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Prognostic Value and Immunological Role of POP7 in Clear Cell Renal Cell Carcinoma

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Background: Studies have found that RNA-binding proteins (RBPs) are participated in the occurrence or development of tumours. However, the role of processing of precursor family (POP family) in clear cell renal cell carcinoma (ccRCC) has not been studied yet. Here, we analyzed the expression and prognostic value of POP family in ccRCC analyzed and subsequently revealed the relationship between POP7 and immune infiltration in ccRCC patients.

Methods: POP family expression in cancer and normal tissues was analyzed in Cancer Genome Atlas pan-cancer (TCGA-pan-cancer). Kaplan–Meier (KM) survival analysis, univariable and multivariable analysis demonstrated the survival of ccRCC with POP family in Kidney Clear Cell Carcinoma (TCGA-KIRC). POP7 mRNA and protein expression were verified by Gene Expression Omnibus (GEO) data, the quantitative real-time polymerase chain reaction (qRT-PCR), and Office of Cancer Clinical Proteomics Research (CPTAC). The diagnostic ability of POP7 mRNA and protein expression was achieved with ROC curves. Gene Set Enrichment Analysis (GSEA) and TiMER2 evaluated pathogenesis role and immune infiltration of POP7in ccRCC.

Results: There is a significant difference in expression of POP family in TCGA-pan-cancer, especially in ccRCC. KM survival analysis, univariable and multivariable analysis demonstrated low expression of POP7 and was associated with poor OS and poor DFS. GEO data, the qRT-PCR, and CPTAC verified the high expression of POP7 mRNA and protein in ccRCC. ROC curves verified a valuable diagnostic ability of POP7 in mRNA and protein expression. GSEA demonstrated POP7 was associated with CD8+cells, CD4+cells, natural killer (NK) cells, and helper T (TH1) cells. TiMER2 results indicated POP7 had a positive correlation with T cell regulatory (Tregs) and myeloid-derived suppressor cells (MDSC) in ccRCC and was an immunosuppressor for ccRCC.

Conclusion: POP7 was a reliable immunosuppressor, predictor and biomarker for ccRCC.

Keywords: POP7, ccRCC, immunotherapy, prognostic indicator

Background

Global cancer statistics from the International Agency for Research on Cancer (IARC) showed 434,419 new cancer and 155,702 new cancer deaths cases with kidney in 2022.[1] During the same period in 2022, there were approximately 77410 new cancer cases and 46345 new deaths from renal cancer in China.[2] It is estimated that among all cancers, renal cell carcinoma will have approximately 81,610 new cases and 14,390 new deaths in the United States in 2024.[3] The estimated number of deaths from renal cancer in China is very large, and the pathogenesis and treatment of renal tumors are serious challenges for researchers. Clear cell renal cell carcinoma (ccRCC) is the main types of RCC and remains an extremely lethal disease.[4] The main treatment for early-stage RCC was partial nephrectomy or radical nephrectomy, while targeted drug therapy was mainly treatment for advanced renal cancer.

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Tumor recurrence was still happening after nephrectomy or metastasectomy, especially for metastatic renal cell carcinoma.[5] Target of tyrosine kinase inhibitor (TKI) drugs (anti-VEGF tyrosine kinase inhibitors) was the main drug treatments for metastatic ccRCC.[6,7] All anti-VEGF tyrosine kinase inhibitors except sunitinib had failed to benefit to patients with locally advanced disease.[8] Immune checkpoint inhibitors were used as the first-line in metastatic ccRCC. Pembrolizumab benefits patients with metastatic disease or at a high risk of recurrence as adjuvant therapy.[9,10] It offered the best risk/benefit ratio, when patients took nephrectomy at high risk of relapse.[11] Drug therapy inevitably develops into drug resistance and urgently needs us to study the mechanism of drug tolerance.

Previous research showed POP1 and POP4 had limited expression in prostate cancer tissue, whereas POP5 were significantly downregulated prostate cancer tissue and benign clinical samples of prostate tissue, POP1 and POP7 Expression were increased whereas POP5 were decreased by androgen.[12] In this study, we investigated the gene expression of POP family and the role of POP7 in TCGA-KIRC, the expression and diagnosability of POP7 in clinical samples, GEO database, and CPTAC of ccRCC. TiMER2 and Gene Set Enrichment Analysis (GSEA) demonstrated that POP7 was a significant marker and immunosuppressor in ccRCC.

Patients and Methods

Patient Samples from Public Database and

Public database from Gene Expression Omnibus (GEO)[13] (GSE16441, which contains 17 pairs of ccRCC tumours and paired normal tissues), The Cancer Genome Atlas Kidney Clear Cell Carcinoma[14] (TCGA-KIRC, which contains 72 pairs of ccRCC tumours and paired normal tissues, and total 533 patients), and Office of Cancer Clinical Proteomics Research (CPTAC, which contains 110 patients).[15]

Clinical Samples Collection, RNA Extraction, RNA Reverse Transcription and qRT-PCR

Twenty-four clinical samples were collected from Wuhan Union Hospital between 2022 and 2023. The patient/participant provided written informed consent, and the research procedures were approved by the Institutional Review Committee of Huazhong University of Science and Technology followed by the Declaration of Helsinki. RNA extraction was then conducted using the TRizol reagent (Thermo, Massachusetts, USA). Next, synthesize the strand cDNA Synthesis with cDNA Synthesis test kit (Vazyme, Nanjing, China) and quantitative real-time polymerase chain reaction (qRT-PCR) with qPCR SYBR® Green Master Mix (Vazyme, Nanjing, China).[16] Finally, we analyzed the POP7 expression with $2^{-\Delta Ct}$ ($\Delta Ct = Ct_{POP7} - Ct_{GAPDH}$).

POP7, (forward, 5′- CCCGGAGACCCAATGACATTT −3′,
reverse, 5′- GGGCCTTAAAGTCCGTCTTCA-3′).
GAPDH (forward, 5’-GAGTCAACGGATTTGGTCGT-3’;
reverse, 5’-GACAAGCTTCCCGTTCTCAG-3’).

Bioinformatics Analysis

Hazard ratio (HR) and confidence interval (CI) of the HR estimated the univariable and multivariable Cox proportional hazards regression. Kaplan Meier (KM) curves evaluated the patient’s survival status of OS and DFS when the survival time was cut at 120 months with surv_cutpoint and ggsurvplot in R 4.1.3. Area Under Curve (AUC) and Receiver Operator Characteristic (ROC) curve evaluated the clinical diagnostic ability of POP7 in patients with ccRCC with SPSS Statistics 22.0 and GraphPad prism 9 as described above.[17]

Gene set enrichment analysis (GSEA) evaluated the role of POP7 in ccRCC. (http://www.broadinstitute.org/gsea). As mentioned before, $p < 0.05$ and false discovery rate (FDR) of <25% had statistically significant difference.[18,19] TiMER2 was used to analyze the role of POP family in pan-cancer and the immune infiltration of POP7 in ccRCC.[20]

Statistical Analysis

RNA and protein results were described with median and SEM. The two paired and unpaired samples were analyzed with paired sample *t*-test or *t*-test, and inter multiple group analysis was analyzed in one way ANOVA as previously describe.[19] Data analyses were performed with GraphPad prism 9 and followed by guidelines for reporting of statistics for clinical research in urology, *p < 0.05, ** p < 0.01,*** p < 0.001.[21]

Results

The Expression of POP Family Had a Significant Expression Difference in ccRCC

Firstly, we want to know the role of POP family in pan-cancer in Supplementary Figure 1. POP1 was significantly increased in bladder urothelial carcinoma (BLCA), breast invasive carcinoma (BRCA), cholangiocarcinoma (CHOL), colon adenocarcinoma (COAD), esophageal carcinoma (ESCA), head and neck squamous cell carcinoma (HNSC), KIRC, liver hepatocellular carcinoma (LIHC), lung adenocarcinoma (LUAD), lung squamous cell carcinoma (LUSC), prostate adenocarcinoma (PRAD), rectum adenocarcinoma (READ), stomach adenocarcinoma (STAD), and uterine corpus endometrial carcinoma (UCEC) but reduced in thyroid carcinoma (THCA) and kidney chromophobe (KICH) in Supplementary Figure 1A. POP4 was significantly increased in BLCA, BRCA, CHOL, ESCA, HNSC, KIRC, kidney renal papillary cell carcinoma (KIRP), LIHC, LUAD, LUSC, STAD, UCEC, but reduced in THCA in Supplementary Figure 1B. POP5 was significantly increased in BLCA, COAD, CHOL, ESCA, HNSC, KIRP, LIHC, LUAD, LUSC, STAD, UCEC, but reduced in KICH, KIRC, and THCA in Supplementary Figure 1C. POP7 was significantly increased in BLCA, BRCA, COAD, CHOL, ESCA, HNSC, KICH, KIRC, KIRP, LIHC, LUAD, LUSC, THCA, PRAD, STAD, UCEC in Supplementary Figure 1D. Then, we focused on the expression of this family in kidney cancer. Heat map showed the mRNA expression levels of the POP1, POP4, POP5, and POP7 in TCGA-KIRC in Figure 1A. POP1, POP4, and POP7 had a higher expression, while POP5 had a lower expression in total ccRCC tissues vs non-tumorous tissues (Normal n = 72, Tumour n = 533) in Figure 1B and C. The same results showed POP1, POP4, and POP7 had a higher expression, while POP5 had a lower expression in paired ccRCC tissues vs non-tumorous tissues (Normal n = 72, Tumour n = 72) in Figure 1D and E.

Prognostic Significance, Univariable and Multivariable Analyses in OS and DFS of POP Family in ccRCC

Next, we analyzed the prognostic significance of POP family in ccRCC. We defined the high- and low-expression groups as the median expression of POP family. The different expression of POP1 has no effect on the prognosis of ccRCC. High expression of POP4, POP5, POP7 had shorter OS and shorter DFS in Figure 2A–F. Univariable and multivariable analysis with Hazard ratio (HR) and confidence interval (CI) of the HR estimated the prognostic ability of POP7. The results of OS were showed as follows: age (HR, 1.60; 95% CI: 1.17–2.20, p = 0.003), T stage (HR, 1.54; 95% CI: 1.07–2.21, p = 0.02), N stage (HR, 2.89; 95% CI: 2.01–4.16, p < 0.0001), POP5 (HR, 1.80; 95% CI: 1.22–2.67, p = 0.003), POP7 expression (HR, 1.64; 95% CI: 1.11–2.41, p = 0.013), (Table 1). DFS: T stage (HR, 1.99; 95% CI: 1.29–3.05, p = 0.002), N stage (HR, 2.60; 95% CI: 1.23–5.48, p = 0.012), M stage (HR, 4.870; 95% CI: 3.14–7.37, p < 0.0001), Grade (HR, 2.42; 95% CI: 1.58–3.73, p < 0.000), POP7 expression (HR, 1.67; 95% CI: 3.14–7.36, p = 0.025), (Table 2). Therefore, we focus on understanding the functional role of POP 7 in ccRCC.

The Relationship Between Clinical Characteristics and POP7 in KIRC

We had analyzed the relationship of POP7 and clinical characteristics in KIRC patient, as the clinical characteristics were related to survival prognosis. POP7 expression was downregulation significantly in living patients (Figure 3A). The expression of POP7 was decreased in patients without recurrence (Figure 3B). Patients with low expression of POP7 lower tumor distant metastasis (Figure 3C), lymph node metastasis (Figure 3D). Patients with high clinical stage (T3 + T4, Figure 3E and F), higher TNM patients (III+IV, Figure 3G and H) and grade (G3 + G4, Figure 3I and J) exhibited significant high expression of POP7.

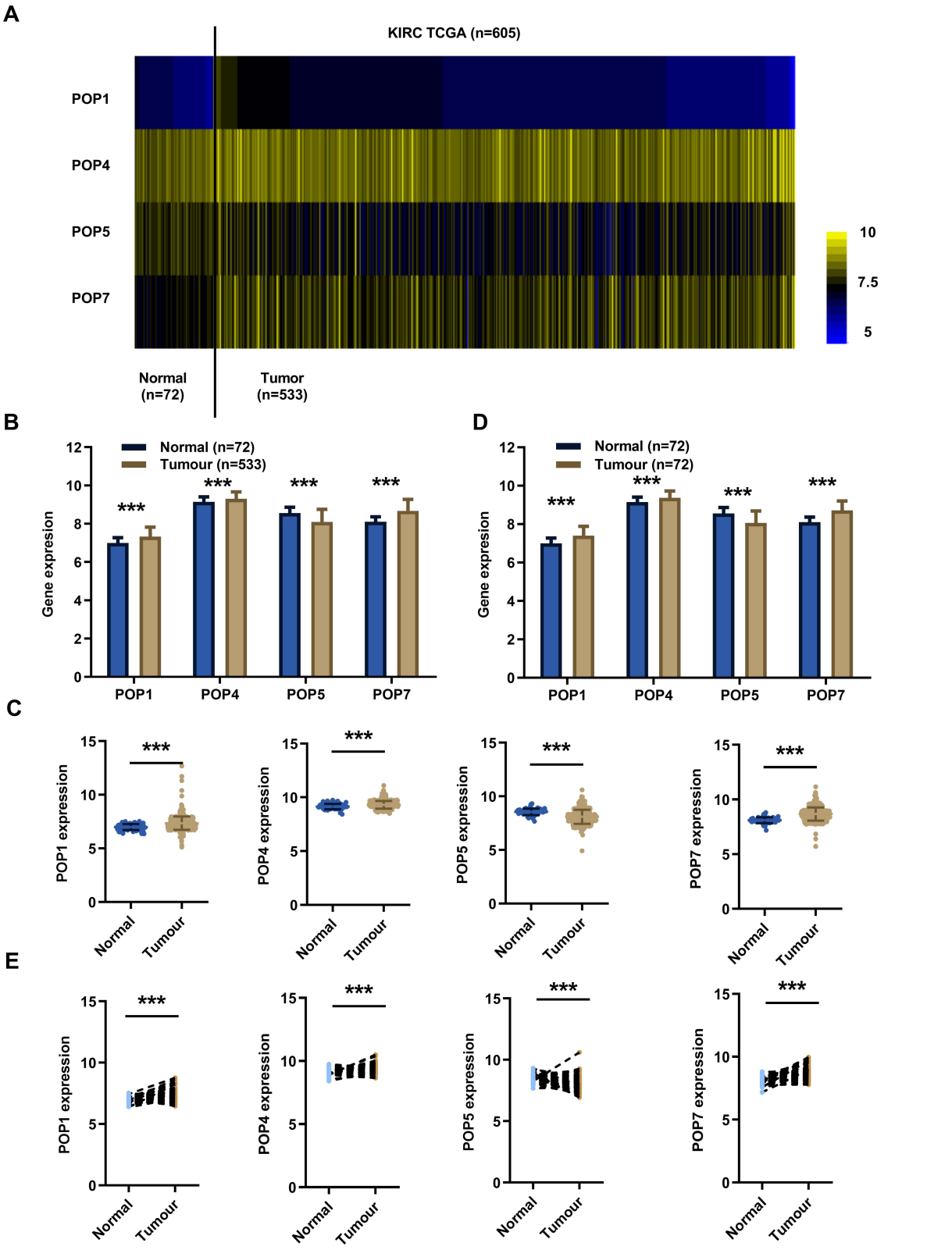

Figure 1 POP family expression in TCGA-KIRC datasets. (**A**) Heat map depicting POP family expression in TCGA-KIRC (n = 605). (**B**) and (**C**) POP1, POP4, and POP7 had a higher expression, while POP5 had a lower expression in paired ccRCC tissues vs non-tumorous tissues (Normal n = 72, Tumour n = 533). (**D**) and (**E**) POP1, POP4, and POP7 had a higher expression, while POP5 had a lower expression in paired ccRCC tissues vs non-tumorous tissues (Normal n = 72, Tumour n = 72). Research. ***P <0.001.

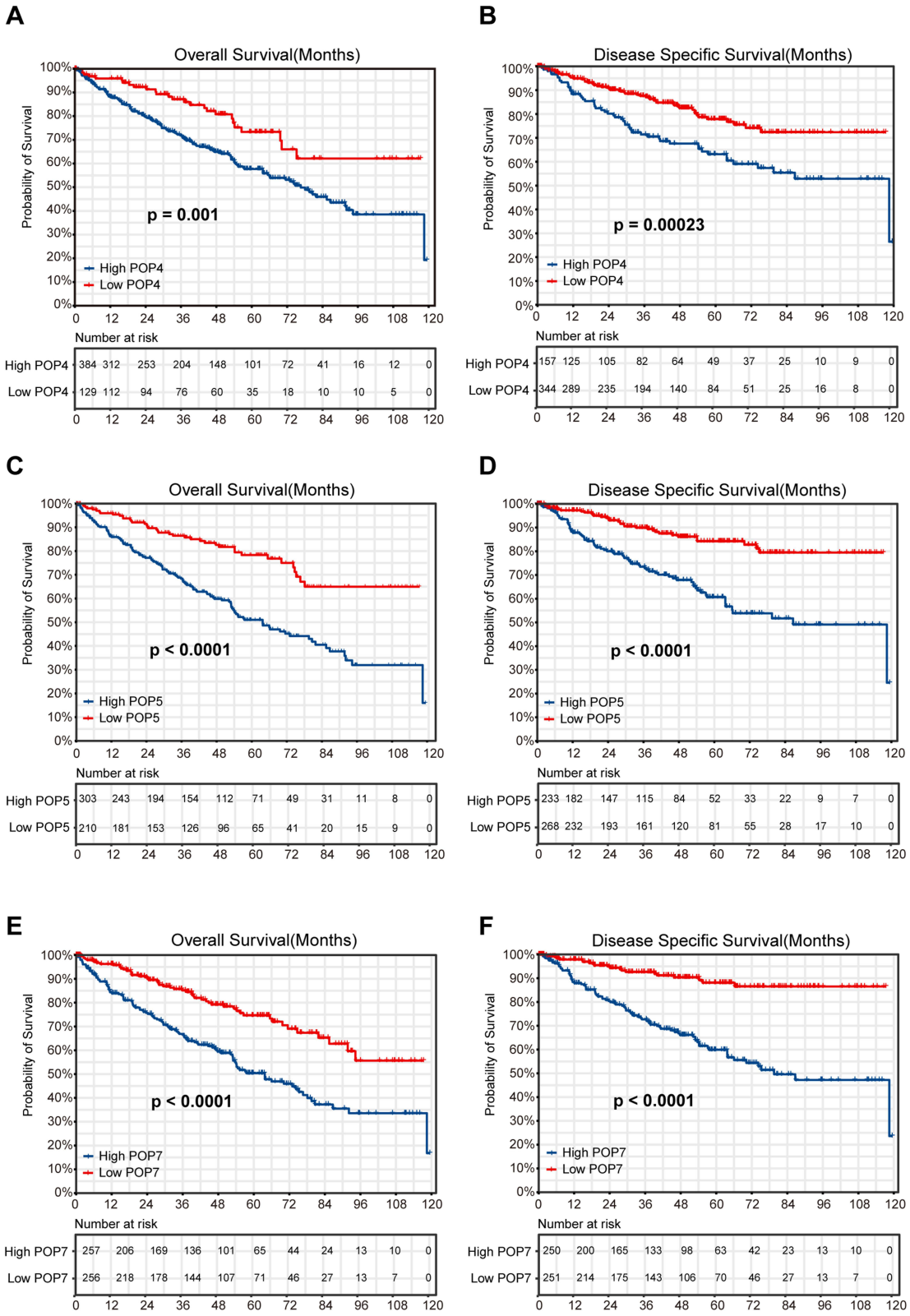

Figure 2 Prognostic significance of POP family in ccRCC. (**A**) and (**B**) Higher POP 4 had shorter OS and DFS than the lower expressers. (**C**) and (**D**) Higher POP 5 had shorter OS and DFS than the lower expressers. (**E**) and (**F**) Higher POP 7 had shorter OS and DFS than the lower expressers.
Abbreviations: OS, overall survival; DFS, disease-free survival.

Table 1 Univariable and Multivariable Analyses of POP Family mRNA Level and Patient Overall Survival

Variables	Univariate analysis			Multivariate analysis		
	HR[a]	95% CI[b]	P value	HR[a]	95% CI[b]	P value
Overall survival						
Age (years)	1.80	1.32–2.47	0.000	1.60	1.17–2.20	0.003
≤60 vs >60						
Sex	0.95	0.70–1.29	0.825			
Female vs Male						
T stage	3.12	2.31–4.22	0.000	1.54	1.07–2.21	0.02
T3 or T4 vs T1 or T2						
N stage	3.83	2.07–7.06	0.000			
N1 vs N0 or NX						
M stage	4.35	3.19–5.92	0.000	2.89	2.01–4.16	0.000
M1 vs M0 or MX						
Grade	2.64	1.89–3.70	0.000			
G3 or G4 vs G1 or G2						
POP1	1.09	0.81–1.47	0.579			
High vs Low						
POP 4	1.42	1.05–1.92	0.025			
High vs Low						
POP 5	2.18	1.59–2.99	0.000	1.80	1.22–2.67	0.003
High vs Low						
POP 7	2.32	1.68–3.12	0.000	1.64	1.11–2.41	0.013
High vs Low						

Notes: [a]Hazard ratio, estimated from Cox proportional hazard regression model. [b]Confidence interval of the estimated HR.

Table 2 Univariable and Multivariable Analyses of POP Family mRNA Level and Patient Disease–Free Survival

Variables	Univariate analysis			Multivariate analysis		
	HR[a]	95% CI[b]	P value	HR[a]	95% CI[b]	P value
Overall survival						
Age (years)	1.37	0.96–1.95	0.084			
≤60 vs >60						
Sex	1.41	0.95–2.10	0.087			
Female vs Male						
T stage	4.53	3.13–6.54	0.000	1.99	1.29–3.05	0.002
T3 or T4 vs T1 or T2						
N stage	5.94	2.98–11.84	0.000	2.60	1.23–5.48	0.012
N1 vs N0 or NX						
M stage	8.53	5.88–12.38	0.000	4.87	3.14–7.37	0.000
M1 vs M0 or MX						
Grade	3.38	2.24–5.10	0.000	2.42	1.58–3.73	0.000
G3 or G4 vs G1 or G2						
POP1	1.05	0.74–1.50	0.770			
High vs Low						
POP 4	1.52	1.06–2.17	0.023			
High vs Low						

(*Continued*)

Table 2 (Continued).

Variables	Univariate analysis			Multivariate analysis		
	HR[a]	95% CI[b]	P value	HR[a]	95% CI[b]	P value
POP 5 High vs Low	1.85	1.29–2.66	0.001			
POP 7 High vs Low	2.55	1.75–3.73	0.000	1.67	1.07–2.61	0.025

Notes: [a]Hazard ratio, estimated from Cox proportional hazard regression model. [b]Confidence interval of the estimated HR.

Verification of POP7 in ccRCC Patients

GEO data and quantitative real-time polymerase chain reaction (qRT-PCR) were used to verify POP7 expression in ccRCC patients. The results exhibited that the mRNA expression of POP7 was lower in normal tissue from GSE16441 in Figure 4A. qRT-PCR indicated mRNA expression of POP7 was lower in normal samples from ccRCC patients in Figure 4B. The mRNA expression of paired and total POP7 from CPTAC database exhibited higher in cancer samples in Figure 4C and D. Similarly, we have found that the protein expression of paired and total POP7 from CPTAC database exhibited higher in cancer samples in Figure 4E and F.

Diagnostic Capability of POP7 in ccRCC

The diagnostic capability of POP7 with ROC curve as AUC was analyzed as the mRNA, and protein level was high in ccRCC cancer tissues. The results showed AUC was 0.8260 (95% CI: 0.7869–0.8650; $p < 0.001$) in total ccRCC patients with RNA expression (Figure 5A). And 0.8807 (95% CI: 0.8245–0.926; $p < 0.001$) in 72 paired patients with RNA expression (Figure 5B). Similar results were represented in GSE16441 (Figure 5C) and clinical samples (Figure 5D) with RNA expression. POP7 had a diagnostic capability in total (AUC = 0.9376, 95% CI: 0.9544–0.9927; $p < 0.001$, Figure 5E) and paired (AUC = 0.9680, 95% CI: 0.9425–0.9935; $p < 0.001$, Figure 5F) ccRCC patients from CPTAC database with mRNA expression. Similar results showed that POP7 had a diagnostic capability in total (AUC: 0.8594, 95% CI: 0.8092–0.9095; $p < 0.001$, Figure 5E) and paired (AUC = 0.8554, 95% CI: 0.8008–0.9101; $p < 0.001$, Figure 5F) ccRCC patients from CPTAC database in protein level.

Functional Prediction of POP7 in ccRCC

POP7 function in ccRCC was analyzed by GSEA and TiMER2. GSEA identified POP7 had a positive correlation with the downregulation of CD4+cells, CD8+cells, and natural killer (NK) cells (Figure 6A–C) but upregulation of helper T (TH1) cells (Figure 6D). In contrast, POP7 had a negative correlation with the upregulation of CD4+cells, CD8+cells, and natural killer (NK) cells (Figure 6E-H). TiMER2 results showed POP7 had a positive correlation with T cell regulatory (Tregs) and myeloid-derived suppressor cells (MDSC) in ccRCC (Figure 7A–C). On the contrary, POP7 had a negative correlation with CD4+cells, CD8+cells, and natural killer (NK) cells (Figure 7D–I). The result displayed POP7 was an immunosuppressor for ccRCC.

Discussion

Previous research reported that the role of RBP had essential roles in progression and neoplasm metastasis. In clinical samples, elevated expression of an RBP, Pumilio 1 (PUM1) was associated with metastasis, recurrence, and poor survival of gastric cancer (GC). PUM1 could bind directly to DEP domain-containing mammalian target of rapamycin-interacting protein mRNA, then induce metabolic reprogramming and activate the PI3K-Akt signal in glycolysis. PUM1 deficiency could suppress glycolytic metabolism in GC.[22] Circular RNAs TET2 interacted with heterogeneous nuclear ribonucleoprotein C (an RBP), which could regulate the lipid metabolism of chronic lymphocytic leukemia cell.[23] Musashi-2 (MSI2, an RBP) deficiency suppressed the growth and survival and promoted ferroptosis by inactivating the MAPK signaling pathway in colorectal cancer.[24] Our previous study showed that downregulation of an RBP (RNA binding

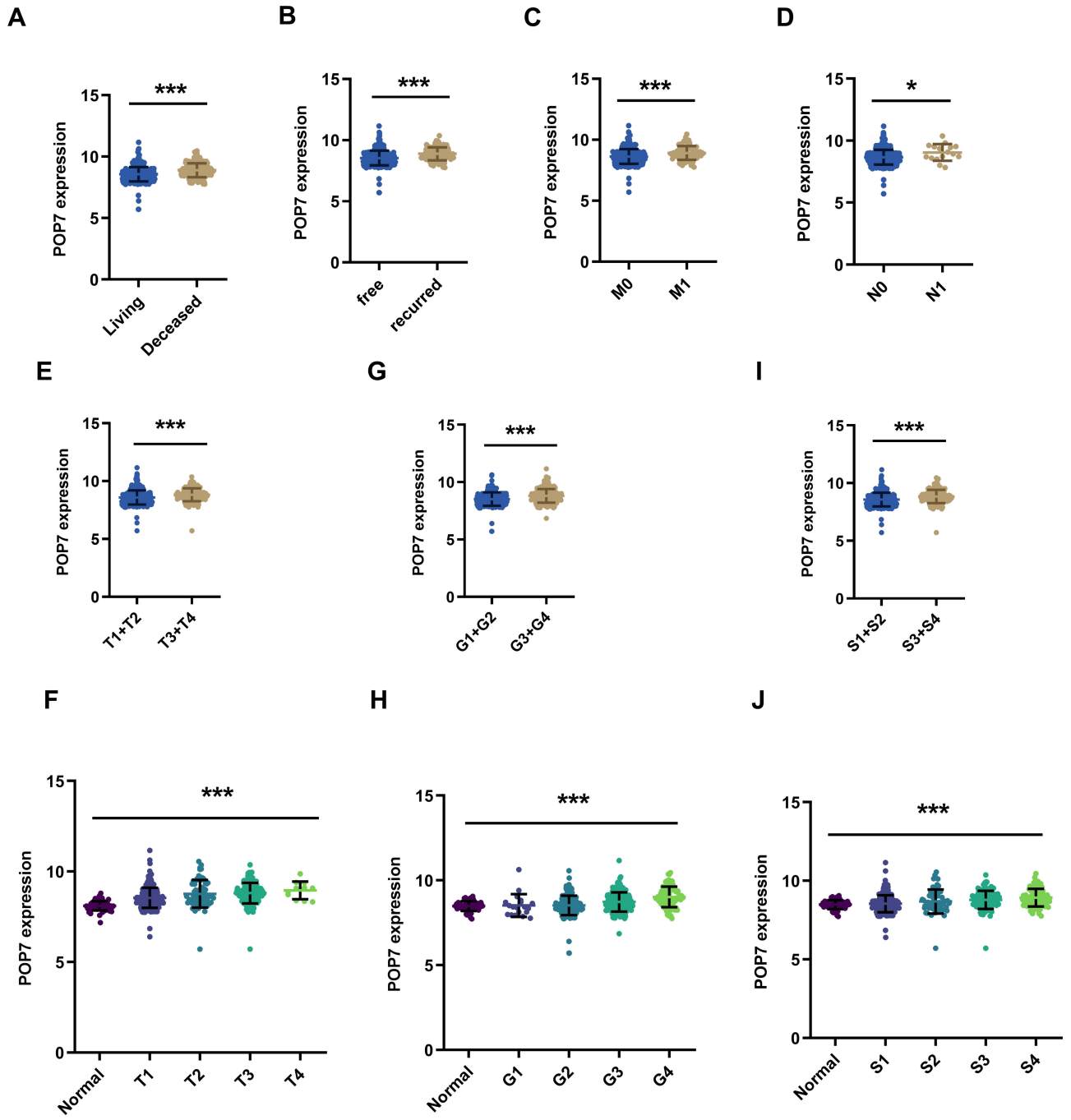

Figure 3 The relationship between clinical characteristics and POP7 in KIRC. (**A**) Survival status. (**B**) disease free status. (**C**) M stage. (**D**) N stage. (**E**) and (**F**) T stage. (**G**) and (**H**) grade. (**I**) and (**J**)TNM stage. *P <0.05, and ***P <0.001.

protein 47) predicted low survival and could modificate RNA stability in ccRCC.[25] Here, we reported the expression of an RBP family (POP family) and POP7 had a prognostic effect in ccRCC for the first time.

The role of POP family in various tumors was reported in the previous research. POP1 was up-regulated in breast cancer (BC). POP1 was one of the high-risk gene in GC.[26] High expression of POP1 had a poor prognosis and more likely to be responded to immunotherapy.[27] POP1 was upregulated in breast cancer (BC) tissues and cancer cell lines. High POP1 expression had poor outcomes, and POP1 overexpression promoted cell progression in BC cells.[28] POP7 mRNA levels are higher in esophageal cancer (ES) tumor tissues when compared with normal tissues. Lower expression

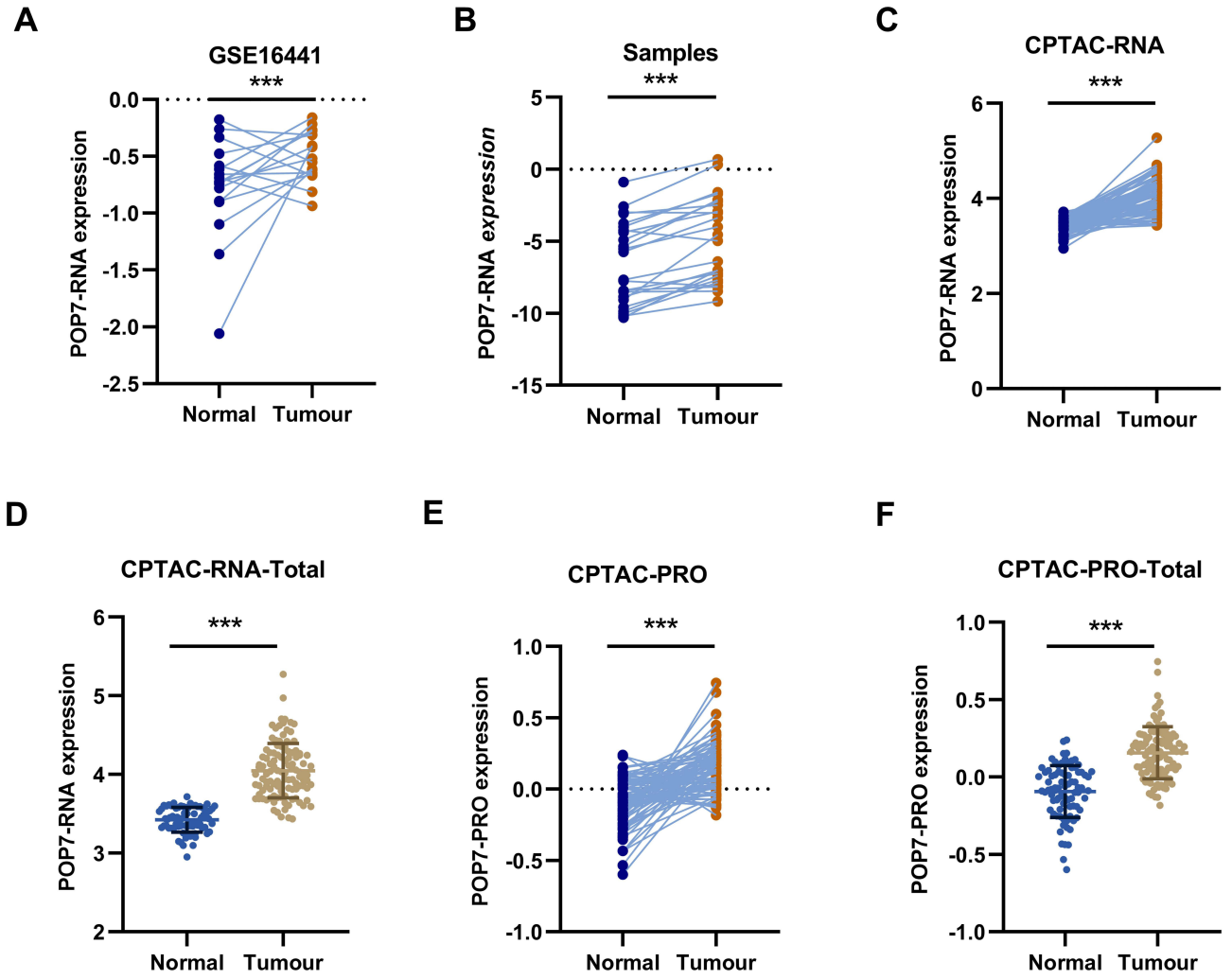

Figure 4 Verification of POP7 in ccRCC patients. (**A**) POP7 mRNA was higher in ccRCC cancer tissue from GSE16441. (**B**) POP7 mRNA was higher in ccRCC cancer samples. (**C** and **D**) The mRNA expression of paired and total POP7 exhibited higher in cancer samples from CPTAC database. (**E**) and (**F**) The protein expression of paired and total POP7 exhibited higher in cancer samples from CPTAC database. ***P <0.001.

of POP7 predicted a poor prognosis in ES.[29] POP5 was upregulated in the uterine corpus endometrial carcinoma cancer tumor tissue compared with normal tissues.[30]

In this research, we found that the expression of POP1, POP4, POP7 was significantly escalated, whereas POP5 was downregulated in ccRCC. POP7 was significantly increased in most cancer types such as BLCA, BRCA, COAD, CHOL, ESCA, HNSC, LIHC, LUAD, LUSC, THCA, PRAD, STAD, and UCEC, especially in all KICH, KIRC, and KIRP. POP7 expression was positively correlated with poor disease progression by multiple Cox proportional hazard regression methods. Patients with high POP7 expression had a poor OS and DFS, high T stage, lymphatic metastasis and distant metastasis, high grade and TNM stages. POP7 mRNA and protein had a significant role in the diagnosis of ccRCC from TCGA-KIRC, GSE16441, clinical samples, and CPTAC database.

The use of immune checkpoint inhibitors (ICIs) in cancer immunotherapy had completely changed the field of cancer treatment.[31,32] ICI had improved the progress for patient care in RCC or urothelial carcinoma.[33,34] CD72 was associated with Pathologic T stage, stage, M stage, N stage and tumour immunity.[35] Our previous research showed LY96 was associated with immunosuppression in ccRCC.[20] Nivolumab plus ipilimumab was the first-line regimen for poor-risk, intermediate-risk or metastatic RCC, and nivolumab monotherapy was used as second-line therapy.[36] A review suggested that ICI-based combination therapy was the standard of care as the first-line treatment of patients with metastatic RCC even after nephrectomy, and it was critical for treatment decisions.[37] The immunotherapeutic predictive role was

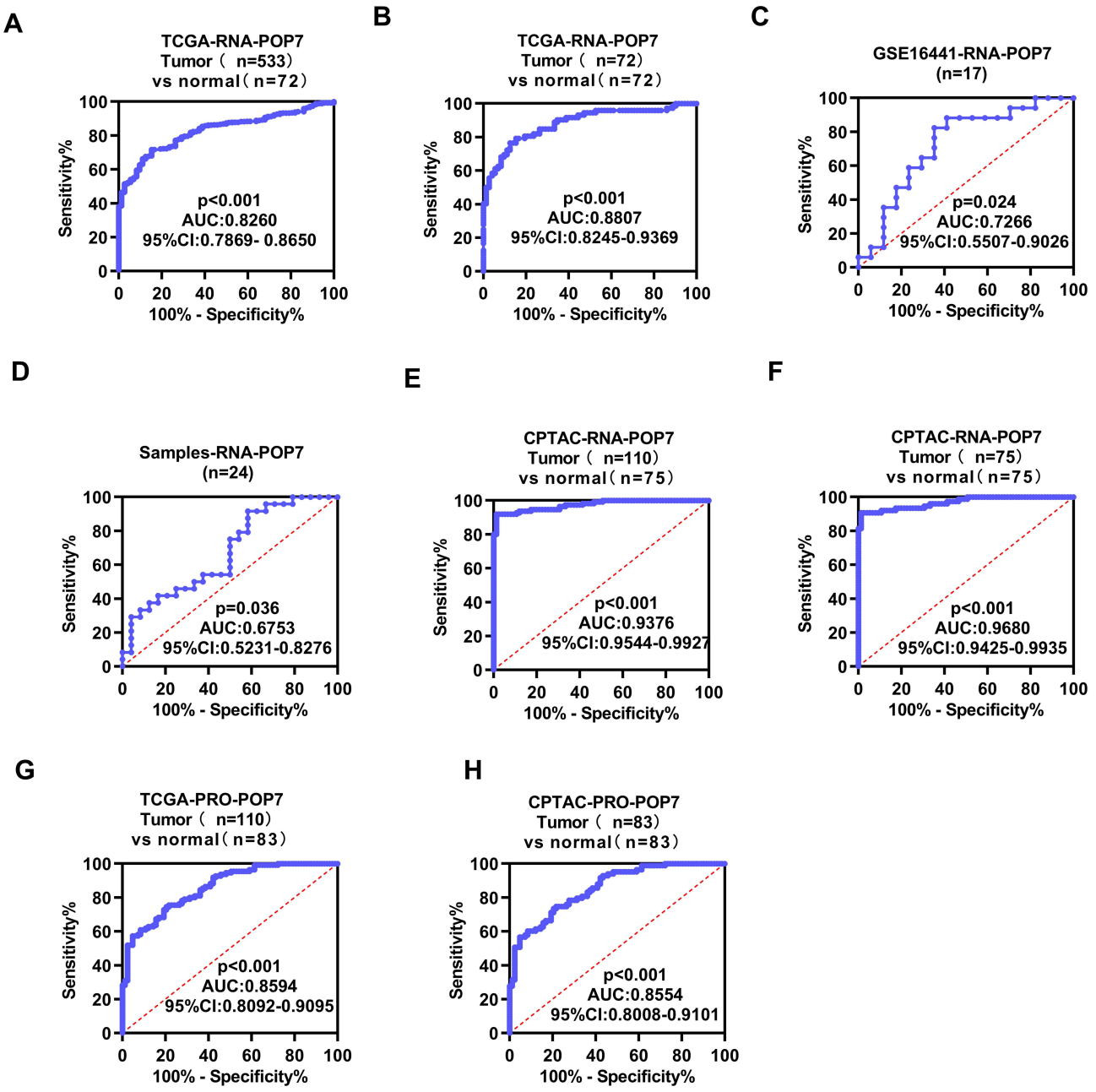

Figure 5 The diagnostic value of POP7 in ccRCC. (**A**) and (**B**) ROC curve of POP7 mRNA between total and paired tumor and non-cancerous normal tissues in TCGA-KIRC, the AUC: 0.8260 and 0.8807 ($p < 0.001$); (**C**) The AUC of POP7 mRNA between tumor and paired non-cancerous normal tissues in GSE16441 was 0.7226 ($p=0.024$). (**D**) The AUC of POP7 mRNA between tumor and paired non-cancerous normal tissues in clinical samples was 0.6753 ($p = 0.036$). (**E**) and (**F**) ROC curve of POP7 mRNA between total and paired tumor and non-cancerous normal tissues in CPTAC, the AUC: 0.9376 and 0.9680 ($p < 0.001$). (**G**) and (**H**) ROC curve of POP7 protein between total and paired tumor and non-cancerous normal tissues in CPTAC, the AUC: 0.8594 and 0.8554 ($p < 0.001$).

validated in an in-house cohort.[38] Patients who did not respond to treatment (primary resistance) or gradually developing into resistance to therapy (acquired resistance) posed a significant obstacle to drug treatment.[39] Chemicals, toxins, and radiation were the general risk factors for cancer.[40] The demand for developing new predictive and prognostic biomarkers can help mRCC patients develop personalized treatment. Then, GSEA and TiMER2 results identified POP7 had a positive correlation with TH1, Tregs cells, and MDSC, but had a negative correlation with CD4 + cells, CD8 + cells, NK cells.

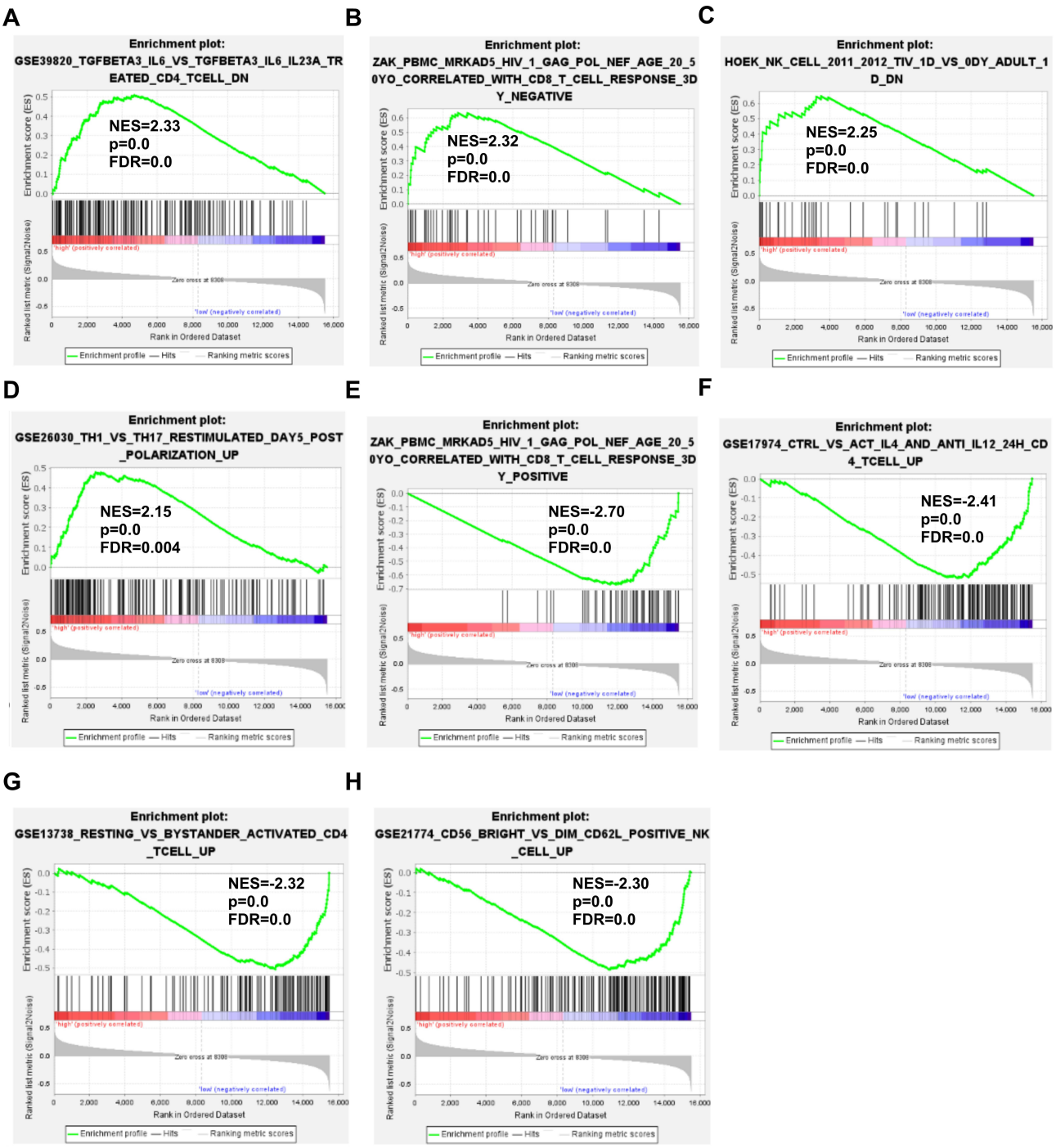

Figure 6 Pathway of POP7 in TCGA-KIRC with Gene Set Enrichment Analysis (GSEA). POP7 had a positive correlation with downregulation of CD4+cells (**A**), CD8+cells (**B**), natural killer (NK) cells (**C**). Upregulation role of POP7 in helper T (TH1) cells (**D**). POP7 had a negative correlation with upregulation of CD4+cells (**E**), CD8+cells (**F** and **G**), natural killer (NK) cells (**H**).

Although we have achieved some research results, the functionality of POP7 has not been proven through in vitro and in vivo experiments, and the role of POP7 in tumor immunity had not been verified in vitro and in vivo experiments. We will take more research to explore the relationship between tumors and immunotherapy in the future.

Conclusion

This paper investigated the gene expression of POP family in pan-cancer, and the role of POP7 in TCGA-KIRC, POP7 was significantly correlated with cancer progression, and was an independent predictor for ccRCC. We then verified the

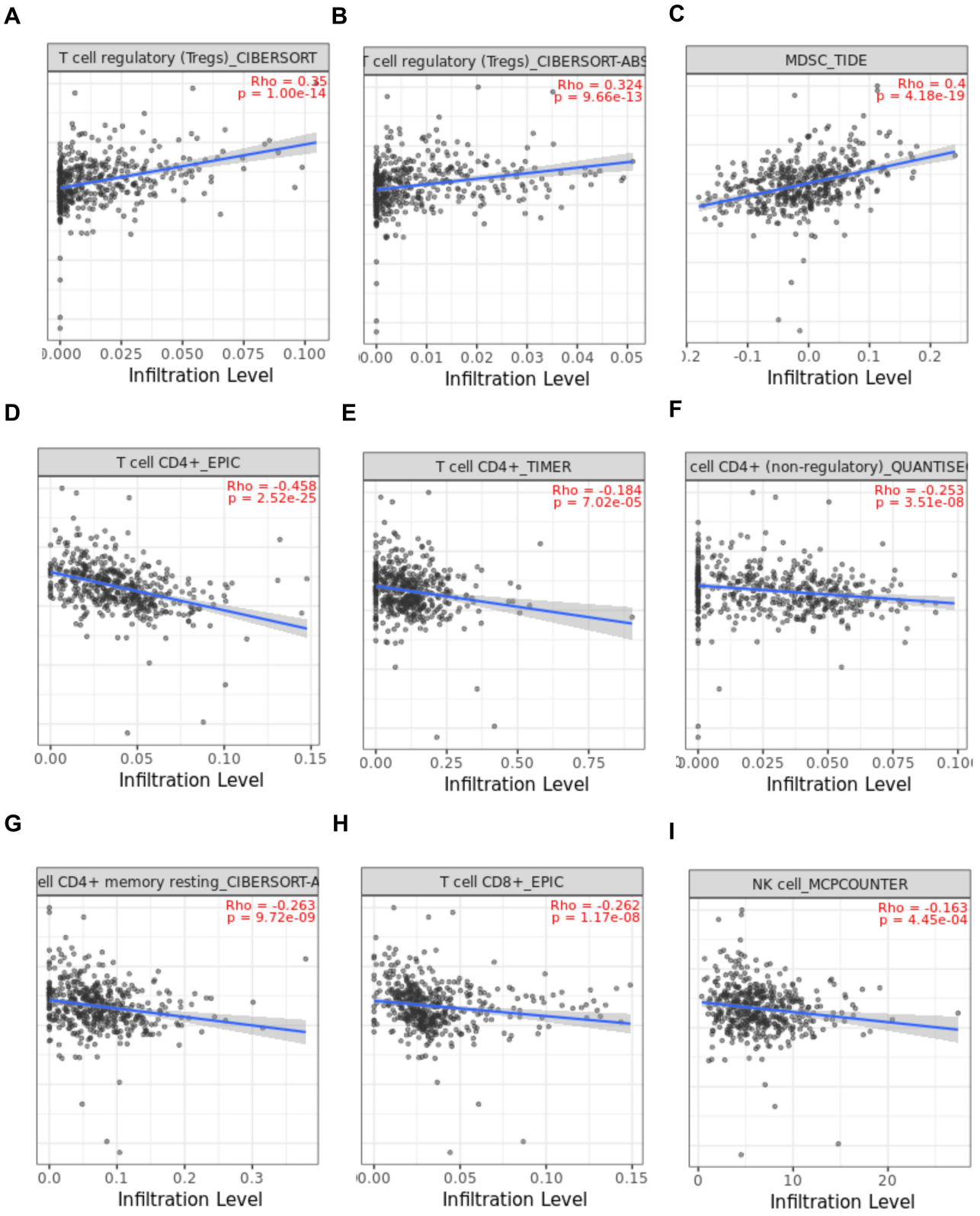

Figure 7 TiMER2 results of POP7 and immune infiltration in ccRCC. POP7 had a positive correlation with Tregs (**A** and **B**), and MDSC (**C**) in ccRCC. POP7 had a negative correlation with CD4+cells (**D**–**G**), CD8+cells(**H**), natural killer (NK) cells (**I**) in ccRCC.

expression and diagnosability of POP7 in clinical samples, GEO database, and CPTAC of ccRCC. The mRNA and protein of POP7 had a significant diagnosability role in ccRCC from TCGA-KIRC, GSE16441, clinical samples, and CPTAC database. GSEA and TiMER2 showed the biological role and immune infiltration of POP7 in ccRCC. This study demonstrated that POP7 was a significant marker and immunosuppressor in ccRCC.

Acknowledgments

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Disclosure

The authors report no conflicts of interest in this work.

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