Clinical Expression, Prognosis and Immune Infiltration of SUV39H1 in Diffuse Large B-cell Lymphoma

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Abstract

Epigenetic regulation plays a crucial part in the oncogenesis and treatment of diffuse large B-cell lymphoma (DLBCL). The H3K9me3-specific histone methyltransferase SUV39H1 is a significantly epigenetic gene that promotes the progression of a variety of malignancies. However, the roles of SUV39H1 in DLBCL remain unclear. By retrieving Oncomine, GEPIA, CCLE, UALCAN, and TCGA databases, we observed that the expression of SUV39H1 was higher in DLBCL tissues than in normal and other cancer tissues. Combined with immunohistochemical validation assay, we analysed clinical characteristics of DLBCL patients. The results showed that high expression of SUV39H1 was closely associated with age over 50 years old (*P*=0.014) and low albumin level (*P*=0.015). In the prognostic analyses, DLBCL patients in GEPIA database showed that the high SUV39H1 expression group had a lower disease-free survival (DFS) rate than the low SUV39H1 expression group (*P*=0.035). Finally, we discovered that expressions of CD86+ and CD163+ macrophages have high correlations with SUV39H1+ in DLBCL tissues(with *P*=0.037 and *P*=0.045,respectively). SUV39H1-associated macrophages may downregulate T lymphocyte subsets, especially Treg cells in DLBCL(*P*=0.003). In summary, SUV39H1 might be not only a potential target for the epigenetic therapy and immunotherapy of DLBCL, but also a clinical indicator for doctors to evaluate the trend of disease development.

Introduction

Diffuse large B-cell lymphoma (DLBCL) is the most common type of non-Hodgkin lymphoma (NHL) and accounts for 30%-40% of all NHLs[1]. According to the HANS classification in 2016, DLBCL is divided into two types: germinal center B cell-like (GCB) and non-germinal center B cell-like (non-GCB)[2]. Its clinical symptoms, immunotypes, histomorphology and genetics are highly heterogeneous. Currently, the frontline standard of care for DLBCL is rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP)[3]. However, 30%-40% of patients become resistant to drugs or relapse after treatment, and their diseases are associated with rapid progression and a poor prognosis. The 5-year overall survival (OS) rate is 60-70%. The occurrence and development of DLBCL are attributed to the abnormal expression of multiple genes and posttranscriptional regulation[4]. In order to solve these problems, research on the molecular origin and mechanism of DLBCL has become the focus of research in order to develop effective therapies[5].

SUV39H1 is a member of the SET gene family and functions as a histone methyltransferase to catalyze the methylation of histone H3 lysine 9 (H3K9me) and generate a specific binding site called heterochromatin protein 1 (HP1)[6, 7]. SUV39H1 protein is a modified histone enzyme that is able to alter the structure of chromosomes[8] and then affect gene expression. SUV39H1 was confirmed to participate in cell senescence[9]. Clemens A. Schmitt et al innovatively found that cells from senescence microenvironment can re-entered the cell cycle, by targeting SUV39H1 transgenic mouse models of senescence condition. It follows that the theory of tumor stemness can be promoted by senescence-associated reprogramming [10]. What's more, SUV39H1 was reported to play a critical part in the functions

of immune cells, which can modify chromatin to silence stem and memory genes in the differentiation of CD8+ T [11]. SUV39H1 can be bounded with an essential repressor of repetitive elements (REs), FBXO44. SUV39H1/FBXO44 inhibition can activate REs, stimulate interferon (IFN) signaling and promote immunotherapy response.[12]

Some studies have shown that SUV39H1 is highly expressed and promotes tumor development in many types of carcinomas, such as gastric cancer[13], liver cancer[14], colon cancer[15], and breast cancer[16]. In DLBCL, scientists have utilized SUV39H1 transgenic mouse model to predict prognosis of DLBCL patients[17], but the real expression of SUV39H1 in DLBCL patients is unkown. Whether SUV39H1 can be applied to clinical therapeutics is a hot topic for scientists and clinicians[17].

Therefore, in our study, differential expressional of SUV39H1 in DLBCL was confirmed by bioinformatics tools Oncomine, Cancer Cell Line Encyclopedia (CCLE), UALCAN, Gene Expression Profiling Interactive Analysis (GEPIA), the Cancer Genome Atlas (TCGA) databases and verified by immunohistochemistry assays. Finally, the correlation between clinical parameters, prognosis, immune cells of SUV39H1 were analyzed to explore new and potent targets to improve the cure rate of DLBCL.

Methods

Database analyses

Oncomine (https://www.oncomine.org/resource/login.html) is an online cancer microarray database that integrates RNA and DNA-Seq data from the Gene Expression Omnibus (GEO), The Cancer Genome Atlas (TCGA) and published literature and incorporates 715 datasets and 86,733 samples.

Gene Expression Profiling Interactive Analysis (GEPIA, http://gepia.cancer-pku.cn/) is an interactive web server used to analyze the expression of RNA sequences, including those of 9, 736 tumor samples and 8,587 normal samples from the TCGA and Genotype-Tissue Expression (GTEx) databases; it was developed by Zefang Tang et al. at Peking University [18] .

The Cancer Cell Line Encyclopedia (CCLE, https://portals.broadinstitute.org/ccle/) is a genomic and pharmacologic web server used to analyze human cancer models. It also provides visualization of genetic data and public access to t over 1100 cell lines; it was conceived by the Broad Institute, the Novartis Institutes for Biomedical Research and the Genomics Institute of the Novartis Research Foundation [19, 20].

UALCAN (http://ualcan.path.uab.edu/) is a public database used to analyze TCGA data, identify biomarkers, provide plots depicting protein-coding, miRNA-coding and lincRNA-coding genes, evaluate epigenetic information and select genes/targets by connecting to GeneCards, PubMed, TargetScan, the Human Protein Atlas and so on. It was developed by Chandrashekar DS, et al. from the University of Alabama at Birmingham, Birmingham[21].

We retrieved information on the differential expression of SUV39H1 in DLBCL from the Oncomine, GEPIA, CCLE, UALCAN and TCGA databases. All the database information on the differential expression, clinical parameters, prognosis and immune infiltration of SUV39H1 in DLBCL was acquired from the five public databases listed above.

Pathological specimens and clinical parameters of patients

Paraffin-embedded biopsy specimens and clinical parameters of the patients, including age, sex, subtype, lymph node involvement, number of extranodal lesions, Ki-67 index, Ann Arbor stage, B symptoms, eastern cooperative oncology group (ECOG) performance status, lactate dehydrogenase (LDH) level, albumin level, hemoglobin level, international prognostic index (IPI), OS and progression-free survival(PFS) times, were collected from the First Affiliated Hospital of Zhengzhou University between 2014.01.01 and 2020.11.01, including 67 cases of DLBCL and 36 cases of reactive lymphoid hyperplasia. All paraffin specimens were diagnosed by two experienced pathologists in our hospital.

Immunohistochemistry (IHC) assays

All the tissues were embedded in paraffin and cut into 4 μm slices. After heating at 70°C 30 min for baking sections, the slices were dewaxed with xylene three times (20 min each time) and rehydrated them with absolute ethanol for 10 min, 95% ethanol for 5 min and 75% ethanol for 5 min. Then, slices were repaired in high temperature and make them cool to 25℃. Afterwards, we blocked sections with bovine serum albumin (BSA) for 50min, following by incubating primary antibody against SUV39H1 (1:200; Affinity Biosciences Inc.), CD86 (1:200; Proteintech Inc.) and CD163 (1:200; Proteintech Inc.) at 4℃ overnight. The sections were incubated with the secondary antibody for 30 min, used DAB for color reaction and sealed with neutral gum. All the images were captured with a digital pathology section scanner (NanoZoomer S210, Hamamatsu Photonics Trading Co. Ltd.)

Grading criteria

The nuclei of positive cells appeared yellow to brown in color. Five nonrepetitive visual fields were selected under high magnification. Based on the intensity of positive staining, the sections were graded as follows: 0 points, negtive; 1 point, weak; 2 points, moderate; and 3 points, strong. The amount of staining was graded as follows: 0 points, 0-10% positive cells; 1 point, 11-25% positive cells; 2 points, 25-50% positive cells; and 3 points, >50% positive cells. The collected images were evaluated by two independent observers, and the above scores from the two evaluations were multiplied. Samples with 0-2 points were classified as the low expression group, and those with ≥3 points were classified as the high expression group.

Statistical analysis

All the databases used (Oncomine, GEPIA, CCLE, UALCAN and TCGA are available online. Student's t-test was used to analyze data from the Oncomine database, and one-way ANOVA was used to analyze data

from the GEPIA database. The χ^2 test was used to determine differential expressions of SUV39H1, CD86 and CD163 in pathology results. Student's t-test was used to analyze data from the UALCAN database, and Fisher's exact test or the χ^2 test was used to analyze clinical characteristics data from our hospital. The response rates were also calculated by Fisher's exact test or the χ^2 test. OS and PFS were analyzed by Kaplan–Meier curves and compared by the log-rank test. Immune cells were analyzed by Spearman rank correlation. SPSS 21.0 software was used to analyze all the data, and values of $P < 0.05$ were considered statistically significant. OS and PFS curves of patients in our hospital were generated with GraphPad Prism 8 software. R software were used to analyze the correlations between SUV39H1 and immune cells.

Results

SUV39H1 has a higher expression levels in DLBCL tissues compared with pan-cancer and normal tissues.

By searching the Oncomine database, we found that the expression of SUV39H1 was significantly higher in DLBCL tissues (P=0.006) than in normal nonlymphoid tissues (skin and tonsillar tissues) in Storz dataset[22](Fig. 1a). According to Compagno dataset[23]. In GEPIA database, SUV39H1 expression was also significantly overexpressed in (P=0.010) 47 DLBCL tissues compared with 337 normal tissues (Fig. 1b). Moreover, in the GEPIA database, we also discovered that the expression of SUV39H1 was higher in DLBCL than other types of cancer (Fig. 1c and 1d).

To verify the expression of SUV39H1 in DLBCL and normal lymphoid tissues in the databases, we collected 67 DLBCL pathological sections and 36 reactive lymphoid hyperplasia sections. Immunohistochemical results showed that in 67 DLBCL tissues, 51 samples had high SUV39H1 expression, and 16 samples had low SUV39H1 expression and the positive rate of SUV39H1 in DLBCL reached up to 76.12% (Table 1). Among 36 cases of reactive lymphoid hyperplasia, 17 had low SUV39H1 expression, and 19 had high SUV39H1 expression. The positive rate in the control group was 52.78%, which is similar to the negative rate occupied 47.22%(Table 1). The expression of SUV39H1 in DLBCL tumor tissues was significantly higher than that in reactive lymphoid hyperplasia tissues(Fig. 1e and 1f).

Table 1 Expression differences between DLBCL and reactive lymphoid hyperplasia

Disease type	Total	High (%)	Low (%)	*P* value
Diffuse large B-cell lymphoma	67	51(76.12%)	16 (23.88%)	**0.015***
Reactive lymphoid hyperplasia	36	19 (52.78%)	17(47.22%)	

SUV39H1 has a high mRNA expression in DLBCL cell lines

By searching the CCLE database, we discovered that the mRNA expression of SUV39H1 was higher in DLBCL cell lines than in other malignant tumor cell lines (RNA-seq) (Fig. 2a). The same result was

obtained from another dataset, the Affymetrix gene chip (Affy), which also includes pan-cancer mRNA expression information from the CCLE database (Fig. 2b).

SUV39H1 is related to DLBCL patients'age and albumin level

To analyze the clinicopathological parameters, we firstly searched UALCAN database. The results indicated that SUV39H1 expression level was not correlated with tumor stage, sex, age, race, or weight in DLBCL patients (Fig. 3, $P>0.05$).

Furthermore, in our immunohistochemical results, DLBCL patients were divided into two groups SUV39H1 high/low expression groups. As shown in Table 2, we found that there was a significant difference between age and SUV39H1 expression. In SUV39H1 high expression group, patients over or equal to 50 years old occupies 76.5% and patients less than 50 years old is 23.5%. In SUV39H1 low expression group, patients over or equal to 50 years old only occupies 43.7% and patients less than 50 years old is 56.3%. These suggest that patients over 50 years old prone to have high expression of the SUV39H1 (Table 2, $P=0.014$). In addition, the results show that SUV39H1 is related to albumin level. In SUV39H1 high expression group, the number of patients whose albumin level is less than 40g/L occupies 27.5% and percentage of patients with normal albumin level is 70.5%. In SUV39H1 low expression group, no patients with low albumin level and patients with normal albumin level occupies 100%. It demonstrated that high expression of SUV39H1 has correlation with low albumin level (Table 2, $P=0.015$), but the probability of this event is low(27.5% approximately).

Table 2 Relationship between SUV39H1 and the clinical characteristics of 67 patients with DLBCL

Clinical characteristics	Variable	Total	High SUV39H1 (%)	Low SUV39H1 (%)	*P* value
Age (years)	<50	21	12 (23.5%)	9 (56.3%)	**0.014***
	≥50	46	39 (76.5%)	7 (43.7%)	
Sex	Male	29	22 (43.1%)	7 (43.8%)	0.966
	Female	38	29 (56.9%)	9 (56.2%)	
Subtype	GCB	32	26 (51.0%)	6 (37.5%)	0.346
	Non-GCB	35	25 (49.0%)	10 (62.5%)	
Lymph node involvement	Involvement	32	32 (62.7%)	13 (81.2%)	0.080
	No involvement	21	19 (37.3%)	2 (12.5%)	
	Unclear	1	0	1 (6.3%)	
Number of lesions	<2	31	24 (47.1%)	7 (43.7%)	0.338
	≥2	35	27 (52.9%)	8 (50.0%)	
	Unclear	1	0	1 (6.3%)	
Ki-67 index	<80%	19	13 (25.5%)	6 (37.5%)	0.360
	≥80%	48	38 (74.5%)	10 (62.5%)	
Ann Arbor stage	I-II	41	31 (60.8%)	10（62.4%）	0.680
	III-IV	25	20 (39.2%)	5 (31.3%)	
	Unclear	1	0	1 (6.3%)	
B symptoms	Present	5	5 (9.8%)	0	0.582
	Absent	60	45 (88.2%)	15 (93.7%)	
	Unclear	2	1 (2.0%)	1 (6.3%)	
IPI	0-2	50	38 (74.5%)	12 (75.0%)	1.000
	3-5	16	13 (25.5%)	3 (18.7%)	
	Unclear	1	0	1 (6.3%)	
ECOG performance status	0-1	43	32 (62.7%)	11 (68.7%)	0.755
	2-5	21	17 (33.3%)	4 (25.0%)	
	Unclear	3	2 (4.0%)	1 (6.3%)	
LDH level	Elevated (more than 245U/L)	33	24 (47.1%)	9 (56.2%)	0.425
	Normal (75-245U/L)	27	22 (43.1%)	5 (31.3%)	

	Unclear	7	5 (9.8%)	2 (12.5%)	
Albumin level	Low (less than 40g/L)	14	14 (27.5%)	0	**0.015***
	Normal (40-55g/L)	52	36 (70.5%)	16 (100%)	
	Unclear	1	1 (2.0%)	0	
Hemoglobin level	Low (less than 110g/L)	43	32 (62.7%)	11 (68.8%)	0.729
	Normal (110-160 g/L)	23	18 (35.3%)	5 (31.2%)	
	Unclear	1	1 (2.0%)	0	

Abbreviations: ECOG, Eastern Cooperative Oncology Group; LDH, lactate dehydrogenase; CR, complete response; PR, partial response; PD, progressive disease; SD, stable disease; IPI, International Prognostic Index. *P<0.05.

High SUV39H1 expresssion has a worse prognosis in DLBCL

To explore the association between short-term prognosis and SUV39H1, we analyzed the CR rate, PR rate and ORR of DLBCL patients who were treated only with R-CHOP in the SUV39H1 high- and low-expression groups. Among 67 DLBCL patients, 59 patients received the R-CHOP therapeutic regimen and required complete evaluations of therapeutic effect. 44 patients with high SUV39H1 expression and 15 patients with low SUV39H1 expression. Specifically, in the group of high SUV39H1 expression, 27 patients achieved CR, 7 patients achieved PR, 2 patients were SD, 8 patients suffered PD and 34 patients achieved objective response. In the group of low SUV39H1 expression, 11 patients achieved CR, 2 patients achieved PR, 1 patient were SD, 1 patient suffered PD and 13 patients achieved objective response. However, these figures indicate that there were no significant differences for SUV39H1 in short-term prognostic analyses (Table 3, P >0.05).

Table 3 Response rates of the high/low SUV39H1 expression groups

Response	Number of patients (%)		*P* value
	High SUV39H1 (N=44)	Low SUV39H1 (N=15)	
CR	27 (61.4%)	11 (73.3%)	0.403
PR	7 (15.9%)	2 (13.3%)	1.000
SD	2 (4.5%)	1 (6.7%)	1.000
PD	8 (18.2%)	1 (6.7%)	0.424
ORR	34 (77.3%)	13 (86.6%)	1.000

Abbreviations: CR, complete response; PR, partial response; ORR, objective response rate; *$P < 0.05$.

To investigate the relation between long-term prognosis and SUV39H1, we obtained DFS and OS data according to SUV39H1 expression in 46 DLBCL patients from GEPIA database (Fig. 4a). Compared with the high and low SUV39H1 expression groups, DFS of the high SUV39H1 expression group were significantly lower than those of the low SUV39H1 expression group (P=0.035). In terms of OS, the survival time was markedly shortened, but the survival rate was not significantly different (P=0.32). The OS/PFS outcomes were also analyzed in 59 patients from our hospital, revealing no statistic differences in OS/PFS between the high and low SUV39H1 expression groups (Fig. 4b, P>0.05).

SUV39H1 has close relations with CD86+/CD163+ macrophages and T lymphocyte subsets in DLBCL

It has reported that SUV39H1 can influence CD8+ T cell differentiation[11] and B lymphopoiesis[24]. In the field of macrophages, SUV39H1 can interfere with lipopolysaccharide (LPS)-induced tolerance in macrophage and promote inflammatory cytokine production[25]. Whether SUV39H1 has some relation with macrophage in DLBCL? We did IHC assay to explore the correlation between SUV39H1 and M1/M2 macrophages. CD86 and CD163 are cell surface markers of M1 and M2 macrophages, respectively. The results indicated that CD86+ M1 macrophages have a higher expression in DLBCL tissues comparing with Reactive lymphoid hyperplasia tissues (Table 4, P=0.021). Moreover, the high expressions of CD86+ M1 macrophages and CD163+ M2 macrophages are relevant to the high expressions of SUV39H1 (Table 5, Fig. 5 a,b,c,d, P=0.037 and P=0.045,respectively).

In order to explore the further connection betweeen macrophages and other immune cells related to SUV39H1 in DLBCL, we retrieved TCGA database and found that T follicular helper (TFH), regulatory CD4+ T (Treg), central memory T cell (Tcm), Th17 cells, Th1 cells are negatively correlated with SUV39H1 high expression (Fig. 5e, P□0.05). It is revealed that SUV39H1-assoiated macrophages may downregulate T lymphocyte subsets, especially Treg cell in DLBCL.

Table 4 Expression differences of immune cell between DLBCL and reactive lymphoid hyperplasia

Immunomarker	Expression	Diffuse large B-cell lymphoma(%)	Reactive lymphoid hyperplasia (%)	*P* value
		CD86 N=47/ CD163 N=47	CD86 N=13/ CD163 N=7	
CD86	High	33 (70.2%)	4 (30.8%)	**0.021***
	Low	14 (29.8%)	9 (69.2%)	
CD163	High	31 (66.0%)	6 (85.7%)	0.412
	Low	16 (34%)	1 (14.3%)	

Table 5 Relationship between SUV39H1 and immune cell of 47 patients with DLBCL

Immunomarker	Expression	Numbers of patients (N=47)		*P* value
		High SUV39H1(%)	Low SUV39H1(%)	
CD86	High	27 (57.4%)	7 (14.9%)	**0.037***
	Low	6 (12.8%)	7 (14.9%)	
CD163	High	25 (53.2%)	6 (12.8%)	**0.045***
	Low	8 (17.0%)	8 (17.0%)	

Discussion

Previous studies have shown that SUV39H1 is associated with cell senescence and apoptosis[26]. The dephosphorylation of p53 intensifies the stability of SUV39H1, which is a critical step in cellular senescence[27]. Recently, Milanovic M et al. discovered that SUV39H1 is a critical signal component with stemness. This senescence-associated stemness has important significance in cancer aggressiveness and clinical prognosis and is enriched in recurrent cancers[10]. In our study, SUV39H1 was confirmed to be associated with age over 50 years old. We speculated that high SUV39H1 expression may reprogramme some signal components of stem cells, leading to the progression and aggressiveness of DLBCL in senescence microenvironment. Furthermore, SUV39H1 relevant mechanism of senescence also correlates with the TGF-beta-related microenvironment [28]. Combined with our results of study, SUV39H1 may promote the functions of macrophage and then downregulate Treg cell expression to reduce immune escape.

In most solid tumors, SUV39H1 expression is high, but its expression in cervical cancer is low. Chiba et al. found that patients with high SUV39H1 expression had a significantly high rate of hepatocellular carcinoma recurrence[14]. In gastric cancer, it has been illustrated that SUV39H1 promotes the expression of BCL-2, C-myc pro-caspase-9, pro-caspase-3 and induces cancer invasion and progression. SUV39H1 repressor has been confirmed a potential therapeutic target in gastric carcinoma[29]. SUV39H1 is found to be upregulated in colorectal carcinoma (CRC) tissues compared to normal colon tissues in the tumor microenvironment to promote immune escape[15]. In addition, SUV39H1-selective inhibitor F5446 can transform the functions of known genes involved in DNA replication at S phase and increase the sensitivity of CRC cells to apoptosis in vitro and in vivo[30]. In prostate cancer, it is reported that the elevated expression of SUV39H1 promotes cancer cell aggression[31]. In breast cancer, SUV39H1 binds to PHACTR2-AS1-30nt-RNA, silences DNA genes and then restrains breast cancer progression and lung metastasis in mice[32]. In malignant brain glioma, tumors can be suppressed by repressive targets of SUV39H1[33]. However, in cervical cancer, the weak chromatin state of SUV39H1 promotes cell migration;

thus, SUV39H1 might be a novel and critical target for epigenetic therapies[34]. In our study, we found that SUV39H1 has a higher expression in DLBCL than other solid tumors by searching the GEPIA and CCLE databases. These results suggest that SUV39H1 may be a potential target for the epigenetic therapy of DLBCL in the future.

In hematological malignancies and lymphomas, previous studies have reported that SUV39H1 is a cancer suppressor gene. The H3K9-mediated senescence mechanism depends on the ability of SUV39H1 to inhibit the formation and progression of primary lymphocytes. Therefore, SUV39H1-deficient lymphoma cells usually grow rapidly[9]. Moreover, some researchers have discovered that SUV39H1 plays a vital role in the differentiation of hematopoietic stem cells (HSCs) into B cells [24]. In T lymphoblastoid and monocytic cell lines, methyltransferase SUV39H1 acts on the HIV-1 promoter, increasing the transcription of HIV-1 and promoting apoptosis [35]. Some researchers have found that therapy-induced senescence (TIS) depends on SUV39H1 in the Eμ-myc transgenic mouse lymphoma model. TIS-competent lymphomas, which are Suv39H1(+) lymphomas, can increase glucose utilization, produce more ATP and prompt tumor regression[36]. However, SUV39H1 also functions as a cancer-promoting gene in lymphoma. Target gene promoters in cutaneous T cell lymphoma (CTCL) can be occluded by H3K9me3. It is worth noting that the repression of SUV39H1 can recover the functions of the target gene and effectively inhibit the growth of Sézary cells [37]. In our DFS prognosis analysis, DLBCL patients of high SUV39H1 expression show a worse in GEPIA database. Although OS rate has no statistical significance no matter in database or in our hospital information, we still consider high SUV39H1 expression group having a poorer prognosis in the future with a follow-up visit of longer time.

Conclusion

Our study confirmed that SUV39H1 expression was higher in DLBCL tissues than in normal and pan-cancer tissues. High expression of SUV39H1 is strongly correlated with age over 50 years old, low albumin level, CD86+/CD163+ macrophages and has a negative correlation with Treg cells, indicating that SUV39H1-assoiated macrophages may downregulate Treg cells in DLBCL. But DLBCL patients with high SUV39H1 expression may have a poor DFS. All these discoveries might provide a potential target for the epigenetic therapy of DLBCL and a special indicator for clinicians to evaluate disease development.

Declarations

Ethics approval and consent to participate

Pathological specimens and clinical information were approved by patients and the Ethics Committee of Scientific Research of The First Affiliated Hospital of Zhengzhou University (approval no. 2022-KY-0038-003; Zhengzhou, China)

Consent for publication

All the authors have read and consented to submit the article to this journal.

Availability of data and materials

The datasets supporting the conclusions of this article are available in the Oncomine (https://www.oncomine.org/resource/login.html), Gene Expression Profiling Interactive Analysis (GEPIA, http://gepia.cancer-pku.cn/), Cancer Cell Line Encyclopedia (CCLE, https://portals.broadinstitute.org/ccle/), UALCAN (http://ualcan.path.uab.edu/), and The Cancer Genome Atlas (TCGA, https://www.cancer.gov/about-nci/organization/ccg/research/structural-genomics/tcga) databases.

Competing interests

All the authors declare that they have no competing interests.

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Authors' contributions

Data curation, Yue Zhang, Qing Wen, Yaxin Lei, Jingjing Ge, Xiaoshuang Kong, Wenhua Wang, Zeyuan Wang, Huting Hou, Siyu Qian and Shaoxuan Wu; Funding acquisition, Mingzhi Zhang, Xudong Zhang and Qingjiang Chen; Investigation, Yue Zhang; Methodology, Mingzhi Zhang and Xudong Zhang; Resources, Guannan Wang and Wencai Li; Software, Yue Zhang and Canwei Tang; Supervision, Mingzhi Zhang, Xudong Zhang and Qingjiang Chen; Writing – original draft, Yue Zhang; Writing – review & editing, Qingjiang Chen. All the authors read and approved the final manuscript.

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Figures

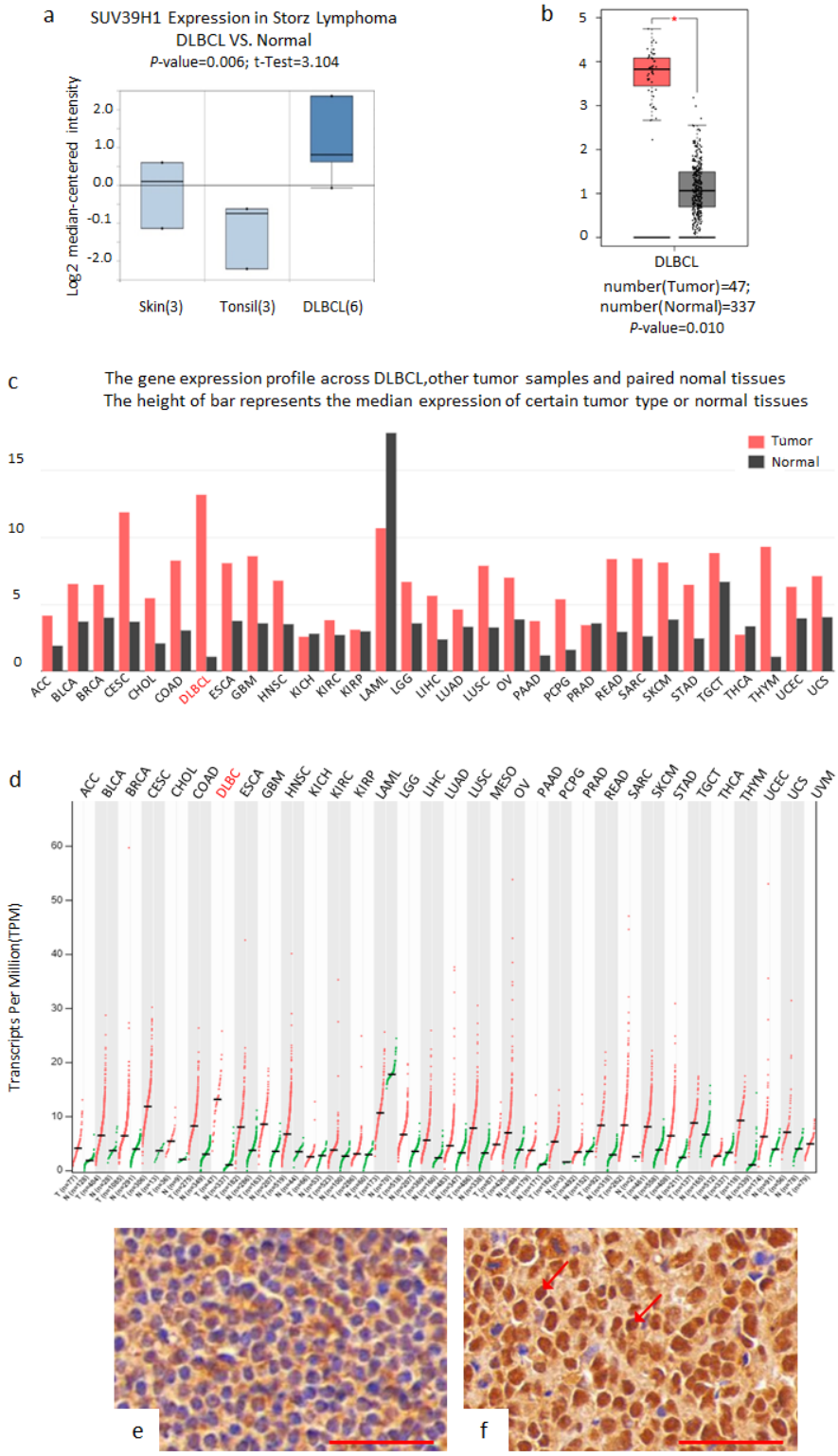


Figure 1

Differential expression of SUV39H1 in DLBCL tissues, normal tissues and pan-cancer tissues.

(a), (b) The differential expression of SUV39H1 between DLBCL and normal tissues in the Oncomine and GEPIA databases.

(c), (d) The differential expression of SUV39H1 between DLBCL and 30 other types of tumors in the GEPIA database.

(e) The expression of SUV39H1 in reactive lymphoid hyperplasia tissue by immunohistochemistry(40×);Scale: 50 μm.

(f) The expression of SUV39H1 in DLBCL tissue by immunohistochemistry(40×); Scale

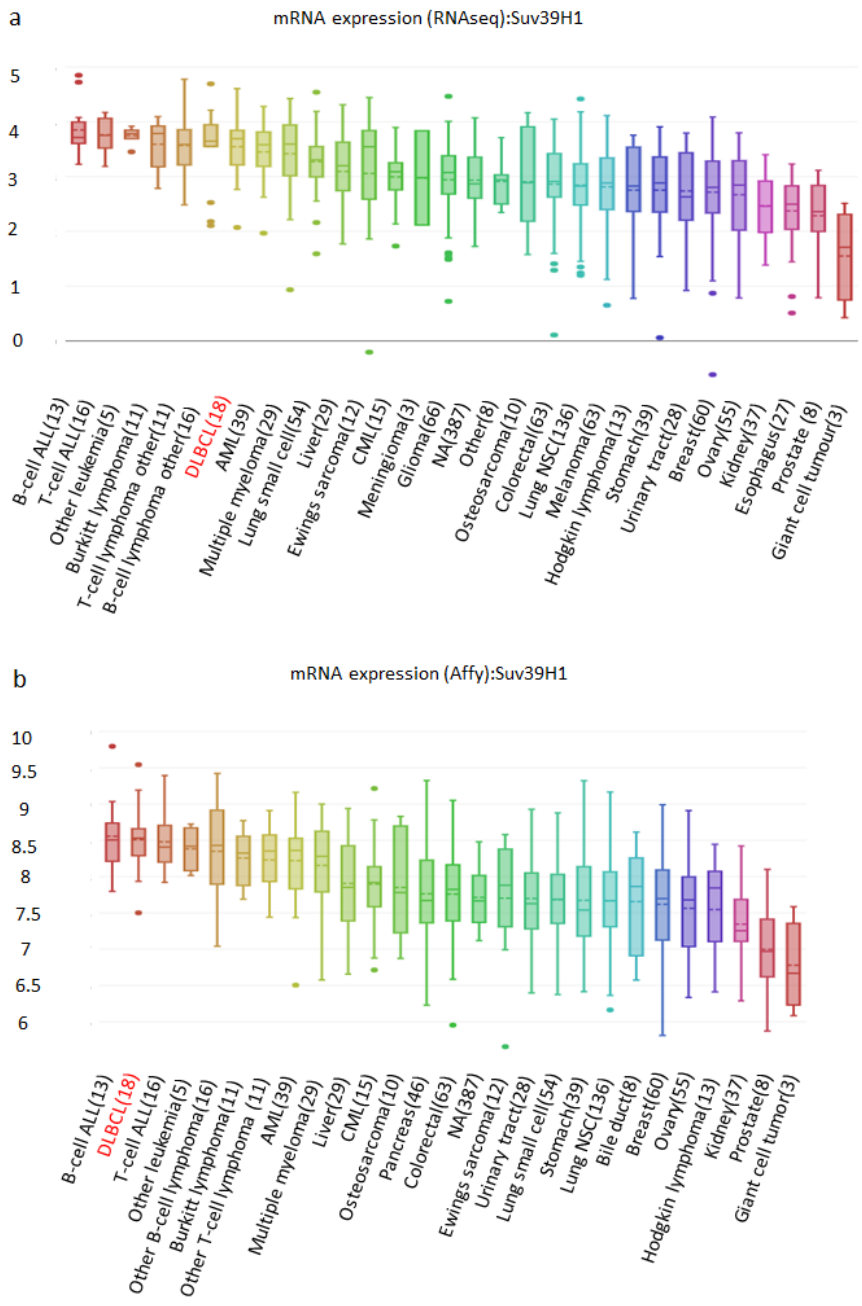


Figure 2

Fig. 2 Expression of SUV39H1 in pan-cancer cell lines from the CCLE database.

(a) The mRNA levels of SUV39H1 in DLBCL and other cancers in RNA sequencing datasets (RNA-seq).

(b) The mRNA levels of SUV39H1 in DLBCL and other cancers in Affymetrix gene chip (affy).

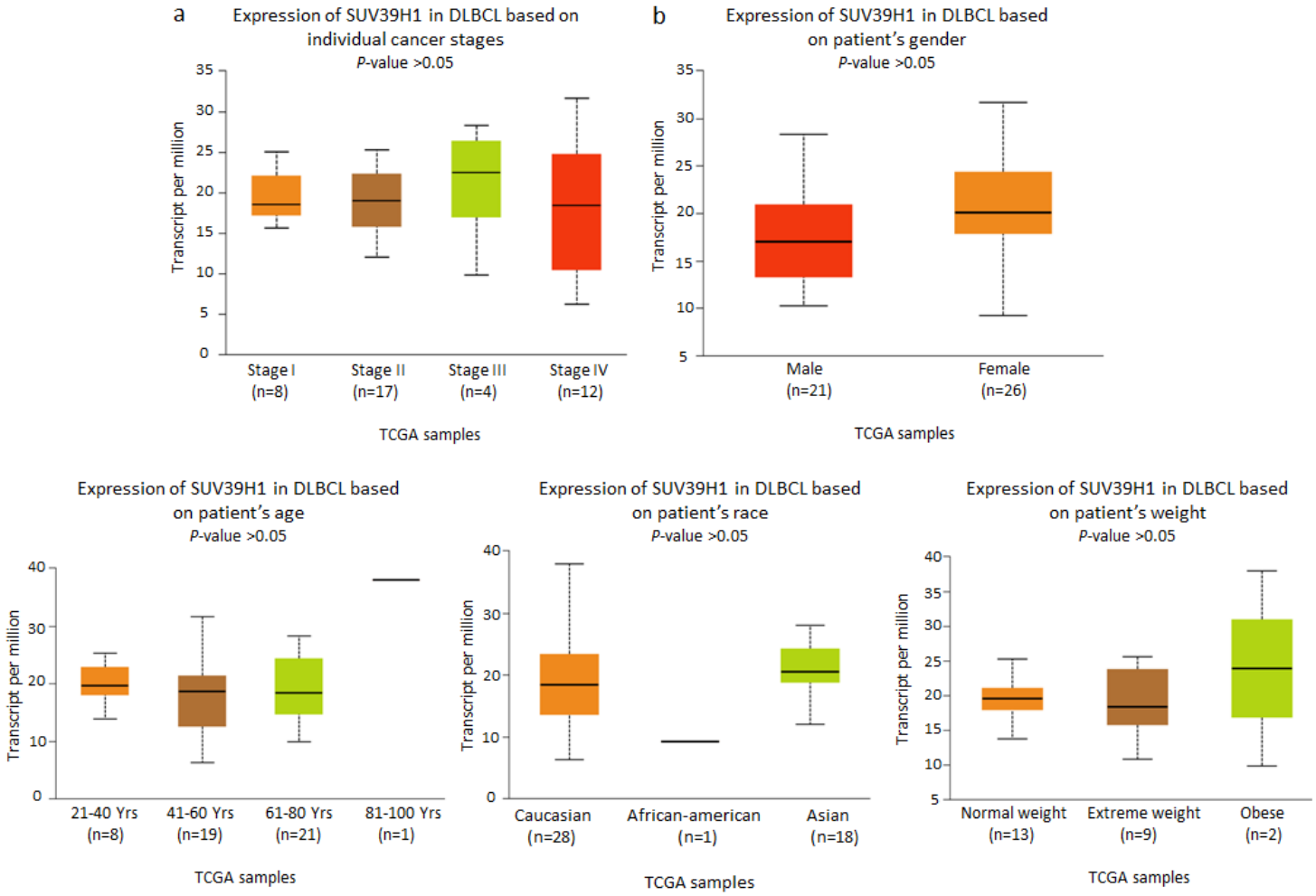


Figure 3

Fig. 3 SUV39H1 expression in DLBCL patients with different clinicopathological parameters in the UALCAN database.

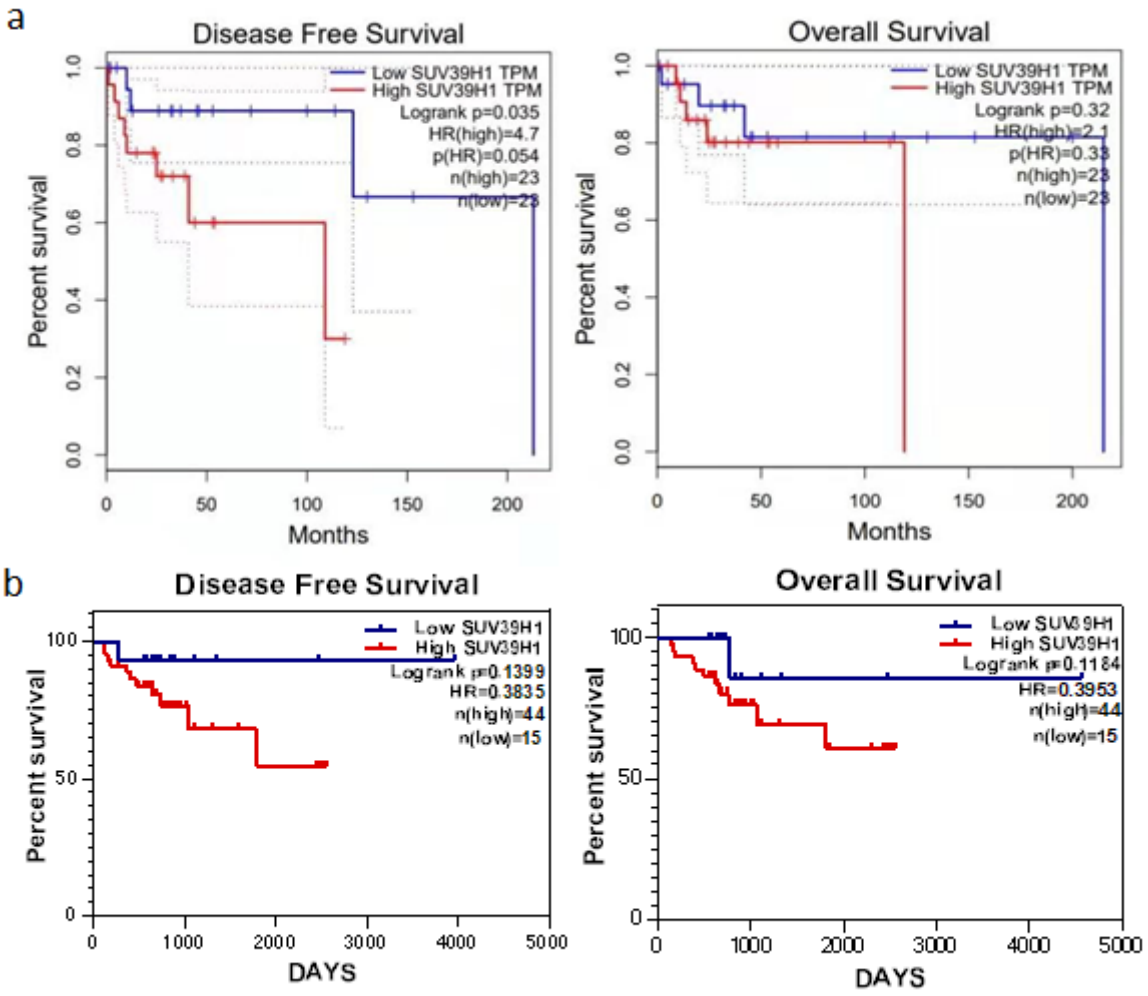
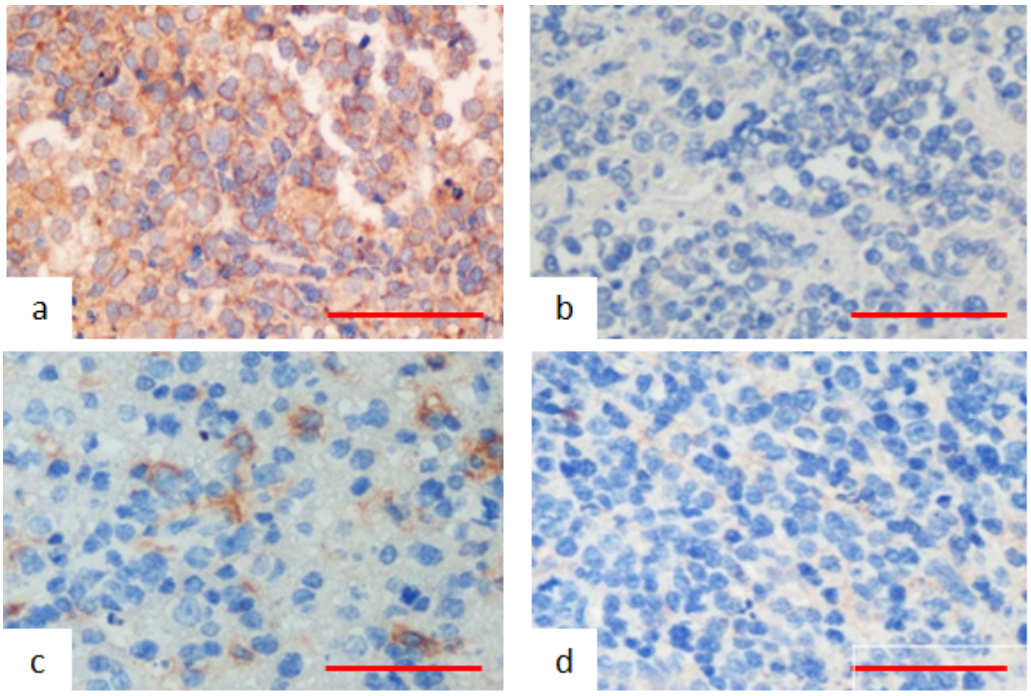


Figure 4

Survival analysis of the high/low SUV39H1 expression groups

(a) DFS and OS differences between the high and low SUV39H1 expression groups in the GEPIA database.

(b) DFS and OS differences between the high and low SUV39H1 expression groups in patients of our hospital.



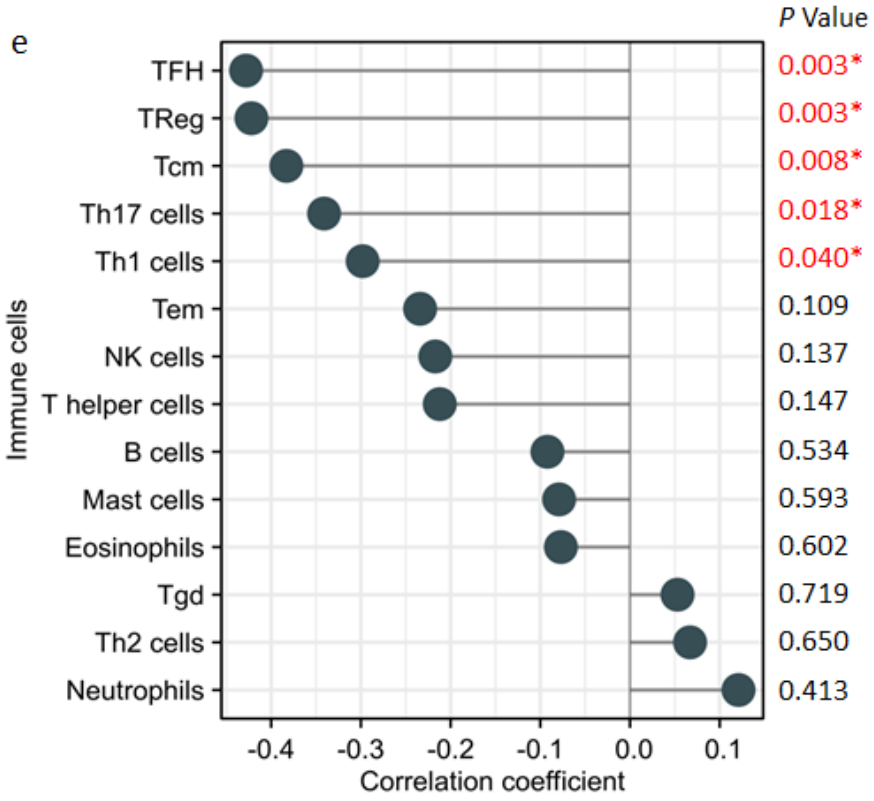


Figure 5

The correlation between SUV39H1 and immune cells.

(a), (b) The differential expression of CD86+ and CD86- in DLBCL tissues (40×), scale: 50 μm.

(c), (d) The differential expression of CD163+ and CD163- in DLBCL tissues (40×), scale: 50 μm.

(e) The correlation between SUV39H1 and all sorts of immune cells in TCGA database.