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LACTOBACILLUS AND *BIFIDOBACTERIUM* INFLUENCE ON THE INDICES OF IMMUNE RESPONSE OF THE ORGANISM SHOWED ON THE EXPERIMENTAL MODEL

It was studied the influence of Lactobacillus and Bifidobacterium on interferonogenesis and functional activity of murine phagocytosis system cells in vivo. It was established that Bifidobacterium Bifidobacterium, Bifidobacterium longum, Lactobacillus acidophilus, Lactobacillus casei and Lactobacillus bulgaricus in vivo had activated the endogenous interferon production proved to be true by essential increase of interferon concentration in murine blood plasma. Lactobacillus acidofillus and Bifidobacterium longum have appeared the most effective inducing agent of both "early" and "late" interferon. These preparation also extended spontaneous and ridostin-induced production of interferon by spleen cells. The probiotic strains of Lactobacillus and Bifidobacterium introduction was accompanied by stimulation of oxygen-depending bactericide and absorbing activity of peritoneal macrophages. Received data testify the obtained composition on the basis of Bifidobacterium longum and Lactobacillus acidophilus is the most perspective for immune correction.

K e y w o r d s: lactobacteria, bifidobacterium, probiotic, interferon, immunity

During the last years humane infectious inflammatory and oncology diseases accompanied by formation of secondary immunodeficiency conditions tend to grow. A perspective direction of purposeful immune correction is used of probiotics and/or prebiotics created on the basis of indigenious normal flora of a gastroenteric path, in particular *Lactobacillus* and *Bifidobacterium* [9, 1, 4, 10, 5]. It is known that probiotic influence on development of cellular and humoral immune response changing variety of production of immune regulating cytokines, first of all Th1-type — interferon-γ and interleukin-2 [1, 8, 3, 2, 5]. Therefore search of *Lactobacillus* and *Bifidobacterium* with immune modulating properties for creation new highly effective probiotics preparations is an actual problem. In connection with the aforesaid it has been laid down for the

aim to define immune modulating properties of *Laktobacillus* and *Bifidobacterium* by investigation of their influence on endogenous interferon production as well as a functional activity of phagocytosis system cells on the murine experimental model.

Materials and methods

There were used freeze-dried *Laktobacillus* and *Bifidobacterium* of different strains: *Bifidobacterium Bifidobacterium* and *Bifidobacterium longum* as well as *Lactobacillus acidofillus*, *Lactobacillus casei* and *Lactobacillus bulgaricus* (Collection of Zabolotny Institute of Microbiology and Virology of NAS, Ukraine). Preparations were separately injected *per os* to mice of line BaLb/c with body mass of about 18-20 g for 4 days once a day. As comparison it was used the official probiotic Lacidofil (Institute Rosell, Canada) *per os* for 4 days once a day and standard interferon inducer ridostin (Vector-Pharm, Russia) was introduced intraperitonealy. The dose of preparations for one mouse was made of: *Bifidobacterium Bifidobacterium* — 100 μg, *Bifidobacterium longum* — 50 μg, *Lactobacillus acidofillus* — 50 μg, *Lactobacillus casei* — 50 μg, *Lactobacillus bulgaricus* — 100 μg, ridostin — 25 μg, lacidofil — 50 μg. Dynamic of interferon production was investigated in blood serum in 6 hours, 1, 3, 6 and 12 days. On the 1st, 3rd, 6th and 12th days the following spontaneous and induced production of interferon by spleen cells was studied. Activity of interferon is defined by microtitration in culture of sensitive cells. Reference preparations of both interferon-α (the international standard B 69/19) and interferon-γ (branch standard) were used. The sample dilution protected 50 % cells from cytopathic action of 100 CTA_{50}/0,1 ml of a test virus (vesicular stomatitis virus, vaccinal strain H) [7] was accepted as interferon titer.

For the 1st, 3rd, 6th and 12th days oxygen-depending bactericide and absorbing activity of peritoneal macrophages was studied using routine methods [7]. While studying the absorbing activity of phagocytes it was calculated the phagocytosis index (PI) — percent of cells in sight of the microscope contained latex particles and phagocytic number (PN) — mean quantity of latex particles which were absorbed by each phagocyte (conventional units (CN)). Oxygen-depending bactericide activity of macrophages was studied in spontaneous reduction test as well as in reduction test with pyrogenal stimulation using nitroblue tetrazolium (NBT-test) cytochemical assay. The percent of cells (among 100) containing dark blue granules of diformazan was calculated in sight of the microscope. The functional reserve (FR, %) defined as a difference between data for spontaneous and stimulated NBT test.

All received data were calculated using the computer program Epi Info (version 6.0) by the variation statistics method supplemented with Student's criterion. In order to estimate the individual indices their mean arithmetic value was taken ± mean error ($M \pm m$).

Results and their discussion

Our results have shown that introduction of *Laktobacillus* and *Bifidobacterium* to mice led to stimulation of endogenous interferonogenesis (tab. 1). However the level and dynamics of interferon synthesis essentially differed depending on strain of *Lactobacteria* as well as *Bifidobacterium*. Among *Lactobacteria* the greatest interferon genesis activity had *Lactobacillus acidophillus*, and among *Bifidobacterium* — *Bifidobacterium longum*. Essential accumulation of interferon in blood serum under the influence of these preparations was observed in 6 hours: an interferon titer increased

Table 1.

Spontaneous production of interferon by spleen cells following the *Laktobacillus* and *Bifidobacterium* introduction

Mice groups	Titer of interferon, $\log_2$ Unit/ml/ period of observation			
	1st day	3rd day	6th day	12th day
Intact (Control)	5,00 ± 0,01	6,00 ± 0,01	5,00 ± 0,01	4,00 ± 0,01
Obtaining of B. longum	7,00 ± 0,01*	7,00 ± 0,01	6,00 ± 0,02	4,00 ± 0,01
Obtaining of B. Bifidobacterium	4,00 ± 0,01	4,00 ± 0,01	3,00 ± 0,01	3,00 ± 0,02
Obtaining of L. acidophilus	7,00 ± 0,04*	7,00 ± 0,01	6,00 ± 0,02	4,00 ± 0,02
Obtaining of L. casei	6,00 ± 0,01	6,00 ± 0,01	4,00 ± 0,01	4,00 ± 0,01
Obtaining of L. bulgaricus	4,00 ± 0,01	5,00 ± 0,01	5,00 ± 0,01	4,00 ± 0,07
Obtaining of lacidofil	5,00 ± 0,01	6,00 ± 0,01	5,00 ± 0,01	3,00 ± 0,01
Obtaining of ridostin	4,00 ± 0,09	6,00 ± 0,01	4,00 ± 0,07	4,00 ± 0,11

Note: *$P < 0,05$ compared with control values.

from 5,30 ± 0,90 $\log_2$ U/ml in the control accordingly to 7,00 ± 0,01 ($P < 0,05$) and 7,00 ± 0,04 $\log_2$ ($P < 0,05$) U/ml. High level of blood serum interferon remained on 1st (accordingly 8,00 ± 0,01 and 7,00 ± 0,01 $\log_2$ U/ml), 3rd (accordingly 9,00 ± 0,05 and 9,30 ± 0,20 $\log_2$ U/ml) and 6th (accordingly 9,00 ± 0,01 and 8,00 ± 0,02 $\log_2$ U/ml) day. Concentration of interferon in blood serum of mice which received *Lactobacillus acidophillus* has appeared increased for 12th day (7,00 ± 0,02 $\log_2$U/ml) too. On the same time following a *Bifidobacterium longum* introduction an interferon titer on the 12th day decreased to control level (4,09 ± 0,06 $\log_2$ U/ml; $P > 0,05$). Under the influence of *Lactobacillus casei* and *Lactobacillus bulgaricus* concentration of serum interferon did not change comparing with control in 6 hours (accordingly 5,00 ± 0,09 and 5,00 ± 0,01 $\log_2$ U/ml) and on 1st day (accordingly 5,30 ± 0,07 and 4,30 ± 0,01 $\log_2$ U/ml), however on 3rd day (accordingly 6,30 ± 0,01 and 7,30 ± 0,05 $\log_2$ U/ml) and 6th (accordingly 6,00 ± 0,01 and 7,00 ± 0,04 $\log_2$ U/ml) the interferon level was seen decreased. In 12 days the interferon level in blood serum of mice received *Lactobacillus casei* or *Lactobacillus bulgaricus*, decreased to control values (accordingly 4,30 ± 0,06 and 4,00 ± 0,03 $\log_2$ U/ml). Following a *Bifidobacterium Bifidobacterium* introduction blood serum interferon titers did not change in 6 hours and on 1st day (accordingly 6,00 ± 0,01 and 4,30 ± 0,10 $\log_2$ U/ml), but increased on 3rd day to 7,30 ± 0,01 $\log_2$ U/ml ($P < 0,05$). On 6th and 12th days the interferon level in blood serum of these mice was seen decreased to control level (accordingly 4,00 ± 0,04 and 4,30 ± 0,06 $\log_2$ U/ml). It is necessary to notice that under the influence of ridostin — the standard inducer of "late" interferon, in 6 hours and on 1st day concentration of blood serum interferon equaled accordingly 5,00 ± 0,01 and 5,60 ± 0,01 $\log_2$ U/ml. Accumulation of its cytokine in blood serum was seen only on 3rd and 6th days: the titers were seen increased to 8,30 ± 0,40 and 7,30 ± 0,50 $\log_2$ U/ml accordingly. For 12 days they did not exceed a control value (4,00 ± 1,00 $\log_2$ U/ml; $P > 0,05$).

It was established that following the introduction of *Bifidobacterium longum* or *Lactobacillus acidophilus* at 1st day ability of splenocytes to produce the interferon spontaneously intensify *in vitro* whereas *Bifidobacterium Bifidobacterium, Lactobacillus casei, Lactobacillus bulgaricus, Lactobacillus lacidophilus* and ridostin did not influence essentially on spontaneous production of interferon by splenocytes *in vitro* (tab. 1).

In reply to the adequate induction the interferon-γ production by spleen cells *in vitro* did not change after introduction of all preparations and interferon-α production was seen increased on 3rd day under the influence of *Bifidobacterium longum* or *Lactobacillus acidophilus* (tab. 2). Interferon-α production by spleen cells did not change following *Lactobacillus casei*, *Lactobacillus bulgaricus*, *Bifidobacterium Bifidobacterium*, lacidofil or ridostin injection.

Our data prove that *Lactobacillus acidophillus* and *Bifidobacterium longum* preparations have appeared effective inducing agent of both "early" and "late" interferon, and also intensify the spontaneous and ridostin-induced interferon production by spleen cells. *Lactobacillus bulgaricus*, *Lactobacillus casei* and *Bifidobacterium Bifidobacterium* induced "late" interferon synthesis as well as standard interferon inducer — ridostin but did not influence on ability of splenocytes to synthesize interferon.

It is shown that following *Laktobacillus* and *Bifidobacterium* introduction functional activity of peritoneal macrophages in particular their oxygen-depending bactericide activity has increased that is confirmed by essential growth of NBT-positive cells number in spontaneous NBT-test. Under the influence of *Bifidobacterium longum, Bifidobacterium Bifidobacterium* or *Lactobacillus acidophilus* oxygen-depending bactericide activity of macrophages increasing was seen on 1st and 6th days and on 12th day following *Bifidobacterium longum* introduction (tab. 3). *Lactobacillus casei* extend quantity of NBT-positive macrophages on 1st and 6th days and *Lactobacillus bulgaricus* — on 1st day. However oxygen-depending bactericide activity of macrophages did not change essentially after lacidofil or ridostin introduction. Under the influence of all studied preparations stimulated NBT-test indices became higher but their FR kept on the control level. *Laktobacillus* and *Bifidobacterium* had stimulating influence on absorbing activity of macrophages. Following *Bifidobacterium longum* introduction PI was seen increased on 1st, 6th and 12th days up to 44,4 ± 2,2, 62,4 ± 1,9 and 60,5 ± 2,5 % accordingly in comparison with 31,5 ± 2,6 % ($P < 0,05$). It was emphasized the tendency of PI to increase on 1st and 6th days (accordingly 4,5 ± 0,2 and 4,3 ± 0,2 conventional U (CU) comparing with 3,1 ± 0,2 CU in control; $P > 0,05$), that index was found out to increase essentially on the 12th day — to 5,7 ± 0,1 CU ($P < 0,05$). Under the influence of *Bifidobacterium Bifidobacterium* the macrophages absorbing activity was stimulated too. PI increased on 1st, 6th and 12th days after its introduction according to 51,9 ± 4,9; 56,0 ± 4,1 and 50,0 ± 3,1 %. However it was established that the PI of macrophages had only tendency to increase: this index on 1st, 6th and 12th days became accordingly 4,5 ± 0,9; 4,0 ± 0,8 and 4,0 ± 1,0 CU. *Lactobacillus acidophilus* also stimulated the phagocytosis activity of macrophages. On 1st, 6th and 12th days following its introduction PI reached accordingly 69,6 ± 2,0; 56,3 ± 1,8 and 57,9 ± 2,7 %. PN on 3rd and 12th days remained at control level (4,2 ± 0,2 and 3,6 ± 0,2 CU accordingly), and on 6th days increased up to 6,7 ± 0,21 CU ($P < 0,05$). Following the *Lactobacillus casei* introduction PN reached 45,7 ± 1,4; 50,1

Table 2.

Production of IFN-α and IFN -γ by spleen cells following the *Laktobacillus* and *Bifidobacterium* introdution in response to adequate induction *in vitro*

Groups of mice observed/time of observation	Interferon production/ period of observation							
	interferon-γ titer, $\log_2$ unit/ml				interferon-α titer, $\log_2$ unit/ml			
	1st day	3rd day	6th day	12th day	1st day	3rd day	6th day	12th day
Intact mice (control)	5,00 ± 0,01	6,00 ± 0,01	3,00 ± 0,01	4,00 ± 0,01	5,00 ± 0,01	6,00 ± 0,01	5,00 ± 0,01	4,00 ± 0,02
Obtaining of B. bifidobacterium	4,00 ± 0,01	4,00 ± 0,01	4,00 ± 0,01	3,00 ± 0,02	4,00 ± 0,01	4,00 ± 0,02	4,00 ± 0,02	3,00 ± 0,01
Obtaining of B. longum	5,00 ± 0,02	6,00 ± 0, 02	4,00 ± 0,01	4,00 ± 0,01	6,00±0,12	8,00 ± 0,01*	5,00 ± 0,20	4,00 ± 0,16
Obtaining of L. acidophilus	5,00 ± 0,01	6,00 ± 0,01	4,00 ± 0,01	4,00 ± 0,03	6,00 ± 0,16	8,00 ± 0,23*	5,00 ± 0,09	4,00 ± 0,06
Obtaining of L. casei	4,00 ± 0,01	4,00 ± 0,01	4,00 ± 0,05	5,00 ± 0,01	5,00 ± 0,08	7,00 ± 0,21	4,00 ± 0,09	3,00 ± 0,01
Obtaining of L. bulgaricus	4,00 ± 0,01	5,00 ± 0,01	4,00 ± 0,01	4,00 ± 0,01	6,00 ± 0,23	7,00 ± 0,16	4,00 ± 0,13	4,00 ± 0,09
Obtaining of lacidofil	5,00 ± 0,01	6,00 ± 0,01	5,00 ± 0,01	4,00 ± 0,01	5,00 ± 0,01	5,00 ± 0,01	4,00 ± 0,01	4,00 ± 0,01
Obtaining of ridostin	4,00 ± 0,09	6,00 ± 0,01	4,00 ± 0,02	4,01 ± 0,03	6,00 ± 0,21	5,00 ± 0,01	4,00 ± 0,01	4,00 ± 0, 01

Note: *$P < 0,05$ compared with control values.

Table *3*.

Oxygen-depending bactericide activity of macrophages following the *Lactobacillus* and *Bifidobacterium* introdution

Groups of mice observed	Values of NBT-test / time of observation								
	Number of NBT- positive cells in spontaneous NBT-test, %			Number of NBT- positive cells in stimulated NBT-test, %			FR, %		
	1st day	6th day	12th day	1st day	6th day	12th day	1st day	6th day	12th day
Intact (control)	42,0 ± 4,3			59,7 ± 1,5			9,9±0,3		
Obtaining of B. bifidobacterium	62,0 ± 3,4*	59,0 ± 5,1*	40,0 ± 3,2	71,4 ± 8,7	60,0 ± 2,1	56,0 ± 5,6	13,2 ± 2,1	10,0 ± 1,7	9,9 ± 3,1
Obtaining of B. longum	70,5 ± 2,3*	60,1 ± 1,6*	57,9 ± 2,0*	75,2 ± 2,1	69,6±1,9	68,4 ± 1,4	10,7 ± 0,3	9,5 ± 0,4	10,5 ± 0,4
Obtaining of L. acidophilus	60,3 ± 1,9*	59,3 ± 1,4*	47,6 ± 1,6	67,1 ± 2,2	68,4 ± 1,8	58,2 ± 1,8	6,7 ± 0,3	9,1 ± 0,2	10,6 ± 0,3
Obtaining of L. casei	55,9 ± 2,6*	52,5 ± 2,9*	48,5 ± 1,4	61,7 ± 1,6	69,6 ± 2,4	57,7 ± 2,3	13,7 ± 0,3	8,5 ± 0,3	9,2 ± 0,3
Obtaining of L. bulgaricus	59,8 ± 1,9*	49,6 ± 2,2	44,3 ± 2,7	68,0 ± 1,2	59,3 ± 2,5	55,0 ± 2,4	8,2 ± 0,5	9,7 ± 0,4	10,7 ± 0,3
Obtaining of lacydofil	35,0 ± 8,7	42,0 ± 4,3	46,0 ± 3,9	39,0 ± 6,6	46,0 ± 5,6	55,0 ± 8,9	8,6 ± 1,1	9,0 ± 2,1	9,0 ± 1,1
Obtaining of ridostin	46,2 ± 1,7	42,2 ± 2,3	39,3 ± 1,9	58,4 ± 2,5	52,6 ± 1,8	47,8 ± 2,4	12,1 ± 0,3	10,4± 0,2	8,5 ± 0,31

Note: *$P < 0,05$ compared with control values.

± 1,3 and 53,2 ± 1,8 % on 3rd, 6th and 12th days respectively. PN on 1st day kept on control level (2,6 ± 0,17 CU), however on 6th and 12th days this index increased up to 5,8 ± 0,2 and 6,9 ± 0,2 CU respectively. Following the *Lactobacillus bulgaricus* introduction PI on 1st, 6th and 12th days increased to 44,4 ± 1,6; 46,4 ± 2,1 and 45,8 ± 1,8 % accordingly. PN on 3rd day (4,4 ± 0,2 CU) kept on the control level, and on 6th and 12th days increased to 6,1 ± 0,2 and 7,3 ± 0,1 CU accordingly. Lacidofil also stimulated absorbing activity of peritoneal macrophages. It was observed PI increase of macrophages on 1st, 6th and 12th days to 47,8 ± 4,3; 53,0 ± 2,9 and 56,0 ± 5,1 % accordingly caused by lacidofil introduction. However PN kept on the control level (accordingly 3,4 ± 0,2; 4,0 ± 1,0 and 5,0 ± 1,1 CU). It is established that ridostin injection did not change phagocytosis activity of macrophages. On 1st, 6th and 12th days PI equaled to 34,6 ± 1,3; 36,7 ± 2,0 and 38,3 ± 1,7 % accordingly and PN was 2,7 ± 0,1; 3,9 ± 0,3 and 4,4 ± 0,2 CU accordingly. So submitting to the influence of *Bifidobacterium Bifidobacterium, Bifidobacterium longum, Lactobacillus acidophilus, Lactobacillus casei* and *Lactobacillus bulgaricus* PI of macrophages increased during the whole term observed as well as phagocyte numbers on 6th day following the *Lactobacillus casei* or *Lactobacillus bulgaricus* introduction and on 12th day after the *Bifidobacterium Bifidobacterium, Bifidobacterium longum, Lactobacillus acidophilus, Lactobacillus casei* or *Lactobacillus bulgaricus* introduction.

Thus our data showed that *Bifidobacterium Bifidobacterium, Bifidobacterium longum, Lactobacillus acidophilus, Lactobacillus casei* and *Lactobacillus bulgaricus in vivo* had stimulated the interferonogenesis and functional activity of phagocytosis system cells. However *Bifidobacterium longum* and *Lactobacillus acidophilus* have appeared to be the most effective. Under their influence both "early" and "late" interferon was produced and also spontaneous and ridostin induced production of interferon by spleen cells increased. *Bifidobacterium longum* and *Lactobacillus acidophilus* had stimulating influence on functional activity of phagocytosis system cells. Therefore it is possible to admit that *Bifidobacterium longum* and *Lactobacillus acidophilus* are the most perspective for development of new probiotic preparations for immune correction.

Conclusions

1. *Bifidobacterium Bifidobacterium, Bifidobacterium longum, Lactobacillus acidophilus, Lactobacillus casei* and *Lactobacillus bulgaricus* have activated endogenous interferon production *in vivo* proved by essential increase of interferon concentration in blood plasma following their introduction to mice. *Lactobacillus acidophillus* and *Bifidobacterium longum* have appeared the most effective both "early" and "late" interferon inducing agents. These preparations also intensified spontaneous and ridostin-induced production of interferon by spleen cells. *Lactobacillus bulgaricus, Lactobacillus casei* and *Bifidobacterium Bifidobacterium* induced "late" interferon production and did not influence on the interferonogenesis activity of splenocytes.

2. Introduction of *Bifidobacterium longum, Bifidobacterium Bifidobacterium, Lactobacillus acidophilus, Lactobacillus casei* or *Lactobacillus bulgaricus* to mice was accompanied by increasing of functional activity of phagocytosis system cells proved by stimulation of oxygen-depending bactericide and absorbing activity of peritoneal macrophages.

3. Creation of new probiotic preparations for immunity correction on the basis of the compositions of *Laktobacillus* and *Bifidobacterium* was studied as a perspective direction of the subsequent researches. As our data testify the composition on the basis of *Bifidobacterium longum* and *Lactobacillus acidophilus* is the most perspective for immune correction.

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ВПЛИВ ЛАКТО- ТА БІФІДОБАКТЕРІЙ НА ПОКАЗНИКИ ІМУНОРЕАКТИВНОСТІ ОРГАНІЗМУ НА ЕКСПЕРИМЕНТАЛЬНІЙ МОДЕЛІ

Реферат

Вивчено вплив лакто- та біфідобактерій на інтерфероногенез та функціональну активність клітин фагоцитарної системи *in vivo*. Встановлено, що *Bifidobacterium Bifidobacterium, Bifidobacterium longum, Lactobacillus acidophilus, Lactobacillus casei* та *Lactobacillus bulgaricus in vivo* мали активуючий вплив на продукцію ендогенного інтерферону, що підтверджувалось суттєвим підвищенням концентрації інтерферону у плазмі крові мишей. *Lactobacillus acidofillus* та *Bifidobacterium longum* виявились найбільш ефективними індукторами як «раннього», так і «пізнього» інтерферону. Ці препарати також посилювали спонтанну та ридостин-індуковану продукцію інтерферону клітинами селезінки. Введення мишам штамів лакто- та біфідобактерій супроводжувалась активацією киснезалежної бактерицидності та поглинальної активності макрофагів черевної порожнини. Отримані дані свідчать, що найбільш перспективною для корекції імунітету є композиція на основі *Bifidobacterium longum* та *Lactobacillus acidophilus*.

К л ю ч о в і с л о в а: лактобактерії, біфідобактерії, пробіотики, інтерферон, імунітет.

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ВЛИЯНИЕ ЛАКТО- И БИФИДОБАКТЕРИЙ НА ПОКАЗАТЕЛИ ИММУНОРЕАКТИВНОСТИ ОРГАНИЗМА НА ЭКСПЕРИМЕНТАЛЬНОЙ МОДЕЛИ

Реферат

Изучено влияние лакто- и бифидобактерий на интерфероногенез и функциональную активность клеток фагоцитарной системы *in vivo*. Установлено, что *Bifidobacterium Bifidobacterium, Bifidobacterium longum, Lactobacillus acidophilus, Lactobacillus casei* и *Lactobacillus bulgaricus in vivo* усиливали продукцию

эндогенного интерферона, что подтверждалось существенным повышением концентрации интерферона в плазме крови мышей. *Lactobacillus acidofillus* и *Bifidobacterium longum* оказались наиболее эффективными индукторами как «раннего», так и «позднего» интерферона. Эти препараты также усиливали спонтанную и ридостин-индуцированную продукцию интерферона клетками селезенки. Введение мышам штаммов лакто- и бифидобактерий сопровождалось активацией кислородзависимой бактерицидности и поглотительной активности макрофагов перитонеальной полости. Полученные данные свидетельствуют, что наиболее перспективной для коррекции иммунитета является композиция на основе *Bifidobacterium longum* и *Lactobacillus acidophilus*.

К л ю ч е в ы е с л о в а: лактобактерии, бифидобактерии, пробиотики, интерферон, иммунитет.