


ABO Blood Group and the Risk and Prognosis of Lymphoma

Ling Qin¹, Dongli Gao¹, Qian Wang¹, Xuwei Zheng², Jingjing Wang², Xingang Chen², Dongliao Fu², Haodi Ma², Junjia Tan³, Qinan Yin² 

¹The First Affiliated Hospital, and College of Clinical Medicine of Henan University of Science and Technology, Luoyang, People's Republic of China; ²Laboratory for Precision Medicine, School of Medical Technology and Engineering, Henan University of Science and Technology, Luoyang, People's Republic of China; ³Section for Statistical Analysis and Data Collection, Luoyang Branch, Bank of China, Luoyang, People's Republic of China

Correspondence: Qinan Yin, School of Medical Technology and Engineering, Henan University of Science and Technology, No. 263 Kaiyuan Avenue, Luoyang, 471000, People's Republic of China, Tel +86-13939928711, Email qinanyin@haust.edu.cn

Abstract: ABO blood group antigens exhibit alternative phenotypes and genetically derived structures that are located on the red cell surface. The role of ABO blood group in cancer biology has been intensely reported by several studies, and it is now widely recognized that ABO antigens are associated with the risk and prognosis of several types of tumors, namely gastric cancer and pancreatic cancer. However, there have been contentious limited issues with the association between the ABO blood group and lymphoma. In this narrative review, based on literature data, we discuss the role of ABO blood group in the risk and prognosis of lymphoma and summarize the current knowledge of the underlying pathogenic mechanisms of the association. The possible association of ABO blood group with racial disparities and pathological classification in lymphoma patients is also discussed.

Keywords: ABO blood group, lymphoma, survival, disease susceptibility, race

Introduction

The ABO blood group is one of the most important human blood group systems. The *ABO* gene is located on chromosome 9q34 and encodes two alleles (i.e., A and B) for specific glycosyltransferases which catalyze the covalent linkage of N-acetyl-D-galactose or D-galactose to a common precursor side chain (i.e., the H antigen), eventually forming A and B antigens respectively.^{1,2} Unlike A and B alleles, the O variant encodes a non-functional glycosyltransferase, so H antigen is unmodified.³ The ABO blood group antigens are defined by carbohydrate moieties on the extracellular surface of red blood cell membranes. ABO blood group is classified into type A, type B, type AB and type O based on the antigens expressed on erythrocytes. People with blood type A have antigen A on their erythrocytes, and those with blood type B have antigen B.⁴ Individuals with blood type AB have both antigens A and B in the surface of erythrocytes, while those with blood type O lack either antigen.⁵ Studies have shown that these antigens are also highly expressed on the surface of a large number of human cells and tissues, including endothelial, neurons, platelets, and body fluids.^{6–8}

The association between ABO blood groups and tumors has been reported in the early stage.⁹ There is also growing evidence from recent literatures of a critical involvement of the ABO blood group in the development of various types of cancers. Relevant studies demonstrated that blood group A significantly increases the risk of gastric and pancreatic cancer.^{10–12} The reason may be that tumor cells expressing “A-like antigen” in individuals with blood type A are not easy to be recognized by the body for immune rejection.^{13–16} A study in Shanghai also showed that blood group AB is associated with significantly increased risk of liver cancer.¹⁷ Study has noted a direct link of single nucleotide polymorphisms at the ABO locus to serum levels of tumor necrosis factor-alpha, an inflammatory cytokine that regulates liver cancer risk.^{18,19} But the mechanism by which blood type AB is associated with an increased risk of liver cancer is not very clear. In addition, patients with blood type O have a poor prognosis for multiple myeloma (MM).²⁰ This may be due to serum levels of lactic dehydrogenase (LDH) is higher in MM patients with blood type O than other blood types.²⁰

High serum LDH levels may be associated with an extramedullary lesion in MM patients.²¹ So far there is limited understanding of ABO blood group in the risk and prognosis of lymphoma. Moreover, the potential mechanisms underlying remain largely unknown. The association between ABO blood groups and lymphoma is addressed in this concise review through analyzing the published literature and pathogenic mechanisms.

Methods

We systematically reviewed the scientific literature published so far on the relationship between ABO blood group and lymphoma. The PUBMED[®] electronic database was searched without time limit under English language restrictions. The following medical subject headings and keywords were used: “ABO blood group”, “lymphoma”, “disease susceptibility”, “distribution”, “survival”, “prognosis”, and “non-Hodgkin’s lymphoma” (HL). Furthermore, we also manually searched the reference lists for relevant items.

The relationships between ABO blood type and clinical variables were assessed using Chi-square test. A two-tailed $P < 0.05$ was considered statistically significant. The statistical software package SPSS 26.0 (SPSS Inc., Chicago, IL, USA) was used for statistical calculations.

Pathogenic Effects of ABO Blood Group on Lymphoma

The underlying mechanisms that the ABO blood group may interact with the development and progression of cancers including lymphoma are still poorly understood. Several plausible potential pathogenic ways encompass: 1) Deletion of ABO blood group antigens caused by multiple regulators enhances the motility and migration of tumor cells, resulting in poor prognosis;^{15,22–27} 2) Tumor markers that are ABO blood group antigens can evade the immune surveillance of host and allow tumors to grow;^{13–16} 3) Dysregulation of ABO glycosyltransferases, which are mainly involved in altering the modulator of angiogenesis during the tumorigenesis, is related to tumor;^{28–31} and 4) The influence of ABO blood group antigens on tumor growth, invasion and migration is mainly related to the ABO gene locus involved in regulating the mediators of inflammation and immune responses (Figure 1).^{18,32–36}

The decrease or absence of ABO blood group antigen expression seems to play a role in the progression of tumors. There are several factors for the decrease or absence of ABO blood group. First, the deletion of ABO allele or hypermethylation of the ABO promoter region causes relative down-regulation of the glycosyltransferase necessary for blood group antigen synthesis.^{22,37–40} Second, some microRNAs (miRNAs) affect the expression of blood group antigens by regulating the activity of glycosyltransferase, such as miR-331-3p and miR-1980-5-p.²⁷ Third, mutations in the ABO gene. For example, the mutation of the GATA motif in intron 1 of the ABO gene could reduce the expression of the B antigen, and mutation of RUNX1 causes the loss of A antigen.^{25,26} Loss of blood group antigen expression may lead to increased cell motility and migration, which enhances malignancy of tumors and is associated with poor prognosis.^{15,23,24} So how does the deletion of blood group antigens enhance malignancy of tumors? It may be ascribable to the glycosylation of ABO blood group antigens on the regulation of integrin receptors activity.⁴¹ Integrin is an important component of cell adhesion molecules. In addition, the glycosylation of ABO blood group antigens can lead to conformational changes in proteins that not only affects intercellular signaling, cell adhesion, and immune surveillance, but also stimulates tumor growth and metastasis.^{42–47} The absence of ABO blood antigen is observed in hematological malignancies, including HL.^{48,49} We hypothesize that some of these factors may cause decreased expression of ABO blood group antigens on the surface of red blood cells in patients with lymphoma, leading to disease progression.

Some tumor antigens, which are the known product of certain blood type precursors/antigens, escape from immune surveillance and cause adverse prognosis. Many of those tumor antigens are similar to the A antigen, which are known as “A-like antigens.” “A-like antigens” was once considered to be an Across-reacting antigen (e.g., Forssman antigen, or Tn antigen), but it was later found to be the real A antigen.^{14–16} The discovery of the A antigen in non-A cancers indicates that ABO antigens can act as cancer risk factors.^{50,51} It is reported that under the immune surveillance theory, tumor cells expressing “A-like antigen” in individuals with blood type O can be detected by host immune surveillance at an early stage and are more likely to suffer immunologic rejection.¹⁵ However, it is difficult for type A persons to recognize tumor cells expressing “A-like antigen” as foreign cells as type O persons do.¹³ This may explain the increase in type A patients compared to type O patients in many malignancies. It is also found that the efficacy of immune checkpoint inhibitors

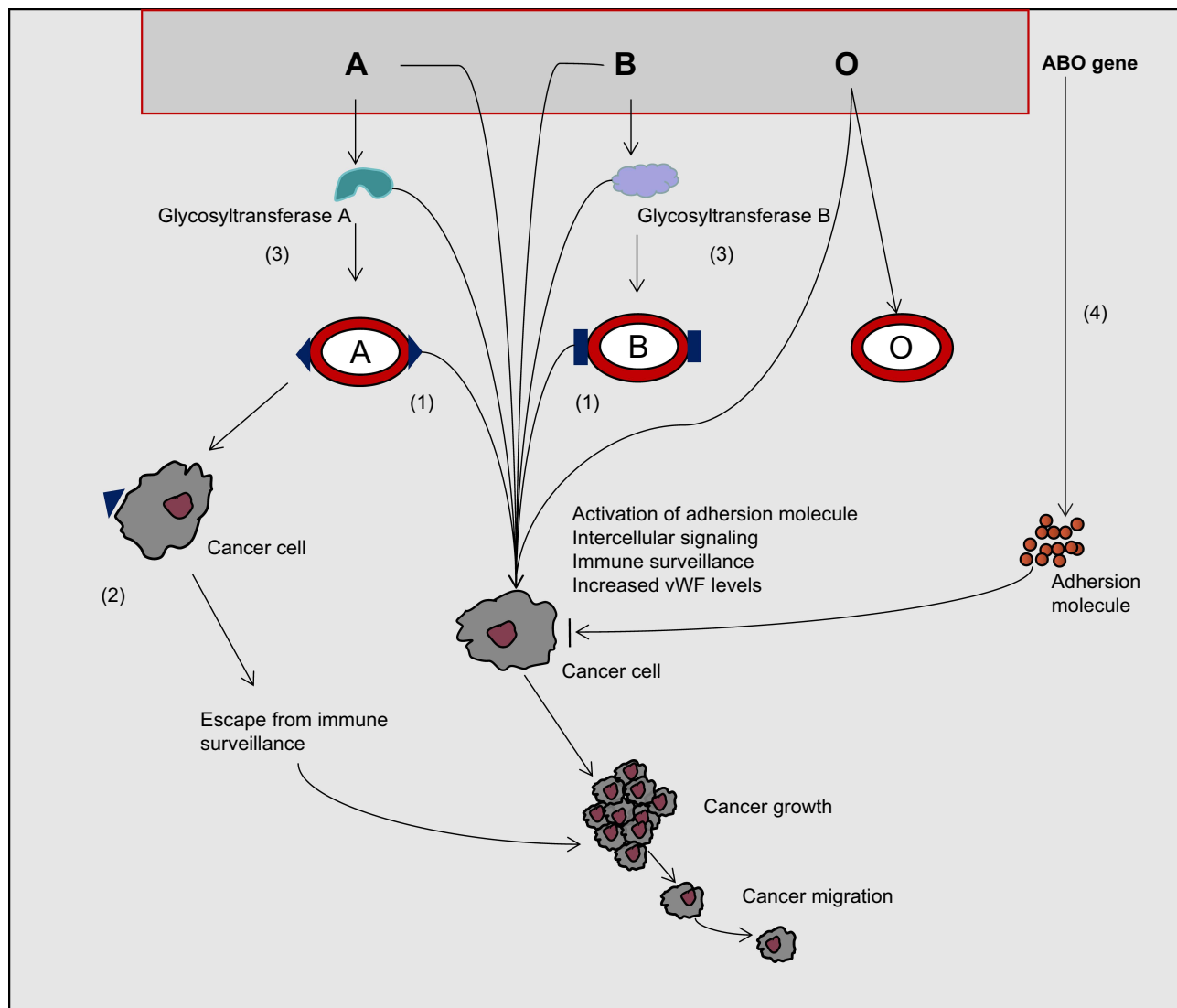


Figure 1 Pathogenic mechanism of ABO blood group on lymphoma. Potential mechanisms by which ABO blood groups may interact with the development and progression of cancers, including lymphoma: 1) Multiple regulators lead to the deletion of ABO blood group antigens, especially the A and B antigens, which enhances the motility and migration of tumor cells, resulting in poor prognosis; 2) Tumor markers that are ABO blood group antigens can evade the immune surveillance of host and allow tumors to grow; 3) Dysregulation of ABO glycosyltransferases, which are mainly involved in altering the modulator of angiogenesis during the tumorigenesis, is related to tumor; and 4) The influence of ABO blood group antigens on tumor growth, invasion and migration is mainly related to the ABO gene locus involved in regulating the mediators of inflammation and immune responses.

(ICIs) could be influenced by the ABO blood group, and advanced malignant melanoma patients with type B or AB had significantly longer overall survival (OS) than other blood types after using ICIs.⁵² Similar findings have been found in other blood group systems. For example, CD44, which is identical to the blood group antigen In b, is associated with lymphocyte (T cell) activation, hematopoietic development, and metastasis of malignant lymphoma.^{53–56} Thus, we hypothesize that there are tumor markers that are essentially ABO blood group antigens in lymphoma that contribute to disease progression.

Dysregulation of ABO glycosyltransferases, which are mainly involved in altering the modulator of angiogenesis during the tumorigenesis, is related to tumor. The mechanism is similar to how ABO glycosyltransferase regulates plasma von Willebrand factor (vWF) levels to affect the risk of venous thromboembolism (VTE).^{29,31,57} VWF plays an important role in inhibiting angiogenesis, promoting wound healing, and promoting tumor cell apoptosis; particularly, angiogenesis and apoptosis are also involved in tumorigenesis.^{28,30,58,59} ABO glycosyltransferase may promote the development of lymphoma by regulating plasma vWF levels.

It is possible that ABO blood group antigens influence tumor progression and metastasis by changing the inflammatory state of the host. The researchers found that the ABO gene locus is associated with circulating levels of tumor necrosis factor- α , soluble intercellular adhesion molecule (ICAM)-1, E-selectin, and P-selectin.^{18,32,33} All of these adhesion molecules are important mediators of chronic inflammation and immune cell recruitment. The correlation between ABO blood group and the occurrence and prognosis of chronic inflammatory diseases, such as inflammatory bowel disease and autoimmune diseases have been reported.^{60–72} Chronic inflammation is related to tumor growth, invasion, and migration.^{34–36} Therefore, we speculate that these inflammatory mediators directly correlate ABO blood groups with tumor development and spread. Chronic inflammation is also associated with lymphatic malignancies.⁷³ For example, Epstein–Barr virus is connected with large B cell lymphoma in immunocompromised patients and in patients with Burkitt's lymphoma or HL.⁷⁴ Another example is the lymphomas that appear in GM-CSF- and IFN γ -deficient mice, which are caused by infections and subside after antibiotic treatment.⁷⁵ Thus, ABO blood group may be associated with lymphoma initiation and spread by changing the inflammatory state of the host.

Epidemiological and Clinical Data

Several epidemiological studies have assessed the impact of ABO blood group antigens on the risk (Table 1) and prognosis of lymphoma (Table 2). ABO blood group is found to be associated with the susceptibility of lymphoma and could be worked as an independent predictor of prognosis in lymphoma patients.^{76,77} It was observed that individuals with blood type A have a lower risk of lymphoma than those with other blood types.⁷⁶ Besides, lymphoma patients with blood type B have a poorer prognosis, while patients with blood type O have a better prognosis.^{77,78} Currently, racial disparities in incidence and survival exist for patients with lymphoma.^{79,80} Racial differences in ABO blood groups also

Table 1 Studies of the Association Between ABO Blood Group and the Risk Factors of Developing Lymphoma

First Author, Year ^{Ref}	Study Design	Subjects	Main Findings
Levitani, 1959 ⁸³	Retrospective	500 patients with Hodgkin's lymphoma	The incidence of blood group B is higher in HL patients than in controls
Williams, 1966 ⁸⁶	Retrospective	100 patients with Burkitt's lymphoma	No significant association between Burkitt's lymphoma and ABO blood groups
Saichua, 1978 ⁸⁷	Retrospective	80 patients with leukemia and 34 patients with lymphoma	No significant association between ABO blood group and lymphoma ($P > 0.05$)
Janardhana, 1991 ⁸⁸	Retrospective	558 Caucasian patients of European descent with leukemia or lymphoma	No significant association between ABO blood group and lymphoma ($P > 0.05$)
Vadivelu, 2004 ⁷⁶	Retrospective	63 patients with HL, 78 patients with non-Hodgkin's lymphoma, 116 patients with acute myeloid leukemia, 522 patients with acute lymphoblastic leukemia	Blood group B (45.6%) was significantly associated with an increased risk for HL (95% CI: 6.8–84.5), blood group A (56.5%; 52.9%) was significantly associated with a decreased risk for HL and NHL (95% CI: 19.9–85.4; 95% CI: 18.1–82.6)
Gharouni, 2008 ⁸⁴	Retrospective	36 patients with primary central nervous system lymphoma	The percentage of patients with blood group A was lower in the PCNSL group ($n = 3$, 8.3%) than in the control group ($n = 371$, 37.1%)
Abouzari, 2012 ⁸⁵	Retrospective	202 patients with secondary central nervous system lymphoma	The percentage of patients with blood group A was lower in the SCNSL group ($n = 10$, 5%) than in the control group ($n = 371$, 37.1%)
Petrosyan, 2022 ⁸²	Retrospective	798 patients with hematological malignancies including 577 patients with acute lymphoblastic leukemia, 84 patients with acute myeloid leukemia (AML), 81 patients with HL, 40 patients with NHL, and 16 patients with chronic myeloid leukemia	Patients with blood group A were more likely to develop hematological malignancies in comparison with the other blood groups

Table 2 Studies of the Association Between ABO Blood Group and Survival in Patients with Lymphoma

First Author, Year ^{Ref}	Study Design	Subjects	Main Findings
Oberhuber, 1997 ⁹⁰	Retrospective	89 patients with gastric mucosa-associated lymphoid tissue lymphoma and 95 patients with upper gastrointestinal complaints including 5 patients with mucosa-associated lymphoid tissue lymphoma	No significant difference in survival was observed among patients with different ABO blood types ($P = 0.18$)
Li, 2017 ⁷⁷	Retrospective	697 patients with extranodal natural killer (NK)/T-cell lymphoma	The 5-year overall survival rate in patients with blood type O was significantly higher than that in patients with non-O blood type (62% vs. 48.9%, $P = 0.001$)
Osada, 2020 ⁷⁸	Retrospective	523 patients with malignant lymphoma	Blood group B was associated with a lower 5-year overall survival rate compared with non-B blood groups (40.9% vs. 57.3%, $P < 0.01$)
Tizro, 2020 ⁸⁹	Retrospective	37 patients with diffuse large B-cell lymphoma	The average number of days of survival was lower in patients with 3 group B patients compared to 5 non-B group patients (254 days vs. 537 days, $P = 0.03$)
Ulu, 2022 ⁹¹	Retrospective	206 patients with diffuse large B-cell lymphoma	Cox regression analysis revealed no significant association of ABO blood groups with prognosis

exist and are well characterized.⁸¹ An awareness could be raised in the effects of racial differences in ABO blood group on clinical variables seen in lymphoma.

ABO Blood Groups and the Risk of Lymphoma

ABO blood groups have been reported to be associated with the occurrence of lymphoma.^{82,83} An increasing proportion of B blood group and a decreasing proportion of A blood group were observed in HL.^{76,83} Furthermore, studies on central nervous system lymphoma showed a significantly lower risk of both primary central nervous system lymphoma (PCNSL) and secondary CNS lymphoma (SCNSL) in blood group A individuals.^{84,85} However, a number of studies indicated that ABO blood group was not associated with lymphoma susceptibility in both children and adult patients (Table 1).^{86–88}

ABO Blood Groups and the Prognosis of Lymphoma

The prognostic value of ABO blood group in lymphoma were evaluated in a number of studies. A study of 697 patients with extranodal natural killer (NK)/T-cell lymphoma (ENKTL) revealed that ABO blood group was an independent predictor of clinical outcome for patients with ENKTL.⁷⁷ Studies in patients with diffuse large B-cell lymphoma (DLBCL) confirmed the association of ABO blood group with OS in lymphoma patients.^{78,89} Blood group B was also identified as an independent predictor of shorter OS in male DLBCL patients.⁷⁸ However, other studies indicated that ABO blood group was not significantly associated with the prognosis of patients with lymphoma (Table 2).^{90,91}

Association of ABO Blood Group with Racial Disparities and Pathological Classification in Lymphoma Patients

We summarized and analyzed the clinical characteristics among a total of 3118 lymphoma patients reported in 13 studies, of which the vast majority were performed in Caucasians and a few in Asians and Africans (Table 3). Among a total of 1623 Caucasian lymphoma patients, the greatest frequency of A, B, AB and O blood group was reported in Turkey (45.2%), Iran (56.7%), America (6.7%) and Australia (49.9%) respectively (Table 3). The Asian lymphoma patients had the greater reported frequency of both B (27.3%) and AB (8.8%) blood group as compared to Caucasian and African (Table 4). A greatest frequency of O blood group (53%) was observed in African patients and that of A blood group (33.3%) in Caucasian (Table 4). There are significant differences in the distribution of ABO blood groups in lymphoma patients of different races ($P < 0.001$, Table 4).

Table 3 Summary of the Characteristics of Lymphoma Patients in Reported Studies

First Author, Year	Region	Race	Lymphoma Classification	Gender		Age Range (Years)	Cases with Different ABO Blood Types (%)				Total
				Males	Females		O	A	B	AB	
Levitan, 1959 ⁸³	America	Caucasian	HL	ND	ND	ND	224 (44.8)	174 (34.8)	73 (14.6)	29 (5.8)	500
Oberhuber, 1997 ⁹⁰	Austria	Caucasian	Gastric MALT lymphoma ^a	44	50	NA	36 (38.3)	39 (41.5)	13 (13.8)	6 (6.4)	94
Janardhana, 1991 ⁸⁸	Australia	Caucasian	N/A	ND	ND	ND	213 (49.9)	158 (37.0)	40 (9.4)	16 (3.7)	427
Gharouni, 2008 ⁸⁴	Iran	Caucasian	PCNSL ^a	24	12	18~73	20 (55.6)	3 (8.3)	10 (27.8)	3 (8.3)	36
Abouzari, 2012 ⁸⁵	Iran	Caucasian	SCNSL ^a	113	89	16~80	60 (29.7)	10 (5.0)	125 (61.9)	7 (3.5)	202
Tizro, 2020 ⁸⁹	America	Caucasian	DLBCL ^a	37	0	37~93	19 (51.4)	11 (29.7)	6 (16.2)	1 (2.7)	37
Ulu, 2022 ⁹¹	Turkey	Caucasian	DLBCL ^a	105	101	24~93	80 (38.8)	93 (45.2)	20 (9.7)	13 (6.3)	206
Petrosyan, 2022 ⁸²	Armenia	Caucasian	HL and NHL	N/A	N/A	0~18	38 (31.4)	52 (43.0)	17 (14.0)	14 (11.6)	121
Saichua, 1978 ⁸⁷	Thailand	Asian	N/A	15	19	15~80	11 (32.4)	7 (20.6)	11 (32.4)	5 (14.7)	34
Vadivelu, 2004 ⁷⁶	Indian	Asian*	HL and NHL	ND	ND	0~12	62 (44.0)	14 (9.9)	59 (41.8)	6 (4.3)	141
Li, 2017 ⁷⁷	China	Asian	ENKTL ^a	492	205	10~82	255 (36.6)	195 (28.0)	188 (27.0)	59 (8.5)	697
Osada, 2020 ⁷⁸	Japan	Asian	N/A	293	230	18~99	164 (31.4)	183 (35.0)	123 (23.5)	53 (10.1)	523
Williams, 1966 ⁸⁶	Nigerians	African	Burkitt's lymphoma ^a	60	40	5~15	53 (53.0)	23 (23.0)	21 (21.0)	3 (3.0)	100

Notes: ^aThe pathological type of these lymphomas is classified as non-Hodgkin lymphoma. ⁹²The study was carried out in Tamil Nadu, a state in southern India where the majority of the population was Asian.

Abbreviations: ND, not done; N/A, not applicable; HL, Hodgkin's lymphoma; NHL, non-Hodgkin's lymphoma; PCNSL, primary central nervous system lymphoma; SCNSL, secondary primary central nervous system lymphoma; Gastric MALT lymphoma, gastric mucosa-associated lymphoid tissue lymphomas; ENKTL, extranodal natural killer (NK)/T-cell lymphoma; DLBCL, diffuse large B-cell lymphoma.

Table 4 ABO Blood Group Distribution of Lymphoma Patients by Race

Race	Total	Cases with Different ABO Blood Types (%)				P value*	Reports
		O	A	B	AB		
Asian	1395	492 (35.3)	399 (28.6)	381 (27.3)	123 (8.8)	0.000	4 studies ^{76-78,87}
Caucasian	1623	690 (42.5)	540 (33.3)	304 (18.7)	89 (5.5)		8 studies ^{82-85,88-91}
African	100	53 (53.0)	23 (23.0)	21 (21.0)	3 (3.0)		1 study ⁸⁶

Notes: *P value was derived from a comparative analysis of ABO blood group distribution of lymphoma patients in Asian, Caucasian and African.

Previous studies in Asians have demonstrated no significant association between ABO blood group and the incidence of lymphoma.^{77,87} Only one study conducted in Tamils in Indian demonstrated the significant decrease of A blood group in HL and non-HL (Table 3).⁷⁶

A total of 3118 lymphoma patients were studied its association with ABO blood groups. Among them, non-HL accounted for 47.8%, followed by HL (20.7%) and the remaining 31.6% was not reported its classification (Table 3). The non-Hodgkin lymphoma patients had the greater reported frequency of B blood group (28.1%) as compared to Hodgkin lymphoma (17.5%), while the greatest frequency of A (33.7%), AB (6.8%) and O (41.9%) blood groups were observed in Hodgkin lymphoma patients (Table 5). There are significant differences in ABO blood group distribution among

Table 5 ABO Blood Group Distribution of Patients by Different Categories of Lymphoma

Lymphoma Classification	Total	Cases with Different ABO Blood Types (%)				P value*	Reports
		O	A	B	AB		
NHL	1490	577 (38.7)	397 (26.6)	419 (28.1)	97 (6.5)	0.000	8 studies ^{76,77, 84–86,89–91}
HL	644	270 (41.9)	217 (33.7)	113 (17.5)	44 (6.8)		3 studies ^{76,82,83}
Classification unreported	984	388 (39.4)	348 (35.4)	174 (17.7)	74 (7.5)		3 studies ^{78,87,88}

Notes: *P value was derived from a comparative analysis of ABO blood group distribution in NHL, HL and classification unreported.

Abbreviations: HL, Hodgkin's lymphoma; NHL, non-Hodgkin's lymphoma.

patients with different classification of lymphoma ($P < 0.001$, Table 5). Whereas these differences may be difficult to explain currently, we could not eliminate a hypothesis that the ABO blood group could be associated with racial disparity and pathological classification in lymphoma patients.

Conclusions

A number of literatures report an association between ABO blood group and lymphoma risk and prognosis. Several plausible mechanisms have been proposed to support this association, including cell motility, inflammation, immune surveillance, and glycosyltransferase activity. However, the molecular mechanisms underlying these association remain poorly understood. The results evaluating the risk and prognostic value of ABO blood groups in lymphoma varied significantly among studies due to unstageable patients, unidentical treatment and unstandardized study design. Besides, an association of ABO blood group with racial disparities and pathological classification in lymphoma patients may exist, yet little is known about the basis for the differences. To be better understand the role of ABO blood groups in lymphoma and the mechanism of their association, future experimental studies are recommended in larger number of lymphoma patients as well as at molecular level of ABO blood groups. Public health endeavors should focus on refining the clinical data of lymphoma patients on race and ethnicity.

Author Contributions

All authors contributed to data analysis, drafting or revising the article, have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Funding

This work was supported by the Fundamental Research Funds for Henan University of Science and Technology (QNY13510001).

Disclosure

The authors report no conflicts of interest in this work.

References

1. Yamamoto F. Molecular genetics of ABO. *Vox Sang.* 2000;78(Suppl 2):91–103.
2. Yamamoto F, Cid E, Yamamoto M, Blancher A. ABO research in the modern era of genomics. *Transfus Med Rev.* 2012;26:103–118. doi:10.1016/j.tmr.2011.08.002
3. Lowe JB. The blood group-specific human glycosyltransferases. *Baillieres Clin Haematol.* 1993;6:465–492. doi:10.1016/S0950-3536(05)80155-6
4. Franchini M, Liumbruno GM. ABO blood group: old dogma, new perspectives. *Clin Chem Lab Med.* 2013;51:1545–1553. doi:10.1515/cclm-2013-0168
5. Li HY, Guo K. Blood group testing. *Front Med.* 2022;9:827619. doi:10.3389/fmed.2022.827619
6. Oriol R, Mollicone R, Coullin P, Dalix AM, Candelier JJ. Genetic regulation of the expression of ABH and Lewis antigens in tissues. *APMIS Suppl.* 1992;27:28–38.
7. Eastlund T. The histo-blood group ABO system and tissue transplantation. *Transfusion.* 1998;38:975–988. doi:10.1046/j.1537-2995.1998.381098440863.x
8. Breimer ME, Molne J, Norden G, Rydberg L, Thiel G, Svalander CT. Blood group A and B antigen expression in human kidneys correlated to A1/A2/B, Lewis, and secretor status. *Transplantation.* 2006;82:479–485. doi:10.1097/01.tp.0000231697.15817.51
9. Hartmann O, Stavem P. Abo blood-groups and cancer. *Lancet.* 1964;1:1305–1306. doi:10.1016/S0140-6736(64)91696-4
10. Pelzer U, Klein F, Bahra M, et al. Blood group determinates incidence for pancreatic cancer in Germany. *Front Physiol.* 2013;4:118. doi:10.3389/fphys.2013.00118

11. Li X, Xu H, Gao P. ABO blood group and diabetes mellitus influence the risk for pancreatic cancer in a population from China. *Med Sci Monit.* 2018;24:9392–9398. doi:10.12659/MSM.913769
12. Chen Y, Hu N, Liao L, et al. ABO genotypes and the risk of esophageal and gastric cancers. *BMC Cancer.* 2021;21:589. doi:10.1186/s12885-021-08334-1
13. Hakomori S. Fucolipids and blood group glycolipids in normal and tumor tissue. *Prog Biochem Pharmacol.* 1975;10:167–196.
14. Hakomori S, Wang SM, Young WW Jr. Isoantigenic expression of Forssman glycolipid in human gastric and colonic mucosa: its possible identity with “A-like antigen” in human cancer. *Proc Natl Acad Sci U S A.* 1977;74:3023–3027. doi:10.1073/pnas.74.7.3023
15. Hakomori S. Antigen structure and genetic basis of histo-blood groups A, B and O: their changes associated with human cancer. *Biochim Biophys Acta.* 1999;1473:247–266. doi:10.1016/S0304-4165(99)00183-X
16. Garratty G. Blood groups and disease: a historical perspective. *Transfus Med Rev.* 2000;14:291–301. doi:10.1053/tmr.2000.16228
17. Huang JY, Wang R, Gao YT, Yuan JM. ABO blood type and the risk of cancer - Findings from the Shanghai Cohort Study. *PLoS One.* 2017;12:e0184295. doi:10.1371/journal.pone.0184295
18. Melzer D, Perry JR, Hernandez D, et al. A genome-wide association study identifies protein quantitative trait loci (pQTLs). *PLoS Genet.* 2008;4:e1000072. doi:10.1371/journal.pgen.1000072
19. Nieters A, Yuan JM, Sun CL, et al. Effect of cytokine genotypes on the hepatitis B virus-hepatocellular carcinoma association. *Cancer.* 2005;103:740–748. doi:10.1002/encr.20842
20. Gocer M, Kurtoglu E. Effect of the ABO blood groups on the development, clinical features and survival of multiple myeloma. *Memo.* 2021;14:235–240. doi:10.1007/s12254-020-00669-y
21. Barlogie B, Smallwood L, Smith T, Alexanian R. High serum levels of lactic dehydrogenase identify a high-grade lymphoma-like myeloma. *Ann Intern Med.* 1989;110:521–525. doi:10.7326/0003-4819-110-7-521
22. Stellner K, Hakomori S, Warner GS. Enzymic conversion of “H1-glycolipid” to A or B-glycolipid and deficiency of these enzyme activities in adenocarcinoma. *Biochem Biophys Res Commun.* 1973;55:439–445. doi:10.1016/0006-291X(73)91106-6
23. Le Pendu J, Marionneau S, Cailleau-Thomas A, Rocher J, Le Moullac-Vaidye B, Clement M. ABH and Lewis histo-blood group antigens in cancer. *APMIS.* 2001;109:9–31. doi:10.1111/j.1600-0463.2001.tb00011.x
24. Dabelsteen E, Gao S. ABO blood-group antigens in oral cancer. *J Dent Res.* 2005;84:21–28. doi:10.1177/154405910508400103
25. Sano R, Nakajima T, Takahashi K, et al. Expression of ABO blood-group genes is dependent upon an erythroid cell-specific regulatory element that is deleted in persons with the B(m) phenotype. *Blood.* 2012;119:5301–5310. doi:10.1182/blood-2011-10-387167
26. Hayakawa A, Sano R, Takahashi Y, et al. RUNX1 mutation in a patient with myelodysplastic syndrome and decreased erythrocyte expression of blood group A antigen. *Transfusion.* 2020;60:184–196. doi:10.1111/trf.15628
27. Kronstein-Wiedemann R, Nowakowska P, Milanov P, et al. Regulation of ABO blood group antigen expression by miR-331-3p and miR-1908-5p during hematopoietic stem cell differentiation. *Stem Cells.* 2020;38:1348–1362. doi:10.1002/stem.3251
28. Franchini M, Frattini F, Crestani S, Bonfanti C, Lippi G. von Willebrand factor and cancer: a renewed interest. *Thromb Res.* 2013;131:290–292. doi:10.1016/j.thromres.2013.01.015
29. Franchini M, Liumbruno GM, Lippi G. The prognostic value of ABO blood group in cancer patients. *Blood Transfus.* 2016;14:434–440. doi:10.2450/2015.0164-15
30. O’Sullivan JM, Preston RJS, Robson T, O’Donnell JS. Emerging roles for von Willebrand factor in cancer cell biology. *Semin Thromb Hemost.* 2018;44:159–166. doi:10.1055/s-0037-1607352
31. Ibrahim-Kosta M, Bailly P, Silvy M, et al. ABO blood group, glycosyltransferase activity and risk of venous thromboembolism. *Thromb Res.* 2020;193:31–35. doi:10.1016/j.thromres.2020.05.051
32. Barbalic M, Dupuis J, Dehghan A, et al. Large-scale genomic studies reveal central role of ABO in sP-selectin and sICAM-1 levels. *Hum Mol Genet.* 2010;19:1863–1872. doi:10.1093/hmg/ddq061
33. Kiechl S, Pare G, Barbalic M, et al. Association of variation at the ABO locus with circulating levels of soluble intercellular adhesion molecule-1, soluble P-selectin, and soluble E-selectin: a meta-analysis. *Circ Cardiovasc Genet.* 2011;4:681–686. doi:10.1161/CIRCGENETICS.111.960682
34. Fernandes JV, Cobucci RN, Jatoba CA, Fernandes TA, de Azevedo JW, de Araujo JM. The role of the mediators of inflammation in cancer development. *Pathol Oncol Res.* 2015;21:527–534. doi:10.1007/s12253-015-9913-z
35. Singh R, Mishra MK, Aggarwal H. Inflammation, Immunity, and Cancer. *Mediators Inflamm.* 2017;2017:6027305. doi:10.1155/2017/6027305
36. Greten FR, Grivnenkov SI. Inflammation and cancer: triggers, mechanisms, and consequences. *Immunity.* 2019;51:27–41. doi:10.1016/j.immuni.2019.06.025
37. Orlow I, Lacombe L, Pellicer I, et al. Genotypic and phenotypic characterization of the histoblood group ABO(H) in primary bladder tumors. *Int J Cancer.* 1998;75:819–824. doi:10.1002/(SICI)1097-0215(19980316)75:6<819::AID-IJC1>3.0.CO;2-Y
38. Iwamoto S, Withers DA, Handa K, Hakomori S. Deletion of A-antigen in a human cancer cell line is associated with reduced promoter activity of CBF/NF-Y binding region, and possibly with enhanced DNA methylation of A transferase promoter. *Glycoconj J.* 1999;16(10):659–666. doi:10.1023/A:1007085202379
39. Kominato Y, Hata Y, Takizawa H, Tsuchiya T, Tsukada J, Yamamoto F. Expression of human histo-blood group ABO genes is dependent upon DNA methylation of the promoter region. *J Biol Chem.* 1999;274:37240–37250. doi:10.1074/jbc.274.52.37240
40. Gao S, Bennett EP, Reibel J, et al. Histo-blood group ABO antigen in oral potentially malignant lesions and squamous cell carcinoma--genotypic and phenotypic characterization. *APMIS.* 2004;112:11–20. doi:10.1111/j.1600-0463.2004.apm1120103.x
41. Ichikawa D, Handa K, Withers DA, Hakomori S. Histo-blood group A/B versus H status of human carcinoma cells as correlated with haptotactic cell motility: approach with A and B gene transfection. *Cancer Res.* 1997;57:3092–3096.
42. Greenwell P. Blood group antigens: molecules seeking a function? *Glycoconj J.* 1997;14:159–173. doi:10.1023/A:1018581503164
43. Pinho SS, Reis CA. Glycosylation in cancer: mechanisms and clinical implications. *Nat Rev Cancer.* 2015;15:540–555. doi:10.1038/nrc3982
44. Stowell SR, Ju T, Cummings RD. Protein glycosylation in cancer. *Annu Rev Pathol.* 2015;10:473–510. doi:10.1146/annurev-pathol-012414-040438
45. Reily C, Stewart TJ, Renfrow MB, Novak J. Glycosylation in health and disease. *Nat Rev Nephrol.* 2019;15:346–366. doi:10.1038/s41581-019-0129-4
46. Laubli H, Borsig L. Altered cell adhesion and glycosylation promote cancer immune suppression and metastasis. *Front Immunol.* 2019;10:2120. doi:10.3389/fimmu.2019.02120
47. Xu Y, Chang R, Xu F, et al. N-glycosylation at Asn 402 stabilizes N-cadherin and promotes cell-cell adhesion of glioma cells. *J Cell Biochem.* 2017;118:1423–1431. doi:10.1002/jcb.25801

48. Scott GL, Rasbridge MR. Loss of blood group antigenicity in a patient with Hodgkin's disease. *Vox Sang.* 1972;23:458–460. doi:10.1111/j.1423-0410.1972.tb03836.x
49. Bianco T, Farmer BJ, Sage RE, Dobrovic A. Loss of red cell A, B, and H antigens is frequent in myeloid malignancies. *Blood.* 2001;97:3633–3639. doi:10.1182/blood.V97.11.3633
50. Clausen H, Hakomori S, Graem N, Dabelsteen E. Incompatible A antigen expressed in tumors of blood group O individuals: immunochemical, immunohistologic, and enzymatic characterization. *J Immunol.* 1986;136:326–330. doi:10.4049/jimmunol.136.1.326
51. Metoki R, Kakudo K, Tsuji Y, Teng N, Clausen H, Hakomori S. Deletion of histo-blood group A and B antigens and expression of incompatible A antigen in ovarian cancer. *J Natl Cancer Inst.* 1989;81:1151–1157.
52. Ergun Y, Esen SA, Bardakci M, et al. Predictive and prognostic effect of ABO blood group on immune checkpoint inhibitors. *Cancer Biomark.* 2022;34:329–336. doi:10.3233/CBM-210455
53. Spring FA, Dalchau R, Daniels GL, et al. The Ina and Inb blood group antigens are located on a glycoprotein of 80,000 MW (the CDw44 glycoprotein) whose expression is influenced by the In(Lu) gene. *Immunology.* 1988;64:37–43.
54. Haynes BF, Telen MJ, Hale LP, Denning SM. CD44—a molecule involved in leukocyte adherence and T-cell activation. *Immunol Today.* 1989;10:423–428. doi:10.1016/0167-5699(89)90040-6
55. Akisik E, Bavbek S, Dalay N. CD44 variant exons in leukemia and lymphoma. *Pathol Oncol Res.* 2002;8:36–40. doi:10.1007/BF03033699
56. Naor D, Wallach-Dayan SB, Zahalka MA, Sionov RV. Involvement of CD44, a molecule with a thousand faces, in cancer dissemination. *Semin Cancer Biol.* 2008;18:260–267. doi:10.1016/j.semcancer.2008.03.015
57. Ward SE, O'Sullivan JM, O'Donnell JS. The relationship between ABO blood group, von Willebrand factor, and primary hemostasis. *Blood.* 2020;136:2864–2874. doi:10.1182/blood.2020005843
58. Starke RD, Ferraro F, Paschalaki KE, et al. Endothelial von Willebrand factor regulates angiogenesis. *Blood.* 2011;117(3):1071–1080. doi:10.1182/blood-2010-01-264507
59. Ishihara J, Ishihara A, Starke RD, et al. The heparin binding domain of von Willebrand factor binds to growth factors and promotes angiogenesis in wound healing. *Blood.* 2019;133:2559–2569. doi:10.1182/blood.2019000510
60. Collet A, Zawadzki C, Jeanpierre E, et al. ABO blood groups in systemic sclerosis: distribution and association with this disease's characteristics. *J Clin Med.* 2022;12:12. doi:10.3390/jcm12010012
61. Klove-Mogensen K, Steffensen R, Masmans TN, et al. ABO, secretor, and Lewis carbohydrate histo-blood groups are associated with autoimmune neutropenia of early childhood in Danish patients. *Transfusion.* 2022;62:1636–1642. doi:10.1111/trf.17002
62. Salem GI, Gamal NM, Talaat EA, El-Hammady DH, Hammam N, Gheita TA. Clinical impact of the ABO blood type in patients with rheumatic diseases: is there a link to the ABO and rhesus? *Mediterr J Rheumatol.* 2021;32:237–242. doi:10.31138/mjr.32.3.237
63. Stoia I, Ramneantu R, Poitas M. Blood groups ABO and Rh (D) factor in the rheumatic diseases. *Ann Rheum Dis.* 1967;26:332–333. doi:10.1136/ard.26.4.332
64. Nik A, Mirfeizi Z, Rezaieyazdi Z, et al. ABO and Rh blood groups in patients with lupus and rheumatoid arthritis. *Caspian J Intern Med.* 2021;12:568–572. doi:10.22088/cjim.12.4.568
65. Islamoglu ZGK, Unal M. Is there an association of ABO blood groups and Rhesus factor with alopecia areata? *J Cosmet Dermatol.* 2018;17:1271–1274. doi:10.1111/jocd.12491
66. Cildag S, Kara Y, Senturk T. ABO blood groups and rheumatic diseases. *Eur J Rheumatol.* 2017;4:250–253. doi:10.5152/eurjrheum.2017.17044
67. Chen J, Chen H, Lin Y, Zheng W, Wang C. Association between ABO blood group and risk of Crohn's disease: a case-control study in the Chinese Han population. *J Clin Lab Anal.* 2022;36:e24195. doi:10.1002/jcla.24195
68. Forni D, Cleynen I, Ferrante M, et al. ABO histo-blood group might modulate predisposition to Crohn's disease and affect disease behavior. *J Crohns Colitis.* 2014;8:489–494. doi:10.1016/j.crohns.2013.10.014
69. Dagdeviren M, Ates I, Demir BF, Ergun E, Yildiz C, Altay M. Investigation of blood groups in benign thyroid diseases in Turkey. *Endocr J.* 2019;66:1001–1009. doi:10.1507/endocrj.EJ18-0582
70. Lopetegi I, Munoz-Lopetegi A, Arruti M, et al. ABO blood group distributions in multiple sclerosis patients from Basque Country; O(-) as a protective factor. *Mult Scler J Exp Transl Clin.* 2019;5:2055217319888957. doi:10.1177/2055217319888957
71. Markovic S, Bozicevic D, Simic D, Brzovic Z. Genetic markers in the blood of multiple sclerosis patients. *Neurol Croat.* 1991;41:3–12.
72. Ye BD, Kim BM, Jung S, et al. Association of FUT2 and ABO with Crohn's disease in Koreans. *J Gastroenterol Hepatol.* 2020;35:104–109. doi:10.1111/jgh.14766
73. Grivennikov SI, Greten FR, Karin M. Immunity, inflammation, and cancer. *Cell.* 2010;140:883–899. doi:10.1016/j.cell.2010.01.025
74. Ferreri AJ, Ernberg I, Copie-Bergman C. Infectious agents and lymphoma development: molecular and clinical aspects. *J Intern Med.* 2009;265:421–438. doi:10.1111/j.1365-2796.2009.02083.x
75. Enzler T, Gillissen S, Manis JP, et al. Deficiencies of GM-CSF and interferon gamma link inflammation and cancer. *J Exp Med.* 2003;197:1213–1219. doi:10.1084/jem.20021258
76. Vadivelu MK, Damodaran S, Solomon J, Rajaseharan A. Distribution of ABO blood groups in acute leukaemias and lymphomas. *Ann Hematol.* 2004;83:584–587. doi:10.1007/s00277-004-0888-1
77. Li YJ, Yi PY, Li JW, et al. Prognostic role of ABO blood type in patients with extranodal natural killer/T cell lymphoma, nasal type: a triple-center study. *Chin J Cancer.* 2017;36:62. doi:10.1186/s40880-017-0229-0
78. Osada Y, Ito C, Nishiyama-Fujita Y, et al. Prognostic impact of ABO blood group on survival in patients with malignant lymphoma. *Clin Lymphoma Myeloma Leuk.* 2020;20:122–129. doi:10.1016/j.clml.2019.09.607
79. Li Y, Wang Y, Wang Z, Yi D, Ma S. Racial differences in three major NHL subtypes: descriptive epidemiology. *Cancer Epidemiol.* 2015;39:8–13. doi:10.1016/j.canep.2014.12.001
80. Vaughn JL, Spies D, Xavier AC, Epperla N. Racial disparities in the survival of patients with indolent non-Hodgkin lymphomas in the United States. *Am J Hematol.* 2021;96:816–822. doi:10.1002/ajh.26198
81. Bloodbook. Racial and ethnic distribution of ABO blood types. Available from: <http://www.bloodbook.com/world-abo.html>. Accessed December 06, 2022.
82. Petrosyan A, Palanjyan A, Melnichenko I, et al. ALL-436 association between ABO and Rh blood groups and pediatric hematological malignancies in Armenia. *Clin Lymphoma Myeloma Leuk.* 2022;22(Suppl 2):S204–S205. doi:10.1016/S2152-2650(22)01204-6
83. Levitan R, Razis DV, Diamond HD, Craver LF. ABO blood groups in Hodgkin's disease. *Acta Haematol.* 1959;22:12–19. doi:10.1159/000205756

84. Gharouni M, Abouzari M, Rashidi A, Sodagari N, Behzadi M. Low frequency of blood group A in primary central nervous system lymphoma. *J Neurooncol.* 2008;87:363–364. doi:10.1007/s11060-008-9516-6
85. Abouzari M, Behzadi M, Rashidi A. Low frequency of blood group A in secondary central nervous system lymphoma. *Surg Neurol Int.* 2012;3:95. doi:10.4103/2152-7806.100179
86. Williams AO. Haemoglobin genotypes, ABO blood groups, and Burkitt's tumour. *J Med Genet.* 1966;3:177–179. doi:10.1136/jmg.3.3.177
87. Saichua S, Chiewsilp P. Red cell ABH antigens in leukaemias and lymphomas. *Vox Sang.* 1978;35:154–159. doi:10.1111/j.1423-0410.1978.tb02915.x
88. Janardhana V, Propert DN, Green RE. ABO blood groups in hematologic malignancies. *Cancer Genet Cytogenet.* 1991;51:113–120. doi:10.1016/0165-4608(91)90016-N
89. Tizro P, Liu ML, Aggarwal A, Nava VE. ABO blood group as a prognostic factor in patients with diffuse large B cell lymphoma. *Clin Lymphoma Myeloma Leuk.* 2020;20:561–562. doi:10.1016/j.clml.2020.03.001
90. Oberhuber G, Kranz A, Dejaco C, et al. Blood groups Lewis(b) and ABH expression in gastric mucosa: lack of inter-relation with *Helicobacter pylori* colonisation and occurrence of gastric MALT lymphoma. *Gut.* 1997;41:37–42. doi:10.1136/gut.41.1.37
91. Ulu BU, Basci S, Bakirtas M, et al. Could blood groups have prognostic significance on survival in patients with diffuse large B cell lymphoma? *Leuk Res.* 2022;115:106810. doi:10.1016/j.leukres.2022.106810
92. Swerdlow SH, Campo E, Pileri SA, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. *Blood.* 2016;127:2375–2390. doi:10.1182/blood-2016-01-643569

Journal of Inflammation Research

Dovepress

Publish your work in this journal

The Journal of Inflammation Research is an international, peer-reviewed open-access journal that welcomes laboratory and clinical findings on the molecular basis, cell biology and pharmacology of inflammation including original research, reviews, symposium reports, hypothesis formation and commentaries on: acute/chronic inflammation; mediators of inflammation; cellular processes; molecular mechanisms; pharmacology and novel anti-inflammatory drugs; clinical conditions involving inflammation. The manuscript management system is completely online and includes a very quick and fair peer-review system. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/journal-of-inflammation-research-journal>