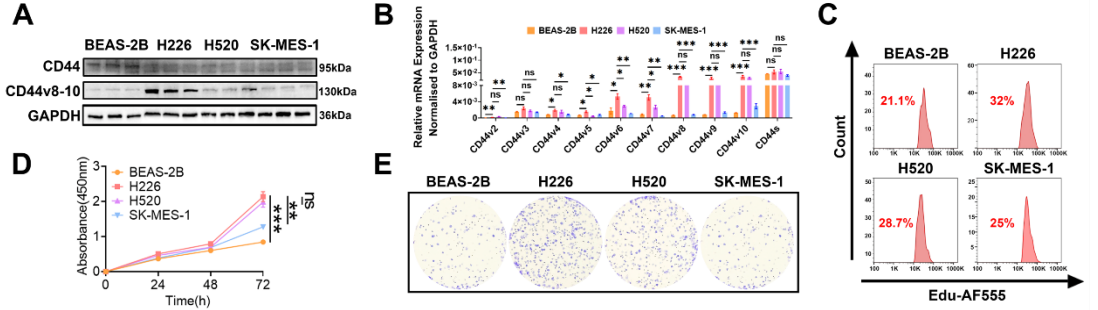


Supplementary Figure 1. CD44v8-10 expression is elevated in LUSC and associated with poor prognosis.

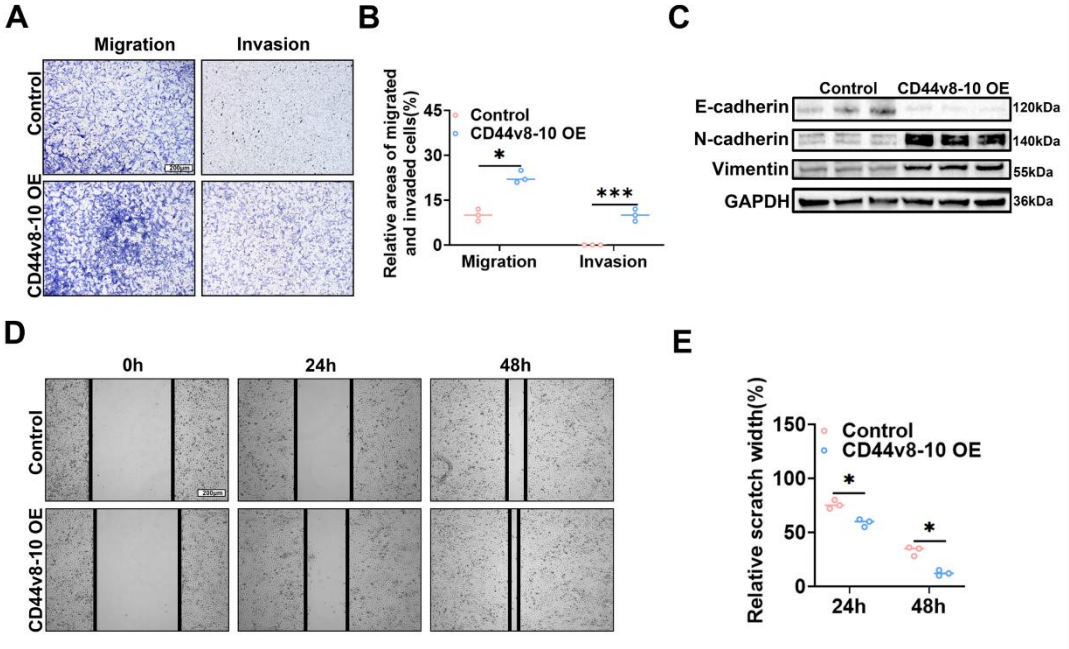
(A) WB analysis of CD44 and its isoforms in different cell lines. Protein levels of CD44 and its isoform CD44v8-10 are shown in BEAS-2B (normal lung epithelial cells), H226, H520, and SK-MES-1 (Lung squamous cell carcinoma cell lines), with GAPDH as a loading control.

(B) qRT-PCR analysis of *CD44* isoform relative mRNA expression of *CD44* isoforms (n=3). Data are presented as mean ± SD.

(C) Cell proliferation analysis using CCK8 assay. The absorbance values at 450 nm indicate the cell proliferation rate at different time points (24, 48, and 72 hours) (n=3). Datas are presented as mean ± SD.

(D) Colony formation assay. Representative images showing colony formation ability of the cell lines. Colonies were stained with crystal violet, and the number of colonies was visually assessed.

(E) EdU incorporation assay analysis of proliferation rate. Flow cytometry histograms showing the percentage of cells undergoing DNA synthesis in each cell line, indicated by Edu incorporation. Statistical analyses were performed using the one-way ANOVA followed by Tukey's post hoc test. for (B and C). NS, not significant for $P > 0.05$, *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.



Supplementary Figure 2. CD44v8-10 OE enhances cell migration, invasion, and epithelial–mesenchymal transition (EMT).

(A) Representative images of Transwell migration and invasion assays in Control and *CD44v8-10* OE cells. Migrated and invaded cells were stained with crystal violet. Scale bars, 2000 μm.

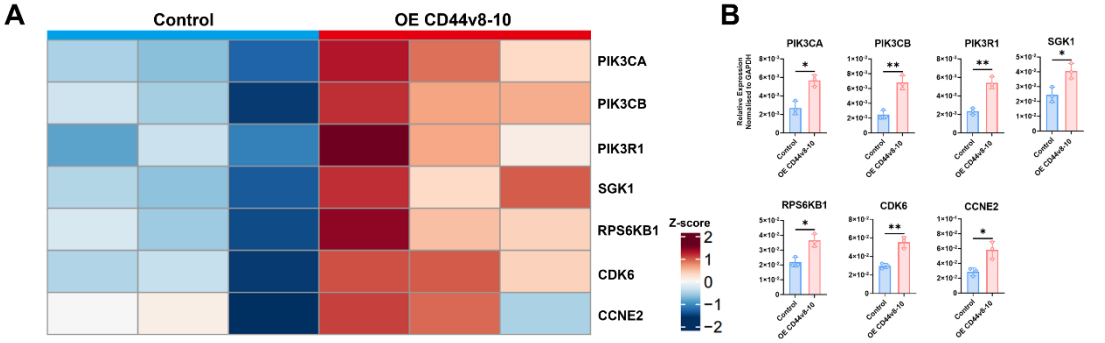
(B) Quantification of migrated and invaded cells. Relative areas of migrated and invaded cells (%) are shown for Control and *CD44v8-10* OE groups (n=3). Data are presented as mean ± SD.

(C) WB analysis of epithelial–mesenchymal transition (EMT)-related proteins in Control and *CD44v8-10* OE cells. Protein levels of E-cadherin, N-cadherin, and Vimentin were detected by western blot, with GAPDH as a loading control.

(D) Representative wound healing assay images of Control and *CD44v8-10* OE cells at 0 h, 24 h, and 48 h. Scale bars, 2000 μm.

(E) Quantification of wound closure. Relative scratch width (%) at 24 h and 48 h in Control and *CD44v8-10* OE cells (n=3). Data are presented as mean ± SD.

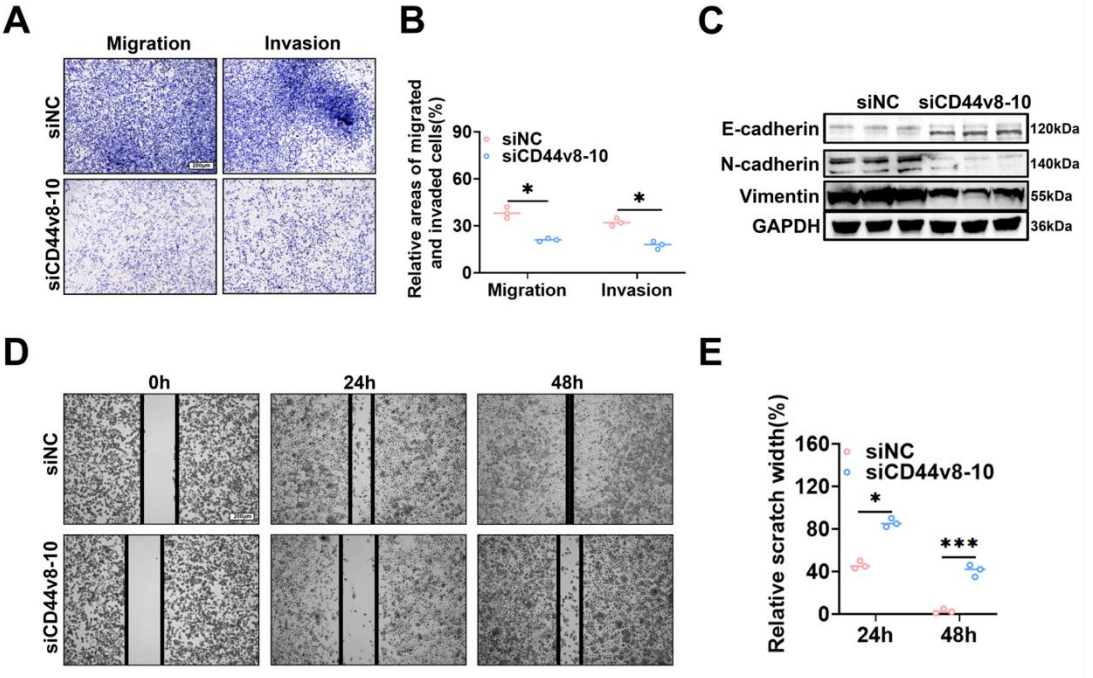
Statistical analyses were performed using the two-tailed unpaired t test for (B and E). NS, not significant for $P > 0.05$, *$P < 0.05$, ***$P < 0.001$.



Supplementary Figure 3. CD44v8-10 overexpression increases the expression of PI3K–AKT signaling- and cell cycle-associated genes in BEAS-2B cells.

(A) Heatmap showing the relative expression patterns (row z-score) of PI3K–AKT signaling- and cell cycle-related transcripts in Control and CD44v8-10-overexpressing (OE) BEAS-2B cells. Compared with control cells, CD44v8-10 overexpression was associated with increased expression of genes involved in PI3K–AKT signaling and cell cycle regulation.

(B) qRT-PCR validation of selected PI3K–AKT signaling-related genes (PIK3CA, PIK3CB, PIK3R1, SGK1) and cell cycle-related genes (RPS6KB1, CDK6, CCNE2) in Control and CD44v8-10 OE BEAS-2B cells. mRNA expression levels were normalized to GAPDH and presented as mean ± SD (n = 3). Statistical significance was determined using a two-tailed unpaired t-test. NS, not significant ($P > 0.05$); *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.



Supplementary Figure 4. *CD44v8-10* knockdown suppresses migration, invasion, and EMT progression in H226 cells.

(A) Representative images of Transwell migration and invasion assays in H226 cells transfected with siNC or si*CD44v8-10*. Migrated and invaded cells were stained with crystal violet. Scale bars, 200 μm.

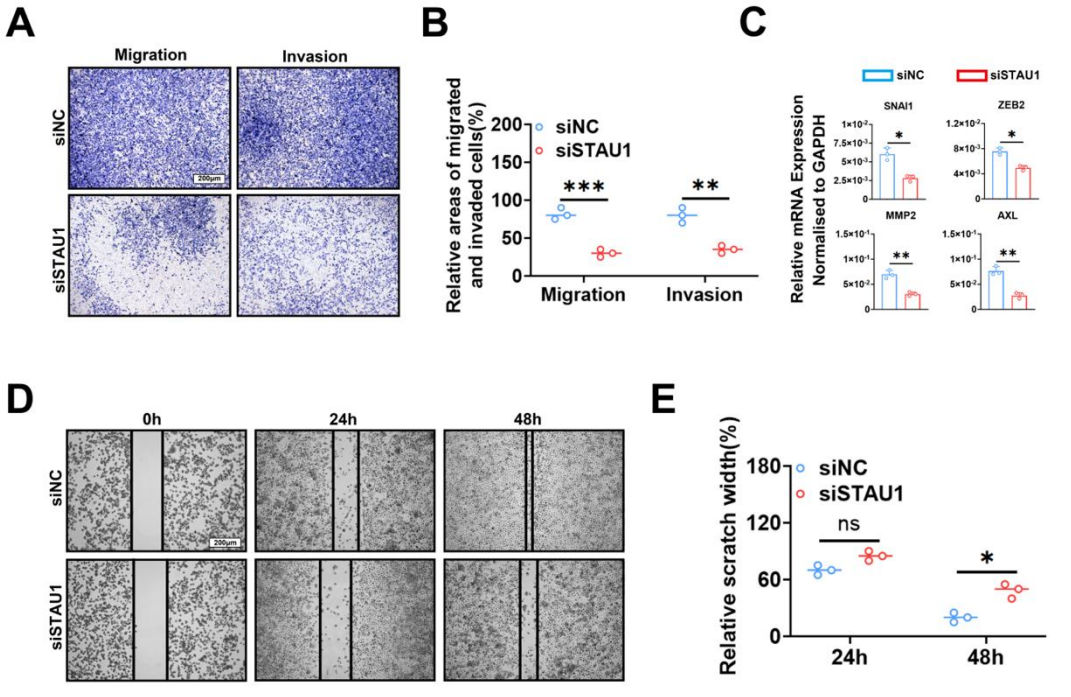
(B) Quantification of migrated and invaded cells in siNC and si*CD44v8-10* groups (n=3). Relative areas of migrated and invaded cells (%) are shown. Data are presented as mean ± SD.

(C) WB analysis of epithelial–mesenchymal transition (EMT)-related proteins in H226 cells following *CD44v8-10* knockdown. Protein levels of E-cadherin, N-cadherin, and Vimentin were detected by western blot, with GAPDH as a loading control.

(D) Representative wound healing assay images of H226 cells transfected with siNC or si*CD44v8-10* at 0 h, 24 h, and 48 h. Scale bars, 200 μm.

(E) Quantification of wound closure in siNC and si*CD44v8-10* cells (n=3). Relative scratch width (%) at 24 h and 48 h is shown. Data are presented as mean ± SD.

Statistical analyses were performed using the two-tailed unpaired t test for (B and E). NS, not significant for $P > 0.05$, *$P < 0.05$, ***$P < 0.001$.



Supplementary Figure 5. STAU1 knockdown suppresses migration, invasion, and EMT/invasion-associated gene expression in H226 cells.

(A) Representative images of Transwell migration and invasion assays in H226 cells transfected with siNC or siSTAU1. Migrated and inva0ded cells were stained with crystal violet. Scale bars, 200 μm.

(B) Quantification of migrated and invaded cells in siNC and siSTAU1 groups (n = 3). Relative areas of migrated and invaded cells (%) are shown. Data are presented as mean ± SD.

(C) qRT–PCR analysis of EMT-and invasion-associated genes in H226 cells following *STAU1* knockdown. The mRNA levels of *SNAI1, ZEB2, MMP2*, and *AXL* are shown relative to siNC. Data are presented as mean ± SD.

(D) Representative wound-healing assay images of H226 cells transfected with siNC or siSTAU1 at 0, 24 h, and 48 h. Scale bars, 200 μm.

(E) Quantification of wound closure in siNC and si*STAU1* cells (n = 3). Relative scratch width (%) at 24 h and 48 h is shown. Data are presented as mean ± SD.

Statistical analyses were performed using the two-tailed unpaired t test for (B, C, and E). NS, not significant (P > 0.05); *P < 0.05; **P < 0.01; ***P < 0.001.

Supplementary Table The sequences of primers used for qRT-PCR.

Primer names	**Primer sequences**
GAPDH	Forward: GGAGTCCACTGGCGTCTTCA
	Reverse: GTCATGAGTCCTTCCACGATACC
CD44v2	Forward: ATCACCGACAGCACAGACAGAAT
	Reverse: AACCATGAAAACCAATCCCAGG
CD44v3	Forward: TACGTCTTCAAATACCATCTCAGCA
	Reverse: AATCTTCATCATCATCAATGCCTG
CD44v4	Forward: AACCACACCACGGGCTTTTG
	Reverse: TCCTTGTGGTTGTCTGAAGTAGCA
CD44v5	Forward:TGCTTATGAAGGAAACTGGAAC
	Reverse: TGTGCTTGTAGAATGTGGGGT
CD44v6	Forward: CCAGGCAACTCCTAGTAGTACAACG
	Reverse: CGAATGGGAGTCTTCTTTGGGT
CD44v7	Forward: GCCTCAGCTCATACCAGCCATC
	Reverse: TCCTTCTTCCTGCTTGATGACCT
CD44v8	Forward: TGGACTCCAGTCATAGTATAACGC
	Reverse: GGTCCTGTCCTGTCCAAATC
CD44v9	Forward: AGCAGAGTAATTCTCAGAGC
	Reverse: TGATGTCAGAGTAGAAGTTGTT
CD44v10	Forward: CCTCTCATTACCCACACACG
	Reverse: CAGTAACTCCAAAGGACCCA
CD44v8-10	Forward: TCCAGTCATAGTACAACGCT
	Reverse: CCAAGATGATCAGCCATTCTGG
CD44s	Forward: GGAGCAGCACTTCAGGAGGTTAC
	Reverse: GGAATGTGTCTTGGTCTCTGGTAGC
PIK3CA	Forward: GAAGCACCTGAATAGGCAAGTCG
	Reverse: GAGCATCCATGAAATCTGGTCGC
PIK3CB	Forward: GGTAATCGGAGGATAGGGCAGT
	Reverse: CGGCAGTATGCTTCAAGGATGAC
PIK3R1	Forward: CGCCTCTTCTTATCAAGCTCGTG
	Reverse: GAAGCTGTCGTAATTCTGCCAGG
SGK1	Forward: GCTGAAATAGCCAGTGCCTTGG
	Reverse: GTTCTCCTTGCAGAGTCCGAAG
RPS6KB1	Forward: TATTGGCAGCCCACGAACACCT
	Reverse: GTCACATCCATCTGCTCTATGCC
CDK6	Forward: GGATAAAGTTCCAGAGCCTGGAG
	Reverse: GCGATGCACTACTCGGTGTGAA
CCNE2	Forward: CTTACGTCACTGATGGTGCTTGC
	Reverse: CTTGGAGAAAGAGATTTAGCCAGG
AKT1	Forward: TGGACTACCTGCACTCGGAGAA
	Reverse: GTGCCGCAAAAGGTCTTCATGG

PTEN	Forward: TGAGTTCCCTCAGCCGTTACCT
	Reverse: GAGGTTTCCTCTGGTCCTGGTA
CDK4	Forward: CCATCAGCACAGTTCGTGAGGT
	Reverse: TCAGTTCGGGATGTGGCACAGA
CCNE1	Forward: TGTGTCCTGGATGTTGACTGCC
	Reverse: CTCTATGTCGCACCACTGATACC
CDKN1A	Forward: AGGTGGACCTGGAGACTCTCAG
	Reverse: TCCTCTTGGAGAAGATCAGCCG
E2F1	Forward: GGACCTGGAAACTGACCATCAG
	Reverse: CAGTGAGGTCTCATAGCGTGAC
PCNA	Forward: CAAGTAATGTCGATAAAGAGGAGG
	Reverse: GTGTCACCGTTGAAGAGAGTGG
MCM2	Forward: TGCCAGCATTGCTCCTTCCATC
	Reverse: AAACTGCGACTTCGCTGTGCCA
SNAI1	Forward: TGCCCTCAAGATGCACATCCGA
	Reverse: GGGACAGGAGAAGGGCTTCTC
TWIST1	Forward: GCCAGGTACATCGACTTCCTCT
	Reverse: TCCATCCTCCAGACCGAGAAGG
ZEB2	Forward: AATGCACAGAGTGTGGCAAGGC
	Reverse: CTGCTGATGTGCGAACTGTAGG
FOXC2	Forward: TCACCTTGAACGGCATCTACCAG
	Reverse: TGACGAAGCACTCGTTGAGCGA
AXL	Forward: GTTTGGAGCTGTGATGGAAGGC
	Reverse: CGCTTCACTCAGGAAATCCTCC
MMP2	Forward:AGCGAGTGGATGCCGCCTTTAA
	Reverse: CATTCCAGGCATCTGCGATGAG