Supplementary Figure S1

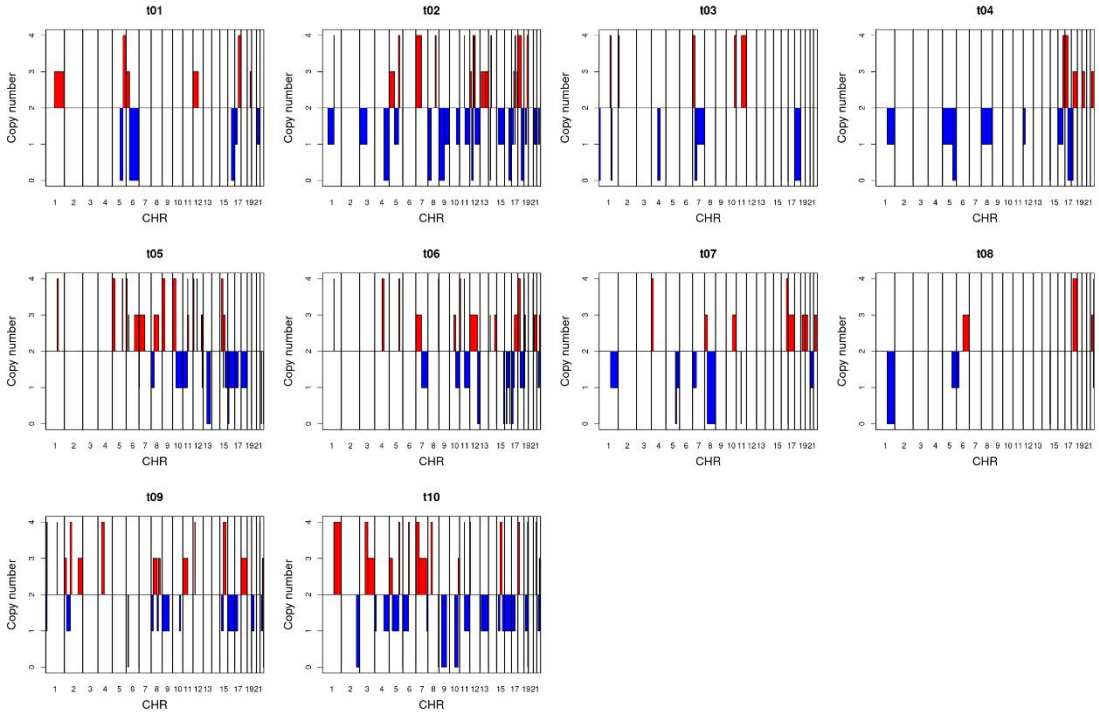

Figure S1. Genome-wide copy-number profiles of tumor cells from all 10 LUAD samples. Each panel (t01–t10) displays copy-number variation of genes along the chromosomes (x-axis, CHR 1–21), with the y-axis indicating inferred copy-number states. Red bars represent copy-number gains and blue bars represent copy-number losses.

Supplementary Figure S2

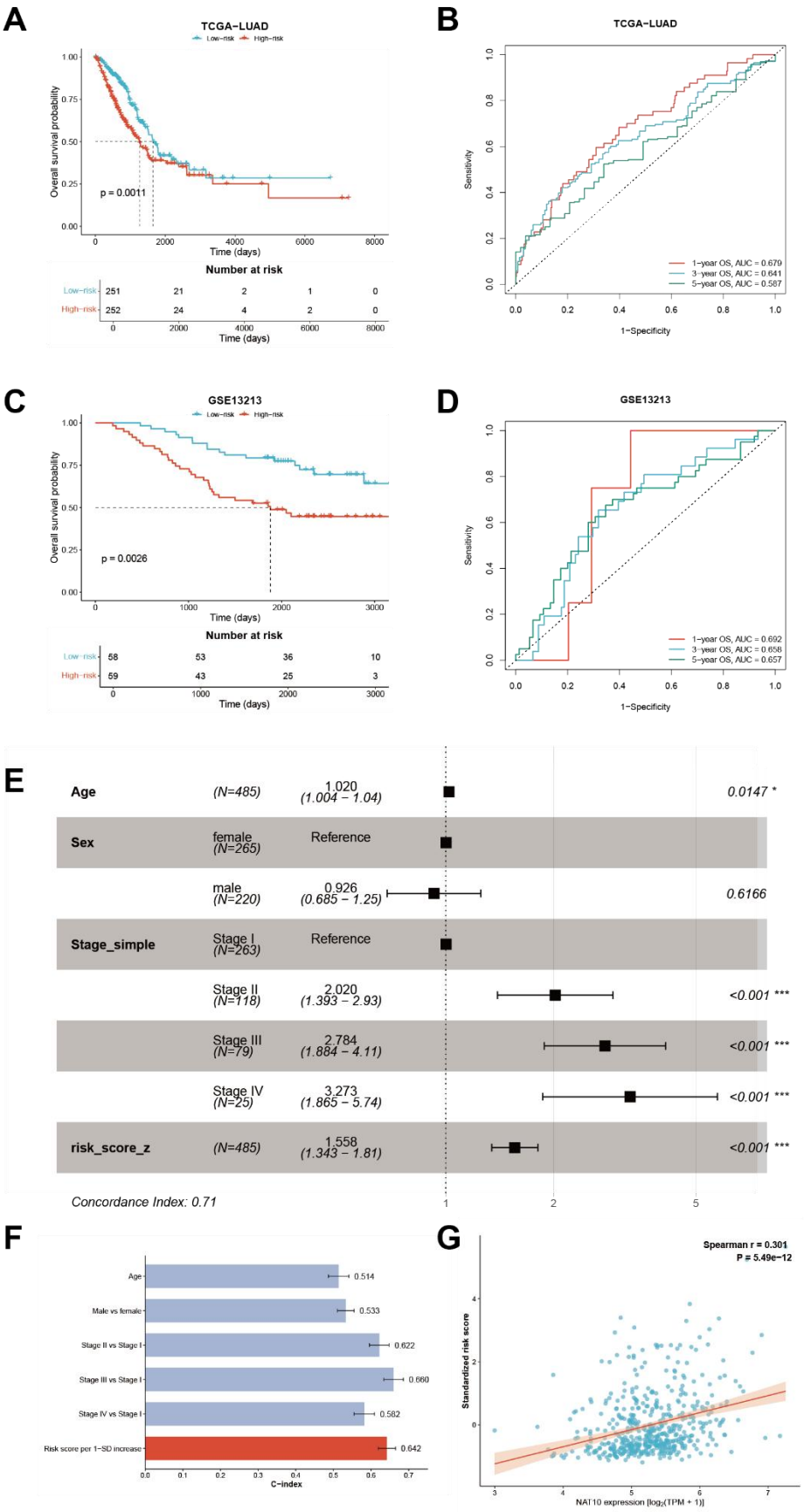

Figure S2. Additional validation and prognostic evaluation of the six-gene ac4C-related signature in LUAD. (A, B) Kaplan–Meier survival curve and time-dependent ROC analysis of the six-gene signature in the TCGA-LUAD cohort. **(C, D)** Kaplan–Meier survival curve and time-dependent ROC analysis of the signature in the independent GSE13213 cohort. **(E)** Multivariate Cox regression analysis of overall survival in the TCGA-LUAD cohort. **(F)** Comparison of C-index values from six univariate Cox models in the TCGA-LUAD cohort. **(G)** Spearman correlation analysis between NAT10 expression and the standardized risk score in TCGA-LUAD.

Supplementary Table S1. Prognostic validation of the six-gene signature

Cohort	N	HR per 1-SD increase in risk score	95% CI	*P* value	C-index	1-year AUC	3-year AUC	5-year AUC
GSE13213	117	1.387	1.068–1.801	0.0142	0.623	0.692	0.658	0.657
TCGA-LUAD internal validation	503	1.593	1.393–1.821	1.04E-11	0.629	0.679	0.641	0.587

HR, hazard ratio; **CI**, confidence interval; **AUC**, area under the curve.

Supplementary Table S2. Multivariate Cox regression analysis of overall survival in the TCGA-LUAD cohort

Variable	HR	95% CI	*P value*
Age	1.020	1.004–1.036	0.0147
Sex: male vs female	0.926	0.685–1.252	0.617
Stage II vs Stage I	2.020	1.393–2.930	0.000209
Stage III vs Stage I	2.784	1.884–4.114	2.74×10^{-7}
Stage IV vs Stage I	3.273	1.865–5.743	3.58×10^{-5}
Risk score per 1-SD increase	1.558	1.343–1.806	4.60×10^{-9}

HR, hazard ratio; **CI**, confidence interval. Female sex and Stage I were used as the reference categories. The analysis included 485 patients with complete clinicopathological information.

Supplementary Table S3. Summary of the six genes in the ac4C-related prognostic signature

Gene	Chromosomal location	Established biological function	Reported cancer-related role	Representative references
CDCA4	14q32.33	E2F-responsive nuclear factor involved in E2F-dependent transcriptional regulation and cell proliferation.	Reported to promote LUAD proliferation through interaction with IGF2BP1 and activation of the PI3K/AKT pathway; related to cell-cycle-dependent tumor growth programs.	[1, 2]
GCLC	6p12.1	Catalytic subunit of glutamate-cysteine ligase, the rate-limiting enzyme for glutathione biosynthesis and cellular redox homeostasis.	Supports antioxidant and redox adaptation in cancer cells; glutathione-related pathways contribute to tumor progression, therapy resistance, and cisplatin resistance in LUAD.	[3, 4]
HMGA1	6p21.31	AT-hook chromatin architectural protein involved in chromatin organization and transcriptional regulation.	Implicated in oncogenic transcriptional programs, chromatin organization, Wnt-associated signaling, lipid metabolic reprogramming, and tumor progression.	[5-7]
PLK1	16p12.2	Mitotic serine/threonine kinase involved in G2/M progression, spindle formation, chromosome segregation, and cytokinesis.	A well-established cancer-associated kinase and therapeutic target; reported to promote Kras/Tp53-mutant LUAD development through RET/MAPK signaling.	[8, 9]
SLC7A5	16q24.2	L-type amino acid transporter 1 mediating uptake of large neutral amino acids and supporting nutrient-dependent growth signaling.	Promotes cancer cell growth through amino acid transport and mTORC1-related metabolic signaling; reported as a LUAD-specific prognostic biomarker associated with an immunosuppressive tumor microenvironment.	[10, 11]
TNNT1	19q13.42	Slow skeletal troponin T isoform and tropomyosin-binding component of the troponin complex involved in thin-filament regulation.	Reported to promote migration, invasion, and epithelial-mesenchymal transition in lung cancer cells, potentially through Wnt/β-catenin signaling.	[12, 13]

Note. Chromosomal locations were annotated according to public gene annotation resources. Biological functions and cancer-related roles were summarized from representative published studies.

Abbreviations: LUAD, lung adenocarcinoma; EMT, epithelial-mesenchymal transition; GSH, glutathione; LAT1, L-type amino acid transporter 1; mTORC1, mechanistic target of rapamycin complex 1.

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