The Oncogenic Role of AXIN1 In Human Tumors: A Pan-Cancer Analysis of AXIN1.

Jinzhou Wang
Beijing Chao-Yang Hospital
Xiangjun Shi
Beijing Chao-Yang Hospital
Xingchen Yao
Beijing Chao-Yang Hospital
Ziyu Xu
Beijing Chao-Yang Hospital
Xinru Du (duxinru@163.com)
Beijing Chao-Yang Hospital

Research Article

Keywords: AXIN1, cancer genomics, phosphorylation, oncogene

Posted Date: September 21st, 2021

DOI: https://doi.org/10.21203/rs.3.rs-745142/v1

Abstract

Background: Although emerging cell- or animal-based evidence supports the correlation between AXIN1(Axis inhibition protein 1) and cancers，no pan-cancer analysis is accessible.

Method: We thus investigate the possible oncogenic characters of AXIN1 by 33 tumor types based on the datasets of TCGA (The cancer genome atlas) and GEO (Gene expression omnibus).

Result: AXIN1 has a high expression in lots of tumors, and obvious relevance between AXIN1 expression and prognosis of cancer patients, such as LICH (Liver hepatocellular carcinoma) and breast cancer. We observed an increase phosphorylation level of S486/S493 in breast cancer and UCEC (Uterine Corpus Endometrial Carcinoma). AXIN1 expression shows a correlation with T cell regulatory in several cancers such as LIHC and LUAD (Lung adenocarcinoma). Furthermore, enrichment exist between Wnt signaling pathway, Hippo signaling pathway and pathways in cancer and the functional mechanisms of AXIN1.

Conclusions: Our first pan-cancer study provides a relatively complete interpretation of oncogenic characters of AXIN1 though different tumors.

Introduction

It is vital to carry out a pan-cancer expression investigation for on genes which have interest and estimate the association with clinical prognosis as well as underlying molecular mechanisms in consideration of the intricacy of tumor. The TCGA task which is sponsored by the public and the accessible data bank consist of genomics data sets of diverse cancers (1-3)，which makes it possible for us to carry out a pan-cancer.

At first，AXIN1 was regarded as retardant of signaling channel of Wnt that interplay with GSK-3beta and beta-catenin as well as reconciling the sign sent by GSK-3beta，thus negatively accommodating the Wnt signaling channel (4) (5).

What's more, it also functions as a main support of numerous signaling channel including JNK (6).At present, diverse species have gained lucid structural and functional awareness in the area of physiology and pathology(7).

The experiments carried out on mice have shown that there are diverse functions between the two kinds Axin proteins though they both accommodate the WNT signaling.Axin1 lies ubiquitously in fetuses and acts as a key factor for survivability, while Axin2 only existed in a very small minority of tissues and acts as the transcriptional target spot of WNT sign(8, 9).

Though we conclude abundant cell- or animal experiment which is based on the evidence of joint between AXIN1 and different tumor kinds. However, it is short of pan-cancer investigation about the connection between AXIN1and various kinds of cancer on basis of abundant clinical data.

Our research, for the first time, utilized the TCGA together with GEO databases for the intention of analyzing the pan-cancer of AXIN1. Furthermore, we also take a series of features into consideration such as genetic adaptation, immune infiltration, pertinent cellular channel and so on in order to analyze the underlying molecular mechanism of SND1 of diverse cancers.

Materials And Methods

Gene expression analysis

In order to look into AXIN1's expressive discrepancy between virulent compositions and consecutive regular compositions in aspect of diverse carcinomas or particular neoplasm hypotypes of TCGA scheme, we adopt the means by entering AXIN1 into "Gene-DE" component of TIMER2.0 (neoplasm immunity assessment source, version 2.0) web(http://timer.cistrome.org/).

We made use of "Expression examination-Box graphs component contained in GEPIA2 server (http://gepia2.cancer-pku.cn/#analysis) (10) so as to obtain box graphs as well as expressive discrepancy between virulent compositions and regular compositions contained in GTEx datum bank, which is under the background of GTEx (Genotype-Tissue Expression) datum in order to deal with the unusual neoplasms without regular or exceedingly restricted compositions such as TCGA-LGG (Brain Lower Grade Glioma) and so on.

In addition, through the "Pathological Stage graph" included in GEPIA2, we succeeded in gaining violin graphs which are contained in AXIN1 manifestation covering all pathological phrase of all TCGA neoplasms. The datum was converted by the violin and box graphs on the foundation of log2[TPM(Transcripts per million)+1].

We succeeded in gaining protein expression examination contained in CPTAC(Clinical proteomic tumor analysis consortium) (https://proteomics.cancer.gov/programs/cptac) by the means of UALCAN (http://ualcan.path.uab.edu/analysis-prot.html), which is a collaborative web source aiming at investigating carcinoma Omics datum. Correspondingly, we input "AXIN1" for the intention of examining expression stage contained in all protein or phosphoprotein contained in AXIN1 (NP_003493.1) between idiopathic neoplasm and regular compositions separately. In order to achieve the goal we utilized economical datum bank contained in three neoplasms, which are Breast invasive carcinoma Colon adenocarcinoma and Uterine Corpus Endometrial Carcinoma.

Survival prognosis examination

By the means of "Survival Map" component contained in GEPIA2 (10), we succeeded in obtaining Overall survival as well as Disease-free survival distinctiveness chart datum contained in AXIN1 which cover all the TCGA neoplasms. By the means of calculating liminality, cutoff high (50) and low (50) values we divided all the datum into high-expression as well as low-expression types.

Genetic alteration examination

In order to gain hereditary adjustment features contained in AXIN1 by the means of inputting “AXIN1” into “TCGA Pan carcinoma Atlas Studies”, we made use of cBio method web (https://www.cbioportal.org/) (11, 12). All the outcome are carried out in “carcinoma Types Summary”. The capricious location information is shown by the “Mutations” component including 3D arrangement as well as other news. What’s more, we gain the datum via “Comparison” component such as existence discrepancy without disease or progression under the circumstances of TCGA carcinoma as well as other information.

Immune infiltration examination

It is “immunity-Gene” component contained in the TIMER2.0 that provides the link between AXIN1 expression and immunity penetration. As a result, we finally selected immunity cells of T cell accommodation. When conducting the Spearman’s level association examination, we gained the scatter graph of P-values as well as partial association value after the pureness degree are reset.

AXIN1-realated gene enrichment analysis

We utilized the designation(“AXIN1”) as well as creature (“Homo sapiens”) of protein to finish the inquiry through STRING website (https://string-db.org/) after which the crucial data is determined on the foundation of Network kind which is “full network” the largest number of interactants which is “less than 50 interactants” as well as the lowest interface mark which is “0.150”.As a result, the proteins which is combined with AXIN1are exported in the form of figure.

Through TCGA neoplasm as well as regular compositions, we succeeded in gaining the first 100 target genes which are related to AXIN1 by the means of utilizing “Similar Gene Detection”. The “association examination” component of GEPIA2 succeeded in conducting the pairwise Pearson association examination of AXIN. The dot graph is finished on the foundation of log2 TPM and the P-value as well as the association factor were finally obtained. In addition, we finally gained the heatmap datum the partial association as well as the P-value in Spearman’s level association examination after the pureness degree are reset.

During the process of KEGG examination, we made full use of two kinds of datasets which are Kyoto encyclopedia of genes and genomes. At the same time, we utilized DAVID as the analysis tool. We also made full use of “tidyr” as well as “gggraph2” R packages during the analysis process. The R language software also played an important role in the investigation process. The statistical distinctiveness was finally confirmed through the two-tailed P-value examination.

Results

The expression of AXIN1 in lots of tumors is higher than normal tissues.

We used the TIMER2.0 to perform the level of expression of in various of benign and malignant tissues. As shown in Fig.1A the level of expression of AXIN1 in BLCA, BRCA, CESC, CHOL, COAD, ESCA, GBM,

HNSC, KICH, KIRC, KIRP, LIHC, LUAD, LUSC, PRAD, READ, THCA, UCEC (Table.S1) is higher than normal tissues.

We regarded the GTEx dataset as control and figured out that the statistical significance of expression difference exists between normal tissues and CHOL, THYM tumor tissues. Fig.1B ($P<0.01$) But there was no difference presenting in DLBC, GBM, LGG, SKCM, TCGT. Simultaneously, the result of CTPAC data base presented a higher protein expression in LUAD ($p<0.05$).

Furthermore, we observed the correlation between the expression of AXIN1 and pathological stages of tumors including KICH, SKCM, COAD, ESCA, ACC, OV and LIHC via the “Pathological Stage Plot” module of GEPIA2. Fig.1 C

Survival analysis data has statistical difference between ESCA, LIHC, SKCM, UCEC, PRAD, ACC.

Firstly, the clinical cancer cases was divided into the high-expression group and low-expression group. Then, we explored the correlation between the expression of AXIN1 and the prognosis. The OS (Overall survival) of ESCA($p=0.0063$), LIHC($p=0.009$), SKCM($p=0.038$) were associated with the high-expression of AXIN1, as well as the DFS (Disease-free survival) of UCEC ($p=0.045$), PRAD ($p<0.001$), ACC($p=0.04$), ESCA($p=0.02$), LIHC($p<0.001$). Among the output results, the DFS of ESCA, UCEC and the OS of ESCA positively correlated with the expression of AXIN1, the others were inverse.

Additionally, we used the Kaplan-Meier plotter to analysis the survival data. The results revealed that the high expression of AXIN1 generates a poor OS (logrank P=3.3e-13), FP (logrank P=1e-08) and PPS (logrank P=6.4e-14) in gastric cancer. Moreover, we found that the OS and RFS of the AXIN1 high expression group in ESCA were significantly higher than the low expression group, as same as the OS of STAD and the RFS of breast cancer.

The R146Q/* mutation is the most frequent genetic alteration of the AXIN1 protein.

We investigated the genetic alteration data of various of tumors of the TCGA cohorts. Fig.3B The most obvious alteration frequency of AXIN1 is the liver hepatocellular carcinoma (>7%) and more than 3% genetic alteration of breast invasive carcinoma is the “Amplification” type. Furthermore, we found that the missense mutation is the largest portion of the genetic alteration of “AXIN1”, especially R146Q/* mutation which is in the RGS domain involved with 3 cases of missense mutation in UCEC, and 1 case of missense mutation in GBM and another one of nonsense in GBM. Fig.3C The 3D structure is presented in the Fig.3A. Besides, we discovered the UCEC with AXIN1 alteration demonstrated better prognosis in overall survival ($p=0.0297$) compared with non-AXIN1 alteration UCEC casesFig3D.

The S486S493 locus protein as shown in Fig.4A demonstrates an increased phosphorylation in phosphorylation analysis.

We used the CPTAC data set to compare the distinction in AXIN1 phosphorylation levels between the benign tissues and malignant tissues. Fig.4B The S77 locus shows a higher level of phosphorylation in

colon cancer (p=4.8e-02) and an opposite result in breast cancer (p=3.9e-02), as well as the S486493 locus which shows an increased phosphorylation level in UCEC(p=1.1e-09) and breast cancer(p=7.2e-11).

Tumor-infiltrating immune cells play an important role in cancer infiltration, progression and metastasis. (10) (11) . Regulatory T cell plays a significant character in tumor's immunity and metastasis. (12, 13). We used the CIBERSORT, CIBERSORT-ABS, QUANTISEQ algorithms to analysis the relationship between the immune infiltration of regulatory T cell and the AXIN1 gene expression in tumors. Fig.5 A positive association was presented between the regulatory T cell immune infiltration value and AXIN1 expression in TCGA tumors of LIHC(p=8.0e-10), LUAD(p=1.26e-06), CARC(p=1.03e-03), STAD(p=1.79e-05), which are shown in Fig5A Fig5B. through one algorithm (CIBERSORT).

Enrichment analysis of AXIN1-related genes shows the potential pathways of AXIN1.

In order to explore the enrichment analysis of AXIN1 related genes, we first used the STRING website to find 50 experimentally verified proteins with the highest correlation with AXIN1, and made a protein interaction network diagram. Fig.6A After that, we used the GEPIA2 tool to screen out the 100 genes with the highest correlation with AXIN1, and made a scatter plot of the top 5 genes with the highest correlated value, RNPS1(R=0.68), RPUSD1(R=0.59), UBE21(R=0.58), TFAP4(R=0.57), TRAF7(R=0.55) . Then we used the TIMER tool to make a heat map of the correlation between AXIN1 and the above 5 genes. Fig.6B A positive correlation was shown in the corresponding heatmap between AXIN1 and the top 5 genes in various cancer types.Fig.6C

Moreover, in order to study the KEGG and GO enrichment analysis of AXIN1 related genes, we collected the above 50 proteins and 100 genes, and used the DAVID website and the ggplot2 package of the R program to perform KEGG enrichment analysis to create bubble charts. Fig.6D At the same time, use the cluster program package to perform GO enrichment analysis on the above-mentioned gene set. Fig.6E And the details of the top 5 most significant pathways was performed in the Fig.6F.

Discussion

A series of previous literatures have reported the relationship between AXIN1 and Wnt signaling pathway and tumors, such as gastrointestinal cancer, colorectal cancer and hepatocellular carcinoma. (14-16)The role of AXIN1 in the occurrence and development of various tumors, and whether AXIN1 has different effects on different tumors is still unknown. Through literature review, we have not found a pan-cancer analysis article related to AXIN1. Therefore, we performed gene expression analysis, survival analysis, gene enrichment analysis, and protein phosphorylation analysis on 33 tumor cells based on the TCGA, CPTAC, and GEO databases.

As mentioned in previous literatures, the overexpression of AXIN1 inhibited hepatocellular carcinoma. (17-19)In this study, we observed a significant increase in the expression of AXIN1 in hepatocellular carcinoma. However, we combined with the TCGA database to perform KM survival analysis and found

that the high expression of AXIN1 is associated with lower OS, DFS, RFS, and DSS. We believe that the expression of AXIN1 is correlated with lower OS, DFS, RFS, and DSS. The amount of expression may be an important factor in judging the prognosis of hepatocellular carcinoma, and its mechanism is currently unclear, which needs to be verified by more clinical studies in the later period. Moreover, we detected a down-regulation of the expression trend in stage IV hepatocellular carcinoma tumors. We analyzed that this may be due to the weakening of the anti-tumor effect of in advanced liver cancer. Not only that, there are reports suggesting that AXIN1 mutation can reduce the immune score of hepatocellular carcinoma. (10)In this study, it was found for the first time that AXIN1 is related to Treg cell infiltration in hepatocellular carcinoma. This may be the immunological basis of AXIN1's inhibitory effect on hepatocellular carcinoma, and provides a direction for future experimental verification.

In this study, the results of survival analysis by GEPIA2.0 and KMplotter showed that the OS and RFS of the AXIN1 high expression group in ESCA were significantly higher than the low expression group, and the mechanism is still unclear, which may be related to the accumulation of β-catenin. Interestingly, through the survival analysis data, we also found that the DFS of UCEC and the RFS of breast cancer were positively correlated with the expression of AXIN1. At the same time, we observed for the first time through CTPAC dataset that the phosphorylation levels of the S486 and S493 locus in AXIN1 in UCEC and breast cancer tumor cells were higher than normal tissues. This phenomenon has not been found in OV, Colon cancer, LUAD. Studies have shown that S486 and S493 are located in the β-catenin binding domain in the AXIN1 protein. Phosphorylated by GSK3B will increase the stability of the binding of AXIN1 and β-catenin, and promote the ubiquitination and degradation of β-catenin. Therefore, we believe that the phosphorylation levels of S486 and S493 in the AXIN1 protein may be related to the prognosis of UCEC and breast cancer. This may provide possible targets for improving the prognosis of UCEC and breast cancer patients. Further experiments are needed in the future. More samples to verify.

We summarized AXIN1-binding components and AXIN1 expression-related genes, and performed enrichment analysis, and mainly obtained "Wnt signaling pathway", "Hippo signaling pathway" and mRNA binding and helicase activity. It has been pointed out in the literature that the mutation or deletion of AXIN1 that induces the occurrence of malignant tumors may not be related to the activation of the Wnt pathway. (19)Based on the results of this study, we speculate that this may be related to the effect of AXIN1 on the activation of the Hippo pathway. The Hippo pathway is known to have a known effect in the occurrence and development of tumors. AXIN1 may have a positive effect on the Hippo pathway, which has not been proposed in the previous literature.

Conclusion

We performed a pan-cancer analysis of AXIN1 for the first time to study the expression of AXIN1 and the occurrence and development of different tumors, clinical prognosis, protein phosphorylation, immune cell infiltration, potential mechanism of action, and enrichment analysis. To better understand the role and potential clinical significance of AXIN1 in various tumors.

Declarations

Ethical approval and consent to participate

Ethical approval and consent to participate are not applicable to this article as no patient's information were involved during the current study.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and analysed during the current study are available in the TIMER2.0, GEPIA2, CPTAC, Cbioportal.

Competing interests

The authors declare that they have no competing interests.

Funding

This study was funded by the Beijing Municipal Natural Science Foundation (No. 7192071).

Authors' contributions

JZW drafted and revised the manuscript. JZW contributed to the data collection and drafting of the manuscript. XCY and XJS contributed to the data analysis and interpretation. XRD and ZYX contributed to the conception of the article and manuscript revision. All authors read and approved the final manuscript.

Acknowledgments

In the analytical methodology, this research was inspired by the brilliant work from Dr.Xiaoteng Cui's team of Department of Biochemistry and Molecular Biology, Tianjin Medical University. (20)

Author's information

Department of orthopaedics, Beijing Chao-Yang hospital, Capital Medical University, No.8 Gongren Tiyuguan Nanlu, Chaoyang district, Beijing ,China.

Jinzhou Wang, Ziyu Xu, Xingchen Yao, Xinru Du

Department of hematology, Beijing Chao-Yang hospital, Capital Medical University, No.8 Gongren Tiyuguan Nanlu, Chaoyang district, Beijing ,China.

Xiangjun Shi

References

1. Tomczak K, Czerwińska P, Wiznerowicz M. The Cancer Genome Atlas (TCGA): an immeasurable source of knowledge. Contemporary oncology (Poznan, Poland). 2015;19(1a):A68-77.

2. Clough E, Barrett T. The Gene Expression Omnibus Database. Methods in molecular biology (Clifton, NJ). 2016;1418:93-110.

3. Blum A, Wang P, Zenklusen JC. SnapShot: TCGA-Analyzed Tumors. Cell. 2018;173(2):530.

4. Zeng L, Fagotto F, Zhang T, Hsu W, Vasicek TJ, Perry WL, 3rd, et al. The mouse Fused locus encodes Axin, an inhibitor of the Wnt signaling pathway that regulates embryonic axis formation. Cell. 1997;90(1):181-92.

5. Ikeda S, Kishida S, Yamamoto H, Murai H, Koyama S, Kikuchi A. Axin, a negative regulator of the Wnt signaling pathway, forms a complex with GSK-3beta and beta-catenin and promotes GSK-3beta-dependent phosphorylation of beta-catenin. The EMBO journal. 1998;17(5):1371-84.

6. Luo W, Lin SC. Axin: a master scaffold for multiple signaling pathways. Neuro-Signals. 2004;13(3):99-113.

7. MacDonald BT, Tamai K, He X. Wnt/beta-catenin signaling: components, mechanisms, and diseases. Developmental cell. 2009;17(1):9-26.

8. Ishizaki Y, Ikeda S, Fujimori M, Shimizu Y, Kurihara T, Itamoto T, et al. Immunohistochemical analysis and mutational analyses of beta-catenin, Axin family and APC genes in hepatocellular carcinomas. International journal of oncology. 2004;24(5):1077-83.

9. Mallick A, Taylor SKB, Ranawade A, Gupta BP. Axin Family of Scaffolding Proteins in Development: Lessons from C. elegans. Journal of developmental biology. 2019;7(4).

10. Fridman WH, Galon J, Dieu-Nosjean MC, Cremer I, Fisson S, Damotte D, et al. Immune infiltration in human cancer: prognostic significance and disease control. Current topics in microbiology and immunology. 2011;344:1-24.

11. Steven A, Seliger B. The Role of Immune Escape and Immune Cell Infiltration in Breast Cancer. Breast care (Basel, Switzerland). 2018;13(1):16-21.

12. Gelber C, Eisenbach L, Feldman M, Goodenow RS. T-cell subset analysis of Lewis lung carcinoma tumor rejection: heterogeneity of effectors and evidence for negative regulatory lymphocytes correlating with metastasis. Cancer research. 1992;52(23):6507-15.

13. Speiser DE, Ho PC, Verdeil G. Regulatory circuits of T cell function in cancer. Nature reviews Immunology. 2016;16(10):599-611.

14. Zucman-Rossi J, Villanueva A, Nault JC, Llovet JM. Genetic Landscape and Biomarkers of Hepatocellular Carcinoma. Gastroenterology. 2015;149(5):1226-39.e4.

15. Zhan T, Ambrosi G, Wandmacher AM, Rauscher B, Betge J, Rindtorff N, et al. MEK inhibitors activate Wnt signalling and induce stem cell plasticity in colorectal cancer. Nature communications. 2019;10(1):2197.

16. Mazzoni SM, Fearon ER. AXIN1 and AXIN2 variants in gastrointestinal cancers. Cancer letters. 2014;355(1):1-8.

17. Zucman-Rossi J, Benhamouche S, Godard C, Boyault S, Grimber G, Balabaud C, et al. Differential effects of inactivated Axin1 and activated beta-catenin mutations in human hepatocellular carcinomas. Oncogene. 2007;26(5):774-80.

18. Satoh S, Daigo Y, Furukawa Y, Kato T, Miwa N, Nishiwaki T, et al. AXIN1 mutations in hepatocellular carcinomas, and growth suppression in cancer cells by virus-mediated transfer of AXIN1. Nature genetics. 2000;24(3):245-50.

19. Abitbol S, Dahmani R, Coulouarn C, Ragazzon B, Mlecnik B, Senni N, et al. AXIN deficiency in human and mouse hepatocytes induces hepatocellular carcinoma in the absence of β-catenin activation. Journal of hepatology. 2018;68(6):1203-13.

20. Cui X, Zhang X, Liu M, Zhao C, Zhang N, Ren Y, et al. A pan-cancer analysis of the oncogenic role of staphylococcal nuclease domain-containing protein 1 (SND1) in human tumors. Genomics. 2020;112(6):3958-67.

Figures

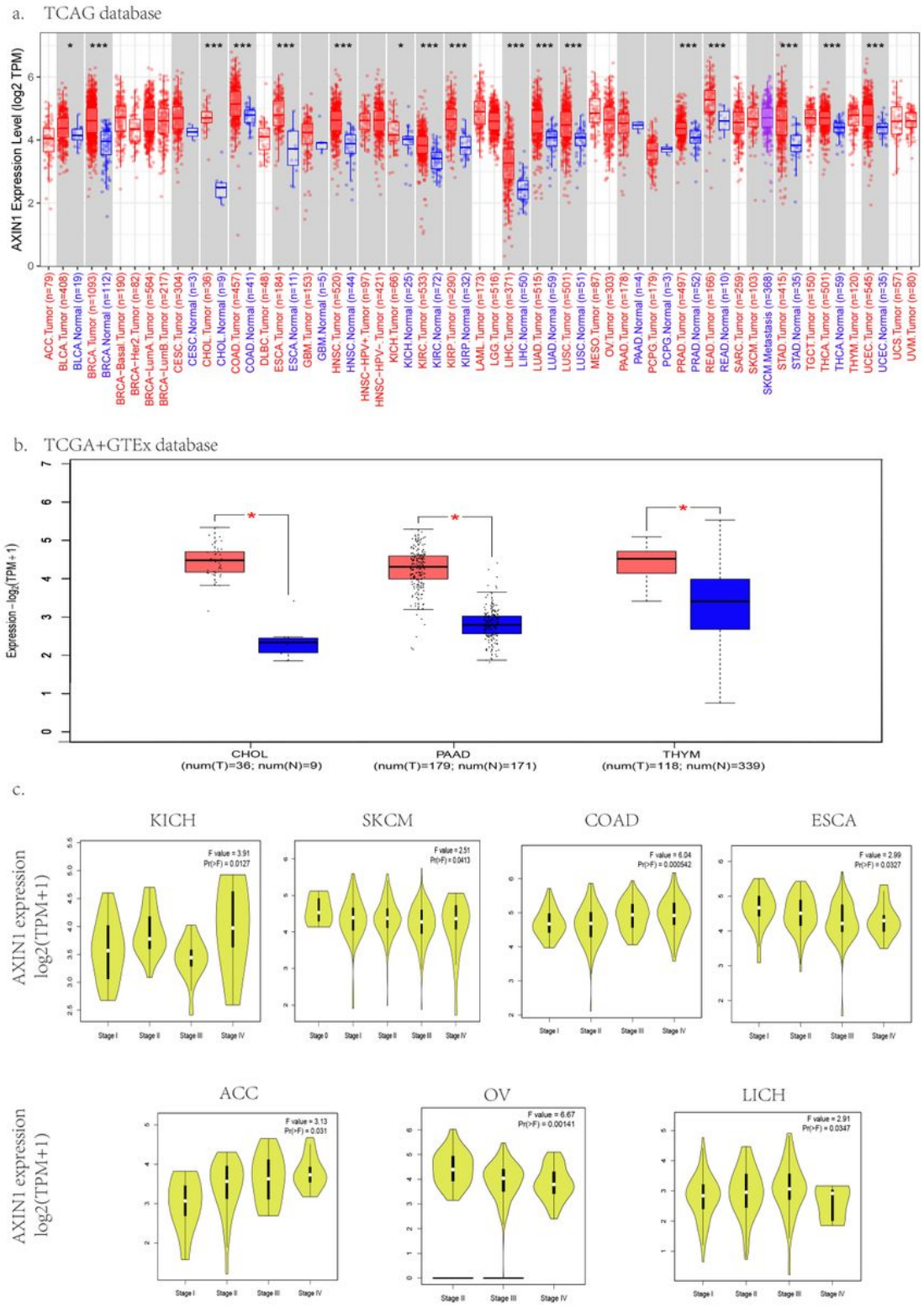

Figure 1

The expression level of AXIN1 in various of cancer types. (a) The expression data of the AXIN1 in different tumors or specific cancer subtypes through TIMER2.0. * P<.05; **P<.01; ***P<.001. (b) For the THYM in the TCGA project, the corresponding normal tissues of GTEx database were chosen as controls, as well as the CHOL and PAAD. (c) Based on the TCGA data, the expression status of AXIN1 was

analyzed by the pathological stages (I, II, III and IV) of KICH, SKCM, COAD, ESCA, ACC, OV, LICH with the log2(TPM+1) served as log-scale.

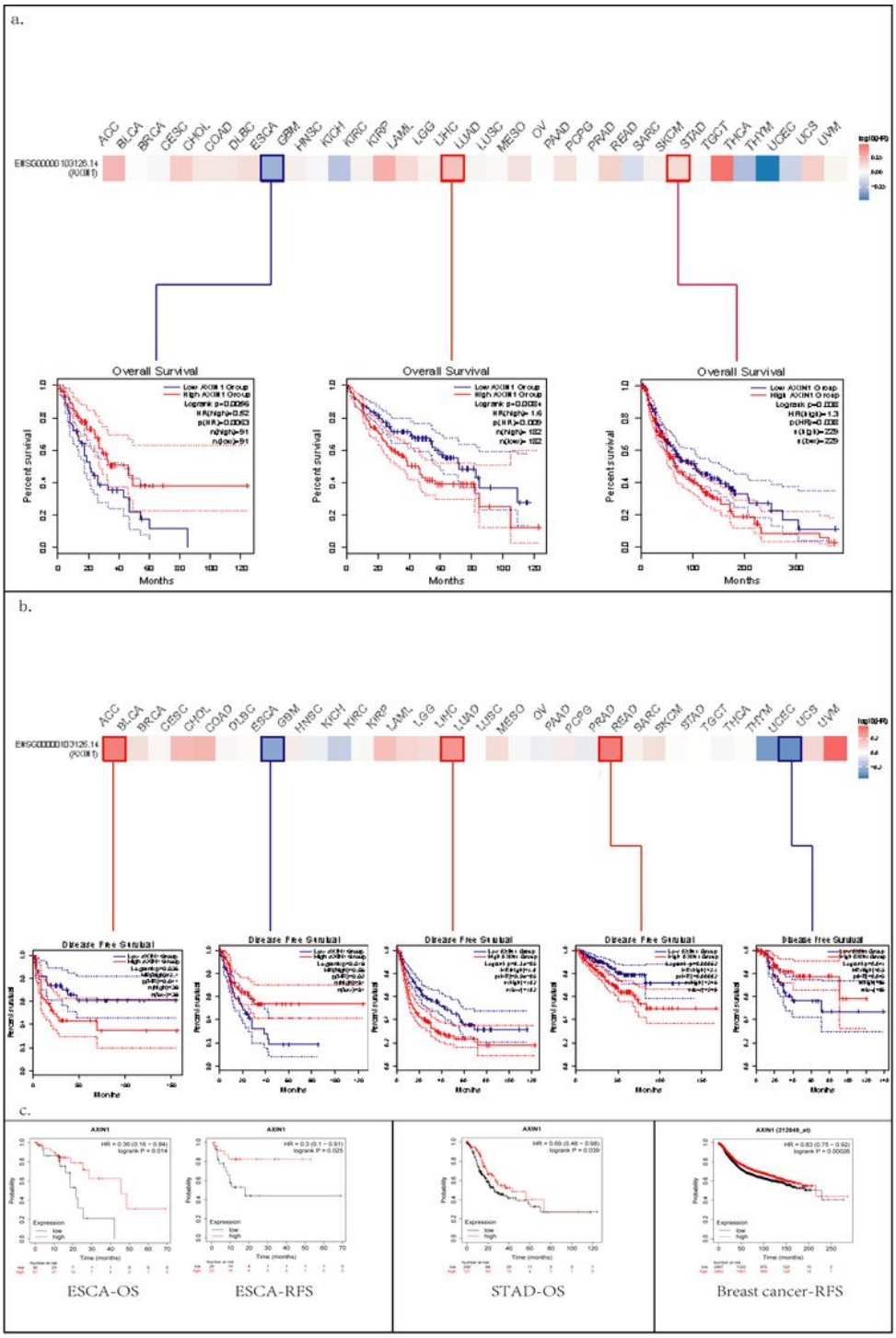

Figure 2

The relationship between AXIN1 gene expression and survival prognosis of cancers in TCGA. We used the GEPIA2 tool to conduct OS (a) and DFS (b). We also used the KMplotter tool to perform the OS, RFS of

ESCA, the OS of STAD and the RFS of breast cancer. The survival map and Kaplan-Meier curves are shown.

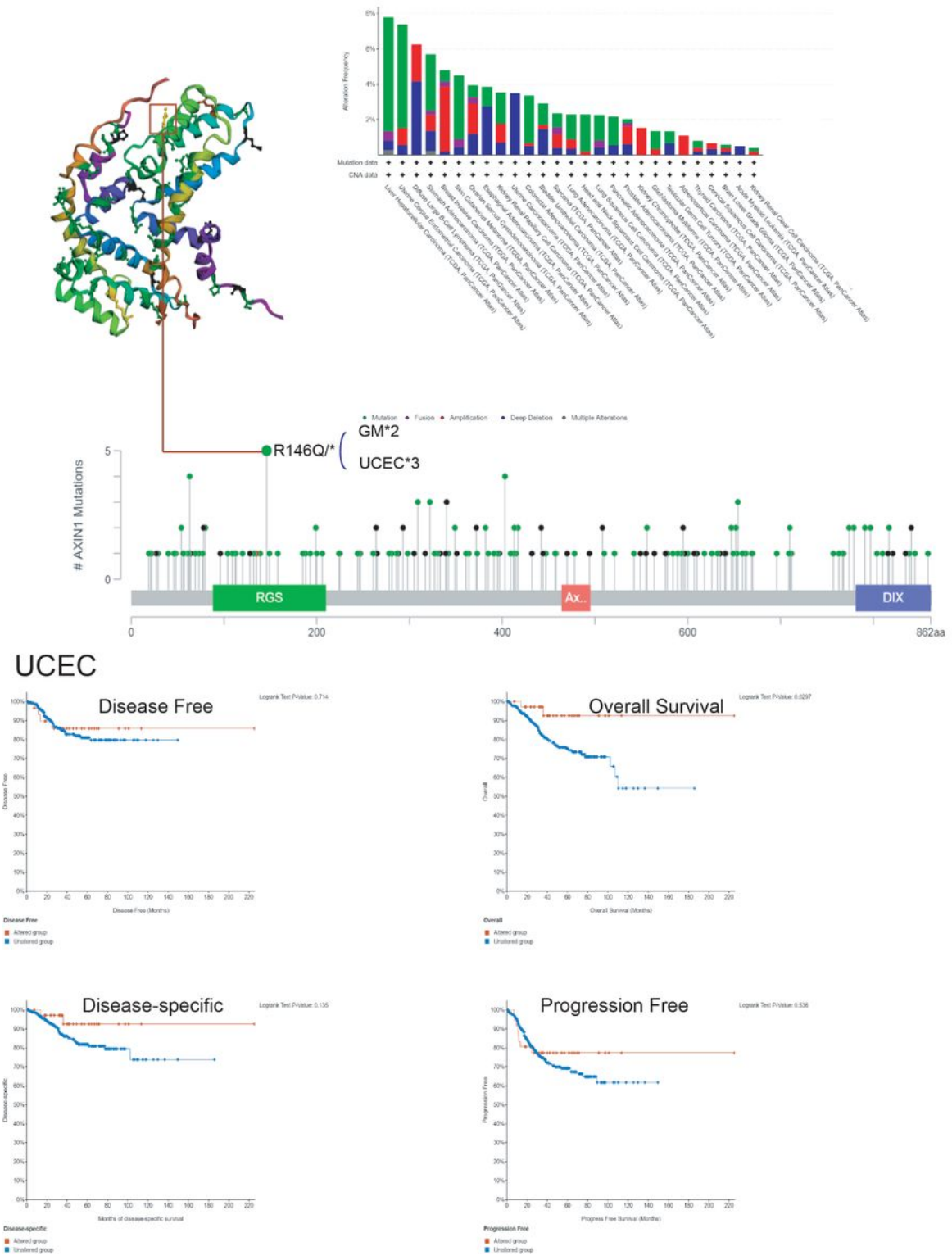

Figure 3

Mutation feature of AXIN1 in different cancer types of TCGA. We used the cBioPortal tool to analyze the mutation data of AXIN1 for the TCGA tumors. (a) We performed the 3D structure of AXIN1 and display the alteration frequency with mutation type (b) and mutation site (c), we also present the mutation site with

the highest alteration frequency (R146Q/*) in the 3D structure. We also performed the potential correlation between mutation status and OS, DFS, DSS, PFS of UCEC through the cBioPortal tool. (d)

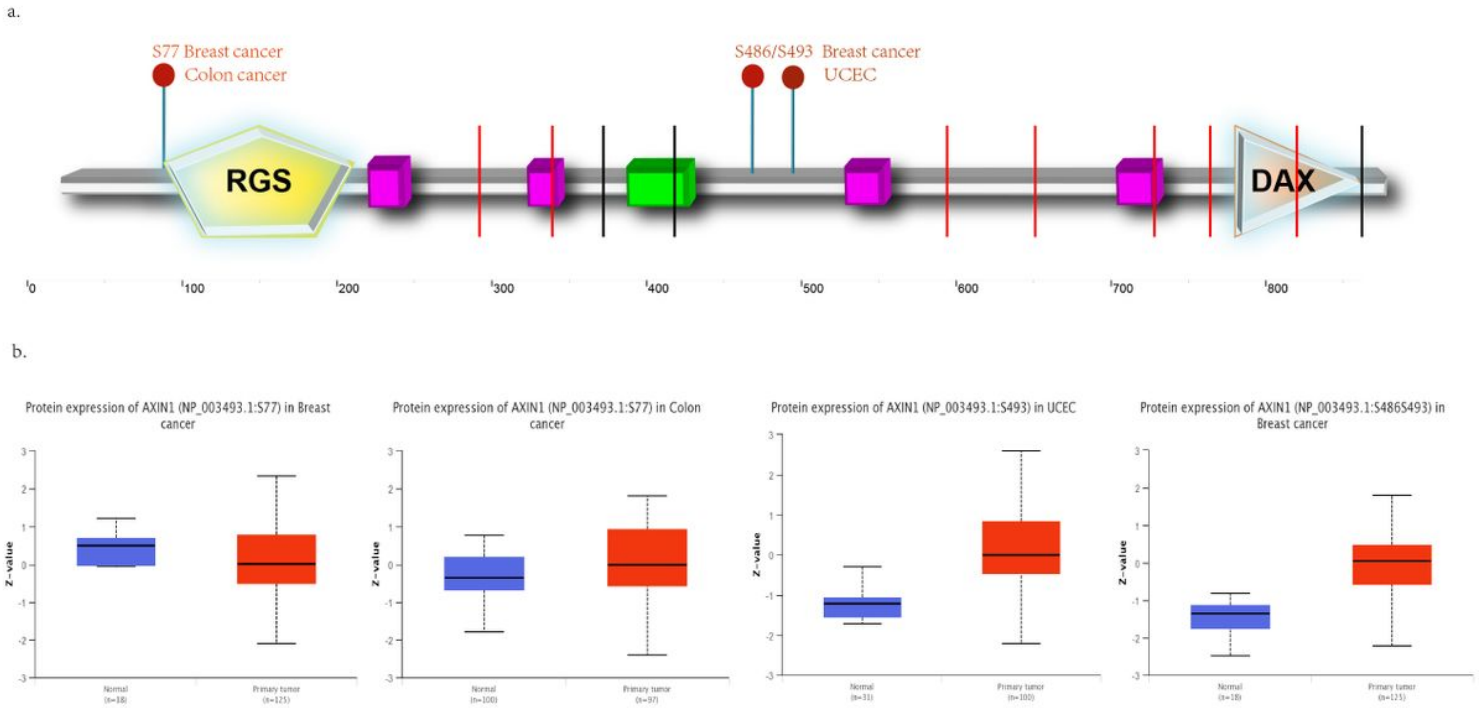

Figure 4

Phosphorylation analysis of AXIN1 in different cancers, based on the CPTAC dataset. (a) We show the box plots for different tumors, including breast cancer, colon cancer and UCEC. (b) Immune infiltration analysis displays a relationship between the regulator T cell immune infiltration and AXIN1 expression in some tumors.

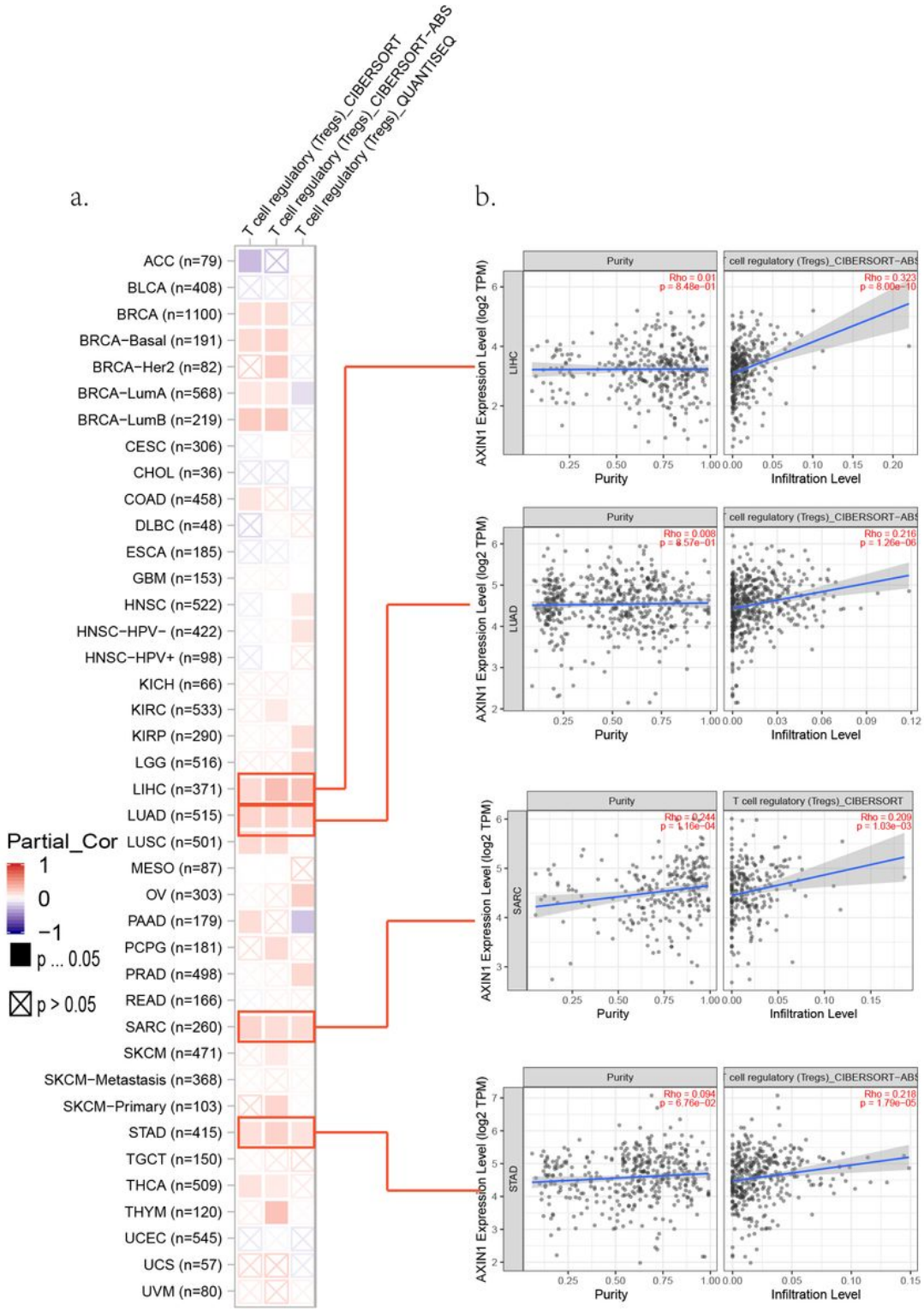

Figure 5

Correlation between AXIN1 expression and the immune infiltration of regulatory T cell. We performed the potential relationship between the expression of AXIN1 gene and the immune infiltration of regulatory T cell across all types of tumor in TCGA through three algorithms, including the CIBERSORT, CIBERSORT-ABS, QUANTISEQ.

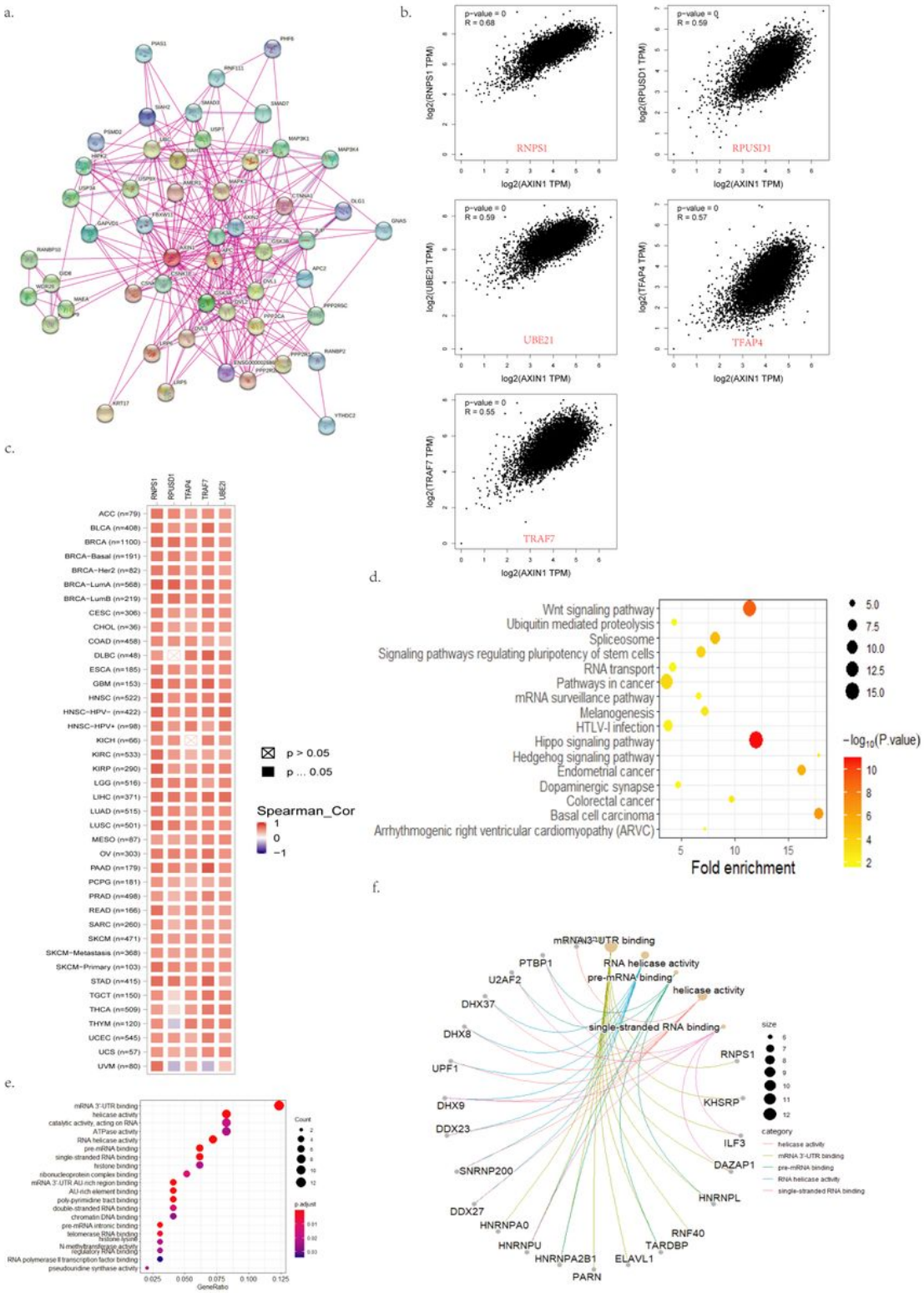

Figure 6

AXIN1-related gene enrichment analysis. (a) We obtained the available AXIN1-bingding proteins through the STRING tool. (b) We also obtained the top 100 AXIN1-correlated genes in TCGA using the GEPIA2 tool and analyzed the expression correlation between AXIN1 and targeting genes, including RNPS1, RPUSD1, UBE21, TFAP4 and TRAF7. (c) We display a corresponding heatmap in specific cancer types. (d) KEGG

pathway analysis was performed based on the AXIN1-binding and interacted genes , as well as the GO analysis (e),(f).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- TableS1.docx