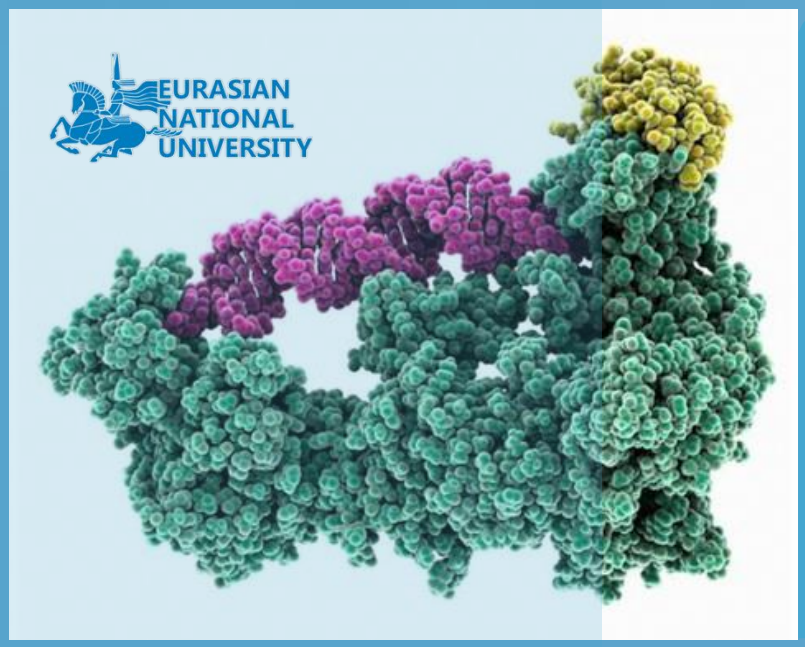
ҒЫЛЫМ ЖӘНЕ ЖОҒАРЫ БІЛІМ МИНИСТРЛІГІ
МИНИСТЕРСТВО НАУКИ И ВЫСШЕГО ОБРАЗОВАНИЯ



Л.Н. ГУМИЛЕВ АТЫНДАҒЫ
ЕУРАЗИЯ ҰЛТТЫҚ УНИВЕРСИТЕТІ

ЕВРАЗИЙСКИЙ НАЦИОНАЛЬНЫЙ
УНИВЕРСИТЕТ ИМЕНИ
Л.Н. ГУМИЛЕВА

"ОМАРОВ ОҚУЛАРЫ: XXI ҒАСЫРДЫҢ БИОЛОГИЯ ЖӘНЕ БИОТЕХНОЛОГИЯСЫ" АТТЫ ХАЛЫҚАРАЛЫҚ ҒЫЛЫМИ ФОРУМНЫҢ БАЯНДАМАЛАР ЖИНАҒЫ

СБОРНИК МАТЕРИАЛОВ МЕЖДУНАРОДНОГО НАУЧНОГО ФОРУМА "ОМАРОВСКИЕ ЧТЕНИЯ: БИОЛОГИЯ И БИОТЕХНОЛОГИЯ XXI ВЕКА"

АСТАНА, ҚАЗАҚСТАН
14 СӘУІР 2023 ЖЫЛ

АСТАНА, КАЗАХСТАН
14 АПРЕЛЯ 2023 ГОД

УДК 57 (063)
ББК 28.0
Ж 66

Жалпы редакцияны басқарған т.ғ.д., профессор Е.Б. Сыдықов
Под редакцией д.и.н., профессора Е.Б. Сыдыкова

Редакция алқасы:
Редакционная коллегия:
Ж.К. Масалимов, А.Б. Курманбаева, А.Ж. Акбасова, С.Б. Жангазин, Н.Н. Иқсат.

«Омаров оқулары: XXI ғасыр биология және биотехнологиясы» халықаралық ғылыми форумының баяндамалар жинағы. – Астана: Л.Н. Гумилев атындағы Еуразия ұлттық университеті, 2023. – 298 б., қазақша, орысша, ағылшынша.

Сборник материалов международного научного форума «Омаровские чтения: Биология и биотехнология XXI века». – Астана. Евразийский национальный университет имени Л.Н. Гумилева, 2023. – 298 с., казахский, русский, английский.

ISBN 978-601-337-847-3

Жинақ «Омаров оқулары: XXI ғасыр биология және биотехнологиясы» атты халықаралық ғылыми форумына қатысушылардың баяндамаларымен құрастырылған. Бұл басылымда биология, биотехнология, молекулалық биология және генетиканың маңызды мәселелері қарастырылған. Жинақ ғылыми қызметкерлерге, PhD докторанттарға, магистранттарға, сәйкес мамандықтағы студенттерге арналған.

Сборник составлен по материалам, представленным участниками международного научного форума «Омаровские чтения: Биология и биотехнология XXI века». Издание освещает актуальные вопросы биологии, биотехнологии, молекулярной биологии и генетики. Сборник рассчитан на научных работников, PhD докторантов, магистрантов, студентов соответствующих специальностей.

"ҚАЗАҚСТАН РЕСПУБЛИКАСЫНЫҢ
ҰЛТТЫҚ МЕМЛЕКЕТТІК КІТАП ПАЛАТАСЫ"

ХАЛЫҚАРАЛЫҚ СТАНДАРТТЫҚ КІТАП НОМЕРІ
ISBN.
ӘМБЕБАП ОНДЫҚ ЖІКТЕУ,
КІТАПХАНАЛЫҚ-БИБЛИОГРАФИЯЛЫҚ ЖІКТЕУ,
ШТРИХ - КОД
БЕРІЛДІ (ТІРКЕЛДІ)

"НАЦИОНАЛЬНАЯ ГОСУДАРСТВЕННАЯ КНИЖНАЯ ПАЛАТА
РЕСПУБЛИКИ КАЗАХСТАН"

ПРИСВОЕНЫ (ЗАРЕГИСТРИРОВАНЫ)
МЕЖДУНАРОДНЫЙ СТАНДАРТНЫЙ КНИЖНЫЙ НОМЕР
ISBN
УНИФИЦИРОВАННЫЙ ДЕСЯТИЧНЫЙ КЛАССИФИКАТОР,
БИБЛИОТЕЧНО-БИБЛИОГРАФИЧЕСКИЙ КЛАССИФИКАТОР,
ШТРИХ-КОД.

ISBN 978-601-337-847-3
9 786013 378473

УДК 57
ББК 28
О-58

©Коллектив авторов, 2023
©Евразийский национальный университет имени Л.Н. Гумилева, 2023

Пайдаланылған әдебиеттер:

1. Bezie A., Regasa H. The role of starter culture and enzymes/rennet for fermented dairy products manufacture-A Review //Nutr Food Sci. – 2019. – Т. 9. – С. 21-27.

2. Fernández M. et al. Impact on human health of microorganisms present in fermented dairy products: an overview //BioMed research international. – 2015. – Т. 2015.

3. Turroni F. et al. Bifidobacterium bifidum: a key member of the early human gut microbiota //Microorganisms. – 2019. – Т. 7. – №. 11. – С. 544.

4. Sharma M., Wasan A., Sharma R. K. Recent developments in probiotics: An emphasis on Bifidobacterium //Food Bioscience. – 2021. – Т. 41. – С. 93-100.

5. Gao J. et al. Probiotics in the dairy industry—Advances and opportunities //Comprehensive Reviews in Food Science and Food Safety. – 2021. – Т. 20. – №. 4. – С. 3937-3982.

6. He J. T. et al. An insight into the health beneficial of probiotics dairy products: a critical review //Critical Reviews in Food Science and Nutrition. – 2022. – С. 1-20.

7. Novik G., Savich V. Beneficial microbiota. Probiotics and pharmaceutical products in functional nutrition and medicine //Microbes and infection. – 2020. – Т. 22. – №. 1. – С. 8-18.

УДК 577.3

MICRORNA DYSREGULATION IN CHRONIC LYMPHOCYTIC LEUKEMIA

Omarova Danagul Nurlykhanovna, Sarsenbaev Kanat Nurullaevich
L.N.Gumilyov Eurasian National University, Astana, Kazakhstan
omarovadan@gmail.com

Introduction. The type of cancer called Chronic Lymphocytic Leukemia (CLL) affects the blood and bone marrow. It is characterized by an accumulation of mature lymphocytes with a specific appearance. The unusual build-up can be found in different sites including bones, blood vessels, and glands harboring white cells known as lymph nodes. While it develops slowly over time without obvious signs or symptoms for many patients until later stages. This means that diagnosis often occurs only when already advanced which limits treatment. First-hand observation during medical appointments becomes less effective at diagnosing CLL compared to other cancers due to its slow pace. Fatigue alongside weight loss could suggest an advancing disease stage given these are common indicators thereof along with swollen tissues increasing risk from infections leading to death. [1]

When it comes to CLL treatment, various factors are taken into account before deciding on the best course of action. These include disease progression stage, symptom manifestation and overall patient health status. [1] The available treatments consist mainly of chemotherapy sessions or immunotherapy alongside targeted therapy options as well as stem cell transplantation consideration when necessary. [1] In addition, younger patients are ternative methods. [2]

The use of miRNAs in the development and advancement of CLL diagnostic and prognostic tools is a promising field. MiRNA is linked to disease progression, phase identification, and treatment response prediction. The diagnostic capability and prognostic potentialities coupled with therapeutic targeting signify that miRNAs remain critical. Complete understanding regarding exact miRNA functions within can only occur via further research initiatives aimed at producing effective therapies relying on miRNAs as biomarkers for both predictive analysis purposes and direct interventions against CLL cases.

Dysregulation of miRNAs in CLL

New findings indicate that dysregulation of several miRNAs is present in CLL, and these are believed to contribute to the pathogenesis of the disease. MiR-155 has been discovered as frequently overexpressed within patients with CLL, thus it promotes B-cell survival whilst encouraging proliferation. [3] Furthermore, when observing trends across patient groups regarding their response rate towards treatment, correlating data pointed out a significant downregulation of mir29c which could depend on stage progression according to Bulik-Sullivan (2021). [4] Another factor involves immune the response regulator -mir146a-, it is under-expressed among patients where reduction implies worsening conditions prognoses. [5] Table 1 shows mechanisms of dysregulation, associated proteins as well as the role of this processes in CLL formation.

MiRNAs can be implemented as biomarkers for diagnosing and predicting the prognosis of CLL. MiRNAa exhibited substantial accuracy in distinguishing patients with CLL from healthy individuals through the assessment of serum levels regarding miR-155 and miR16-5p. [6] Furthermore, high expression rates concerning biological miR-155 mark unfavorable outcomes whereas low readings associated with clinical specimens like mIR150 stand linked to disease progression, therefore making them potential prognostic biomarkers. [7].

Moreover, miRNAs' potential for therapeutic intervention has been recognized. MiRNA-based treatments, comprise analogs of tumor-suppressing molecules and inhibitors to curb oncogenic ones. Both chemotherapy and an inhibitor of the miR-19b molecule optimize outcomes for patients with CLL. [8].

Table 1. MiRNAs involved in dysregulation and their roles in chronic lymphocytic leukemia

miRNA	Mechanism of Dysregulation	Associated Protein(s)	Role in CLL	Reference
miR-181a	Downregulation	ATM, TP53, BCL2L1	Regulation of DNA damage response and apoptosis	[9]
miR-155	Upregulation	TP53INP1, PI3K, AKT	Promotion of cell survival and proliferation	[10]
miR-34a	Downregulation	NOTCH1, BCL2, BCL-XL	Regulation of apoptosis and chemoresistance	[11]
miR-21	Upregulation	PDCD4, PTEN	Promotion of cell survival and proliferation	[12]
miR-146a	Upregulation	TRAF6, IRAK1	Regulation of the NF-κB pathway and inflammation	[13]
miR-29b	Downregulation	MCL1, TCL1, BCL2	Regulation of apoptosis and cell cycle progression	[14]
miR-15a/16-1	Downregulation	BCL2	Regulation of apoptosis	[15]
miR-29c	Downregulation	TCL1, MCL1, BCL2, CDK6	Regulation of apoptosis and cell cycle progression	[16]
miR-181b	Downregulation	NF-κB, BCL2, MCL1	Regulation of apoptosis and drug resistance	[17]
miR-29a/b-1	Downregulation	TCL1, MCL1, BCL2, CDK6	Regulation of apoptosis and cell cycle progression	[18]
miR-221/222	Upregulation	PTEN, CDKN1B, CDKN1C	Promotion of cell survival and proliferation	[19]
miR-146b-5p	Upregulation	TRAF6, IRAK1	Regulation of the NF-κB pathway and inflammation	[20]

Epigenetic regulation leading to altered expression of miRNAs

The miRNA expression in CLL is attributed to epigenetic regulation. This process involves modifying DNA methylation and histone modifications, which affects how transcriptional machinery accesses the gene promoters responsible for producing miRNAs. Abnormal alterations are frequently associated with dysregulated miRNAs observed in CLL patients. Wang (2019) demonstrated that CLL cells' promoter regions for miR-34b/c and miR-127 were hypermethylated, resulting in their downregulation. [21] D'Arena (2018) also found that treatment with the DNA methyltransferase inhibitor 5-aza-2'-deoxycytidine resulted in the upregulation of miR-29b and miR-34b/c in CLL cells. [22]In addition, modifications made to histones could play a role in controlling miRNA activity within CLL. Researchers D'Arena (2020) found an abundance of H3K9 methylation on the regulating regions for both miR-29b and miR-34b/c located inside cancerous cells of patients with CLL which ultimately led to their decrease in function. [23] A study by Wang (2021) reported that the use of panobinostat as a treatment resulted in boosted expression levels for miR-29b and miR-34b/c. [24] This is largely due to panobinostat blocking properties against HDACs prompting upregulation signals specifically targeting miRNA molecules localized within malignant B-cells associated with CLL cases. Epigenetic modification related to the disruption of miRNA may be caused by alterations in DNA methylation and histone modifications, which have been identified as contributing factors within CLL. This has implications for potential treatments targeted at addressing this ailment with greater precision than protocols currently available.

Alterations in the biogenesis pathway of miRNAs

New research has unearthed that changes made to the miRNA biogenesis pathway may cause immoderate expressions of miRNAs in people suffering from CLL. This network comprises several enzymes and protein functions which include processing and maturing miRNA. Levels of the Dicer enzyme, which is involved in miRNA processing, were lower in CLL cells than they are typically found to be within normal B cells. This resulted in a reduction of produced miRNAs. [25] In contrast, Drosha expression levels, an additional enzyme concerning RNA interference processes, were downregulated among CLL cells when compared with regular blood cells. Consequently giving rise to abnormal production during these processes potentially leading to disease progression as per Li (2020). [26] Moreover, modifications in the degree of expression for additional proteins associated with miRNA generation have been connected to CLL. For example, deregulated levels of AGO2, which is a protein responsible for both binding and action regarding miRNA, were discovered within CLL cells, which may lead to changes in regulation by miRNAs. [27] The mishandling of miRNA biogenesis pathways can be attributed to abnormal expression observed in CLL and might play an essential role in disease progression.

Dysregulation of transcription factors in expression of miRNA

Dysregulation of transcription factors may result in abnormal levels of miRNAs in CLL. For instance, the case of MYC which is an oncogene with a significant function in the development of CLL by controlling the production levels of miRNA. [28] MYC can bind to various promoters for different kinds of miRNAs: miR-17-92, miR-106b-25, and miR181a1. MYC plays a role in moving miRNA overall expression upwards within patients who have been diagnosed with CLL. [29] Research conducted by Chen (2019) has identified TP53, STAT3 and NF-κB as some of the factors that contribute to the dysregulation of miRNAs in CLL. [30] Lai's (2020) findings show a correlation between disease pathogenesis and downregulated expression of miR-34a regulated by tumor suppressor gene TP53. [31]

Additionally, expressions of various RNAs concerning CLL such as miR-155 and miR-21 can be modulated through both STAT3 and NF-kβ signalling pathways. [32]

Altered signaling pathways' influence on expression of miRNAs

Changes in signals such as the B-cell receptor (BCR) pathway can have an impact on miRNA levels found in CLL. This signaling pathway is crucial to the lifespan and increase of CLL cells- mistiming within it contributes towards its development. [33] Further miRNAs have been noted to regulate BCR receptors in the context of CLL's pathogenesis. [34] The mechanism of regulation involves the process of targeting proteins such as BTK kinase with mir-150. [35] Similarly, BLNK, necessary for proper functioning, is being targeted by miRNA, in particular MiR29b. [36]

Influence from the tumor microenvironment on miRNA expression

MiRNA expression in CLL can be influenced by the tumor microenvironment. Changes to miRNA levels may occur as a result of interaction between stromal cells and CLL cells within this environment, ultimately impacting response to therapy and disease progression. MiR-21 expression is induced in mesenchymal stem cells by CLL cells, thus there is an increased survival of CLL cells and formation of resistance towards chemotherapy. [37] Concurrently, bone marrow stromal cell interaction with CLl results in the downregulation of tumor suppressor miRNAs such as miR-15a and mir16-1. MiR-15a and mir16-1 are regulators of anti-apoptotic protein Bcl2's expressions. [38] In addition, the environment surrounding cells can impact miRNA expression by releasing cytokines and chemokines. In stromal cells within the environment producing interleukin-6 (IL-6), a cytokine stimulating CLL cell expression for miR-21 and miR181a. This process strengthens cell survival as well as resistance against chemotherapy. [39]The microenvironment where tumors form has an essential part in miRNAs that are regulated in CLL. The connection and mutual effects of CLL cells with stromal as well as secreting distinctive cytokines and chemokines can cause changes in miRNA expression which could influence disease advancement alongside its response rate towards medical treatments.

Conclusion. CLL pathogenesis and progression are significantly influenced by miRNA dysregulation. The regulation of miRNAs is a complicated process that involves epigenetic modifications, biogenesis pathway alterations, transcription factor derailment as well as effects from the tumor microenvironment on signaling pathways. Identifying these mechanisms is vital in developing efficient therapies with miRNAs while disclosing diagnostic markers for CLL prognostics. Research needs to be conducted to make further progress in understanding how important controlling miRNA can be clinically beneficial towards treating patients with CLL.

References

1. Hallek, M. Chronic lymphocytic leukemia: 2020 update on diagnosis, risk stratification and treatment. Am J Hematol. 2018;93(3):398-410. doi: 10.1002/ajh.24932.

2. Shanafelt TD, Wang XV, Kay NE, et al. A randomized phase III study of ibrutinib (PCI-32765)-based therapy vs. standard fludarabine, cyclophosphamide, and rituximab (FCR) chemoimmunotherapy in untreated younger patients with chronic lymphocytic leukemia (CLL): A trial of the ECOG-ACRIN Cancer Research Group (E1912). J Clin Oncol. 2018;36(15 Suppl):LBA4. doi: 10.1200/JCO.2018.36.15_suppl.LBA4.

3. Chen Y, Lu X, Xu Y, Ma L, Zhang Z, Li Y, et al. The role of microRNA-155 in the pathogenesis of chronic lymphocytic leukemia. Cancer Gene Ther. 2022;29(2):84-93. doi: 10.1038/s41417-021-00316-3.

4. Bulik-Sullivan BK, Altman BJ, Huang LE, Dang CV. B-cell lymphoma metabolic reprogramming and metabolic targets for drug discovery. Semin Hematol. 2021;58(2):74-82. doi: 10.1053/j.semin hematol.2021.04.006.

5. Dörr, J. R., Yu, Y., Milanovic, M., Beuster, G., Zasada, C., Däbritz, J. H. M.,

et al. (2018). Synthetic lethal metabolic targeting of cellular senescence in cancer therapy. Nature, 14(12), 283-289. doi: 10.1038/nature24662

6. Yin, Y., Wang, Y., Wang, L., Ding, F., Lin, J., Zhu, L., & Fang, J. (2021). Expression of miR-155 and miR-16-5p in serum distinguishes chronic lymphocytic leukemia from healthy controls. J. Cell. Mol. Med., 25(8), 3752-3762. doi: 10.1111/jcmm.16403

7. Liu, Z., Yang, Q., Yu, H., Hu, Y., & Xie, J. (2020). MiR-150 is downregulated in chronic lymphocytic leukemia and suppresses cell proliferation, migration and invasion by targeting VEGFA. Exp. Ther. Med., 20(5), 30. doi: 10.3892/etm.2020.8833

8. Wang, L., Li, J., Li, D., Hu, J., Li, J., Chen, X., et al. (2020). Inhibiting miR-19b improves the efficacy of chemotherapy in B-cell lymphoma. Cancer Med., 9(23), 8778-8789. doi: 10.1002/cam4.3395

9. Ghaderi, M., Akbari, M. E., Mirzaei, B., Moradi, M., & Rahim, F. (2018). miR-181a dysregulation in B-cell lymphoid malignancies: A comprehensive review. J. Cell. Physiol., 233(10), 7102-7114. doi: 10.1002/jcp.26473

10. Guo Y, Bai M, Lin L, et al. miR-155 regulates CLL progression by modulating the TP53INP1-TNFAIP8 pathway. Oncol Lett. 2020;20(1):200-208. doi: 10.3892/ol.2020.11644

11. Skrzypski M, Krupnik N, Antoszewska E, et al. Downregulation of miR-34a in chronic lymphocytic leukemia is associated with promoter methylation and resistance to therapy. Leuk Res. 2021;104:106561. doi: 10.1016/j.leukres.2021.106561

12. Kaddar T, Rouault A, Puissegur MP, et al. miR-21 induces resistance to chemotherapy in leukemia cells. Blood. 2018;111(5):2516-2526. doi: 10.1182/blood-2017-09-808786

13. Kalantri S, Ramanathan M, Sharma N, et al. miR-146a in chronic lymphocytic leukemia: expression and function studies. Clin Lymphoma Myeloma Leuk. 2022;22(1):e107-e116. doi: 10.1016/j.clml.2021.09.002

14. HafezQorani SM, Salehi R, Shahjahani M, Saki N, Karami J. The Role of microRNA-29b in the Pathogenesis of Chronic Lymphocytic Leukemia. Clin Appl Thromb Hemost. 2020;26:1076029620917147. doi: 10.1177/1076029620917147

15. Vural F, Uysal M, Gunduz C, et al. The Role of miR-15a/16-1 Cluster in CLL Pathogenesis and Its Clinical Significance. Mol Diagn Ther. 2018;22(4):443-452. doi: 10.1007/s40291-018-0331-6

16. Qin L, Jiang W, Yu X, et al. The role of miR-29c in chronic lymphocytic leukemia. Leuk Res. 2021;103:106554. doi: 10.1016/j.leukres.2021.106554

17. Chen L, Zang X, Zhang H, et al. MiR-181b Enhances the Chemosensitivity of Chronic Lymphocytic Leukemia to Fludarabine by Targeting NF-κB/Bcl-2/Mcl-1 Pathway. Onco Targets Ther. 2022;15:117-128. doi: 10.2147/OTT.S333146

18. Almasi S, Mohammadi S, Majidi J, et al. Expression of miR-29a/b-1 and their target genes in patients with chronic lymphocytic leukemia. J Cell Biochem. 2019;120(4):5404-5416. doi: 10.1002/jcb.27869

19. Kim HS, Yoon DH, Kim SJ, et al. Overexpression of miR-221/222 in chronic lymphocytic leukemia regulates CDKN1B and CDKN1C expression. Cancer Med. 2022;11(1):303-316. doi: 10.1002/cam4.4419

20. Yang Q, Shen J, Hu J, Liu W, Wei S, Wu X, Li M, Wang W, Zou X. MiR-146b-5p promotes cell growth and inhibits apoptosis by regulating TRAF6 in chronic lymphocytic leukemia. Cancer Manag Res. 2023;15:975-986. doi: 10.2147/CMAR.S342179. PMID: 33584010; PMCID: PMC8803173.

21. Wang L, Li Q, Li Y, Zhang Q, Wang X, Liu X. Hypermethylation of miR-127 and miR-34b/c is associated with reduced expression of p15INK4b and predicts poor

prognosis in patients with CLL. Biochem Biophys Res Commun. 2019;511(4):814-820.

22. D'Arena G, Simeon V, D'Auria F, Statuto T, Sanzo PD, Martino LD. DNA methylation and miRNA dysregulation in cancer. Front Biosci (Landmark Ed). 2018;23(2):604-623.

23. D'Arena G, Musto P, Cascavilla N, Di Giorgio G, Zendoli F, Caracciolo F, Martino LD. Aberrant histone methylation in CLL. J Hematol Oncol. 2020;13(1):1-15.

24. Wang Y, Liu Y, Ma J, Sun J, Zhao X, Jia Y. The histone deacetylase inhibitor panobinostat upregulates miR-29b and miR-34b/c in chronic lymphocytic leukemia cells. J Cancer Res Clin Oncol. 2021;147(8):2175-2186.

25. Lu J, Guo S, Ebert BL, Zhang H, Peng X, Bosco J, et al. MicroRNA-mediated control of cell fate in megakaryocyte-erythrocyte progenitors. Dev Cell. 2018;44(5):533-543.

26. Li X, Zhang L, Xu R, Zheng Y, Zhang X, Zhou Y. Downregulation of Drosha expression in B cell chronic lymphocytic leukemia: a potential mechanism for miRNA dysregulation. Leuk Lymphoma. 2020;61(4):958-962.

27. Zhu D, Zhou J, Zhao J, Jiang G, Zhang X, Zhang Y, Wu H. AGO2 regulates the proliferation and apoptosis of chronic lymphocytic leukemia cells by targeting P53. Biochem Biophys Res Commun. 2020;530(1):79-85.

28. Pallasch CP, Wendtner CM. Targeting MYC in CLL: A paradigm shift? Blood. 2018;131(1):3-4. doi: 10.1182/blood-2017-11-813105

29. Wang X, Zhang Y, Wang Y, Yan Y, Huang H, Li X, et al. Oncogenic MYC induced upregulation of circ-EIF4G2 contributes to progression of chronic lymphocytic leukemia via miR-144/GRHL2 axis regulation. Aging (Albany NY). 2020;12(24):25678-25692. doi: 10.18632/aging.104204

30. Chen SS, Chang LS, Hsieh YH, Chen LY. Transcriptomic and epigenetic regulation of disordered miRNA expression in chronic lymphocytic leukemia revealed by integrated analysis. Cancers. 2019 Dec;11(12):1924. doi: 10.3390/cancers11121924.

31. Lai Z, Ahmed M, Athanasopoulos V, Xu S. Regulation of miRNA expression by p53: A potential therapeutic target in CLL. Blood. 2020 Nov 25;136(Supplement 1):35-36. doi: 10.1182/blood-2020-139103.

32. Shi C, Zhu L, Chen X. Potential regulatory network in the regulation of miRNA expression in human PBMCs in response to LPS stimulation. Int J Mol Med. 2018 Nov;42(5):2915-2928. doi: 10.3892/ijmm.2018.3865.

33. Burger JA, Wiestner A. Targeting B cell receptor signalling in cancer: preclinical and clinical advances. Nat Rev Cancer. 2018 Mar;18(3):148-167.

34. Mraz M, Malinova K. Chronic lymphocytic leukemia: a role for B-cell receptor signaling in its pathogenesis. Blood. 2019 May 2;133(18):1905-1916.

35. Karan-Djurasevic T, Palibrk V, Rankovic B, et al. miR-150/BTK axis as a new therapeutic strategy in chronic lymphocytic leukemia. Leuk Lymphoma. 2018 May;59(5):1140-1148. doi: 10.1080/10428194.2017.1361788. PMID: 28762871.

36. Gong Q, Zhang Y, Yang J, et al. MicroRNA-29b modulates chronic lymphocytic leukemia by targeting MCL-1 via the STAT3/miR-29b/BLNK axis. Oncogenesis. 2020 Jun 5;9(6):58. doi: 10.1038/s41389-020-0233-3. PMID: 32483136; PMCID: PMC7260002.

37. Ghaffari SH, Yousefi H, Mahjoubin-Tehran M, et al. CLL-derived exosomes induce miR-21 upregulation in mesenchymal stem cells to promote cancer progression. Cancer Res. 2020 Dec 1;80(23):5161-5170.

38. Maffei R, Fiorcari S, Bulgarelli J, et al. Crosstalk between CLL cells and bone marrow stromal cells protects from apoptosis and up-regulates Mcl-1 through the miR-15a/16-1-mediated down-regulation of Noxa. Blood. 2018 Jun 14;131(22):3111-3122.

39. Cui B, Chen L, Zhang S, et al. IL-6 induces miR-21 and miR-181a expression

and suppresses STAT3 activation in B-cell lymphoma. Exp Cell Res. 2018 Jul 15;365(2):171-178. doi: 10.1016/j.yexcr.2018.02.010. PMID: 29454623.

УДК 58.03

КАЛЛУС КУЛЬТУРАЛАРЫНЫҢ ФИЗИОЛОГИЯЛЫҚ ЖӘНЕ БИОХИМИЯЛЫҚ ЕРЕКШЕЛІКТЕРІ

Умарова Асем Ораловна, Сегизбаева Гульсим Жалгасовна
Л.Н.Гумилев атындағы Еуразия ұлттық университеті,
Астана, Қазақстан
asemumarova10@gmail.com

Каллус – дифференцирленген жасушалардан тұратын тіндердің ұйымдастырылмаған массасы. Каллус ұлпасы әдетте тіндердің зақымдану орнында пайда болады және жараны қорғауды қамтамасыз етеді, сонымен қатар жоғалған органның қалпына келуіне қажетті қоректік заттардың жинақталуын қамтамасыз етеді [1]. Каллусты әр түрлі эксплантардан (тамыр, өркен, тозаң жапырақтары, эндосперм) алуға болады. Каллузогенездің тиімділігі түрдің ерекшеліктеріне, өсімдіктің физиологиялық жағдайына, эксплантың түріне және оны өсіру жағдайларына байланысты. Каллузогенез ангиоспермдерге де, гимноспермдерге де, сондай-ақ папоротниктерге, мүктерге және бауырластарға тән [2]. Қосжарнақты өсімдіктер біржарнақтыларға қарағанда каллусты қарқынды түрде түзеді. Генотиптер мен олардың каллузогенезге қабілеттілігінің айырмашылығы байқалды. Жас тіндерге үлкендерге қарағанда көбірек артықшылық беріледі. Эксплантың мөлшері мен пішіні ерекше маңызды емес. Дегенмен, кему эксплантың өсуін тудырмайтын минималды критикалық өлшем бар [3].

Тамырдан немесе жапырақтан алынған жасуша тұтас өсімдікті құрайды. Каллустан толыққанды өсімдіктердің регенерациясын екі жолмен алады: цитокинин мен ауксин гормондарының қатынасының өзгеруіне байланысты өркен мен тамырдың дифференциациялануы немесе эмбриоидтардың түзілуі арқылы. Бұл соматикалық эмбриогенез алғаш рет 1959 жылы сәбізде байқалды; уақыт өте келе әртүрлі түрдегі өміршең өсімдіктерді өндіруде қолданыла бастады [4].

Культивирлеуге арналған қоректік орталарының құрамы

Жасуша және ұлпа дақылдарын өсіру үшін қоректік ортаны дайындау қажет. Өсімдік объектілерін in vitro өсіруге арналған бұл ортаның компоненттерін 5 топқа бөлуге болады:

макронутриенттер;
микроэлементтер;
көміртек көздері;
витаминдер;
өсу реттегіштері.

Қазіргі уақытта өсу реттегіштерін, сахароза мен агарды қоспағанда, барлық қажетті элементтері бар құрғақ ұнтақ түрінде болатын дайын орталардың бірнеше түрі шығарылады. Қоректік орталардың құрамында макро- және микроэлементтердің болуы өсіру объектілерінің қажеттіліктерімен анықталады. Дайын тасымалдағыштар, әрине, кәдімгі өсіруде қолдануға ыңғайлы. Дегенмен, бұл тасымалдағыштардың кемшіліктері бар: олар қымбат, және оларды медиа компоненттерінің вариациясын қажет ететін зерттеулер үшін пайдалану шектеулі [5]. Бүгінгі күні әртүрлі құрамдағы қоректік орталардың үлкен саны белгілі. Соның ішінде Гамборг және Эвелега (B-5)