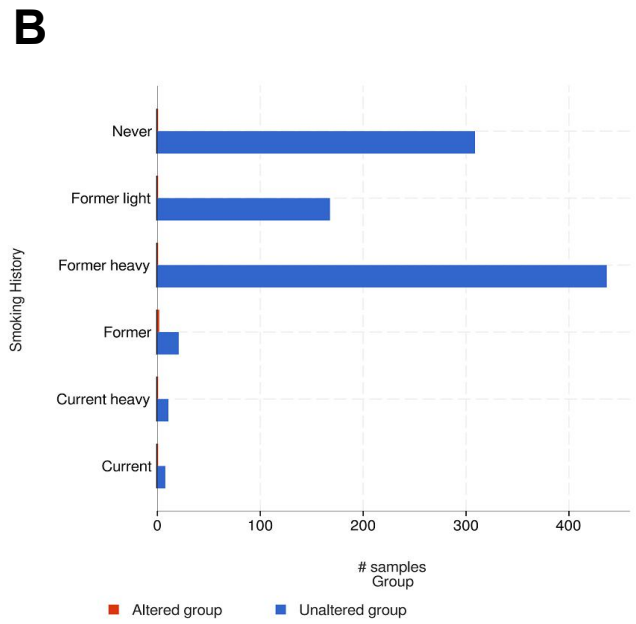
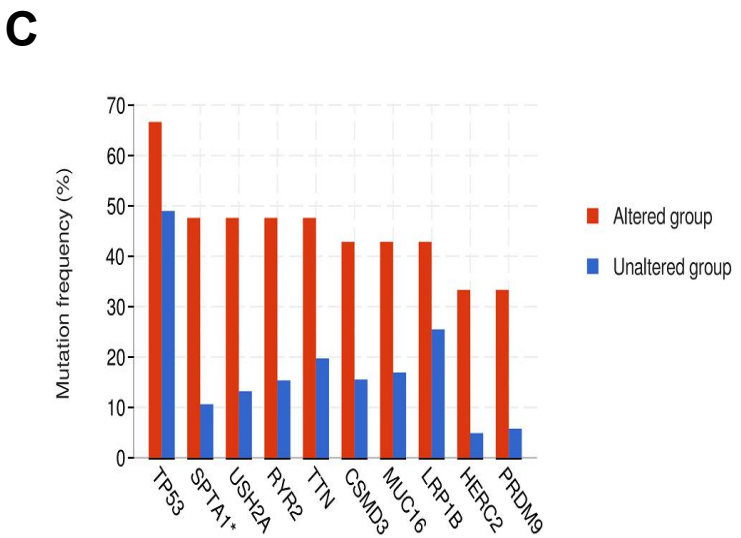
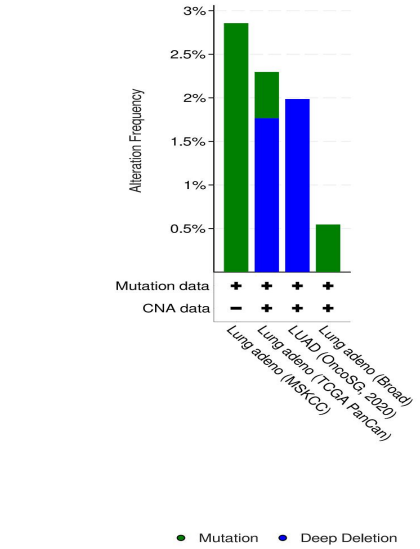
Supplementary Figure 1

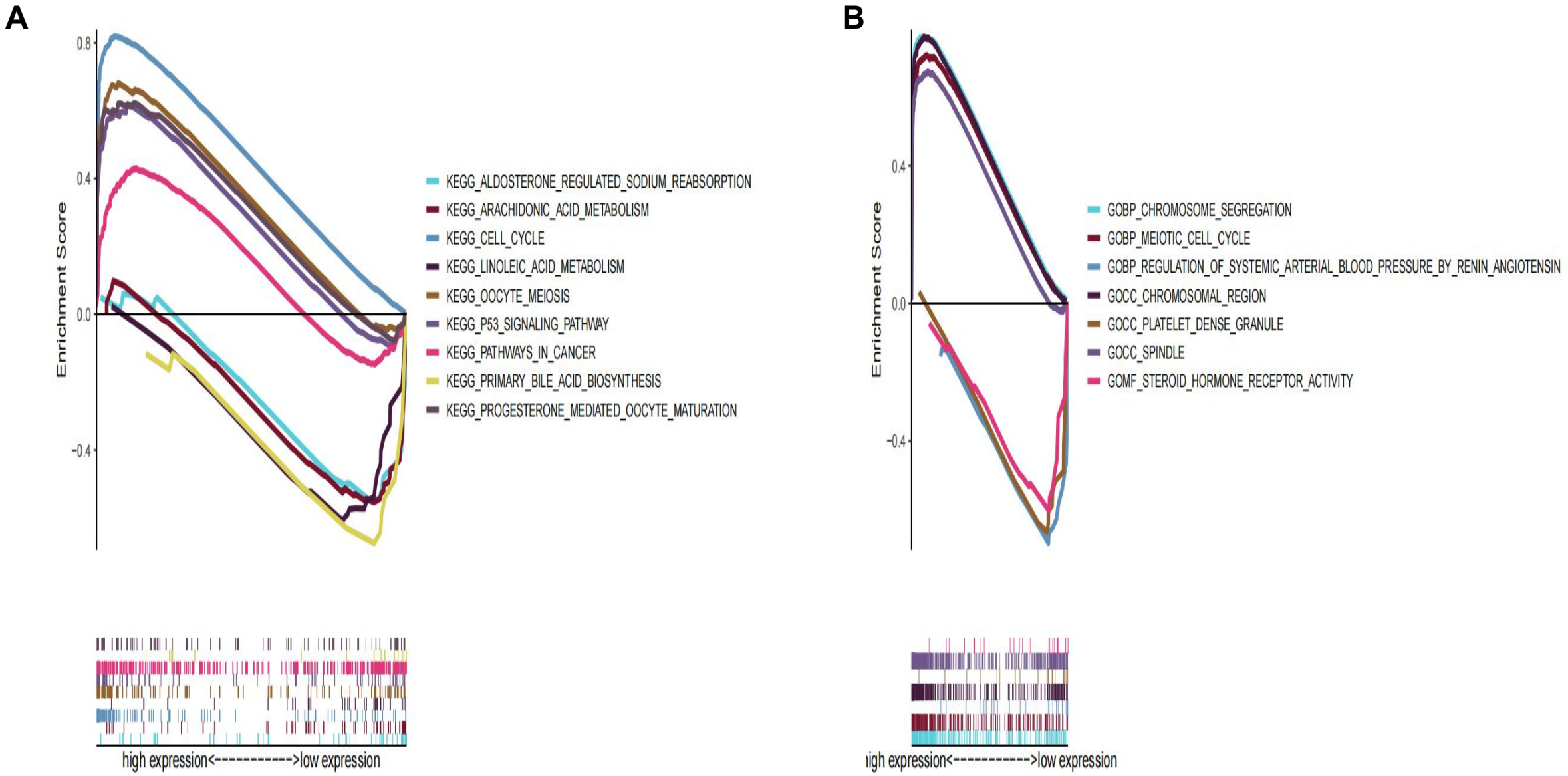








Supplementary Figure 2



Supplementary Figure 3

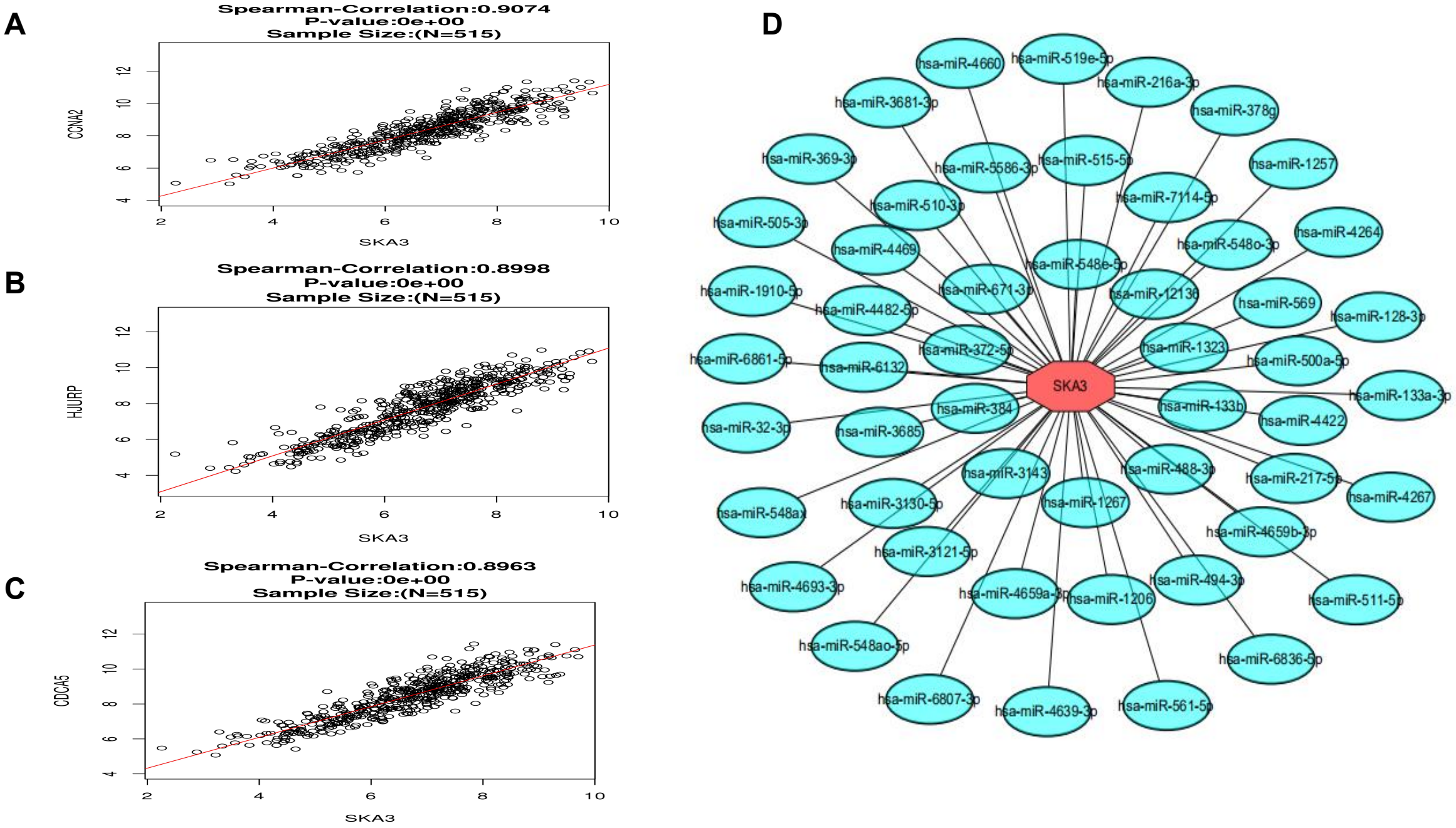


Figure Legend

Figure 1. SKA3 expression levels in diverse kinds of human cancers and transcription level in LUAD. (A): Workflow of this study. (B): SKA3 expression levels in diverse kinds of tumors in TCGA web resource (TIMER).(C): Increased or decreased SKA3 in diverse tumors vs healthy tissues in Oncomine web resource. (D, E): Levels of SKA3 mRNA remarkably higher in LUAD than in healthy tissue. Box plot indicating SKA3 mRNA levels in selamat lung, okayama lung by Oncomine. (F): The expression levels of SKA3 in tumor and non-cancer tissues of LUAD patients in TCGA database. (G): Comparison of SKA3 expression pre-disease and post-disease in the same sample. (H): Histogram of the difference between SKA3 expression levels in lung adenocarcinoma tissues of mice and normal lung tissues. (I): Immunohistochemical (IHC) staining of SKA3 expression in lung adenocarcinoma samples and normal tissues in the Human Protein Atlas. a and b represent the expression of SKA3 in tumors and normal tissues, respectively. ***, $p < 0.001$.

Figure 2. Kaplan-Meier survival curves comparing the high and low expression of SKA3 in LUAD. (A-C): Survival curves of PFS, OS and RFS in two LUAD cancer cohorts (PrognoScan) [GSE13213 (n = 125) and GSE31210 (n = 204)]. (D, E): OS and FP survival curves of lung cancer (Kaplan-Meier Plotter). (n = 1114, n = 596).

Figure 3. SKA3 transcription in subgroups of LUAD patients, stratified on the baisis of types, gender, age, race, smoking and stages (UALCAN). (A): Boxplot

shows expression of SKA3 in LUAD and normal patients. (B): Boxplot shows expression of SKA3 in normal people of either gender or male or female LUAD patients. (C): Boxplot shows relative expression of SKA3 in normal people of any ethnicity or Caucasian, African-American or Asian ethnicity in LUAD. (D): Boxplot shows relative expression of SKA3 in normal people of either smoker or non-smoker, smoker, reformed smoker (<15years) or reformed smoker (>15years). (E): Boxplot shows relative expression of SKA3 in normal people or in LUAD patients in stages 1, 2, 3 or 4. (F): Boxplot shows relative expression of SKA3 in healthy individuals of any age or in LUAD patients aged 21-40, 41-60, 61-80, or 81-100 years. The edges of the box are the 25th and 75th percentiles. The significance of difference in SKA3 expression between groups by the t-test. **, $p < 0.01$; ***, $p < 0.001$.

Figure 4. The expression of SKA3 in LUAD was related to immune infiltration and Prognostic value. (A): SKA3 expression has remarkable negatively correlations with the infiltration levels of B cells, CD4+ T cells and macrophages in LUAD. (B): SKA3 CNV influences the infiltration level of B cells, CD4+ T cells and macrophages in LUAD. P-value Significant Codes: *** < 0.001, ** for p < 0.01, * for p < 0.05. (C-N): Kaplan Meier analysis of prognostic correlation with different immune cells subgroup in LUAD.

Figure 5. SKA3 promoter methylation level in LUAD, stratified based on types，stage, nodal metastasis, age, gender and smoking (UALCAN). (A): DNA

methylation and mRNA expression of SKA3 from TCGA. (B): SKA3 promoter methylation profile based on individaul cancer stages. (C): SKA3 promoter methylation profile based on nodal metastasis stutas. (D): SKA3 promoter methylation profile based on patients‘s gender. (E): SKA3 promoter methylation profile based on patients‘s age. (F): SKA3 promoter methylation profile based on smoking stutas. The difference of SKA3 expression among groups through the t-test. *, $p < 0.05$; **, $p < 0.01$.

Figure 6. SKA3 co-expression genes in LUAD. (A): Identification of highly related genes of SKA3 by Pearson test in LUAD cohort (LinkedOmics). (B, C): Heat maps showed that the top 50 genes were positively and negatively linked to with SKA3 in LUAD. Red represents positive correlation gene, blue represents negative correlation gene (LinkedOmics). (D, E): Remarkably enriched GO annotations, as well as KEGG pathways correlated with SKA3 showing top 15 genes positively in LUAD cohort (webgestalt).

Supplementary Figure 1. SKA3 genomic alterations in LUAD (cBioPortal). (A): OncoPrint of SKA3 alterations in LUAD cohort. The different types of genetic alterations are highlighted in different colors. (B): Distribution of SKA3 CNV frequency in different smoking history. The percentage figure of the bar chart shows the proportion of patients in the altered and non-altered SKA3 groups. (C): Distribution of SKA3 mutation frequency at different mutation points. The bar chart

percentage figures represent the proportion of patients in the altered and non-altered SKA3 groups. (D): CNA and mutation frequency data from cBioPortal.

Supplementary Figure 2. A GSEA for SKA3. GSEA, Gene Set Enrichment Analysis

A and B: GSEA results showing gene sets in KEGG and GO of GSEA suggested that SKA3 levels were associated with cell cycle, pathways in cancer, p53 signaling pathway and meiotic cell cycle in LUAD.

Supplementary Figure 3. SKA3 was associated with the top three positive genes (CCNA3, HJURP and CDCA5) and miRNA-target. The scatter plot showed Pearson correlation of SKA3 expression with expression of CCNA3 (A), HJURP (B), and CDCA5 (C) (LinkedOmics). (D): miRNA-target regulatory network predicted by miRDB (Cytoscape).