Comprehensive bioinformatics analysis of NCAPH expression and its clinical importance in endometrial cancer

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Abstract. Emerging evidence has implicated non-SMC condensin I complex subunit H (NCAPH) as a key regulator of mitosis and driver of tumorigenesis. However, its expression profiling and clinical relevance in endometrial cancer (EC) remain inadequately characterized. The present study aimed to systematically investigate the expression profiling, mutational landscape, co-expression networks and prognostic importance of NCAPH in EC through integrated bioinformatics approaches. NCAPH expression was evaluated in pan-cancer and EC cohorts derived from The Cancer Genome Atlas and Genotype Tissue Expression databases. Mutational analysis was performed using the 'maftools' package in R software. Genes co-expressed with NCAPH (with a significance threshold of P<0.05) were subjected to functional enrichment analysis using Metascape. Single-sample Gene Set Enrichment Analysis (ssGSEA) was used to evaluate the correlation between gene expression and pathway scores. The Tumor Immune Estimation Resource database was utilized to explore the correlation between NCAPH expression and the abundance of tumor-infiltrating immune cells in EC. The prognostic importance of NCAPH was assessed by Kaplan-Meier survival analysis and receiver operating characteristic curve analysis. Immunohistochemistry and western blotting was performed to validate NCAPH protein expression in clinical specimens. Results indicated that NCAPH mRNA and protein expression were significantly elevated in EC compared with normal endometrium. In addition, NCAPH expression was found to be positively correlated with advanced International Federation of Gynecology and Obstetrics stage, advanced age, TP53 mutation and aggressive histological subtypes. Somatic mutations of NCAPH occurred in 4.92% of EC cases, with missense mutations being the predominant type (79.3%). Functional enrichment analysis indicated that NCAPH-associated genes were involved in 'cell cycle', 'DNA replication' and 'oocyte meiosis'. ssGSEA exhibited a positive correlation between NCAPH and DNA repair, G_2M checkpoint, tumor cell proliferation and the PI3K/AKT/mTOR pathway. NCAPH expression exhibited a significant negative correlation with $CD8^+$ T cell infiltration, whereas positive correlations were observed with $CD4^+$ T helper 2 cell infiltration, CD163 and programmed death-ligand 1. In addition, high NCAPH expression was found to predict reduced 5-year overall survival and exhibited certain diagnostic efficacy (area under the curve=0.628). Overall, NCAPH may promote endometrial carcinogenesis through dysregulation of mitotic processes, induction of chromosomal instability as well as modulation of the tumor immune microenvironment and thus may serve as both a prognostic biomarker and a therapeutic target in EC.

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Introduction

Endometrial cancer (EC) has become the most prevalent gynecologic malignancy, with ~420,000 new cases and 97,000 deaths worldwide in 2022 (1). Critically, EC is among the few malignancies with rising incidence and mortality trends. Incidence has increased by 0.7% annually overall and mortality has risen by 1.3-1.6% per year over the past decade (2). This dual increase underscores the urgent need for improved biomarkers and therapeutic targets to reverse these trends (3,4). Despite advancements in therapeutic approaches, persistent challenges such as high recurrence rates and metastatic potential have led to stagnant survival outcomes, especially in cases of advanced-stage disease and aggressive histological subtypes (5-7). These therapeutic challenges have

highlighted the urgent need for novel molecular biomarkers to facilitate early detection, optimize risk stratification and develop targeted treatment strategies (8).

Non-SMC condensin I complex subunit H (NCAPH), localized at chromosome 2q11.2, functions as a key regulatory component of the condensin I complex important in mitotic chromosome condensation and faithful sister chromatid segregation (9,10). Accumulating evidence has indicated that dysregulation of NCAPH is involved in oncogenesis across numerous malignancies (11-13). Its upregulation activates proliferative signaling pathways (including MEK/ERK, β-catenin and PI3K/Akt) and contributes to the acquisition of aggressive phenotypes (14-16). NCAPH is also involved in regulating apoptosis by modulating key signaling pathways, including Akt/mTOR, checkpoint kinase (Chk)-1/Chk2 and MEK/ERK (14,17,18). Mechanistically, NCAPH promotes chromosomal instability, DNA damage tolerance and treatment resistance-features intrinsically associated with poor prognosis in cancer types such as bladder carcinoma, advanced colon adenocarcinoma and estrogen receptor-positive breast cancer (14,19-21). Recent molecular profiling of endometrial carcinomas has further identified NCAPH amplification as a characteristic enriched in high-risk subtypes, suggesting its potential role in the pathogenesis of EC (22).

Despite these advances, comprehensive analyses regarding expression patterns, mutational landscape, functional networks and the clinical utility of NCAPH in endometrial carcinogenesis remain insufficient. The molecular mechanisms underlying NCAPH-driven progression of EC, especially its interactions with cell cycle regulators and its contribution to genomic instability, are poorly characterized. Furthermore, the prognostic and diagnostic value of NCAPH in the clinical management of EC remains unclear.

Subsequently, the present study conducted an integrated multi-omics investigation of NCAPH in endometrial cancer. By leveraging bioinformatics analyses supplemented with experimental validation, the expression dynamics of NCAPH across different histological subtypes and clinical stages was systematically evaluated. The present study also characterized the somatic mutation profiles and co-occurring genomic alterations of NCAPH, delineated co-expression networks and enriched biological pathways, investigated its correlation with immune infiltration and established clinical correlations with survival outcomes and diagnostic performance. Collectively, the present findings identify NCAPH as a key molecular driver of EC progression and a promising biomarker for precision oncology applications.

Materials and methods

Analysis of NCAPH expression. The EC-specific cohort (GDC project ID: TCGA-UCEC) (23) was obtained from https://portal.gdc.cancer.gov/projects/TCGA-UCEC and included 546 patients, all female, with a median age of 64 years (range: 31-90 years). Pan-cancer expression data were obtained through Gene Expression Profiling Interactive Analysis 2 (GEPIA2; http://gepia2.cancer-pku.cn/) (24), which integrates all TCGA tumor cohorts from the GDC portal (https://portal.gdc.cancer.gov/). The R software (Posit Software, PBC) package 'limma' (version 3.54.0) (25) was employed to compare NCAPH expression between EC and normal endometrial tissues. In addition, the associations between NCAPH expression and clinicopathological parameters (tumor stage and histological subtype) were evaluated using UALCAN (http://ualcan.path.uab.edu/) (26,27).

Mutational landscape analysis. Somatic mutation data from TCGA-UCEC were processed using the R package 'maftools' (version 2.14.0) (28). Samples were stratified into high/low NCAPH expression groups based on median values. The top 10 significantly mutated genes ($q<0.05$) were visualized.

Co-expression and functional enrichment. Co-expressed genes with NCAPH were identified using Spearman correlation analysis ($P<0.05$). Functional enrichment analysis of the gene sets was conducted using Metascape (http://metascape.org). A false discovery rate (FDR)<0.05 was considered to indicate a statistically significant difference for Gene Ontology (GO) terms and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways.

Immune cell infiltration analysis. The Tumor Immune Estimation Resource (TIMER) web server (https://compbio.cn/timer3/) (29) was used to examine the correlations of NCAPH expression with the abundance of tumor-infiltrating immune cells, M2 macrophage markers, and programmed death-ligand 1 (PD-L1). Immune infiltration was estimated using the TIMER, XCELL, CIBERSORT-absolute (ABS) and TIDE (Tracking of Indels by Decomposition) algorithms, all accessed through the TIMER platform. Purity-adjusted Spearman's rank correlation test was applied to calculate correlation coefficients and corresponding P-values.

Survival analysis. Kaplan-Meier survival curves were generated using the R packages 'survival' (version 3.5-7; https://CRAN.R-project.org/package=survival) and 'survminer' (version 0.4.9; https://cran.r-project.org/package=survminer), with log-rank tests applied to assess differences in survival outcomes between the high and low NCAPH expression groups. Time-dependent ROC analysis was performed using the 'timeROC' package (version 0.4) (30) to evaluate the diagnostic accuracy at 1, 3 and 5 years.

Single-sample Gene Set Enrichment Analysis (ssGSEA). Spliced Transcripts Alignment to a Reference-counts data and corresponding clinical information from the TCGA-UCEC cohort were extracted and normalized using the $\log_2$ (transcripts per million +1) transformation. Subsequently, the genes included in the corresponding pathways were collected and then analyzed using the 'GSVA' package in R software (31), with the parameter method 'ssgsea' for ssGSEA. Finally, Spearman's correlation analysis was used to evaluate the correlation between gene expression and pathway scores.

Immunohistochemical (IHC) validation. A total of 108 patients (all female; median age 56 years; range: 30-79 years) who underwent surgical resection for endometrial cancer at The Affiliated Huai'an No.1 People's Hospital of Nanjing Medical University (Huai'an, China) between January 2018 and June 2023 were enrolled in the present study. The inclusion

criteria were as follows: i) Met EC diagnostic criteria, which was confirmed by pathological examination; ii) diagnosed and treated at The Affiliated Huai'an No. 1 People's Hospital of Nanjing Medical University between 2018 and 2023; and iii) complete clinicopathologic data were available. The exclusion criteria were as follows: i) Pathological diagnosis of other uterine tumor types; and ii) incomplete clinicopathologic data.

Formalin-fixed (10%, room temperature for 24 h) paraffin-embedded tissue sections (4 μm) from 26 EC specimens and their paired normal endometrial tissues were subjected to antigen retrieval (citrate buffer; pH 6.0; 95˚C; 15 min). Following endogenous peroxidase inactivation with 3% H_2O_2 at room temperature for 10 min, the sections were blocked with 5% goat serum (cat. no. G1208; Wuhan Servicebio Technology Co., Ltd.) at room temperature for 1 h. Then, the sections were incubated with anti-NCAPH antibody (cat. no. 11515-1-AP; Proteintech Group, Inc.) at a dilution of 1:200 overnight at 4˚C, followed by incubation with a HRP-conjugated secondary antibody (1:5,000; cat. no. bs-0295G; BIOSS) at room temperature for 1 h. DAB detection kit (cat. no. G1212; Wuhan Servicebio Technology Co., Ltd.) was used for chromogenic detection. Then, the slides were examined under a light microscope (Olympus BX53; Olympus Corporation). The intensity of nuclear staining was quantified as integrated optical density using ImageJ software (version 2.1.0/1.53c; National Institutes of Health) and statistical analyses were performed using GraphPad Prism (version 10.2.0; Dotmatics).

Western blotting analysis. Tissues were lysed by RIPA buffer (cat. no. G2002; Wuhan Servicebio Technology Co., Ltd.) and quantified by BCA protein quantitative kit (cat. no. G2026; Wuhan Servicebio Technology Co., Ltd.). Equal amounts of protein (30 μg per lane) were separated by 10% SDS-PAGE and transferred onto PVDF membranes. After blocking with 5% non-fat milk in TBST (0.1% Tween-20) at room temperature for 1 h, the membranes were incubated overnight at 4˚C with primary antibodies against NCAPH (1:2,000; cat. no. 11515-1-AP; Proteintech Group, Inc.) and GAPDH (1:8,000; cat. no. 60004-1-Ig; Proteintech Group, Inc.). After washing, membranes were then incubated with HRP-conjugated secondary antibodies: Goat anti-rabbit IgG (cat. no. SA00001-1; Proteintech Group, Inc.) and goat anti-mouse IgG (cat. no. SA00001-2; Proteintech Group, Inc.) for 1 h at room temperature. Finally, the immune complexes were detected by an ECL kit (cat. no. G2014; Wuhan Servicebio Technology Co., Ltd.).

Statistical analysis. Comparisons between NCAPH expression and clinicopathological characteristics were evaluated using Student's t-tests and logistic regression analysis. The Kaplan-Meier method was employed to assess the prognostic impact of NCAPH expression. $P<0.05$ was considered to indicate a statistically significant difference.

Results

NCAPH expression is significantly elevated in pan-cancer and EC. Pan-cancer analysis using GEPIA2 revealed significant upregulation of NCAPH in numerous malignancies, including bladder urothelial carcinoma, breast invasive carcinoma, cervical squamous cell carcinoma, colon adenocarcinoma, diffuse large B-cell lymphoma, esophageal carcinoma, glioblastoma, head and neck squamous cell carcinoma, lower-grade glioma, liver hepatocellular carcinoma, lung adenocarcinoma, lung squamous cell carcinoma, ovarian cancer, pancreatic adenocarcinoma, rectal adenocarcinoma, skin cutaneous melanoma, stomach adenocarcinoma, thymoma, endometrial carcinoma and uterine carcinosarcoma. By contrast, NCAPH was downregulated in acute myeloid leukemia (Fig. 1A).

Analysis of the TCGA-UCEC cohort demonstrated significantly elevated NCAPH expression in 546 endometrial carcinoma samples compared with 35 normal endometrial samples (Fig. 1B). Furthermore, high NCAPH expression was significantly associated with more advanced International Federation of Gynecology and Obstetrics (FIGO) stages (Fig. 1C), serous histotype (Fig. 1D) and older age (Fig. 1E). Given that TP53 mutation is frequently observed in endometrial carcinoma and is associated with poor prognosis (32), the association between NCAPH and TP53 status was also evaluated. NCAPH expression was found to be positively associated with TP53, particularly in tumors carrying mutant TP53 (Fig. 1F). Collectively, these results established NCAPH as a robust molecular marker in EC. Elevated NCAPH expression was found to be associated with advanced disease stage and adverse clinical outcomes, highlighting its potential prognostic utility.

Missense mutations predominate the NCAPH mutational landscape. Analysis of transcriptome data from 528 endometrial cancer samples within TCGA-UCEC dataset identified 26 samples harboring NCAPH mutations, accounting for 4.92% of all analyzed cases. A total of 29 NCAPH mutations were detected among these 26 samples, with missense mutations being the predominant type, representing 79.3% of all alterations (Fig. 2A). Besides NCAPH, other genes were also frequently altered, demonstrating high mutation burdens within this cohort. The ten most frequently mutated genes across all the 26 samples were NCAPH, TTN, DNAH5, MUC16, APOB, CSMD3, SYNE1, RYR2, NEB and USH2A (Fig. 2B).

NCAPH co-expressed genes are enriched in cell cycle and DNA repair pathways and correlate with PI3K/Akt/mTOR activation and p53 attenuation. To investigate the potential biological functions of NCAPH in endometrial cancer, the TCGA dataset was analyzed and 189 genes co-expressed with NCAPH were identified (correlation coefficient ≥0.7). Functional enrichment analysis of these genes was performed using Metascape. Biological processes were significantly enriched in 'mitotic cell cycle process', 'regulation of cell cycle process' and 'DNA metabolic process' (Fig. 3A). Molecular functions showed primary enrichment in 'microtubule binding', 'macromolecular conformation isomerase activity' and 'single-stranded DNA binding' (Fig. 3B). Cellular components were predominantly enriched in the 'chromosomal region', 'spindle' and 'centrosome' (Fig. 3C). KEGG pathway enrichment analysis further implicated NCAPH in endometrial cancer pathogenesis through 'cell cycle', 'DNA replication' and 'oocyte meiosis' (Fig. 3D). ssGSEA was then performed to evaluate correlation between NCAPH expression

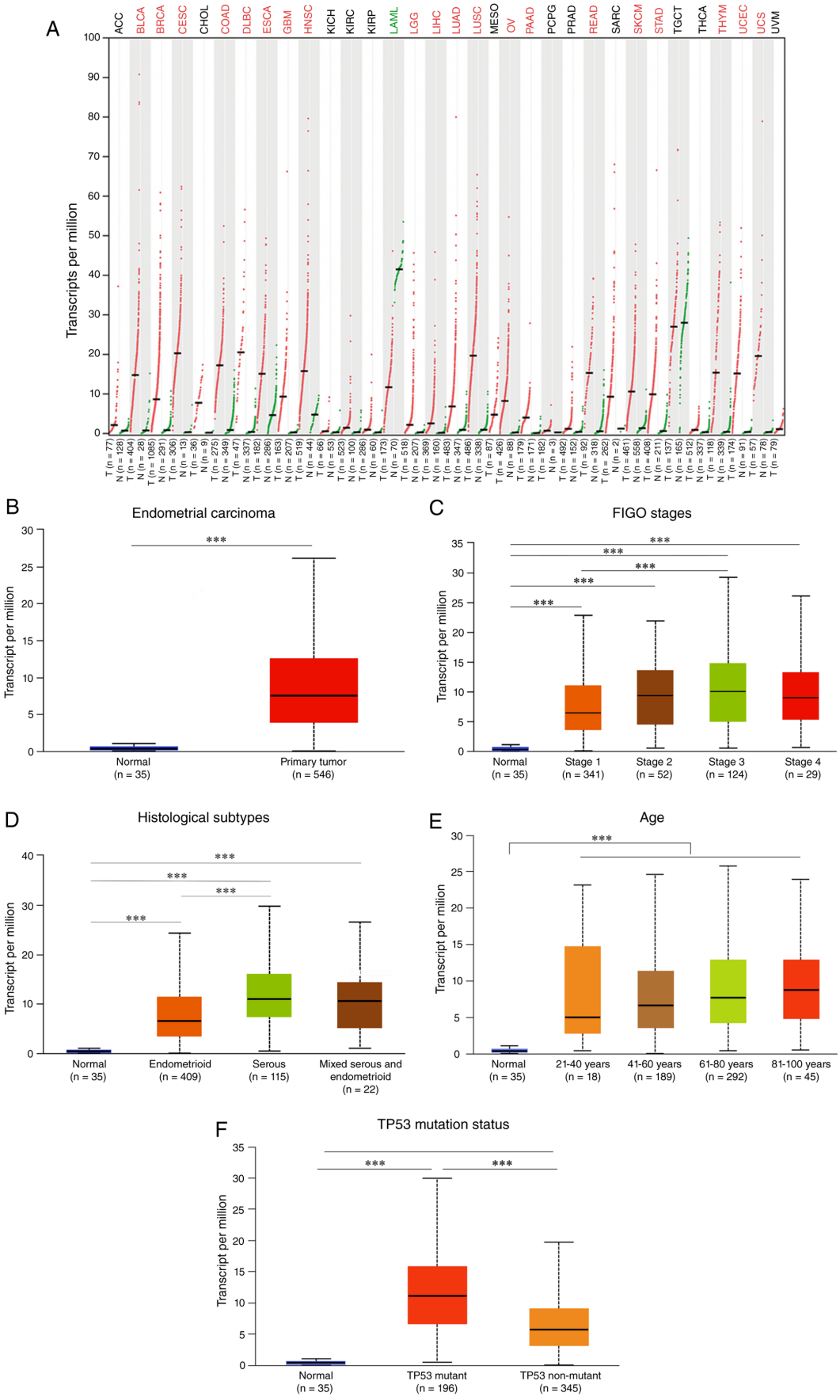

Figure 1. NCAPH upregulation identifies aggressive endometrial carcinoma. (A) NCAPH mRNA levels were significantly higher in T compared with matched N tissues for the majority of cancer types examined. (B) The expression levels of NCAPH were significantly higher in endometrial cancer tissues compared with normal tissues. (C) NCAPH expression stratified by tumor stage relative to normal tissues. (D) NCAPH expression across histological subtypes (endometrioid vs. serous) relative to normal tissue. (E) NCAPH expression across different ages. (F) NCAPH expression relative to TP53 mutation status. ***P<0.001. NCAPH, non-SMC condensin I complex subunit H; FIGO, International Federation of Gynecology and Obstetrics stage; T, tumor tissue; N, normal control.

Figure 2. Analysis of NCAPH Mutations in The Cancer Genome Atlas-Endometrial Cancer cohort. (A) Lollipop chart showing the mutation distribution of the NCAPH gene. (B) Oncoplot displaying the somatic mutation landscape of the 26 samples. Genes are sorted by mutation frequency. NCAPH, non-SMC condensin I complex subunit H.

and numerous signaling pathways in the TCGA-UCEC cohort. The results revealed that NCAPH expression was positively correlated with 'DNA repair', 'G_2M checkpoint', 'tumor proliferation' and the PI3K/AKT/mTOR pathway' but negatively associated with 'p53 pathway' (Fig. 3E). These findings suggested that NCAPH may promote endometrial cancer progression through dysregulation of cell cycle progression and DNA damage response, concomitant with PI3K/AKT/mTOR pathway activation and p53 pathway attenuation.

NCAPH interacts with key mitotic regulators in the protein-protein interaction network. Based on the Search Tool for the Retrieval of Interacting Genes/Proteins database, the top 50 proteins co-expressed with NCAPH were selected for PPI

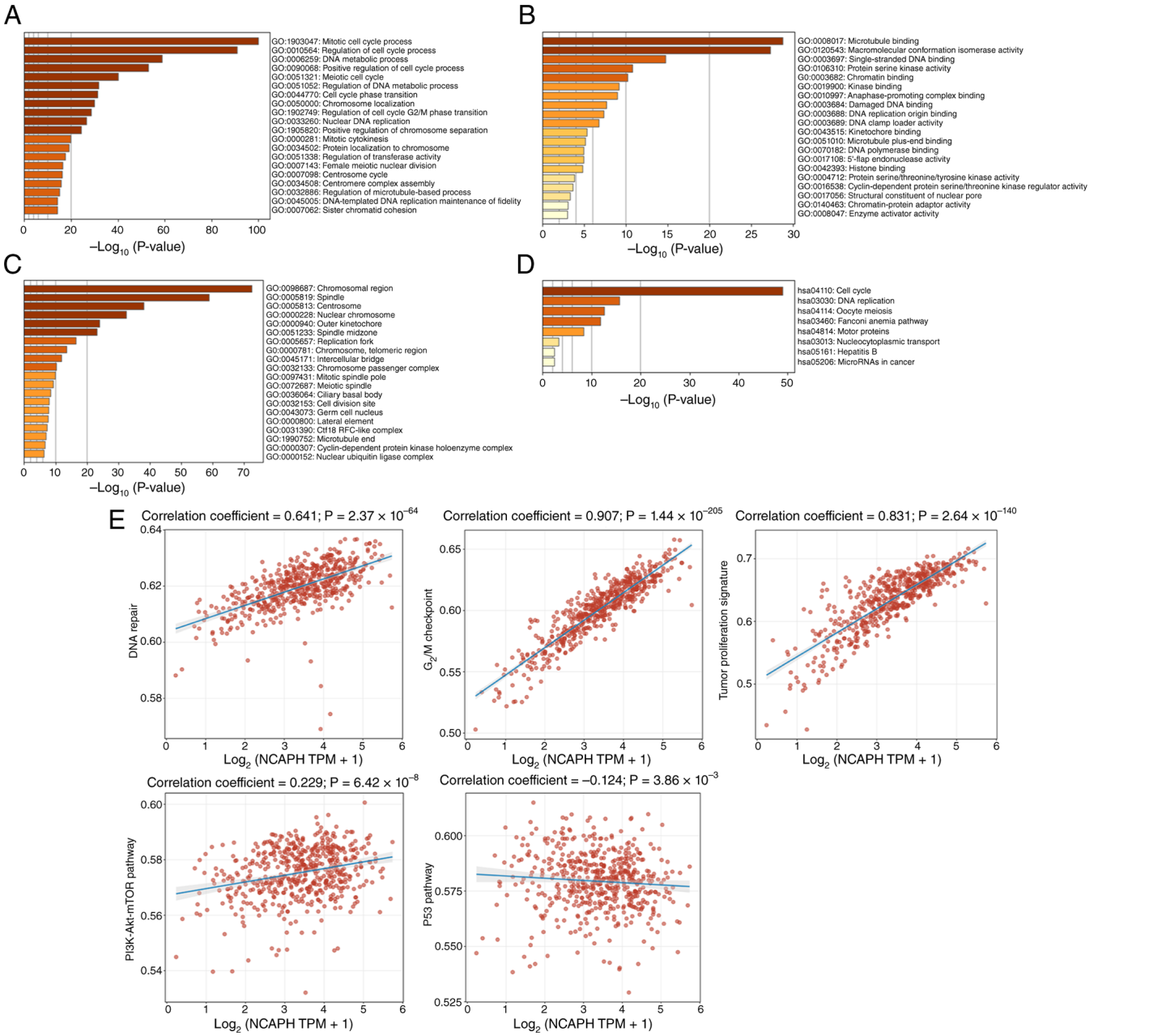

Figure 3. Functional enrichment analysis of NCAPH co-expressed genes in endometrial cancer. (A) Significantly enriched GO biological processes. (B) Enriched GO molecular functions. (C) Enriched GO cellular components. (D) Kyoto Encyclopedia of Genes and Genomes pathway enrichment. Enriched terms are ranked by adjusted P-value (false discovery rate <0.05). (E) Spearman correlation analysis exhibiting the correlation between NCAPH and numerous signaling pathways. GO, Gene Ontology; NCAPH, non-SMC condensin I complex subunit H; TPM, transcripts per million.

network analysis. As illustrated in Fig. 4, the resulting network consisted of 50 nodes and 640 edges, with an average local clustering coefficient of 0.822. The top 10 proteins most associated with NCAPH were identified as non-SMC condensin I complex subunit D (NCAPD)-2, non-SMC condensin I complex subunit G (NCAPG), kinesin family member (KIF)-4A, budding uninhibited by benzimidazoles (BUB)-1, BUB1B, CDCA8, KIF11, maternal embryonic leucine zipper kinase (MELK), cellular communication network (CCN)-B2 and KIF15. Functional clustering analysis revealed that the majority of these proteins are involved in mitotic sister chromatid segregation and the mitotic spindle checkpoint signaling pathway. These findings suggested that dysregulation of NCAPH may promote tumorigenesis in EC by disrupting mitotic processes.

NCAPH expression correlates with an immunosuppressive microenvironment in EC. To explore the correlation between NCAPH expression and the abundance of tumor-infiltrating immune cells in EC, the TIMER database (https://compbio.cn/timer3/) (29) was next used. Analysis revealed a significant negative correlation between NCAPH expression and the abundance of $CD8^+$ T cells (R=-0.318; P<0.01; Fig. 5A). To validate these findings, additional computational methods (XCELL, CIBERSORT-ABS and TIDE) were employed for immune cell quantification. Consistent with the TIMER

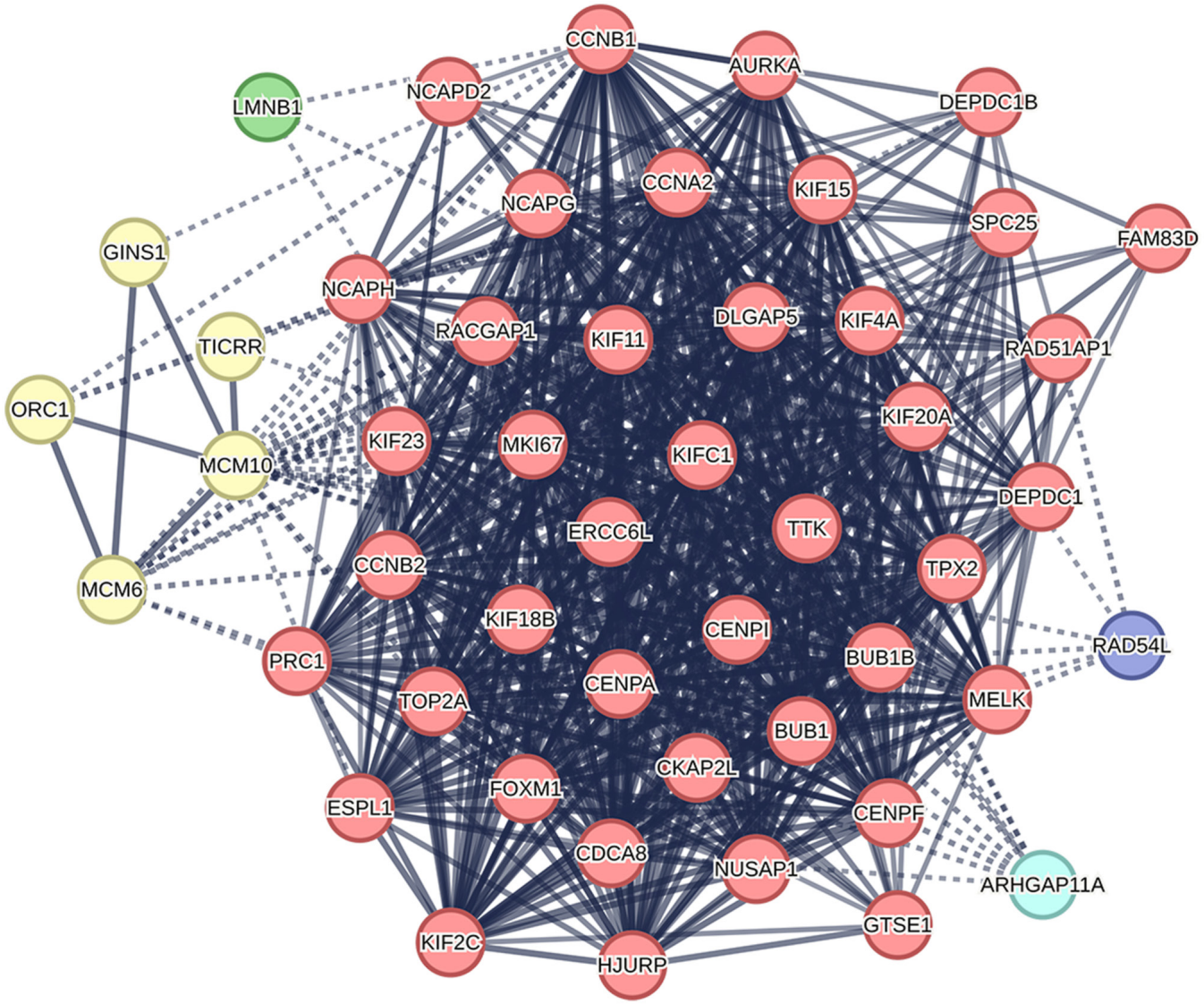

Figure 4. Establishment of protein-protein interaction network of NCAPH and its closely connected proteins. A network of NCAPH and its co-expression proteins set up visually by Search Tool for the Retrieval of Interacting Genes/Proteins. Red cluster indicates mitotic sister chromatid segregation and mitotic spindle checkpoint signaling pathway. Yellow cluster indicates DNA replication initiation and activation of the pre-replicative complex and GINS1 complex. Green cluster indicates LMNB1. Cyan cluster indicates ARHGAP11A. Blue cluster indicates RAD54L. NCAPH, non-SMC condensin I complex subunit H; GINS, GINS complex subunit 1; LMNB1, lamin B1; ARHGAP11A, ϱ-GTPase Activating Protein 11A.

results, the CIBERSORT-ABS method also demonstrated a negative correlation between NCAPH expression and $CD8^+$ T cell infiltration (R=-0.28; P<0.01; Fig. 5B). Furthermore, NCAPH expression exhibited a marked positive correlation with the infiltration of $CD4^+$ T helper (Th)-2 cells (R=0.499; P<0.001 by XCELL; Fig. 5C) and myeloid-derived suppressor cells (MDSCs; R=0.397; P<0.001; TIDE; Fig. 5D). No significant association was observed between NCAPH and regulatory T cells (Tregs) by either CIBERSORT-ABS or XCELL (Fig. S1).

The present study subsequently investigated whether NCAPH associates with M2 macrophage markers, since M2 polarization is a well-recognized mechanism of tumor immune evasion (33). NCAPH exhibited a significant positive correlation with CD163 (R=0.252; P<0.001); V-set and immunoglobulin domain-containing 4 (VSIG4; R=0.113; P=0.053) and mannose receptor C-type 1 (MRC1)/CD206 (R=0.108; P=0.064) trending in the same direction but not reaching significance (Fig. 5E). This pattern suggested an M2-like shift in tumor-associated macrophages in the context of high NCAPH expression in EC.

PD-L1, a key immune checkpoint gene with established relevance to immunotherapy response (34), was also examined. Results showed that NCAPH was positively correlated with PD-L1 (CD274; R=0.231; P<0.001; Fig. 5F). Collectively, NCAPH-high EC showed fewer infiltrating $CD8^+$ T cells, more $CD4^+$ Th2 cells and MDSCs, M2-skewed macrophage marker expression and higher PD-L1, collectively pointing to an immunosuppressive microenvironment. In addition, these findings suggested that patients with NCAPH-high EC may potentially benefit from immune checkpoint therapy.

NCAPH serves as a prognostic biomarker and predicts poor survival in EC. To investigate the association

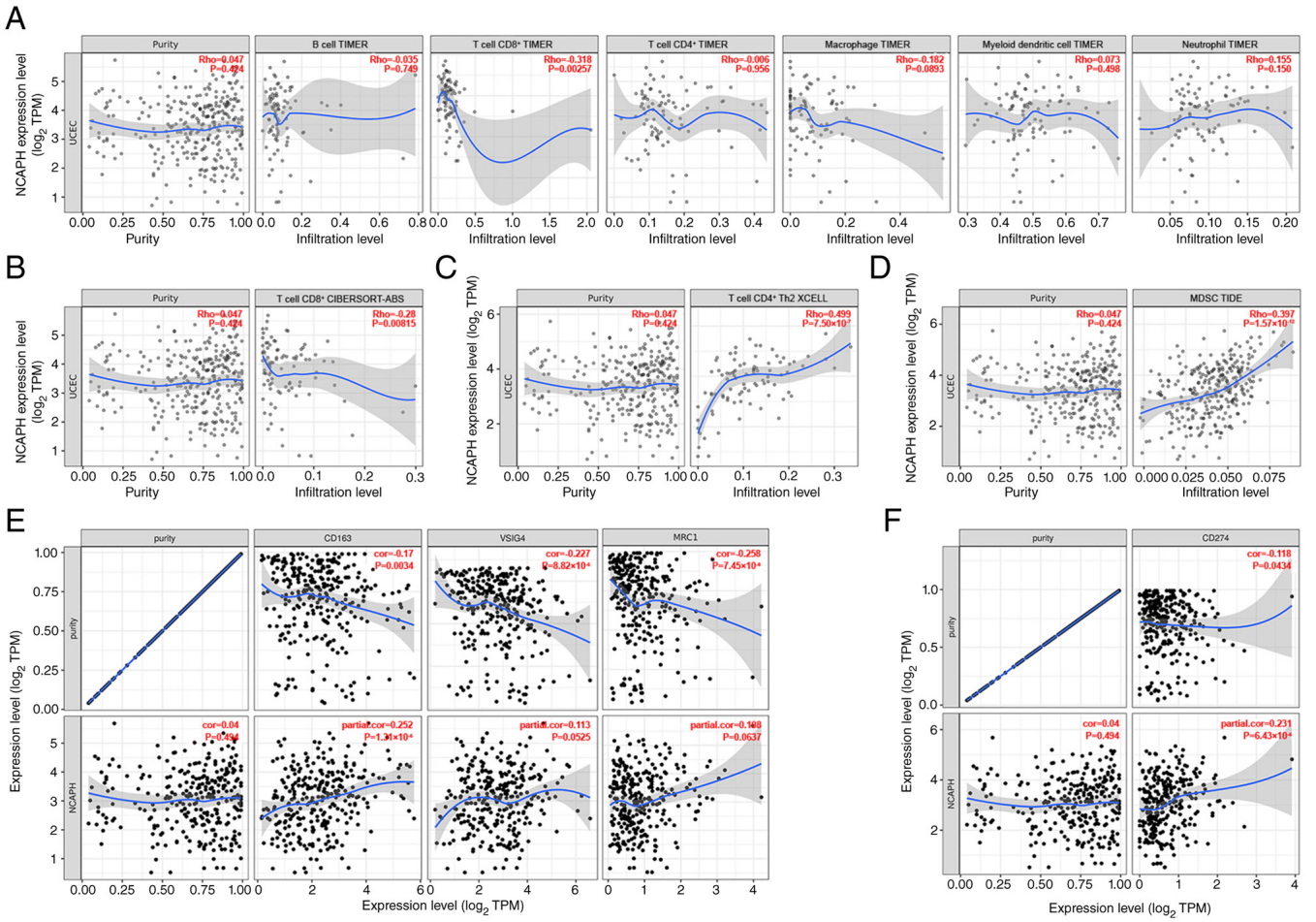

Figure 5. Correlation between NCAPH expression and immune infiltration. Association between NCAPH expression level and immune cells in endometrial cancer using (A) TIMER (B) CIBERSORT-ABS, (C) XCELL and (D) TIDE methods. (E and F) Purity-adjusted partial spearman correlation analysis to show the correlation between NCAPH with numerous markers. NCAPH, non-SMC condensin I complex subunit H; TPM, transcripts per million; cor, correlation; TIMER, Tumor Immune Estimation Resource; CIBERSORT-ABS, CIBERSORT absolute; TIDE, Tracking of Indels by Decomposition.

between NCAPH expression and prognosis, a risk score was computed for each individual. Using the 'ggrisk' and 'survminer' R packages, an optimal cut-off value was determined to stratify patients into a high-risk group (n=401) and a low-risk group (n=143) (Fig. 6A, upper panel). Fig. 6A (middle panel) shows the survival status of all patients in the TGCA-UCEC cohort and Fig. 6A (lower panel) presents the expression level of NCAPH. Kaplan-Meier survival analysis revealed that patients in the high-risk group had significantly shorter overall survival compared with those in the low-risk group (Fig. 6B). To predict the prognostic value of NCAPH in EC, diagnostic performance was assessed through time-dependent ROC analysis at 1-, 3- and 5-year intervals, yielding area under the curve (AUC) values of 0.602, 0.614 and 0.630 respectively (Fig. 6C), indicating moderate but consistent discriminatory capacity for EC. These results demonstrate that elevated NCAPH expression is associated with adverse prognosis in EC and may serve as a valuable prognostic biomarker.

NCAPH protein upregulation in EC is validated by IHC and western blotting and is associated with aggressive clinicopathological features. To further validate NCAPH expression in clinical EC samples, a cohort of 108 patients was retrospectively collected (all female; median age 56 years; range: 30-79 years) who underwent surgical resection for EC at The Affiliated Huai'an No. 1 People's Hospital of Nanjing Medical University (Jiangsu, China) between January 2018 and June 2023 (ethics approval no. KY-2025-195-01). As shown in Fig. 7A, NCAPH was predominantly localized in the cytoplasm of EC tissues. IHC analysis revealed significantly higher NCAPH expression in EC samples compared with normal endometrial controls (Fig. 7B). This upregulation was further determined by paired analysis of tumor tissues and adjacent normal endometrium (Fig. 7C). Consistent with the IHC findings, the western blotting results demonstrated that the NCAPH protein levels were significantly upregulated in EC tumor tissues relative to normal endometrial controls in 3 of 4 paired samples (N-1 vs. T-1, N-2 vs. T-2 and N-4 vs. T-4; $P<0.05$), with the remaining pair showing no significant difference (N-3 vs. T-3) (Fig. 7D). Correlations between NCAPH expression and clinicopathological characteristics in patients with EC were then further evaluated. As summarized in Table I, elevated NCAPH levels were significantly correlated with aggressive histological subtypes, higher tumor grade and advanced FIGO stages. These results provided robust pathological validation of NCAPH upregulation in EC and support its potential role in tumor progression. The correlation

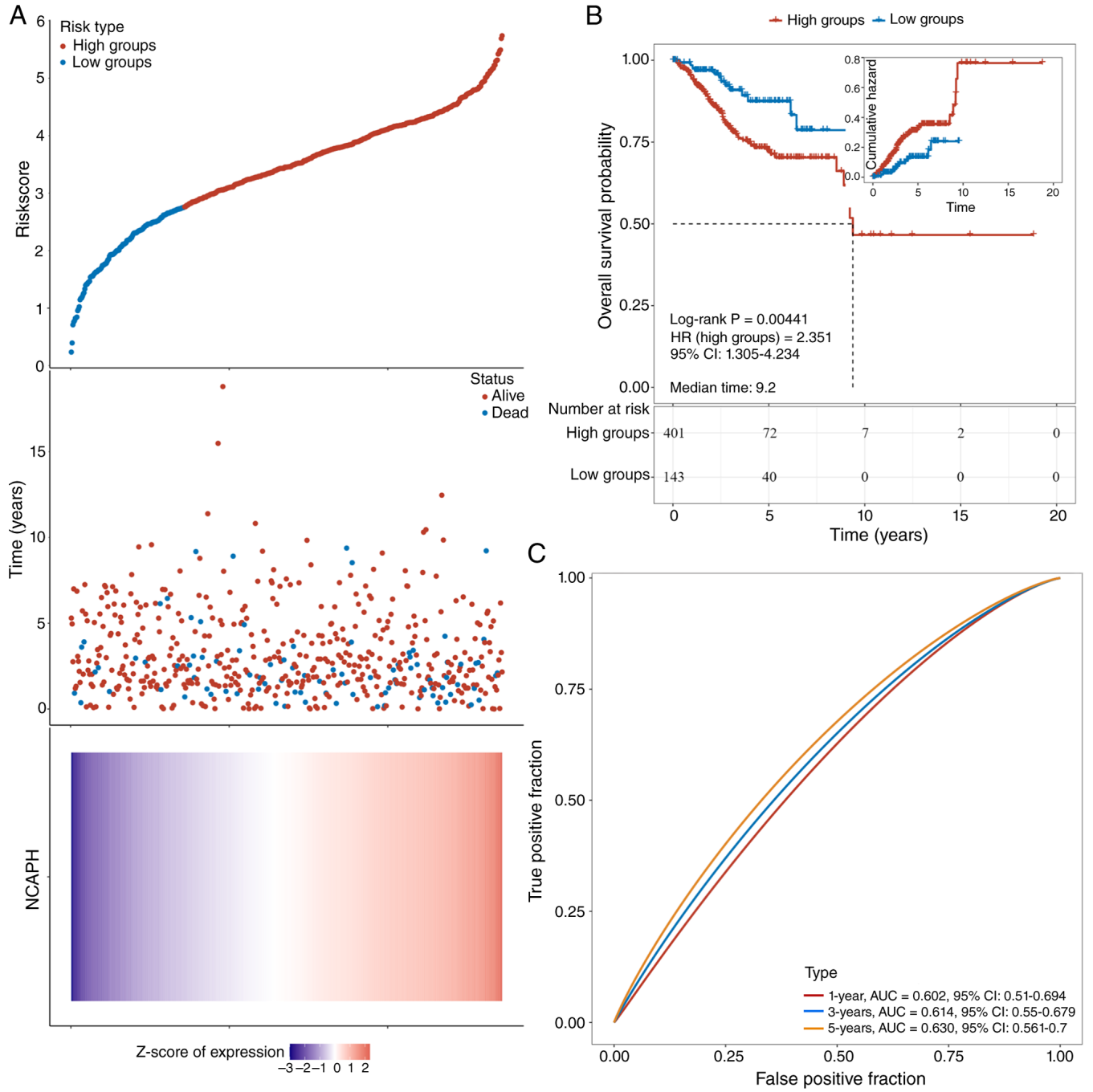

Figure 6. Prognostic importance and diagnostic performance of NCAPH in endometrial cancer. (A) Association between NCAPH expression and overall survival in The Cancer Genome Atlas-Uterine Corpus Endometrial Carcinoma. Upper panel indicates the correlation between NCAPH expression level and risk score stratification. Middle panel indicates distribution of survival time and status corresponding to NCAPH expression in different groups. Lower panel indicates the expression level of NCAPH. (B) Kaplan-Meier survival analysis with an additional cumulative hazard curve in the top right corner. Table indicates the number of patients at risk in different groups at each time point. (C) Time-dependent receiver operating characteristic curve with the AUC assessed at 1, 3 and 5 years. NCAPH, non-SMC condensin I complex subunit H; AUC, area under the curve; HR, hazard ratio.

with adverse clinicopathological features underscores the utility of NCAPH as a diagnostic biomarker and suggested its involvement in EC.

Discussion

As a core subunit of the condensin I complex, NCAPH serves a key role in maintaining the structural integrity of mitotic chromosomes and ensuring genome stability (35,36). Previous studies have demonstrated its oncogenic functions across a number of malignancies (11,12,37); however, the role of NCAPH in EC remains incompletely characterized.

The present study provided a comprehensive multi-omics characterization of NCAPH in EC, integrating genomic, transcriptomic, proteomic and clinicopathological data to establish its role as a key oncogenic driver. The present findings demonstrated that NCAPH expression was significantly upregulated in a number of cancer types, including EC.

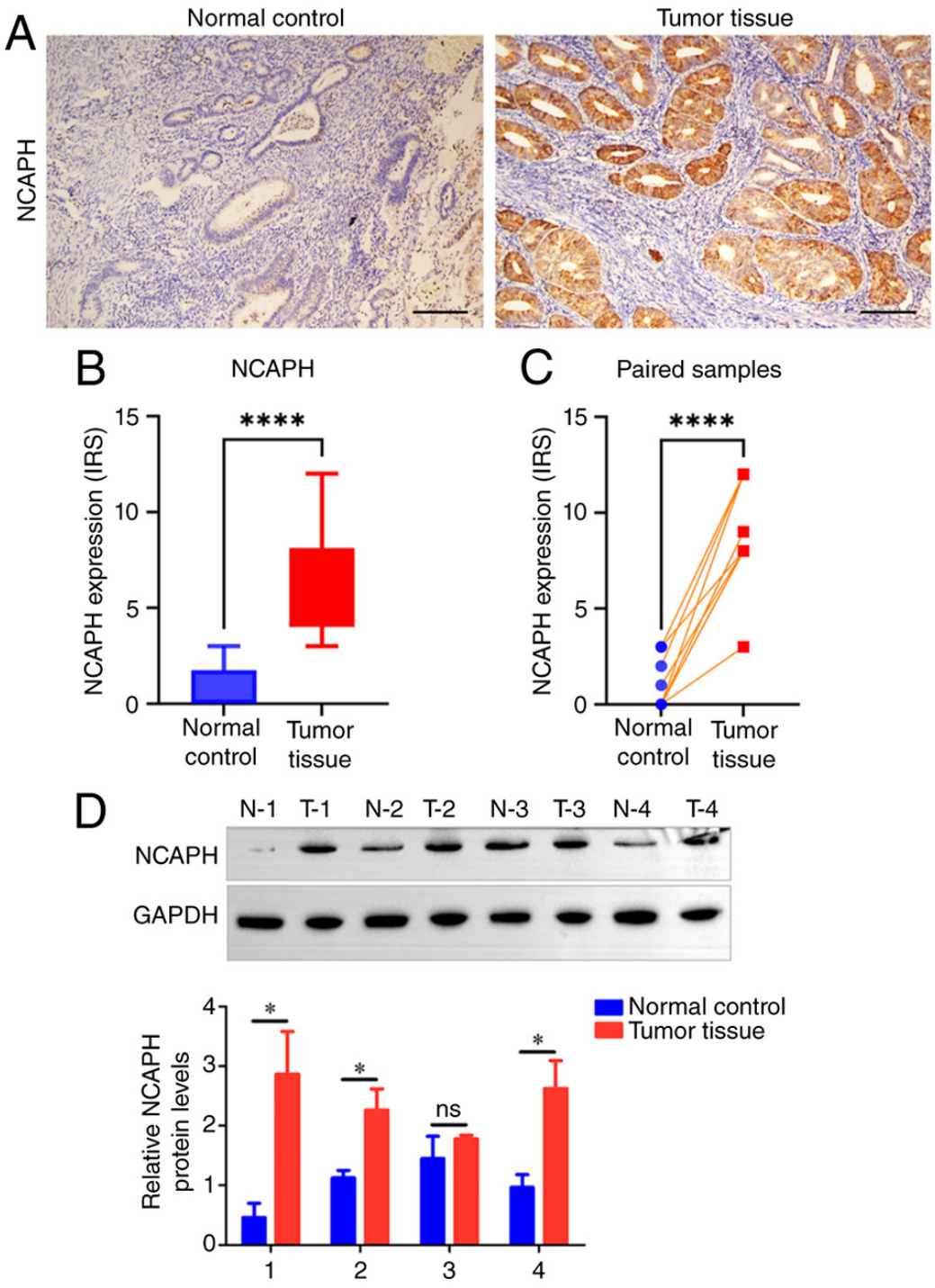

Figure 7. NCAPH protein expression in EC tissues. (A) Representative immunohistochemical staining of NCAPH in T and N endometrial tissues. Scale bar, 100 μm. (B) IRS of NCAPH expression in T (n=108) and N (n=12) endometrial tissues. (C) IRS of NCAPH expression in EC tumor tissues and paired paracancerous normal controls (n=12). (D) Western blotting results and quantification of NCAPH in T and N endometrial tissues. Relative protein level was normalized to GAPDH. Experiments were independently repeated three times. *P<0.05 and ****P<0.0001. NCAPH, non-SMC condensin I complex subunit H; EC, endometrial cancer; T, tumor tissue; N, normal control; IRS, immunoreactive score; ns, not significant.

Increased NCAPH expression was associated with aggressive clinicopathological features, including advanced age, TP53 mutation, higher tumor grade, advanced FIGO stages and the serous histological subtype. These results aligned with and extended previous reports of NCAPH dysregulation in other malignancies such as breast, glioma, gastric, lung and bladder cancers, supporting its broad oncogenic potential across tissue types (13,14,35,38,39).

A notable finding of the present study was the significant positive correlation between NCAPH and TP53, particularly in tumors harboring mutant TP53. Furthermore, NCAPH expression was negatively associated with p53 pathway activity, consistent with the enrichment of TP53 mutations in the NCAPH-high subgroup. This observation is of marked clinical relevance, given the well-established role of TP53 mutations in defining high-risk molecular subtypes of EC (23,40),

Table I. Association between clinicopathological characteristics and NCAPH expression.

		NCAPH		
Characteristic	n	Low	High	P-value
Age, years				0.432
<45	75	31	44	
≥60	33	11	22	
Histological subtype				0.025
Endometriod	94	41	53	
Serous	9	0	9	
Other	5	1	4	
Grade				0.020
1	29	18	11	
2	49	18	31	
3	11	2	9	
FIGO stage				0.023
Stage I	77	36	41	
Stage II	21	3	18	
Stage III	6	3	3	
Stage IV	3	0	3	
LVSI				0.203
Negative	94	39	55	
Positive	13	3	10	

NCAPH, non-SMC condensin I complex subunit H; FIGO, International Federation of Gynecology and Obstetrics; LVSI, lymphovascular space invasion.

particularly serous and copy-number high endometrioid carcinomas, which are characterized by aggressive clinical behavior, chromosomal instability and poor prognosis (41,42). The co-occurrence of elevated NCAPH expression and TP53 mutation suggested a potential synergistic role in driving genomic instability and tumor progression. TP53 loss or mutation impairs cell cycle checkpoint control and DNA damage response, leading to the accumulation of genetic alterations (43,44). Meanwhile, NCAPH, as a core condensin subunit, is key in faithful chromosome condensation and segregation (36,45,46). Dysregulation of NCAPH may further exacerbate chromosomal missegregation and aneuploidy, particularly in a TP53-deficient background where cell cycle surveillance is compromised. This mechanistic synergy might contribute to the more aggressive phenotype observed in TP53-mutant EC.

At the genomic level, NCAPH mutations were identified in 4.92% of EC cases, with a predominance of missense mutations. Although the mutation rate was modest, the high frequency of loss-of-function alterations suggested that NCAPH may contribute to tumorigenesis through haploinsufficiency or dominant-negative effects, warranting further functional validation. Condensin I is a multiprotein complex that acts as a core regulator of mitotic chromosome assembly and faithful segregation in eukaryotes. It consists of the structural maintenance of chromosomes (SMC)-2-SMC4 ATPase core, two HEAT-repeat subunits (NCAPD2/CAP-D2 and NCAPG/CAP-G) and the kleisin NCAPH that bridges the SMC core to the HEAT-repeat subunits (47,48). Physical interactions between NCAPH and the HEAT-repeat subunits are important in chromosome condensation and DNA repair. Among the 29 NCAPH mutations from 26 samples, it was found that numerous mutations clustered in regions important for interaction with HEAT-repeat subunits: The missense mutation D74Y resides within the N-terminal short linear motifs (~55-77 amino acids) that mediate the autoinhibitory interaction with NCAPG (49) and truncating mutations E427* and D469Ifs*25 abolish the entire C-terminal NCAPG-interaction domain (motif IV; ~460-515 amino acids) (50). Given that the HEAT-repeat subunits are central to DNA repair and cell cycle control, the aforementioned mutations are likely to disrupt the physical interaction between NCAPH and its HEAT-repeat partners, leading to impaired DNA damage repair (DDR) and cell cycle control. Notably, a single amino acid substitution in the N-terminal region of Cnd2 (the fission yeast ortholog of NCAPH) has been shown to disrupt both UV-induced DDR and hydroxyurea-induced cells arrest recovery, providing genetic evidence that kleisin N-terminal mutations compromise condensin function in these processes (51). Systematic mutagenesis in fission yeast has further demonstrated that single-amino-acid substitutions in condensin subunits, including both the HEAT-repeat components and the kleisin subunit, confer hypersensitivity to DNA-damaging agents and cause ploidy maintenance defects (52). Collectively, these findings suggested that disruption of HEAT-kleisin interactions represents a potential key mechanism underlying NCAPH mutation-driven chromosomal instability in EC.

Co-expression and functional enrichment analyses revealed that NCAPH-associated genes were significantly enriched in biological processes key in genome integrity, including mitotic cell cycle regulation, DNA replication as well as DNA and microtubule binding. These findings were consistent with the established role of NCAPH in chromosomal condensation and segregation (10) and further suggest that its dysregulation may promote EC progression by inducing chromosomal instability and impaired DDR. PPI analysis identified strong associations between NCAPH and key mitotic regulators such as NCAPD2, NCAPG, BUB1 and KIF family members, reinforcing its central role in cell division. Notably, a number of these interactors have been implicated in cancer pathogenesis (53-55) and represent potential co-targets in NCAPH-driven tumors.

An additional notable finding from the present PPI network analysis was the enrichment of migration and invasion-associated proteins within the NCAPH interactome: The strongest interactor, NCAPG, directly enhances EC invasion through PI3K/Akt signaling (56). KIF4A, which competes with NCAPH for NCAPG binding (49), drives epithelial-mesenchymal transition across numerous cancer types, including glioma and lung, breast, gastric and colorectal cancer (57). Similarly, MELK, KIF11 and aurora kinase A each contributes to migration and invasion through distinct signaling routes. Furthermore, the present KEGG pathway enrichment analysis determined enrichment of the motor protein pathway, a key regulatory axis for cell migration and metastatic progression. This pathway included 12 KIF genes, among which three

(KIF4A, KIF11 and KIF15) were identified as direct binding partners of NCAPH in the present PPI network. These findings suggested that NCAPH may drive the pro-invasive phenotype of EC by orchestrating a prometastatic protein interaction network and modulating motor protein-associated signaling. In addition, NCAPH has been shown to activate a number of oncogenic signaling pathways that promote cancer cell migration and invasion, including PI3K/Akt in glioma (38) and cervical cancer (58), NF-κB/p65 in lung adenocarcinoma (59) and Hippo-yes-associated protein 1 in breast cancer (60). To explore whether similar associations exist in EC, the present study performed ssGSEA and observed a positive correlation between NCAPH expression and PI3K/Akt/mTOR pathway activity, lending independent support to this association. Collectively, these results indicated that NCAPH upregulation may promote metastatic potential in EC through both its network of invasion-associated partners and directly PI3K/Akt pathway activation.

Accumulating evidence from numerous other cancer types has demonstrated that NCAPH upregulation is associated with resistance to platinum-based chemotherapy, including direct experimental evidence in oral squamous cell carcinoma (61) and bioinformatic identification in serous ovarian cancer (62). The underlying mechanisms appear to involve DDR pathways: NCAPH regulates the expression of key homologous recombination repair proteins such as RAD54 and p95/nibrin 1 (35) and directly participates in DNA damage resolution by stabilizing GEN1 for ultra-fine DNA bridge repair (36). Consistent with these findings, the present PPI network analysis revealed an enrichment of DDR proteins within the NCAPH interactome, including direct interactions with DNA topoisomerase II-α and RAD51AP1. Further ssGSEA analysis also determined a positive correlation between NCAPH expression and DNA repair pathway activity, indicating that NCAPH-high EC possess elevated DNA repair capacity. Notably, the present PPI network also identified marked overlap between the NCAPH and RAD51AP1 interactomes, including BUB1, BUB1B, CCNA2, CCNB2, DLG associated protein 5, KIF11, KIF15, KIF20A, KIF4A, MELK, NCAPG and TTK protein kinase. These shared interactors are predominantly involved in mitotic regulation and cell cycle control, processes associated with DNA damage checkpoint signaling and repair, suggesting that NCAPH and RAD51AP1 function within the same biological module. Given that RAD51AP1 has been directly implicated in chemoresistance in gynecological cancer types (63,64), it is plausible that NCAPH upregulation may similarly contribute to chemoresistance in EC. Collectively, these findings imply that NCAPH upregulation may enhance DNA repair capacity in EC through a multi-component DDR axis, thereby promoting resistance to DNA-damaging agents such as cisplatin and paclitaxel. This NCAPH-DDR axis represents a promising therapeutic target for overcoming chemoresistance in EC and warrants further experimental investigation.

A particularly novel aspect of the present study was the investigation into the association between NCAPH expression and the tumor immune microenvironment (TME). A significant negative correlation was observed between NCAPH levels and $CD8^+$ T cell infiltration, along with a positive correlation with $CD4^+$ Th2 cells, indicating an immunosuppressive TME in EC tumors. No significant correlation was detected between NCAPH expression and Treg infiltration using either the CIBERSORT-ABS or XCELL method, indicating that the immunomodulatory effects of NCAPH in EC are unlikely to be mediated by the direct expansion of Tregs. Further analyses regarding canonical M2 macrophage markers (including CD163, MRC1/CD206 and VSIG4) revealed that NCAPH was positively correlated with CD163, while VSIG4 and MRC1/CD206 trended in the same direction but did not reach statistical significance. This expression profile suggested an M2-like shift in tumor-associated macrophages in the context of high NCAPH expression in EC and extends the pan-cancer observation previously reported in breast cancer (37) to EC. The association between NCAPH and PD-L1 (CD274) was further evaluated, given its established role in predicting immunotherapy response (34). NCAPH exhibited a significant positive correlation with PD-L1, consistent with prior mechanistic evidence that NCAPH upregulated PD-L1 expression by inhibiting β-catenin degradation in clear cell renal cell carcinoma (65). The NCAPH-PD-L1 correlation has direct clinical relevance given recent Food and Drug Association approval of PD-1/PD-L1 checkpoint inhibitors (pembrolizumab and dostarlimab) for EC (66-68), suggesting that NCAPH expression could help identify patients most likely to benefit from immunotherapy. Furthermore, a strong immune correlation with MDSC infiltration was also observed. MDSCs are central to tumor immune evasion as they directly inhibit $CD8^+$ T cell cytotoxicity, deplete L-arginine through arginase-1 to starve T cells and drive M2 macrophage polarization. The NCAPH-MDSC correlation therefore provides a mechanistic association that may explain numerous features of the NCAPH-associated immune landscape, the reduced $CD8^+$ T cell infiltration, elevated M2 markers and overall immunosuppression may all converge through MDSC-mediated effects. Collectively, these analyses characterized the immunosuppressive role of NCAPH in EC, supported its potential utility as a candidate biomarker for immunotherapy patient stratification and highlighted the NCAPH/MDSC/PD-L1 axis as a promising target for future mechanistic and functional investigations.

Lastly, the robust prognostic importance of NCAPH upregulation corroborated by Kaplan-Meier survival analysis and time-dependent ROC curves, supports its potential utility as a clinical biomarker for risk stratification. The consistent diagnostic performance of NCAPH across numerous timepoints (AUC=0.602, 0.606, 0.628 at 1, 3, 5 years, respectively) further highlights its reliability in predicting patient outcomes.

Despite these strengths, numerous limitations of the present study should be acknowledged. The bioinformatics analyses were conducted primarily on retrospective datasets and although IHC validation was performed, the sample size was relatively limited. in addition, the precise molecular mechanisms by which NCAPH influences mitotic regulation, genomic instability and immune modulation have not been fully elucidated. In particular, the crosstalk between NCAPH and TP53 signaling remains poorly defined. As such, these questions warrant further investigation using both *in vitro* and *in vivo* models. Furthermore, the potential implications of NCAPH in cancer immunotherapy, though suggestive, remain largely speculative. Despite the present results indicating an association between NCAPH expression and an

immunosuppressive microenvironment, it is still unclear whether NCAPH contributes to primary or acquired resistance to immune checkpoint inhibitors in EC.

In conclusion, the present integrated analysis established NCAPH as a multifaceted oncoprotein in EC, contributing to tumor progression through the dysregulation of mitotic processes, induction of chromosomal instability and modulation of the TME. Its significant association with advanced disease stage, aggressive histologic subtypes and poor survival outcomes underscores its value as a prognostic biomarker. Furthermore, the strong immune correlations observed suggested that NCAPH may influence response to immunotherapy, positioning it as a potential target for future combination therapeutic strategies. The present findings provide a compelling rationale for further mechanistic and translational studies aimed at exploiting NCAPH as both a predictive biomarker and a therapeutic target in EC.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

YH was responsible for conceptualization of the present study, conducting formal analysis, performing the investigation and writing, reviewing and editing the manuscript. KK was responsible for conducting formal analysis, performing the investigation and writing the original manuscript draft. QZ was responsible for pathological diagnosis confirmation, histological quality assessment and the resources used. QM was responsible for IHC staining validation, results interpretation and conducting formal analysis. YX performed tissue sample collection, clinicopathological data acquisition and was responsible for the resources used. YZ and MH conceptualized the present study, provided supervision and were responsible for writing, reviewing and editing the manuscript. All authors read and approved the final version of the manuscript. YH and MH confirm the authenticity of all the raw data.

Ethics approval and consent to participate

Ethical approval was granted from the Medical Ethics Committee of The Affiliated Huai'an No.1 People's Hospital of Nanjing Medical University (Huai'an First People's Hospital, Nanjing, China; approval no. KY-2025-195-01). All methods were performed in accordance with the Declaration of Helsinki. Written informed consent was waived for this retrospective non-interventional study.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Use of artificial intelligence tools

During the preparation of this work, artificial intelligence tools were used to improve the readability and language of the manuscript or to generate images, and subsequently, the authors revised and edited the content produced by the artificial intelligence tools as necessary, taking full responsibility for the ultimate content of the present manuscript.

References

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I and Jemal A: Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 74: 229-263, 2024.
2. Siegel RL, Giaquinto AN and Jemal A: Cancer statistics, 2024. CA Cancer J Clin 74: 12-49, 2024.
3. Cronin KA, Scott S, Firth AU, Sung H, Henley SJ, Sherman RL, Siegel RL, Anderson RN, Kohler BA, Benard VB, *et al*: Annual report to the nation on the status of cancer, part 1: National cancer statistics. Cancer 128: 4251-4284, 2022.
4. Nierengarten MB: Annual report to the nation on the status of cancer: This latest report, a collaboration from the American Cancer Society, the Centers for Disease Control and Prevention, the National Cancer Institute, and the North American Association of Central Cancer Registries, shows that cancer mortality rates have accelerated, and incidence rates remain stable, with pancreatic cancer showing an increase in both incidence and mortality: This latest report, a collaboration from the American Cancer Society, the Centers for Disease Control and Prevention, the National Cancer Institute, and the North American Association of Central Cancer Registries, shows that cancer mortality rates have accelerated, and incidence rates remain stable, with pancreatic cancer showing an increase in both incidence and mortality. Cancer 129: 8, 2023.
5. Murali R, Soslow RA and Weigelt B: Classification of endometrial carcinoma: More than two types. Lancet Oncol 15: e268-e278, 2014.
6. Makker V, MacKay H, Ray-Coquard I, Levine DA, Westin SN, Aoki D and Oaknin A: Endometrial cancer. Nat Rev Dis Primers 7: 88, 2021.
7. Tronconi F, Nero C, Giudice E, Salutari V, Musacchio L, Ricci C, Carbone MV, Ghizzoni V, Perri MT, Camarda F, *et al*: Advanced and recurrent endometrial cancer: State of the art and future perspectives. Crit Rev Oncol Hematol 180: 103851, 2022.
8. Corr B, Cosgrove C, Spinosa D and Guntupalli S: Endometrial cancer: Molecular classification and future treatments. BMJ Med 1: e000152, 2022.
9. Zhou W, Hu J and Zhao J: Non-SMC condensin I complex subunit H (NCAPH), a regulator of cell cycle, predicts poor prognosis in lung adenocarcinoma patients: A study mainly based on TCGA and GEO database. Transl Cancer Res 9: 7572-7587, 2020.
10. Hirano T: Condensins: Organizing and segregating the genome. Curr Biol 15: R265-R275, 2005.
11. Song Z, Xia Y, Zhang G, Wang Z, Yang J and Fan W: NCAPH as an onco-structural hub linking chromatin architecture to metabolic reprogramming, immune evasion, and therapy resistance. Crit Rev Oncol Hematol 222: 105273, 2026.

12. Liu C, Han X, Zhang S, Huang M, Guo B, Zhao Z, Yang S, Jin J, Pu W and Yu H: The role of NCAPH in cancer treatment. Cell Signal 121: 111262, 2024.
13. Li C, Meng J and Zhang T: NCAPH is a prognostic biomarker and associated with immune infiltrates in lung adenocarcinoma. Sci Rep 12: 9578, 2022.
14. Li B, Xiao Q, Shan L and Song Y: NCAPH promotes cell proliferation and inhibits cell apoptosis of bladder cancer cells through MEK/ERK signaling pathway. Cell Cycle 21: 427-438, 2022.
15. Zhang T, Li P, Guo W, Liu Q, Qiao W and Deng M: NCAPH promotes proliferation as well as motility of breast cancer cells by activating the PI3K/AKT pathway. Physiol Int 109: 334-347, 2022.
16. Xiong Q, Jiang L, Liu K, Jiang X, Liu B, Shi Y, Cheng D, Duan Y, Yang C and Chen Y: miR-133b targets NCAPH to promote beta-catenin degradation and reduce cancer stem cell maintenance in non-small cell lung cancer. Signal Transduct Target Ther 6: 252, 2021.
17. Xiong YC, Wang J, Cheng Y, Zhang XY and Ye XQ: Overexpression of MYBL2 promotes proliferation and migration of non-small-cell lung cancer via upregulating NCAPH. Mol Cell Biochem 468: 185-193, 2020.
18. Kim JH, Youn Y, Kim KT, Jang G and Hwang JH: Non-SMC condensin I complex subunit H mediates mature chromosome condensation and DNA damage in pancreatic cancer cells. Sci Rep 9: 17889, 2019.
19. Liao L, Cheng H and Liu S: Non-SMC condensin I complex subunit H promotes the malignant progression and cisplatin resistance of breast cancer MCF-7 cells. Oncol Lett 24: 317, 2022.
20. Ogura T, Azuma K, Sato J, Kinowaki K, Takayama KI, Takeiwa T, Kawabata H and Inoue S: OCT1 is a poor prognostic factor for breast cancer patients and promotes cell proliferation via inducing NCAPH. Int J Mol Sci 22: 11505, 2021.
21. Lei Y, Wang D, Chen W, Tian X and Wei J: FOXM1/NCAPH activates glycolysis to promote colon adenocarcinoma stemness and 5-FU resistance. Anticancer Drugs 34: 929-938, 2023.
22. Qiu X, Gao Z, Shao J and Li H: NCAPH is upregulated in endometrial cancer and associated with poor clinicopathologic characteristics. Ann Hum Genet 84: 437-446, 2020.
23. Levine D and Cancer Genome Atlas Research Network: Integrated genomic characterization of endometrial carcinoma. Nature 497: 67-73, 2013.
24. Tang Z, Kang B, Li C, Chen T and Zhang Z: GEPIA2: An enhanced web server for large-scale expression profiling and interactive analysis. Nucleic Acids Res 47: W556-W560, 2019.
25. Ritchie ME, Phipson B, Wu D, Hu Y, Law CW, Shi W and Smyth GK: limma powers differential expression analyses for RNA-sequencing and microarray studies. Nucleic Acids Res 43: e47, 2015.
26. Chandrashekar DS, Karthikeyan SK, Korla PK, Patel H, Shovon AR, Athar M, Netto GJ, Qin ZS, Kumar S, Manne U, *et al*: UALCAN: An update to the integrated cancer data analysis platform. Neoplasia 25: 18-27, 2022.
27. Chandrashekar DS, Bashel B, Balasubramanya SAH, Creighton CJ, Ponce-Rodriguez I, Chakravarthi BVSK and Varambally S: UALCAN: A portal for facilitating tumor subgroup gene expression and survival analyses. Neoplasia 19: 649-658, 2017.
28. Mayakonda A, Lin DC, Assenov Y, Plass C and Koeffler HP: Maftools: Efficient and comprehensive analysis of somatic variants in cancer. Genome Res 28: 1747-1756, 2018.
29. Cui H, Zhao G, Lu Y, Zuo S, Duan D, Luo X, Zhao H, Li J, Zeng Z, Chen Q and Li T: TIMER3: An enhanced resource for tumor immune analysis. Nucleic Acids Res 53: W534-W541, 2025.
30. Blanche P, Dartigues JF and Jacqmin-Gadda H: Estimating and comparing time-dependent areas under receiver operating characteristic curves for censored event times with competing risks. Stat Med 32: 5381-5397, 2013.
31. Hanzelmann S, Castelo R and Guinney J: GSVA: Gene set variation analysis for microarray and RNA-seq data. BMC Bioinformatics 14: 7, 2013.
32. Moretti NR, Kamitani HZ, de Souza Wagner PH, Matheus GTFU, Talah BAD, Tanimoto LE, de Oliveira Barretto IC and de Moraes FCA: Impact of TP53 somatic mutations on prognosis in endometrial cancer: A systematic review and meta-analysis. Clin Transl Oncol 28: 1324-1339, 2025.
33. Zhang W, Wang M, Ji C, Liu X, Gu B and Dong T: Macrophage polarization in the tumor microenvironment: Emerging roles and therapeutic potentials. Biomed Pharmacother 177: 116930, 2024.
34. Doroshow DB, Bhalla S, Beasley MB, Sholl LM, Kerr KM, Gnjatic S, Wistuba II, Rimm DL, Tsao MS and Hirsch FR: PD-L1 as a biomarker of response to immune-checkpoint inhibitors. Nat Rev Clin Oncol 18: 345-362, 2021.
35. Wang Y, Li JQ, Yang ZL, Wang L, Zhang JC, Sun YF, Li ZY and Qin L: NCAPH regulates gastric cancer progression through DNA damage response. Neoplasma 69: 283-291, 2022.
36. Kim JH, Youn Y and Hwang JH: NCAPH Stabilizes GEN1 in chromatin to resolve Ultra-fine DNA bridges and maintain chromosome stability. Mol Cells 45: 792-805, 2022.
37. Liu Y, Ma X, Feng L, Lin Z and Zhou X: An integrative pan-cancer analysis reveals the carcinogenic effects of NCAPH in human cancer. Math Biosci Eng 20: 76-92, 2023.
38. Liang J, Yun D, Jin W, Fan J, Wang X, Wang X, Li Y, Yu S, Zhang C, Li T and Yang X: NCAPH serves as a prognostic factor and promotes the tumor progression in glioma through PI3K/AKT signaling pathway. Mol Cell Biochem 480: 589-605, 2025.
39. Mendiburu-Elicabe M, Garcia-Sancha N, Corchado-Cobos R, Martínez-López A, Chang H, Hua Mao J, Blanco-Gómez A, García-Casas A, Castellanos-Martín A, Salvador N, *et al*: NCAPH drives breast cancer progression and identifies a gene signature that predicts luminal a tumour recurrence. Clin Transl Med 14: e1554, 2024.
40. Anca-Stanciu MB, Manu A, Olinca MV, Coroleucă C, Comandașu DE, Coroleuca CA, Maier C and Bratila E: Comprehensive review of endometrial cancer: New molecular and FIGO classification and recent treatment changes. J Clin Med 14: 1385, 2025.
41. Espinosa I, D'Angelo E and Prat J: Endometrial carcinoma: 10 years of TCGA (the cancer genome atlas): A critical reappraisal with comments on FIGO 2023 staging. Gynecol Oncol 186: 94-103, 2024.
42. Bogani G, Ray-Coquard I, Concin N, Ngoi NYL, Morice P, Enomoto T, Takehara K, Denys H, Nout RA, Lorusso D, *et al*: Uterine serous carcinoma. Gynecol Oncol 162: 226-234, 2021.
43. Tornesello ML: TP53 mutations in cancer: Molecular features and therapeutic opportunities (Review). Int J Mol Med 55: 7, 2025.
44. Wang H, Guo M, Wei H and Chen Y: Targeting p53 pathways: Mechanisms, structures, and advances in therapy. Signal Transduct Target Ther 8: 92, 2023.
45. Hirano T: Condensins: Universal organizers of chromosomes with diverse functions. Genes Dev 26: 1659-1678, 2012.
46. Wood AJ, Severson AF and Meyer BJ: Condensin and cohesin complexity: The expanding repertoire of functions. Nat Rev Genet 11: 391-404, 2010.
47. Onn I, Aono N, Hirano M and Hirano T: Reconstitution and subunit geometry of human condensin complexes. EMBO J 26: 1024-1034, 2007.
48. Schleiffer A, Kaitna S, Maurer-Stroh S, Glotzer M, Nasmyth K and Eisenhaber F: Kleisins: A superfamily of bacterial and eukaryotic SMC protein partners. Mol Cell 11: 571-575, 2003.
49. Cutts EE, Tetiker D, Kim E and Aragon L: Molecular mechanism of condensin I activation by KIF4A. EMBO J 44: 682-704, 2025.
50. Hara K, Kinoshita K, Migita T, Murakami K, Shimizu K, Takeuchi K, Hirano T and Hashimoto H: Structural basis of HEAT-kleisin interactions in the human condensin I subcomplex. EMBO Rep 20: e47183, 2019.
51. Aono N, Sutani T, Tomonaga T, Mochida S and Yanagida M: Cnd2 has dual roles in mitotic condensation and interphase. Nature 417: 197-202, 2002.
52. Xu X, Nakazawa N and Yanagida M: Condensin HEAT subunits required for DNA repair, kinetochore/centromere function and ploidy maintenance in fission yeast. PLoS One 10: e0119347, 2015.
53. Cai X, Gao J, Shi C, Guo WZ, Guo D and Zhang S: The role of NCAPG in various of tumors. Biomed Pharmacother 155: 113635, 2022.
54. Kim T and Gartner A: Bub1 kinase in the regulation of mitosis. Anim Cells Syst (Seoul) 25: 1-10, 2021.
55. Zhong M, Gong L, Li N, Guan H, Gong K, Zhong Y, Zhu E, Wang X, Jiang S, Li J, *et al*: Pan-cancer analysis of kinesin family members with potential implications in prognosis and immunological role in human cancer. Front Oncol 13: 1179897, 2023.
56. Ren Z, Zheng CY, Xiao X, Yang X, Li X, Cai H and Fu C: Non-SMC Condensin I complex subunit G promotes the proliferation, invasion and homologous recombination repair of endometrial cancer through PI3K/AKT signaling pathway. J Biomed Nanotechnol 19: 1422-1439, 2023.

57. Liu Y, Li Y, Tang C, Wen H, Tang J, Chen G and Wu Y: KIF4A in disease pathogenesis and therapeutics: From molecular mechanisms to clinical translation. Biol Direct 20: 116, 2025.
58. Wang M, Qiao X, Cooper T, Pan W, Liu L, Hayball J, Lin J, Cui X, Zhou Y, Zhang S, *et al*: HPV E7-mediated NCAPH ectopic expression regulates the carcinogenesis of cervical carcinoma via PI3K/AKT/SGK pathway. Cell Death Dis 11: 1049, 2020.
59. Huang P, Zhao H, Sun R, Liu C, Wu L, Wang Y, Gan Z, Yang X and Du J: MiR-1976/NCAPH/P65 axis inhibits the malignant phenotypes of lung adenocarcinoma. Sci Rep 14: 11211, 2024.
60. Qiu C, Wei Y and Li J: NCAPH-YAP1 interaction promotes breast cancer stemness and tumor progression. Stem Cell Res Ther 16: 494, 2025.
61. Shimomura H, Sasahira T, Nakashima C, Kurihara-Shimomura M and Kirita T: Non-SMC condensin I complex subunit H (NCAPH) is associated with lymphangiogenesis and drug resistance in oral squamous cell carcinoma. J Clin Med 9: 72, 2019.
62. Zhan SJ, Liu B and Linghu H: Identifying genes as potential prognostic indicators in patients with serous ovarian cancer resistant to carboplatin using integrated bioinformatics analysis. Oncol Rep 39: 2653-2663, 2018.
63. Huang X, Wu Z, Xiao C and Chen XI: E2F7/RAD51AP1 axis inhibits endometrial cancer sensitivity to 5-FU via the fatty acid metabolic pathway. Anticancer Res 43: 4905-4914, 2023.
64. Zeng SH, Yan ZQ, Ren Q, Lin LH and Chen Z: Knocking down RAD51AP1 enhances chemosensitivity by inhibiting the self-renewal of CD133 positive ovarian cancer stem-like cells. Discov Oncol 15: 410, 2024.
65. Chen Z, Ruan W, Guo C, Chen K, Li L, Tian J, Hu Z, Peng D and Zeng X: Non-SMC condensin I complex subunit H participates in anti-programmed cell death-1 resistance of clear cell renal cell carcinomas. Cell Prolif 56: e13400, 2023.
66. O'Malley DM, Bariani GM, Cassier PA, Marabelle A, Hansen AR, De Jesus Acosta A, Miller WH Jr, Safra T, Italiano A, Mileshkin L, *et al*: Pembrolizumab in patients with microsatellite Instability-High advanced endometrial cancer: Results from the KEYNOTE-158 study. J Clin Oncol 40: 752-761, 2022.
67. Mirza MR, Chase DM, Slomovitz BM, dePont Christensen R, Novák Z, Black D, Gilbert L, Sharma S, Valabrega G, Landrum LM, *et al*: Dostarlimab for primary advanced or recurrent endometrial cancer. N Engl J Med 388: 2145-2158, 2023.
68. Powell MA, Bjorge L, Willmott L, Novák Z, Black D, Gilbert L, Sharma S, Valabrega G, Landrum LM, Gropp-Meier M, *et al*: Overall survival in patients with endometrial cancer treated with dostarlimab plus carboplatin-paclitaxel in the randomized ENGOT-EN6/GOG-3031/RUBY trial. Ann Oncol 35: 728-738, 2024.