Exp Oncol 2022
44, 3, 208–212

Experimental ONCOLOGY

EXPRESSION OF IMMUNOGLOBULIN SEQUENCES HOMOLOGOUS TO ANTI-SARS-CoV-2 ANTIBODIES AND HIV IN CHRONIC LYMPHOCYTIC LEUKEMIA CASES

I. Abramenko, N. Bilous, A. Chumak, Z. Martina, I. Dyagil, D. Bazyka*
National Research Center for Radiation Medicine, National Academy of Medical Sciences of Ukraine, Kyiv 03115, Ukraine

Background: **Identification of epitopes recognized by leukemic B cells could provide insights into the molecular mechanisms of B cell transformation in chronic lymphocytic leukemia (CLL). The *aim* of this paper was to compare nucleotide sequences of immunoglobulin heavy chain variable region (*IGHV*) genes in CLL with known sequences directed against antigens of different origins available in public databases.** ***Materials and Methods:*** **Analysis was performed in the groups of 412 unselected CLL patients with productive *IGHV* gene using polymerase chain reaction followed by direct sequencing.** ***Results:*** **Homology between CLL Ig sequences and antibodies directed against autoantigens was found in 12 patients (2.9%), homology between CLL Ig sequences and antiviral antibodies — in 35 patients (8.5%). Most of these sequences belonged to stereotypical clusters. Among the sequences that have homology to antiviral antibodies, the most prevalent were cases homologous with antibodies against HIV (14 cases, 3.4%) and SARS-CoV-2 antigens (10 cases, 2.4%). None of the patients in our cohort was HIV-infected and the study was conducted before the emergence of SARS-CoV-2 virus.** ***Conclusions:*** **Suggestions could be made about the possible impact of past infection of SARS-CoV-2 virus on the pathogenesis of CLL. In particular, an increase in the proportion of CLL cases with the expression of some stereotyped BCR and/or an increase of CLL risk in the long-term period after SARS-CoV-2 virus infection is not excluded. This assumption needs to be verified by epidemiological data.**

***Key Words*: chronic lymphocytic leukemia, immunoglobulin variable heavy chain (*IGHV*) gene, SARS-CoV-2 antibodies.**

DOI: 10.32471/exp-oncology.2312-8852.vol-44-no-3.18414

One of the characteristics of the B-cell receptor (BCR) in chronic lymphocytic leukemia (CLL) is the nonrandom repertoire of immunoglobulin heavy chain variable region (*IGHV*) genes and the presence of a significant proportion of patients with similar or almost identical variable heavy chain complementarity-determining region 3 (HCDR3) sequences, strongly suggesting recognition of a common antigenic determinant. Different subsets of CLL cases carrying highly similar (stereotyped) BCR immunoglobulins (Ig) were identified, which gradually increased the frequency of stereotyped cases among examined CLL patients [1–4]. It has been hypothesized that either autoantigens or antigens derived from apoptotic cells or pathogens as well as antigens of viral and bacterial origin are essential to trigger CLL pathogenesis [5]. The list of the most antigens recognized by CLL BCRs is presented in the overview of Kostareli *et al*. [6]. Identification of epitopes recognized by leukemic B cells could provide insights into the molecular mechanisms of B cell transformation in CLL. Various approaches are used for this purpose. The aim of this paper was to compare nucleotide sequences of *IGHV* genes in CLL with known sequences directed against antigens of different origins available in public databases.

Submitted: August 17, 2022.
*Correspondence: E-mail: abramenko_iryna@ukr.net
Abbreviations used: BCR – B-cell receptor; CLL – chronic lymphocytic leukemia; HCDR3 – heavy chain complementarity-determining region 3; Ig – immunoglobulins; IGHV – immunoglobulin heavy chain variable region; M – mutated; UM – unmutated.

MATERIALS AND METHODS

Our cohort included 412 unselected CLL patients with productive *IGHV* gene rearrangements (307 men and 105 women) aged 57.63 ± 0.47 years (median 58 years) referred to the National Research Center for Radiation Medicine, Kyiv in 2002–2017. The study was approved by the local Medical Ethics Committee, and all patients gave informed consent to participate. The diagnosis of CLL was based on clinical history, lymphocyte morphology, and immunophenotypic criteria. Stage of disease was established according to the Rai [7, 8] and Binet [9]. None of the patients was HIV-infected. Diagnosis of the disease and molecular analysis were carried out before the onset of the SARS-CoV-2 epidemic.

Genomic DNA for molecular analysis was extracted from peripheral blood mononuclear cells with the QIAamp Blood Mini Kit (Qiagen, UK). The *IGHV* gene mutational status was assessed by polymerase chain reaction amplification followed by a direct sequencing, as described earlier [10]. Sequences were analyzed using the databases IgBlast (https://www.ncbi.nlm.nih.gov/igblast/) and IMGT (https://www.imgt.org/IMGT_vquest/input). Sequences with > 98% homology with the corresponding germ-line *IGHV* gene were considered as unmutated (UM), and cases with < 98% homology were considered to be mutated (M) [11, 12]. Cases with stereotyped BCRs were identified according to Agathangelidis *et al*. [13].

For identification of stereotyped cases and homology with non-CLL sequences we used criteria of Agathangelidis *et al.* [13]: (1) utilization of *IGHV* genes from the same phylogenetic clan, (2) at least 50% amino acid identity and 70% similarity within the HCDR3,

(3) identical HCDR3 length and, (4) identical offset of the shared amino acid pattern.

All statistical analyses were performed with SPSS software (version 17.0; SPSS, Inc., Chicago, IL). The significance of the differences between distribution frequencies of IGHV gene families was calculated by chi-square test. The differences were considered significant at $p < 0.05$.

RESULTS

Nucleotide sequences of *IGHV* genes from 47 CLL patients (11.4%) met the specified stereotypy criteria.

Homology between CLL Ig sequences and antibodies directed against autoantigens was found in 12 patients (2.9%), between CLL Ig sequences and antiviral antibodies was found in 35 patients (8.5%) (Suppl. Table)*. Among CLL Ig sequences directed against autoantigens the most prevalent were cases homologous with antibodies against cardiolipin (six cases, all UM and belonged to subset #6). Other specificities included antibodies produced by B cells in myasthenia gravis patients (four cases: UM, subset #9D1; M, subset #201; M, subset #148A; UM, subset #19A), antibodies produced by B cells in Sjogren's syndrome (one case, UM, subset #V1-69|J3.4.6|16|6) and in Wegener disease (one case, UM, subset #10).

CLL cases, which showed homology with Ig from HIV-positive persons (14 cases) and anti-SARS-CoV-2 antibodies (10 cases), prevailed among sequences directed against viral antigens. Anti-HIV antibodies homologous to CLL Ig were derived mostly from B cells expressing the transcription factor T-bet in infected individuals with chronic viremia (9 of 14 cases) [14]. Anti-SARS-CoV-2 antibodies homologous to CLL Ig have been characterized in COVID-19$^+$ patients (7 cases) and in vaccinated individuals (3 cases) (Table). Besides that, four CLL Ig sequences had homology with anti-HCV (hepatitis C virus) antibodies, three of them also showed homology with anti SARS-CoV-2 antibodies. Six CLL Igs showed homology with antibodies of donors after influenza vaccination (one case also showed homology with anti-SARS-CoV-2 antibodies and one case with anti-HIV antibody). Homology of other specificity was found in single patients (anti-respiratory syncytial virus — two cases; anti-rotavirus — two cases, anti-rabies and anti-yellow fever 17D vaccine — one case each).

The autoantigen-directed CLL Igs sequences were mostly UM (83.3%, *vs* 67.7% in whole cohort; $p = 0.198$) and all belonged to stereotyped subsets (100% *vs* 48.9% in whole cohort; $p = 0.0001$). CLL Igs sequences homologous to antiviral antibodies did not differ in mutational status of *IGHV* genes from the whole cohort of patients ($p = 0.32$), but also mostly belonged to stereotyped subsets (80% *vs* 48.9% in whole cohort; $p = 0.001$). Three of the six cases of cluster #2, identified in our cohort, had homology with anti-SARS-CoV-2 antibodies.

The frequency of *IGHV1* family genes expressing cases was higher among the autoantigen-directed *IGHV* CLL Ig sequences compared to CLL Ig sequences homologous to antiviral antibodies (66.7% *vs* 11.4%; $p = 0.00015$) and the whole CLL cohort (66.7% *vs* 33.5%; $p = 0.017$). The frequencies of *IGHV3* family genes expressing cases was higher among the CLL sequences homologous to antiviral antibodies compared to autoantigen-directed *IGHV* CLL sequences (57.1% *vs* 8.3%; $p = 0.0033$), but did not differ from the whole cohort of patients *IGHV3-15* (57.1% *vs* 41.7%; $p = 0.132$) (Figure).

DISCUSSION

IGHV sequences from CLL patients, which showed homology with anti-autoantigen antibodies, were found in 2.9% cases. All these cases belonged to stereotyped subsets (the most indisputable was the homology of cases belonged to cluster #6 with antibodies against cardiolipin). However, in this group we did not find cases of subset #1, which according to data of some authors showed reactivity with antigens of apoptotic cells, vimentin, calreticulin in functional tests [22, 23]. Therefore, taking into account all obtained data, it seems likely that CLL Ig sequences are more often directed against self-antigens.

Among the sequences that have homology with antiviral antibodies, of greatest interest are CLL cases, with Ig similar to antibodies against HIV and SARS-CoV-2 antigens. None of the patients in our cohort was HIV-infected, and the study was conducted before the emergence of the SARS-CoV-2 virus. Previously, Hwang *et al*. [24] showed in ELISA test the reactivity of *IGHV1-69* CLL Ig with HIV-1 envelope gp41 as well as antigens of influenza, hepatitis C virus E2 protein and intestinal commensal bacteria. They concluded that B-CLL cell population is an expansion of members of the innate polyreactive B cell repertoire with reactivity to a number of infectious agent antigens. This assumption is also supported by our data, namely, the homology of some CLL Ig sequence not only with antibodies against SARS-CoV-2 virus, but also with antibodies directed against antigens of influenza and hepatitis C viruses. Kim *et al.* [25] observed stereotyped neutralizing antibodies against SARS-CoV-2 spike protein receptor binding domain in COVID-19 patients and in healthy persons. The authors suggested that the population of naive B-lymphocytes with a certain configuration of the BCR exist in healthy individuals, which subsequently may provide protective immunity against viral infections.

Our data allow us to speculate that such naive lymphocytes may often become targets for malignant transformation in B-CLL. The incidence of CLL in our cohort homologous with anti-HIV antibodies was 3.4%, and with anti-SARS antibodies — 2.4%. Most of these sequences (80% cases with homology to anti-SARS-CoV-2 antibodies and 71.4% cases with homol-

*The supplementary materials are posted at https://www.researchgate.net/profile/Chumak-Anatolii

Table. Characteristics of CLL cases with homology to anti-SARS-COV-2 antibodies

Sequence, GenBank N, IGHV_IGHD (RF)_IGHJ_mutational status_ stereotyped subset	HCDR3	% of homology within the HCDR3 of CLL and anti-SARS-Cov-2 sequences	Characteristics of anti-SARS-Cov-2 antibodies
MW458616 3-53*01_short_6*02_M	ARDAYGMDV		Convalescent; virus neutralizing; binding with RBD, hACE2 competitive [15]
CLL: EU814964, 3-21*01/02_short_6*02_M_#2	ARDANGMDV	88.8	
CLL: FJ694872, 3-21*01/02_short_6*02_M_#2	ARDANGMDV	88.8	
CLL: EF407838, 3-21*01/02_short_6*02_M_#2	VRDANGMDV	77.7	
MW806142, 1-46*01_3-3*01(2RF) _4*02_UM	ARSPYYDFWSGYHYYFDY		COVID-19+ patient; non-neutralizing [16]
CLL: GU358672, 7-04-1*02_3-3*01(2RF) _4*02_UM_ #V1|J5|18|3	AEVPYYDFWSGYSYAFDI	72.2	
MW293188, 1-2*02_3-22*01(2RF) _4*02_M	AKSPYYYDSSGYLGGFDY		Convalescent, without clarification [17]
CLL: EF407822, 1-58*01_3-22*01(2RF) _4*02_UM_ #V5-51|J4|18|2	AASPYYYDSSGYYSRFDY	77.8	
MW458229, 5-51*01_5-18*01(3RF) _6*02_M	ARLSRGYNYGAYYYYGMDV		Recovering patient; virus neutralizing; binding with RBD, non-hACE2 competitive [15]
CLL: GU358657, 1-69*13_5-24*01(3RF) _6*02_UM	AREGDGYNYGYYYYYGMDV	78.9	
7LJR_S	ARADYYYDSSGYFFDY		Fab fragment of SARS-CoV-2 neutralizing antibodies from COVID-19+ patient; binding with RBD: hACE2 competitive [18]
CLL: EF175440, 4-59*01_3-22*01(2RF) _4*02_UM	ARARYYYDSSGYYFDY	87.5	
MW926465, 3-30*04_3-22*01(2RF) _4*02_M	ASDSSGWYYFDY		After vaccination; non-neutralizing, binding with S2 domain [19]
CLL: EU350426, 3-66*01_3-22*01(2RF) _4*02_M_#73	ARDSSGYYYFDY	83.3	
MZ555540, 3-7*01_3-22*01(2RF) _3*02_M	ARDPYARGGYGAFDI		After vaccination, without clarification [20]
CLL: EF441757, 3-7*01_3-22*01(2RF) _3*02_M_ # V3|J3.4|15|40	ARDPYGSGGYGAFDI	86.7	
MZ292501, 3-20*04_6-13*01(2RF) _4*02_UM	ARGTGAADY		Monoclonal antibodies from single-cell-sorted S-binding germinal centre B cells after vaccination; virus neutralizing; cross-reactive with seasonal beta-coronaviruses OC43 and HKU1 [21]
CLL: EF4078433, 3-48*03 6-13*01(2RF) _4*02 UM #93	ARGTGAGDN	77.7	

Notes: RBD – receptor binding domain; hACE2 – human angiotensin-converting enzyme 2.

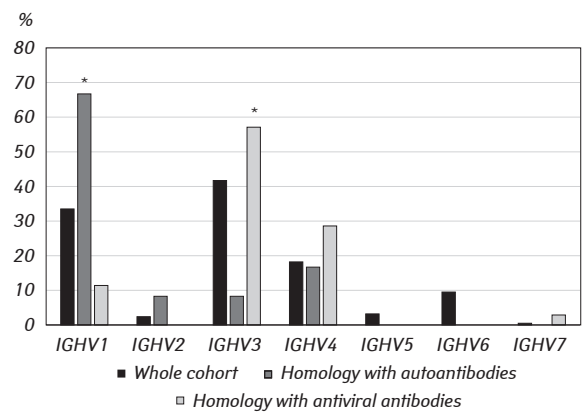

Figure. The distribution of IGHV gene families among observed CLL patients

*Differences between subgroups are significant in chi-square test ($p < 0.05$).

ogy to anti-HIV antibodies) belonged to stereotypical clusters, which indicates their increased frequency compared to heterogeneous *IGHV* cases in various patient groups. In addition, the frequency of some stereotyped clusters is significantly higher in other examined CLL cohorts compared to our CLL group. First, this concerns cases of cluster #2, half of which, according to our data, had homology with anti-SARS-CoV-2 antibodies. The frequency of cluster #2 was only 1.45% in our group compared to 2.51% in the joint European-American CLL cohort [13]. A detailed analysis of Agathangelidis's data showed that in some countries the frequency of cluster #2 was higher. The highest frequencies of subset #2 were observed in the UK (5.07%), the Netherlands (4.67%), Sweden (4.43%), and in northern Germany (4.17%) [13].

SARS-CoV-2 virus infection is widespread throughout the world. By March 2022, the number of infected cases rose to 520,372,492 persons [27]. Persistence of cells directed against coronavirus antigens was shown in the work of Turner *et al.* [21]. They characterized B cells (MZ292501) that targeted the receptor-binding domain of the S protein and also cross-reactive with seasonal coronaviruses OC43 and HKU1. This case showed homology to CLL Ig sequence EF4078433 in our study. The authors concluded that such cells initially directed against the antigens of seasonal coronaviruses can persist in the lymph nodes and become activated during SARS-CoV-2 virus infection [21]. In this regard, it is possible that SARS-CoV-2 virus infection may contribute to the activation and persistence of B cell precursors that are predisposed to their subsequent oncological transformation in CLL. Therefore, in our opinion, an increase in the proportion of CLL cases with the expression of some stereotyped BCR and/or an increase of CLL risk in the long-term period after SARS-CoV-2 virus infection could not be excluded. A similar idea about a possible increase in the risk of developing various oncohematological diseases in the persons who suffered from COVID-19 was expressed earlier by Gluzman *et al*. [28, 29]. This assumptions needs to be verified by epidemiological data.

ACKNOWLEDGEMENTS

The authors express their sincere gratitude to Mr. Thomas Harms, the president of the Charitable Organization "KiHeV-Kinderhilfe Kiew e.V" for his help in acquiring the reagents. The idea to assess the homology of nucleotide sequences in CLL patients with sequences directed against anti-SARS-CoV-2 antibodies was largely inspired by Prof. D.F. Gluzman. The work was performed with the financial support of the National Academy of Medical Sciences of Ukraine, state registration № 0120U100749.

REFERENCES

1. **Tobin G, Thunberg U, Johnson A, *et al***. Chronic lymphocytic leukemias utilizing the VH3-21 gene display highly restricted Vlambda2-14 gene use and homologous CDR3s: implicating recognition of a common antigen epitope. Blood 2003; **101**: 4952–7. doi: 10.1182/blood-2002-11-3485

2. **Ghiotto F, Fais F, Valetto A, *et al***. Remarkably similar antigen receptors among a subset of patients with chronic lymphocytic leukemia. J Clin Invest 2004; **113**: 1008–16. doi: 10.1172/JCI19399.

3. **Messmer BT, Albesiano E, Efremov DG, *et al***. Multiple distinct sets of stereotyped antigen receptors indicate a role for antigen in promoting chronic lymphocytic leukemia. J Exp Med 2004; **200**: 519–25. doi: 10.1084/jem.20040544

4. **Agathangelidis A, Darzentas N, Hadzidimitriou A, *et al***. Stereotyped B-cell receptors in one-third of chronic lymphocytic leukemia: a molecular classification with implications for targeted therapies. Blood 2012; **119**: 4467–75. doi: 10.1182/blood-2011-11-393694

5. **Chiorazzi N, Ferrarini M**. Cellular origin(s) of chronic lymphocytic leukemia: cautionary notes and additional considerations and possibilities. Blood 2011; **117**: 1781–91. doi: 10.1182/blood-2010-07-155663.

6. **Kostareli E, Gounari M, Agathangelidis A, Stamatopoulos K**. Immunoglobulin gene repertoire in chronic lymphocytic leukemia: insight into antigen selection and microenvironmental interactions. Mediterr J Hematol Infect Dis 2012; **4**: e2012052. doi: 10.4084/MJHID.2012.052.

7. **Rai KR, Sawitsky A, Cronkite EP, *et al***. Clinical staging of chronic lymphocytic leukemia. Blood 1975; **46**: 219–34.

8. **Rai KR**. A critical analysis of staging in CLL. In: Gale RP, Rai KR, eds. CLL recent progress and future directions, vol. 59. UCLA Symposia on Molecular and Cellular Biology. New York: Alan R. Liss; 1987. 253 p.

9. **Binet JL, Auquier A, Dighiero G, *et al***. A new prognostic classification of chronic lymphocytic leukemia derived from a multivariate survival analysis. Cancer 1981, **48**; 198–206. doi: 10.1002/ 1097-0142(19810701) 48:1<198::aid-cncr2820480131>3.0.co;2-v

10. **Abramenko I, Bilous N, Chumak A, *et al***. Chronic lymphocytic leukemia patients exposed to ionizing radiation due to the Chernobyl NPP accident--with focus on immunoglobulin heavy chain gene analysis. Leuk Res 2008; **32**: 535–45. doi: 10.1016/j.leukres.2007.08.013

11. **Hamblin TJ, Davis Z, Gardiner A**, ***et al***. Unmutated Ig V(H) genes are associated with a more aggressive form of chronic lymphocytic leukemia. Blood 1999; **94**: 1848–54. PMID: 10477713

12. **Damle RN, Wasil T, Fais F, *et al***. Ig V gene mutation status and CD38 expression as novel prognostic indicators in chronic lymphocytic leukemia. Blood 1999; **94**: 1840–7. PMID: 10477712

13. **Agathangelidis A, Chatzidimitriou A, Gemenetzi K, *et al***. Higher-order connections between stereotyped subsets: implications for improved patient classification in CLL. Blood 2021; **137**: 1365–76. doi: 10.1182/blood.2020007039

14. **Austin JW, Buckner CM, Kardava L, *et al***. Overexpression of T-bet in HIV infection is associated with accumulation of B cells outside germinal centers and poor affinity maturation. Sci Transl Med 2019; **11**: eaax0904. doi: 10.1126/scitranslmed.aax0904

15. **Sakharkar M, Rappazzo CG, Wieland-Alter WF, *et al***. Prolonged evolution of the human B cell response to SARS-CoV-2 infection. Sci Immunol 2021; **6**: eabg6916. doi: 10.1126/sciimmunol.abg6916

16. **Jennewein MF, MacCamy AJ, Akins NR, *et al***. Isolation and characterization of cross-neutralizing coronavirus antibodies from COVID-19+ subjects. Cell Rep 2021; **36**: 109353. doi: 10.1016/j.celrep.2021.109353

17. **Wang Z, Lorenzi JCC, Muecksch F, *et al***. Enhanced SARS-CoV-2 neutralization by dimeric IgA. Sci Transl Med 2021; **13**: eabf1555. doi: 10.1126/scitranslmed.abf1555.

18. **Li D, Edwards RJ, Manne K, *et al***. In vitro and in vivo functions of SARS-CoV-2 infection-enhancing and neutralizing antibodies. Cell 2021, 1**84**:4203–19.e32. doi: 10.1016/j.cell.2021.06.021

19. **Amanat F, Thapa M, Lei T, *et al***. SARS-CoV-2 mRNA vaccination induces functionally diverse antibodies to NTD, RBD, and S2. Cell 2021; **184**: 3936–48.e10. doi: 10.1016/j.cell.2021.06.005

20. **Chen EC, Gilchuk P, Zost SJ, *et al***. Convergent antibody responses to the SARS-CoV-2 spike protein in convalescent and vaccinated individuals. Cell Rep 2021; **36**: 109604. doi: 10.1016/j.celrep.2021.109604

21. **Turner JS, O'Halloran JA, Kalaidina E, *et al***. SARS-CoV-2 mRNA vaccines induce persistent human germinal centre responses. Nature 2021; **596**: 109–13. doi: 10.1038/s41586-021-03738-2

22. **Chu CC, Catera R, Zhang L, *et al***. Many chronic lymphocytic leukemia antibodies recognize apoptotic cells with exposed nonmuscle myosin heavy chain IIA: implications for patient outcome and cell of origin. Blood 2010; **115**: 3907–15. doi: 10.1182/blood-2009-09-244251

23. **Binder M, Lechenne B, Ummanni R, *et al***. Stereotypical chronic lymphocytic leukemia B-cell receptors recognize survival promoting antigens on stromal cells. PLoS One 2010; **5**: e15992. doi: 10.1371/journal.pone.0015992

24. **Hwang KK, Trama AM, Kozink DM, *et al***. IGHV1-69 B cell chronic lymphocytic leukemia antibodies cross-react with HIV-1 and hepatitis C virus antigens as well as intestinal commensal bacteria. PLoS One 2014; **9**: e90725. doi: 10.1371/journal.pone.0090725

25. **Que X, Widhopf GF 2nd, Amir S, *et al***. IGHV1-69-encoded antibodies expressed in chronic lymphocytic leukemia react with malondialdehyde-acetaldehyde adduct, an immunodominant oxidation-specific epitope. PLoS One 2013; **8**: e65203. doi: 10.1371/journal.pone.0065203

26. **Kim SI, Noh J, Kim S, *et al***. Stereotypic neutralizing V_H antibodies against SARS-CoV-2 spike protein receptor binding domain in patients with COVID-19 and healthy individuals. Sci Transl Med 2021; **13**: eabd6990. doi: 10.1126/scitranslmed.abd6990

27. WHO (World Health Organization). Coronavirus (COVID-19) dashboard. https://covid19.who.int/. Updated on 7:41pm CEST, 18 May 2022. Accessed 19 May 2022.

28. **Gluzman DF, Zavelevich MP, Philchenkov AA**, ***et al***. Long-term exposure to low doses of ionizing radiation and COVID-19 pandemic: oncohematological aspects. Exp Oncol 2021; **43**: 189–92. doi: 10.32471/exp-oncology.2312-8852.vol-43-no-2.16434

29. **Gluzman DF, Zavelevich MP, Philchenkov AA, *et al***. Immunodeficiency-associated lymphoproliferative disorders and lymphoid neoplasms in post-COVID-19 pandemic era. Exp Oncol 2021; **43**: 87–91. doi: 10.32471/exp-oncology.2312-8852.vol-43-no-1.15795

ЕКСПРЕСІЯ ПОСЛІДОВНОСТЕЙ ІМУНОГЛОБУЛІНІВ З ГОМОЛОГІЄЮ ДО АНТИТІЛ ПРОТИ ВІРУСІВ SARS-CoV-2 ТА ВІЛ У ВИПАДКАХ ХРОНІЧНОЇ ЛІМФОЦИТАРНОЇ ЛЕЙКЕМІЇ

І.В. Абраменко, Н.І. Білоус, А.А. Чумак, З.В. Мартіна, І.С. Дягіль, Д.А. Базика

Національний науковий центр радіаційної медицини Національної академії наук України, Київ 03115, Україна

Стан питання: Ідентифікація епітопів, які розпізнають лейкемічні клітини, є одним з підходів до розкриття молекулярних механізмів трансформації В-клітин при хронічній лімфоцитарній лейкемії (ХЛЛ). ***Мета роботи***: Провести порівняння нуклеотидних послідовностей генів варіабельних ділянок важких ланцюгів імуноглобулінів (*IGHV*) при ХЛЛ з відомими послідовностями, спрямованими проти антигенів різного походження, доступними у відкритих базах даних. ***Матеріали та методи***: Аналіз проводився в групі 412 хворих на ХЛЛ з продуктивним *IGHV* реаранжуванням з використанням полімеразної ланцюгової реакції та наступним прямим секвенуванням. ***Результати***: Гомологія між імуноглобуліновими (Ig) послідовностями хворих на ХЛЛ і антитілами, спрямованими проти автоантигенів, виявлена у 12 хворих (2,9%), з противірусними антитілами — у 25 (8,5). Більшість гомологічних ХЛЛ Ig послідовностей належала до стереотипних кластерів. Серед ХЛЛ Ig послідовностей, що мали гомологію з противірусними антитілами, найчастіше визначали гомологію з антитілами проти антигенів вірусу імунодефіциту людини (ВІЛ, 14 випадків, 3,4%) та анти-SARS-CoV-2 (10 випадків, 2,4%). Жоден із хворих не був ВІЛ-інфікованим, та обстеження проведено до початку епідемії SARS-CoV-2. ***Висновки***: Висловлено припущення щодо вірогідного внеску перенесеної інфекції SARS-CoV-2 в патогенез ХЛЛ. Не виключено підвищення відносної частки випадків ХЛЛ з експресією окремих стереотипних В-клітинних рецепторів та/або підвищення ризику розвитку ХЛЛ у віддалений період після епідемії SARS-CoV-2. Це припущення потребує перевірки епідеміологічними даними.

Ключові слова: хронічна лімфоцитарна лейкемія, варіабельні ділянки важких ланцюгів імуноглобулінів, антитіла проти SARS-CoV-2.