UDC 577.112.385:579.61:615.37 **https://doi.org/10.15407/biotech18.01.047**

POTENTIAL APPLICATIONS OF *Lactobacillus* CELL COMPONENTS IN THE BIOTECHNOLOGY OF HUMAN LYMPHOBLASTOID INTERFERON

V.V. Pits[1]
O.P. Trokhimenko[2]
V.Yu. Polishchuk[1]
S.O. Soloviov[1, 2]
I.V. Dziublyk[2]
I.M. Fedianovych[3]
Z.F. Kysil[3]
N.A. Bobyr[3]

[1]Igor Sikorsky Kyiv Polytechnic Institute, Kyiv, Ukraine

[2]Shupyk National Healthcare University of Ukraine, Kyiv, Ukraine

[3]Bogomolets National Medical University, Kyiv, Ukraine

E-mail: vadimpitsofficial@gmail.com

Received 2024/12/11
Revised 2025/02/06
Accepted 2025/02/28

Aim. The study aimed to investigate the role of lactobacillus cell components and their effective use in increasing the efficiency of human lymphoblastoid interferon production.

Methods. The study was conducted on the Namalva cell line, a known producer of human lymphoblastoid IFN-α. Newcastle disease virus (NDV) was used as an inducer of interferon production Lactobacillus cell components and metabolites cultured in MRS and its iodine- and Tween-modified variants were evaluated as co-inductors. Macromolecular platinum complexes were used to synchronize Namalva cells in the G1 phase, with synchronization assessed using flow cytometry.

Results. Lactobacillus metabolites grown in MRSjt medium substantially increased interferon production when combined with NDV in synchronized Namalva cultures. The interferon yield increased 16-fold relative to the control. Synchronization of Namalva cells in the G1 phase using macromolecular platinum complex resulted in 96% of cells in the G1 phase, substantially boosting interferon production.

Conclusions. Synchronizing Namalva cells in the G1 phase significantly improved IFN-α production when induced with NDV. The macromolecular platinum complex effectively synchronizes Namalva cells, optimizing interferon production. Lactobacillus metabolites from MRSjt medium serve as cost-effective, natural co-inductors for biotechnological IFN-α production.

Key words: *Lactobacillus* cell components, human leukocyte interferon-alpha, namalva cell line, macromolecular platinum complex.

Human leukocyte interferon (IFN-α) is a type I interferon produced in response to a viral infection as a key signal of the innate immune response with potent antiviral, antiproliferative, and immunomodulatory effects. This cytokine, like other type I interferons, binds to specific receptors on the plasma membrane of almost all cells in the body and is able to affect them [1]. Interferon has species specificity, which means that only human IFN-α is suitable for medical use. It is known that 15 genes and 9 pseudogenes encode natural human IFN-α and are a mixture of many proteins with similar multifunctional properties [1]. Various biotechnological approaches are used to produce it, including isolation from donor blood leukocytes after stimulation

Citation: Pits, V. V., Trokhimenko, O. P., Polishchuk, V. Yu., Soloviov, S. O., Dziublyk, I. V., Fedianovych, I. M., Kysil, Z. F., Bobyr, N. A. (2025). Potential applications of *Lactobacillus* cell components in the biotechnology of human lymphoblastoid interferon. *Biotechnologia Acta*, 18(1), 47–54. https://doi.org/10.15407/biotech18.01.047

with viruses or inducers [2, 3]. The obtained interferon is purified, stabilized, and prepared into dosage forms for medical use: eye drops, ointments, creams, gels, solutions for injection, inhalation forms, and suppositories.

The main therapeutic properties of exogenous IFN-α are antiviral, immunomodulatory, antiproliferative, and antitumor effects. IFN can prevent the initiation of viral matrix RNA translation and destroy viral matrix RNA, enhance the activity of T lymphocytes, macrophages, and NK cells, prevent tumor growth and metastasis, and promote tumor apoptosis. Therefore, leukocyte interferon is used to treat influenza, herpes, hepatitis B and C, etc., both in mono- and complex etiotropic therapy of viral infections. Interferon is also effective in the prevention of viral infections in people at high risk of infection by inducing an antiviral state of cells that are potentially susceptible to the virus [4, 5].

Along with leukocytes, recombinant IFN-α is widely used in clinical practice, which is usually a product of only one human interferon gene, whose DNA is embedded in cells of bacteria, yeast, or other organisms. Such transgenic cells, under controlled conditions, produce the target protein in large quantities, which is then isolated, purified, and prepared for medical use [6].

However, leukocyte and recombinant human interferons have specific differences in terms of the method of production, purity, stability, and the possibility of medical use. For example, leukocyte interferon contains a mixture of different subtypes of interferons and possible impurities from leukocyte proteins that can cause adverse allergic or immune reactions. Recombinant interferon is a homogeneous product containing only one specific subtype of interferon (e.g., interferon-alpha-2a or interferon-alpha-2b), which ensures stability and predictability of their biological action.

Leukocyte interferon may carry a risk of transmitting infections associated with donated blood, although modern purification methods significantly reduce this risk. In addition, the production of leukocyte interferon is very complex, multi-stage, and expensive. In contrast, recombinant interferon is safe against infections because it is synthesized under artificially controlled conditions, does not depend on donor blood, and can be produced in large quantities at lower economic costs.

Due to its natural origin, leukocyte interferon has a wide range of biological effects but can cause variability in results due to heterogeneity of composition. In contrast, the pharmacological effect of recombinant interferon is more specific and predictable, which is essential for clinical use.

Thus, recombinant interferon is a more modern, safe, and controlled option for clinical use. In contrast, leukocyte interferon has a broader spectrum of biological action and multifunctional properties but is less standardized and, therefore, requires careful monitoring of dosage and regimen [7]. Thus, natural and recombinant human IFN-α are not interchangeable drugs, so the development of biotechnologies for the production of natural human interferon is relevant today and requires new approaches and further improvement.

An alternative approach to obtaining natural human IFN-α with a wide range of biological effects is to use transfected cell cultures as producers, stimulate them to produce interferon with viruses or inducers, and then purify and use them for medical use or research. Most often, the Namalwa human lymphoblastoid cell suspension culture is used for this purpose. According to Welcome Research Laboratories (England, 1978), its use is justified for the production of high-activity interferon [8]. In -the analysis of interferon produced by Namalva lymphoblastoid cells, it was shown that about 85% of its total activity is due to leukocyte-type interferon and at least 13% to fibroblast-type interferon [9]. At the same time, the yield of the target product is highly dependent on the concentration of cells in the culture, the composition of the culture medium, the type of viral inducer, and the time of cultivation is also essential. Thus, in a study of the ability of various viruses to stimulate interferon production, it was shown that RNA-genomic viruses, namely measles virus, Newcastle disease virus (NDV), human parainfluenza viruses (types II and III), Semliki forest virus, Sendai virus (SFV) and vesicular stomatitis virus (VSV) are able to stimulate interferon production in Namalwa lymphoblastoid cell culture. This culture has proven to be the best interferon producer [10]. At the same time, when Namalwa is cultivated in serum-free media with a cell concentration

of 3 to 4×10^6 cells/ml, the yield of the target product is up to 10,000 U/ml of interferon upon induction with Newcastle disease virus, strain B1. The maximum accumulation of interferon was obtained approximately 13 hours after induction [11]. Cultivation in serum-free medium indicates that Namalva cell culture did not proliferate during interferon induction, i.e. most of its cells were in the interphase that is most favorable for the reproduction of RNA-genomic viruses, of which Newcastle disease virus is a representative.

In previous studies, we have shown that the reproduction of RNA-genomic viruses in synchronized cell systems is increased relative to the control [12]. At the same time, results showed that lactobacillus components act as co-inducers of interferon production during viral infections in model cell systems [13]. Based on the above and the relevance of developing biotechnological methods for the production of human leukocyte interferon, it is expected that lactobacillus components, as a cheap inducer of natural origin, will contribute to the efficiency of obtaining the target product.

The aim of the study was to investigate the role of lactobacillus cell components and their effective use in increasing the efficiency of human lymphoblastoid interferon production.

Materials and Methods

The objects of the study were filtrates of culture fluids of probiotic strains of lactobacilli *L. delbrueckii* subsp. *lactis LE* and *L. rhamnosus LB3*. The test objects used in the study were the lymphoblastoid suspension cell line of Burkitt's lymphoma Namalwa, substrate-dependent transplantation culture of HEp-2 cells strain Cincinnati, Newcastle disease virus (NDV), vesicular stomatitis virus strain Indiana.

HEp-2 and Namalwa cell cultures, obtained from the cell culture bank of the R.E. Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology of the National Academy of Sciences of Ukraine as cryopreserved samples, were revitalized by the standard method and cultured for three consecutive passages for stabilization.

Substrate-dependent HEp-2 cells were cultured in DMEM medium supplemented with 10% fetal bovine serum and antibiotics (100 U/ml penicillin and 100 µg/ml streptomycin). The quality of cell monolayers was monitored microscopically. The suspension culture of Namalwa cells was maintained in RPMI-1640 medium with 10% fetal serum and antibiotics under standard cultivation conditions.

For interferon induction, Namalwa cell suspensions with at least 85–90% viable cells, determined by trypan blue staining, were prepared. Newcastle disease virus (NDV) and vesicular stomatitis virus (VSV) were used as inducers, with standardized titers and storage conditions. Virus-containing suspensions were aliquoted and stored at 2–8 °C until use.

Lactobacilli were cultured in MRS-based media, including modifications with Tween-80 and iodized water. Structural components (peptidoglycans, teichoic acids, nucleotides, peptides) and exogenous metabolites of lactobacilli were obtained via centrifugation and standardized by protein concentration using the Lowry method.

Synchronization of Namalwa cells in the G1 phase was performed using a macromolecular platinum complex (MPC) at an optimized concentration. Flow cytometry was used to determine the relative number of synchronized cells. The optimal MPC concentration allowed the synchronization of 96% of cells without cytotoxic effects.

Standard laboratory procedures, including cell detachment from the growth surface, washing, and resuspension steps, were performed using established protocols and omitted for brevity to maintain focus on key experimental conditions.

Safety of work

Work with HEp-2 and Namalva cell cultures poses a medium risk to humans, as they are stable cell lines derived from transformed human tissues and blood. According to European Directive 2000/54/EC and WHO [19], VSV and NDV belong to safety group 1, infection with which is very unlikely. Viruses of this group do not pose an individual or public danger. Therefore, work with cell cultures and viruses was carried out in a safety level 1 (BSL-1) laboratory under aseptic conditions in class 2A biological safety cabinets using personal protective equipment. Waste disposal was carried out in accordance with safety requirements in BSL-1 laboratories.

Results and Discussion

As a result of the conducted studies, it was shown that the optimal medium for the cultivation of suspension culture of Namalva cells is RPMI-1640, compared to DMEM, with the addition of 20% conditioned culture medium in the presence of 10% fetal serum. This composition of the nutrient medium allows acceleration of the recovery of the cell pool during the current passage. Also, the optimal for the production of interferon was the use of a suspension at a concentration of 4×10^6 cells/ml. When the concentration of producer cells was reduced or increased, the titers of the resulting interferon decreased, which can be explained by the insufficient number of producer cells in the first case and the decrease in cell viability at high density, and as a result, the inhibition of interferon synthesis — in the second. The obtained results are consistent with the data of the work [20], in which the authors show that it is the concentration of cells (4×10^6 cells/ml) in the suspension that is optimal for the preparative production of human lymphoblastoid interferon. In addition, according to the authors, the high concentration of producer cells does not allow for optimal purification of the target product during its preparative preparation.

The ability of structural components of lactobacilli cells and their exogenous metabolites, when cultivated on MRS medium and its modifications: MRSj, MRSt, and MRSjt, to act as coinductors of interferon production stimulated by NDV was determined. In this case, the study was carried out at an optimal concentration of Namalva cells of 4×10^6 cells/ml. The results are presented in Table 1. It was shown that the structural components of Lactobacillus spp. cells or exogenous metabolites of these lactobacilli grown on MRSjt medium significantly enhance the interferon-inducing effect of NDV in Namalva cell culture, i.e., act as effective coinductors. When they are used, the interferon titers in the target product increase by 8.9 times (up to 3236 U/ml) and 5.7 times (up to 2048 U/ml), respectively, relative to the control (NDV only). At the same time, the most effective coinductive effect of the studied components was observed in the structural elementsof lactobacteria and their exogenous metabolites grown on an MRSjt medium. Thus, those mentioned above biologically active components exhibit a coinductive

Table 1. **Induction of lymphoblastoid interferon with different combinations of interferon production inducers**

Interferon genesis inducers	Average values of interferon titers, U/ml, depending on the concentration of producer cells		
	$1\cdot10^6$ cells/ml	$4\cdot10^6$ cells/ml	$8\cdot10^6$ cells/ml
NDV (Control)	< 2	362	256
NDV + structural components of *Lactobacillus* spp. cells	< 2	3236	2896
NDV + exogenous metabolic products of *Lactobacillus* spp. grown on MRS medium	< 2	1024	512
NDV + exogenous metabolic products of *Lactobacillus* spp. grown on MRSt medium	< 2	1448	1448
NDV + exogenous metabolic products of *Lactobacillus* spp. grown on MRSj medium	< 2	1024	1448
NDV + exogenous metabolic products of *Lactobacillus* spp. grown on MRSjt medium	2	2048	1024
MPC at a final concentration of 0.9×10^{-1} mg/ml	< 2	8	8
MPC at a final concentration of 0.9×10^{-2} mg/ml	2	32	32
MPC at a final concentration of 0.9×10^{-3} mg/ml	< 2	16	4

effect not only upon induction of interferon production *in vitro* by the synthetic inducer ryodostin, which was shown in our previous publication [13], but also upon induction by the NDV, a natural inducer of interferon production.

The ability of MPC at different concentrations to influence the induction of interferon production in Namalva cell culture at the corresponding cell concentrations in suspension was investigated. The results of the studies showed that MPC exhibits weak interferon inducer properties, depending on the final platinum concentration in the producer cell suspension at their optimal concentration (4×10^6 cells/ml), the titers of induced interferon ranged from 8 to 32 U/ml. The highest interferon-inducing ability of this compound was demonstrated at a final concentration of 0.9×10^{-2} mg/ml (32 U/ml) (Table 1). It can be assumed that the stimulation of interferon production by MPC, the general formula of poly{h exakis[chloroaminoaquaplatinum(II)]}-μ-deoxyribonucleate, (chemical formula $[PtCl(NH_3)(H_2O)]_6C_{39}H_{49}O_{32}N_{15}P_{41}$), [21] has weak interferon inducer properties, which are carried out through the exact mechanisms that are known for viruses and viral double-stranded RNA, [22].

The effectiveness of using structural components of lactobacilli cells and lactobacilli metabolites as coinductors of interferon production in response to the induction of human lymphoblastoid IFN-α in synchronized cell culture was investigated.

Previously, the number of cells in different phases of the cell cycle in the Namalva producer culture after its synchronization with the MPC was determined by flow cytofluorimetry on a Partec Pas (Table 2).

It was shown that the most effective induction of interferon using NDV occurred in Namalva, synchronized in the G1 phase of the cycle at a final concentration of MPC of 0.9×10^{-2} mg/ml when 96% of the culture cells were in the G1 phase of the cycle. At the same time, the yield of the target product increased by 2.8 times (from 362 to 1024 U/ml) compared to the induction of interferon using only NDV in a non-synchronized culture, where only 60% of the cells were in the G1 phase of the cycle. However, the use of MPC at a concentration of 0.9×10^{-1} led to a decrease in interferon production by 2.8 times relative to the control (from 362 to 128 U/ml) due to the toxic effect of MPC, which was confirmed by the detection of a significant number of dead cells in the suspension when stained with a mortal dye. Along with this, the use of MPC at a concentration of 0.9×10^{-3} mg/ml led to the synchronization of only 76% of cells in the G1 phase of the cycle, which caused an increase in interferon production induced by NDV-only 2 times (from 362 to 724 U/ml). This can be explained by the insufficient concentration of MPC for synchronization. Thus, the synchronization of producer culture cells in the G1 phase of the cell cycle significantly affects the output of interferon in response to its induction by NDV.

Table 2. **Induction of lymphoblastoid interferon by different combinations of interferon genesis drivers and under conditions of synchronization of the Namalva cell line**

Final concentration of MCP during Namalva synchronization, g/dm^3	**Cell distribution by cycle phases during induction of interferon production**	**IFN-α titers (U/ml) in culture fluid when using NDV and coinductors**		
		NDV	NDV + structural components of lactobacilli cells	NDV + exogenous metabolites of lactobacteria cultured on MRSjt medium
No synchronization	G_1 (60%)	362	3236	2048
	+17%S+23%G_2M)			
0.9×10^{-1}	G_1 (53 %)	128	512	512
	(+28%S+19G_2M) toxicity, few live cells			
0.9×10^{-2}	G_1 (96 %)	1024	512	5793
	(+2%S+2% G_2M)			
0.9×10^{-3}	G_1 (76 %)	724	1218	512
	(+10% S+12 %G_2M)			

However, the most effective induction of IFN-α by NDV in Namalva cell culture synchronized with MPC at an optimal concentration of 0.9×10^{-2} g/l in the G1 phase of the cycle occurred in the presence of a coinducer, which is exogenous metabolites of lactobacteria grown on MRSjt medium. In this case, the yield of the target product increases 16 times (from 362 to 5793 U/ml) compared to NDV induction in an unsynchronized culture (Table 2).

Thus, the conducted studies have shown the effectiveness of using lactobacilli metabolites as coinductors of interferon production in response to viral induction of human lymphoblastoid IFN-α in synchronized cell culture. The conducted studies show that metabolites of lactobacilli grown on MRS medium modified with iodine and tween can be used as a cheap coinductor of interferon production of natural origin in the biotechnology of obtaining human lymphoblastoid interferon, increasing the yield of the target product during viral induction of interferon production in synchronized cell systems.

Conclusions

1. Synchronization of the producer cell culture in the G1 phase significantly affects interferon yield in response to its induction by the Newcastle disease virus. The use of a macromolecular platinum complex with a DNA polyanion at a concentration of 0.9×10^{-2} g/dm^3 allows synchronization of 96% of Namalva cells without toxic effects.

2. Increasing the concentration of the macromolecular platinum complex during Namalva cell culture synchronization is toxic, while a lower concentration is less effective.

3. Metabolites of lactobacilli grown on MRSjt medium are effective co-inducers of interferon production, increasing the production efficiency of human lymphoblastoid interferon 16-fold relative to the control (362 to 5793 U/mL), as confirmed by statistically significant results ($P < 0.05$).

4. Structural components of lactobacilli also exhibit a co-inducing effect, increasing interferon yield 8.9-fold (up to 3236 U/mL) compared to control conditions.

5. The use of lactobacilli metabolites reduces the cost of interferon production and may become an economically viable approach in the biotechnological production of human lymphoblastoid interferon.

Author contributions

Pits V.V. — analysis of results and writing of the article; Soloviov S.O. — development of the research concept; Trokhimenko O.P. — planning the experiment, conducting the study, analysis of the results, and writing the article; Dziublyk I.V. — development of the research concept; Polishchuk V.Yu. —preparation of the experiment, processing of research results; Fedianovych I.M. —conducting the research; Kysil Z.F. — final editing of the article, arrangement of literary sources; Bobyr N.A. — conducting the research. All authors agree with the final version of the manuscript.

The authors declare no conflict of interest.

This article does not contain any human or animal studies conducted by any of the authors.

REFERENCES

1. National Center for Biotechnology Information [Internet]. IFNA1 interferon alpha 1 [Homo sapiens (human)] — *Gene — NCBI*. https://www.ncbi.nlm.nih.gov/gene/3439
2. Rubinstein, M., Rubinstein, S., Familletti, P. C., Miller, R. S., Waldman, A. A., Pestka, S. (1979). Human leukocyte interferon: production, purification to homogeneity, and initial characterization. *Proc. National Acad. Sci*. [Internet]. 1 Feb. 76(2), 640–644. https://doi.org/10.1073/pnas.76.2.640
3. Imanishi, J., Hoshino, S., Matsuoka, H., Kita, M., Kishida, T., Minowada, J. (1982). Production and characterization of human T leukemic lymphoblastoid cell interferon. *Biken. J. Jun*., 25(2), 79–87. PMID: 6182877. https://pubmed.ncbi.nlm.nih.gov/6182877/
4. Viscomi, G. C., Grimaldi, M., Palazzini, E., Silvestri, S. (1995). Human leukocyte interferon alpha: structure, pharmacology, and therapeutic applications. *Med. Res. Rev*. [Internet]. September. 15(5), 445–478. https://doi.org/10.1002/med.2610150504
5. Cantell, K. (1986). Clinical performance of natural human leukocyte interferon.

Immunobiology [Internet]. September. 172(3-5), 231–242. https://doi.org/10.1016/s0171-2985(86)80103-6
6. Production of recombinant interferon proteins WO2009073975A1 https://patents.google.com/patent/WO2009073975A1/en
7. Cantell, K. (1977). Prospects for the clinical use of exogenous interferon. *Med. Biol.* Apr; 55(2), 69–73. PMID: 194114. https://pubmed.ncbi.nlm.nih.gov/194114/
8. Havell, E. A., Vilcek, J. (1972). Production of high-titered interferon in cultures of human diploid cells. *Antimicrob. Agents Chemother* [Internet]. 1 Dec. 2(6), 476–484. https://doi.org/10.1128/aac.2.6.476
9. Havell, E. A., Yip, Y.K., Vilcek , J.(1978). Characteristics of human lymphoblastoid (Namalva) interferon. *J. Gen. Virol.* [Internet]. 1 Jan. 38(1), 51–59. https://doi.org/10.1099/0022-1317-38-1-51
10. Heremans, H., de Ley, M., Volckaert-Vervliet, G., Billiau, A. (1980). Interferon production and virus replication in lymphoblastoid cells infected with different viruses. *Arch. Virol.* [Internet]. Sept. 63(3–4), 317–320. https://doi.org/10.1007/bf01315039
11. Zoon, K. C., Bridgen, P.J., Smith, M. E. (1979). Production of human lymphoblastoid interferon by namalwa cells cultured in serum-free media. *J. Gen. Virol.* [Internet]. 1 Jul. 44(1), 227–229. https://doi.org/10.1099/0022-1317-44-1-227
12. Girin, V. M., Dziublyk, I. V., Trokhymenko, O. P., Kovalchuk, V. K. (1999). Reproduction of viruses in cell cultures synchronized by macromolecular platinum complexes. *Microbiol. Journal*. 61(3), 37–45.
13. Soloviov, S., Trokhimenko, O., Polishchuk, V., Pits, V., Vasylenko, V., Vasylenko, Y., Hol, I., Symchuk, A., Kostiuk, O. (2024). *In vitro* modeling of the effect of lactobacillus metabolites on the systemic response of the body in intestinal viral infection. *Innov. Biosyst. Bioeng.* [Internet]. 21 June. 8(2), 38–52. https://doi.org/10.20535/ibb.2024.8.2.306587
14. Lowry, O., Rosebrough, N., Farr, A. L, Randall, R. (1951). Protein measurement with the folin phenol reagent. *J. Biol. Chem.* [Internet]. 193(1), 265–275. https://doi.org/10.1016/s0021-9258(19)52451-6
15. Dziublyk, I. V., Trokhymenko, O. P., Keysevich, L. V. (1997). Method of synchronization of cells in the G1 phase of the cell cycle. Patent No. 24026, Ukraine, MPK6, C12N 5/02; C12N5/00. Bull. *Industrial Property of Ukraine*. No. 4, 31.08.98, 247 p. (In Ukrainian).
16. Drug Directory Compendium [Internet]. (POLYPLATILLENUM*) Active ingredient. https://compendium.com.ua/uk/akt/80/94441/polyplatillenum/.
17. Burleson, F. G., Chambers, T. M., Wiedbrauk, D. L. (1992). Virology: a laboratory manual. *Academic Press*, London, pp 244–246. https://books.google.com.ua/books/about/Virology.html?id=5s3SBQAAQBAJ&redir_esc=y
18. Lei, C., Yang, J., Hu, J., Sun, X. (2020). On the calculation of TCID50 for quantitation of virus infectivity. Virol SIn [Internet]. 26 May. 36(1), 141–144. https://doi.org/10.1007/s12250-020-00230-5
19. Directive 2000/54/EC of the European Parliament and of the Council of 18 September 2000 on the protection of workers from risks related to exposure to biological agents at work (seventh individual directive within the meaning of Article 16(1) of Directive 89/391/EEC) Directive 2000/54/EC of the European Parliament and of the Council of 18 September 2000 on the protection of workers from risks related to exposure to biological agents at work (seventh individual directive within the meaning of Article 16(1) of Directive 89/391/EEC). http://data.europa.eu/eli/dir/2000/54/oj
20. Zoon, K. C., Buckler, C. E., Bridgen, P. J. (1978). Gurari-Rotman D. Production of human lymphoblastoid interferon by Namalva cells. *J. Clin. Microbiol.* [Internet]. Jan. 7(1), 44-51. https://doi.org/10.1128/jcm.7.1.44-51.1978
21. EP 0374267 A1 Platinum (II) derivatives from polyanion of deoxyribonucleic acid, a method for their preparation and a medicinal product with antitumor action based on them / Volchenskova I.I., Maidanevych N.N., Budaryn L.I., Keysevich L.V., Trokhymenko O.P., Shalimov S.O. (*International application PCT WO* 89/11861. https://patentimages.storage.googleapis.com/30/e1/a9/2b4760e4f7a298/WO1989011861A1.pdf
22. Chen, Y., Lin, J., Zhao, Y., Ma, X., Yi, H. (2021). Toll-like receptor 3 (TLR3) regulation mechanisms and roles in antiviral innate immune responses. *J. Zhejiang Univ. Sci. B* [Internet]. July. 22(8), 609–632. https://doi.org/10.1631/jzus.b2000808

МОЖЛИВОСТІ ЗАСТОСУВАННЯ КОМПОНЕНТІВ КЛІТИН ЛАКТОБАКТЕРІЙ В БІОТЕХНОЛОГІЇ ЛІМФОБЛАСТОЇДНОГО ІНТЕРФЕРОНУ ЛЮДИНИ

В.В. Піць[1], *О.П. Трохименко*[2], *В.Ю. Поліщук*[1], *С.О. Соловйов*[1, 2], *І.В. Дзюблик*[2], *І.М. Федянович*[3], *З.Ф. Кисіль*[3], *Н.А. Бобир*[3]

[1]Київський політехнічний інститут ім. Ігоря Сікорського, Київ, Україна
[2]Національний університет охорони здоров'я України імені П. Л. Шупика, Київ, Україна
[3]Національний медичний університет імені О.О. Богомольця, Київ, Україна

E-mail: vadimpitsofficial@gmail.com

Природний і рекомбінантний ІФН-α людини не є взаємозамінними лікарськими засобами, тому розробка біотехнологій отримання природного інтерферону людини є сьогодні актуальною і потребує нових підходів та подальшого вдосконалення. Альтернативним підходом до отримання природного ІФН-α людини з широким спектром біологічної дії є використання перещеплюваних культур клітин як продуцентів, їх стимуляція до продукції інтерферону вірусами або індукторами з подальшим очищенням і використанням у медичній практиці або наукових дослідженнях.

Мета. Дослідження ролі компонентів клітин лактобактерій та ефективного їх застосування для підвищення ефективності отримання лімфобластоїдного інтерферону людини.

Методи. Дослідження проводили із застосуванням клітинної культури Namalva як продуцента лімфобластоїдного інтерферону. Вірус хвороби Ньюкасла використовували як індуктор інтерфероногенезу. Коіндукторами були структурні компоненти клітин та метаболіти лактобактерій, культивованих на модифікованих середовищах MRS. Синхронізацію клітин у G1-фазі здійснювали за допомогою макромолекулярного комплексу платини з поліаніоном ДНК полі{гексакис[хлороаміноаквaплатина(II)]}-μ-дезоксирибонуклеат. Аналіз проводили методом проточної цитофлуориметрії із застосуванням пропідію йодиду.

Результати. Оптимізація складу живильного середовища для клітин Namalva та використання метаболітів лактобактерій, вирощених на середовищі MRSjt, дозволили підвищити продуктивність інтерфероногенезу у 16 разів порівняно з контролем. Найвищі результати були досягнуті при синхронізації 96% клітин культури у G1-фазі, що забезпечувалося застосуванням макромолекулярного комплексу платини у нетоксичній концентрації.

Висновки. Синхронізація клітин культури продуцента у G1-фазі значно впливає на вихід інтерферону у відповідь на його індукцію вірусом хвороби Ньюкасла. Макромолекулярний комплекс платини з поліаніоном ДНК, полі{гексакис[хлороаміноаквaплатина(II)]}-μ-дезоксирибонуклеат у нетоксичній концентрації синхронізує 96% клітин культури Namalva — відомого продуцента лімфобластоїдного інтерферону людини в G1-фазі клітинного циклу. Метаболіти лактобактерій, вирощені на середовищі MRSjt, можуть стати ефективними коіндукторами для біотехнологічного отримання лімфобластоїдного інтерферону людини, підвищуючи його продуктивність та знижуючи витрати на виробництво.

Ключові слова: компоненти клітин *Lactobacillus*, людський лейкоцитарний інтерферон-альфа, клітинна лінія Namalva, макромолекулярний платиновий комплекс.