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[1]L.M. Burova, [1]E.P. Korneichuk, [2]A.I. Kushkina, [2]F.I. Tovkach

[1]Danylo Halytsky Lviv National Medical University; 69 Pekarskaia St., Lviv, 790014, Ukraine
[2] Zabolotny Institute of Microbiology and Virology, National Academy of Sciences of Ukraine, 154 Acad. Zabolotny St., Kyiv, GSP, D03680, Ukraine

PLASMID PROFILE, COLICINOGENY AND PHAGE SENSITIVITY AS INDICATORS OF THE DYNAMICS OF *ESCHERICHIA COLI* POPULATIONS IN THE HUMAN GUT

A possibility to use such bacterial phenotypes as plasmid profiles, colicinogeny and phage sensitivity as dynamics indicators of enterobacterial population in the human intestine was considered in the present work. All these three phenotypes, considered together with the type of enterobacterial association and age of the patients may reflect the dynamic state of the individual E. coli population that is currently prevailing in the intestinal microflora. The data on plasmid profile structure, colicinogeny and phage sensitivity indicate to considerable quantitative and qualitative diversity of E. coli genetic elements and the intensive interaction between bacteria in the human gut. This diversity is reflected on the formation of the dynamic population of intestinal bacteria, which obviously depends on the host age. The evaluation of the three above mentioned phenotypes confirmed that the E. coli isolates are closely coordinating with other members of the intestinal microbial association. It is noted that the plasmid frequency increases, the colicin range expands and phage sensitivity decreases in E.coli cells simultaneously with the increase of the number of enterobacterial species in the gut. The dynamics of changes in the biological features was observed among E. coli strains from different age groups of patients. The most significant was high frequency of colicinogenic strains in adult patients and di-associated E. coli containing one large plasmid in the youngest patients with dysbiosis.

K e y w o r d s: intestinal microflora, Escherichia coli, plasmids, colicinogeny, phage sensitivity, enterobacterial association, patient age.

Intestinal microflora is one of the key factors in homeostasis control being in strong mutualistic relations with the host [7]. In humans the normal composition of the intestinal microflora is formed in several stages. The occupation of the human gut by microbes begins within the first hours of life. Recently, it has been shown that the most "favorable" intestinal microflora develops in children, which were born in natural way, were on breast feeding and were not exposed to treatment with antibiotics [18]. The largest fluctuations in the number of the intestinal microorganisms are observed in children at the age under 1 year.

The composition of the intestinal flora is stabilized finally within the first two years of life [8]. Modern molecular techniques have revealed more than 500 species of bacteria living in the human gut, most of which are not cultivated [23]. It is interesting, that the host genotype may take influence on individual features of the bacterial and virus associations in the gut [19, 27]. In general, the intestinal microflora represents one of the most complex econiches, often considered as a separate organ of the human body [17].

Despite the fact that *E.coli* makes up about 1% of the total microbial number of the gut bacteria, it plays an important role in implementing various functions of the intestinal flora. Colicinogeny is one of the most important properties of this bacterium which is significant for the gut health. Colicins are one of the killer factors that bacteria may use to suppress competing microbial species [6], they are essential for establishing normal microflora in children [9] and may be responsible for the rapid invasion [24]. It is also shown that colicins can provoke apoptosis of the cells in the intestinal mucosa [4] and can be involved in the development of Crohn's disease [3]. In addition, colicins can perform the dual role and act both as antibiotics and probiotics [10].

Plasmids as extrachromosomal genetic elements perform diverse functions which increase adaptive capabilities of bacterial cells [22]. At the same time, plasmids may be regarded as a hallmark of a bacterial species and/or a strain because of their physical and functional features. Usually, plasmids of just isolated bacteria have specific genes which are needed for survival in the environment and may be helpful in identification of the infection origin. Plasmids of *E. coli are* directly related to colicinogeny [6] and are often the cause of phage resistance [16] in *E. coli*. The last phenotype – the phage sensitivity of bacterial population – is essential to development and administration of phage therapy products for prophylactics and treatment of bacterial infections [2].

The present research is a continuation of the previous ones [5, 14]. Its aim was to study the plasmids composition, colicinogeny and phage sensitivity of *E. coli* strains isolated from patients with impaired bowel eubiosis, as well as to determine the relations of these phenotypes with the level of dysbiosis and age of the patients. The objects of the study were strains of *E. coli*, isolated from the faeces of patients which were living in the Lviv Region (Ukraine) with suspected intestinal dysbiosis of different etiologies. Dysbiosis was diagnosed based on microbial paysage of patient`s faeces (data not shown). Overall, 94 patients aged between 2 weeks and 57 years were examined for the composition of the association of gut bacteria.

Materials and Methods. *Selection and identification of bacterial isolates*. Identification of opportunistic enterobacterial pathogens was performed by commercial test systems ENTEROtest 24 M and NEFERMtest 24 N (Erba Lachema, Czech Republic), and commonly known differential media for Enterobacteriaceae [1]. In most cases one *E. coli* isolate was collected from each sample. As a result, 94 isolates of *E. coli* were collected and analyzed.

Extraction of plasmid DNA was performed by alkaline lysis method [13] with modifications. *E. coli* isolates were grown on LB-plates overnight at 37 °C. The fresh cells were collected with calibrated loop and carefully suspended in 100 μl of TAE buffer (40 mM Tris-acetate, pH 7.9; 2 mM sodium EDTA). The suspension turbidity corresponded to the optical density at 600 nm of 0.8. Then the cells were mixed with two volumes of the lysis solution (3% SDS; 50mM Tris, pH 12.6). The samples were heated during 60 min at 55 °C in a water bath and carefully mixed with an equal volume of acid phenol with chloroform (1:1). After centrifugation of the mix at 11000g for 5-10 min, the aqueous phase was carefully collected and analyzed for the presence of plasmid DNA. Electrophoretic separation of the plasmid DNA samples was carried out in 0.7%-1% agarose gels in TAE buffer-system, strength 6-10 V/cm during 4-6 hours. The gels were stained with ethidium bromide (1 mg\ml) and visualized in UV. Plasmids F (100 kb), RP4 (54 kb), pBR322 (4.4 kb) from *E. coli*, and pCA25::Tn9 (12 kb) from *Pectobacterium carotovorum* 7/4b [21] served as plasmid size markers.

Colicin production was examined by the stunted antagonism method [20]. The *E. coli* isolates were grown overnight at 37 °C on LB-plates until individual colonies appeared. The single colonies were treated with chloroform vapor for 50 minutes following which the indicator strains were applied by the agar overlay method: 5ml of soft LB (0.5 % agar) containing 0.1 ml of an active indicator bacterium was applied to the solid LB layer. To obtain an active culture the cells were grown for 18 hours with aeration in LB-broth at 37 °C, then the overnight cultures were diluted 1:100 in fresh LB-broth and grown under the same conditions to the concentration 2 x 10^8 cells/ml. The well known laboratory strains of *E.coli* K12 and C600, B^E and CIa belong to groups K, B and C, respectively, they were used as the colicin sensitive indicators [5]. *E. coli* M-17 which is a component of the commercial product "Colibacterin" (Biofarma, Ukraine) was also used as an indicator. The results were estimated after 18 hours of incubation of the plates at 37 °C. If there was a noticeable area of the growth inhibition of the indicator strain around a single colony this *E. coli* isolate was considered as a producer of colicins. The diameter of the inhibition zone was measured in mm. The conditional definition "a broad range of colicin activity " was used for those *E. coli* isolates, which produced the colicins active against three or more indicator strains listed above.

Phage sensitivity of the *E.coli* isolates was evaluated against some sets of coliphages: T4-like bacteriophages - T2, T4, RB43, Lw1 [15], T7-like bacteriophages - T7 and FE44 [25], phage-satellite P4 and F pili-specific bacteriophage MS2. The agar overlay method was also used here. The *E. coli* isolates were used as phage sensitive indicators. After solidification the drops of 5 ml of the phage suspensions which contained 10^8-10^9 PFU/ml were applied to the surface of the two-layer plate. The same phage suspensions dropped on specific phage-sensitive indicator strains of *E. coli* were used as a control.

Sensitivity to antibiotics of some *E. coli* isolates was studied using the paper-discs agar plate method. Results were interpreted as "sensitive" and "resistant" strains of *E. coli*, in accordance with the recommendations for each group of antibiotics. The sensitivity to 19 antibiotics of 7 different groups was established: aminoglycosides (amikacin, gentamycin, kanamycin), fluoroquinolones (gatifloxacin, norfloxacin, ofloxacin, pefloxacin, ceprofloxacin), nitrofurans (furagin, furamag),

cephalosporins of I, II, and III generations (cephalothin, cefuroxime, cefotaxime and ceftriaxone), as well as amoxiclav, chloramphenicol, tetracycline were evaluated.

Analysis of the results. Regardless of the proposed selection criteria (the type of the gut enterobacterial association, the patient's age and presence of family relationships) the plasmid frequency, colicinogeny and phage sensitivity for each group of *E. coli* isolates were evaluated. Plasmid frequency for the strains carrying two or more plasmids (named "polyplasmid strains") or containing one large or one small plasmid (named "monoplasmid strains") was determined among all plasmid carrying *E. coli* isolates in the group. The frequency of large plasmids was also calculated. Among the colicinogenic *E. coli* isolates the frequency of strains with broad range of colicin activity (killing three or more indicators) was determined.

Results. *E. coli* isolates of 94 items were originally selected. From this group 89 *E. coli* strains were selected after the initial screening for the microbial composition of the faeces samples. Five *E. coli* isolates were not included in this group because the normal microbial status of the gut was observed in five cases.

Finally, two groups of *E. coli* isolates were formed: a group of strains isolated from the patients with gut dysbiosis (89 strains) and a group of strains isolated from the patients with gut eubiosis (5 strains). A comparative study of these isolates was performed taking into account such parameters as: plasmid profile and frequency, the ability to produce colicins and phage sensitivity. The analysis also considered the structure of the gut enterobacterial association and age of the patients.

Characteristics of E. coli isolates of patients with gut dysbiosis depending on the type of association of the gut enterobacteria.

When analyzing the number and species composition of the enteric bacteria, we have identified *E. coli* without concomitant enterobacteria in 27% of patients. *E. coli* associated with one species of opportunistic enterobacteria (such as *Klebsiella, Sitrobacter, Pantoea, Enterobacter, Proteus, Providencia* and *Morganella*) were isolated in 39% of the cases, and *E. coli* associated with two or more opportunistic enterobacteria were isolated in 34% of cases. Therefore, the group of dysbiotic *E. coli* strains (n=89) was divided into three subgroups: mono-culture (just *E. coli*), di-association (*E. coli* associated with one opportunistic enterobacteria) and poly-association of enterobacteria (*E. coli* associated with two or more other enterobacteria), respectively (Table 1).

Table 1.

Plasmid frequency, colicinogeny and phage sensitivity of the *E. coli* isolates (n=89) depending on the composition of enterobacterial associations

Frequency of phenotypes	Type of enterobacterial association		
	Monoculture of *E. coli* (n=24; 27%)	Di-association (n=35; 39%)	Poly-association (n=30; 34%)
Plasmid *E. coli* isolates	58%	66%	70%
Poly-plasmid *E. coli* strains*	50%	52%	71%
The isolates carrying large plasmids*	79%	78%	86%
Colicinogenic strains	30%	37%	33%
E. coli isolates producing colicins with broad range of killer activity**	43%	62%	80%
Phage sensitive *E. coli* isolates***	54%	60%	33%

Note: in this Table and Table 2:
* - among all plasmid strains;
** - the «colicins of broad range of killer activity» – those ones which are active on three or more indicator *E. coli* strains;
*** - the «phage sensitive *E. coli* isolate» display phage killer effect or phage plaques on their lawns; see the list of bacteriophages in **Materials and Methods**.

The number of the plasmid carrying *E. coli* isolates (Fig.1) increases in the direction "mono-culture – di-association – poly-association", and is 58, 66 and 70%, respectively (Table 1). In *E. coli* strains isolated from the poly-association the plasmids were found more often than in the two other subgroups (Table 1). Large plasmid frequency in the first two subgroups is similar and is 79% and 78%, respectively, while for the poly-associated *E. coli* isolates the value increases to 86%.

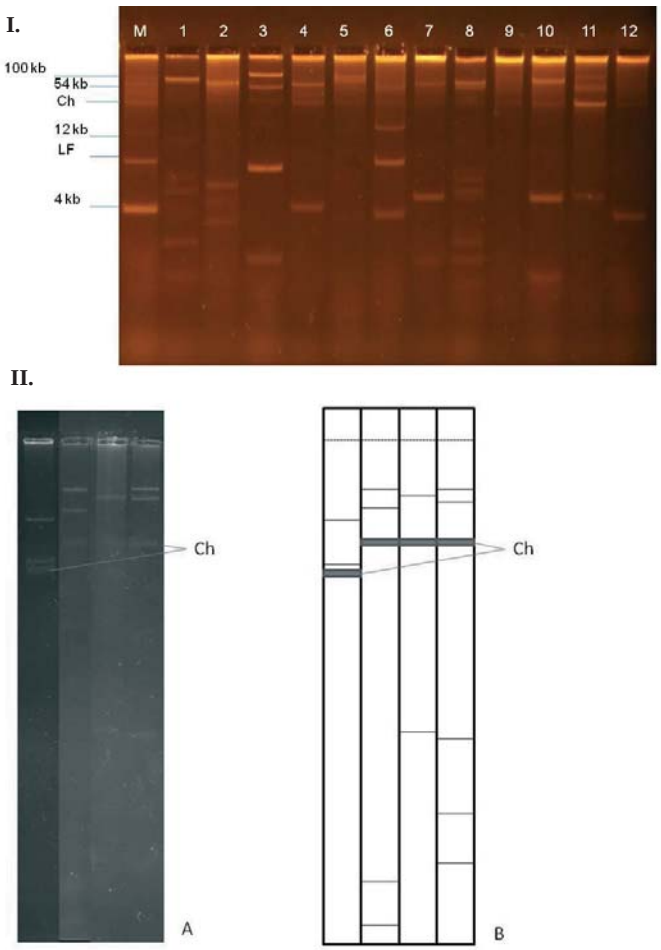

Fig. 1. I. The plasmid profiles of 12 diverse *E. coli* strains isolated from patients with dysbiosis. Electrophoresis in 1% agarose gel, 2 h. II. A. Plasmid profiles of *E. coli* strains isolated from patients with gut eubiosis. Electrophoresis in 0.8 % agarose gel, 4 h. The gel track numbers match to the strain numbers which are pointed out in the Table 4. B. A scheme of localization of small plasmids in the gel. Ch – remnants of bacterial chromosome, LF – linear form of pBR322.

In each of the three sub-groups of *E. coli* strains, based on the type of enterobacterial association, approximately one third of the strains turned out to be colicinogenic (Table 1). However, the range of colicin activity naturally expanded depending on the number of the enterobacterial species. Thus, the number of the *E. coli* strains of the broad range of colicin activity has also increased consistently from *E. coli*, isolated in mono-culture (43%), through *E. coli* from the di-association (62%) to the poly-associated *E. coli* strains (80%).

Phage sensitivity among the *E. coli* strains isolated in the mono-culture and di-association was similar (54% and 60% sensitive strains, respectively). The noticeable decreasing of sensitivity to the phages was detected among strains of *E. coli*, isolated from enterobactrerial poly-association (33%).

Properties of E. coli, isolated from patients of different age groups.

The *E. coli* isolates were also grouped based on the patient age. We were able to identify the three age categories: 1) patients aged from 1 month to 1 year (group I strains, n = 30), 2) patients aged from 1 to 6 years (group II strains, n = 18), 3) adult patients aged from 18 to 45 years (group III strains, n = 25). Thus, the dependence of the type of bacterial association, plasmid diversity, colicinogeny and phage sensitivity of *E. coli* on the age of the patients was analyzed for 73 strains (Table 2).

In pediatric patients (Table 2, group I and II), *E. coli* is most often isolated in association with one additional type of enterobacteria (46 and 50%, respectively). In the group I strains (1 month - 1 year) 36% of *E. coli* isolates were also in poly-association. At the same time, in adult patients (group III strains) *E. coli* was most frequently isolated in the mono-culture and in poly-association (44 and 40%, respectively).

Table 2.

Features of the *E. coli* isolates depending on the patient age

Features	Group I patients 1month-1 year age (n= 30)	Group II patients 1-6 years age (n=18)	Group III patients 18-45 years (n= 25)
Type of enterobacterial association:			
Mono-culture of *E.coli*	17%	22%	44%
Di-association	47%	50%	16%
Poly-association	36%	28%	40%
Plasmid *E. coli* isolates	73%	56%	56%
Poly-plasmid strains*	41%	70%	93%
The strains carrying large plasmids*	73%	90%	86%
Colicinogenic strains	27%	22%	44%
E. coli isolates producing colicins with broad range of killer activity among them **	63%	50%	64%
Phage sensitive *E. coli* isolates***	53%	40%	52%

*, **, *** - see Notes to Table 1.

Plasmid containing *E. coli* isolates were most frequently observed in group I, in the youngest patients (73%). In two other groups a little more than a half of the strains contained plasmids of different sizes. However, in these groups poly-plasmid *E. coli* strains were found more often, whereas in the group I mono-plasmid strains were found in 59% of the cases. The large plasmids (50 kb and more) were detected in most plasmid containing strains in all age groups (73%, 90% and 86%, respectively), and *E. coli* strains containing only small plasmids were rarely detected.

Colicinogenic strains were more often isolated in adult patients (42% of the strains, and 25%, and 26% in children's groups, respectively), but the activity range of colicins did not depend on the age of the patients.

Correlations between phage sensitivity of the *E. coli* isolates and the patient`s age was not observed. About a half of the strains in each group were sensitive to bacteriophages (Table 2).

E. coli isolated from patients with the gut eubiosis.

In five patients, aged from 3 months to 2 years, the intestinal microflora was normal. Five *E. coli* strains were isolated and taken as a comparison group. As it is seen in Fig. 2, four of the five comparison strains contained multiple circular plasmid DNA of various sizes - from 2 to 5 plasmids per cell. The general properties of the strains are presented in Table 3. It should be noted that two of the five reference strains produced colicins, all the five strains were insensitive to the T4-like phages, but sensitive to phages T7 and FE44. Multiple resistance to antibiotics was shown for three of them.

Table 3.

Phenotypes of *E. coli* strains isolated from patients aged from 3 months to 2 years with gut eubiosis.

N	Plasmids[1]	Colicin production[2]	Phage sensitivity[3]	Antibiotic resistance[4]
1	2 (2/0)	–	FE44	3
2	4 (2/2)	–	MS2	11
3	2 (1/1)	+	FE44	–
4	5 (2/3)	+	T7, FE44	16
5	0	–	FE44	–

[1] Here and in Table 4, the common number of plasmids in the strain is pointed out at the front of a parenthesis; the numbers of large and small plasmids, respectively, are pointed out in the parentheses after a slash; 0 – plasmids were not found;

[2] (–) – colicin lysis zones were absent on the lawns of all used indicator *E. coli* strains,
(+) – a colicin lysis zone appeared on at least one indicator strain;

[3] the bacteriophages killing the cells of the *E. coli* isolate as pointed out in the column;

[4] the number of the antibiotics to which the presented E. *coli* isolates are resistant is in the column; there is the list of used antibiotics in **Materials and Methods**; (–) – the test was not done.

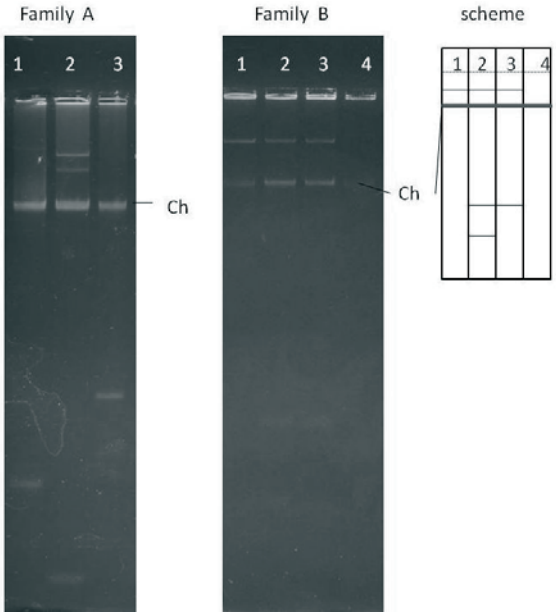

Fig. 2. Plasmid range of relatives living in one family. Family A. 1, 2 – mother, 3 – daughter; Family B. 1 and 2 – twins, brother and sister, respectively, 3 – mother, 4 – father; the scheme – localization of small plasmids. Electrophoresis in 0.8% agarose gel, 4 h.

E. coli isolated from patients living in one family.

There are strains isolated from relatives living in one family in our sample. These strains also appeared very diverse. As it can be seen from Fig. 2, plasmid profiles of "family" strains did not coincide simultaneously for all family members. They could only coincide for the *E. coli* of two relatives of the family consisting of 3 or more persons. However, in this case, colicinogeny and phage sensitivity of those strains could be different (Table 4). In the non-plasmid isolates the biological diversity manifested in sensitivity to phages.

Table 4

The «Family» *E. coli* isolates

Family	Relation-ships	Plasmids[1]	Colicin production[2]	Phage sensitivity							
				T2	T4	RB43	Lw1	T7	FE44	MS2	P4
A	mother	3 (2\1)	-	-	+	-	-	-	-	-	-
	the same	2 (1\1)	-	-	-	+	+	+	+	-	-
	daughter	1 (0\1)	M-17, B^E	-	-	-	-	-	-	+	-
B	mother	2 (1\1)	all	+	-	-	-	-	-	+	+
	sister twin	2 (1\1)	all	-	-	-	-	-	-	-	-
	brother twin	1 (1\0)	-	-	+	-	-	+	+	-	-
	father	0	C600	-	-	-	-	-	+	-	-
C	mother	0	all	-	-	+	-	-	-	+	-
	daughter I	1 (1\0)	-	-	+	-	-	+	+	-	-
	daughter II	0	-	-	-	-	-	-	-	+	+
D	mother	0	-	-	+	+	+	+	+	-	-
	father	0	-	-	+	+	-	-	+	-	-
	the same	0	-	-	-	-	-	-	-	-	-
	daughter	0	-	-	-	-	-	-	-	-	-
E	sister I twin	0	-	+	+	+	-	-	+	-	-
	sister II twin	0	-	-	-	+	-	-	-	-	-

[1] see Note 1 of Table 3;

[2] the *E. coli* strains pointed out in the column were sensitive to colicins produced of the «family» *E. coli* isolate. The list of colicin indicator *E. coli* strains is in **Materials and Methods**; (-) – colicins were not found for the set of the *E. coli* indicator strains used in the study.

Discussion. The data on plasmid profile structure, colicinogeny and phage sensitivity indicate to considerable quantitative and qualitative diversity of *E. coli* genetic elements and intensive interaction between bacteria in the human gut. This diversity is reflected on the formation of the dynamic population of intestinal bacteria, which obviously depends on the age of the host [12]. The *E. coli* isolates containing a single large plasmid were more similar because plasmid DNA of the same size could be detected in their cells, but these strains were different in colicinogeny and sensitivity to bacteriophages. Any similar couple of the *E. coli* isolates having identical plasmid profile was not found between the strains carrying a single small plasmid or polyplasmid *E. coli*. At the same time there were no strains with identical colicinogeny and phage sensitivity among the non-plasmid *E. coli* isolates.

Biological diversity was also detected among *E. coli* isolates obtained from the patients living in one family. Similarities in two of the three phenotypes could be found here, so that the properties of the "family" strains may partially overlap. Despite the fact that the absolute identity was not observed, these *E. coli* can also be collected in distinct "family" groups [26].

The expression of bacterial features is influenced by the microbial environment. It is noted the plasmid frequency increases, the colicin range expands and phage sensitivity decreases simultaneously with the increase of the number of enterobacterial species in the gut. Most of the *E. coli* strains (73%) were isolated from the association with other opportunistic enterobacteria such as *Klebsiella* sp., *Citrobacter* sp., *Pantoea* sp., *Enterobacter* sp., *Proteus* sp., *Providencia sp and Morganella* sp. that indicate to the imbalanced gut microflora. However, the evaluation of the three above mentioned phenotypes confirmed that the *E. coli* isolates are closely coordinating with other members of the intestinal microbial association.

Polyassociated *E. coli* more often contain plasmids and their plasmid profile usually consists of more than one plasmid. The fact that the detection of colicin producing strains does not correlate with the type of enterobacterial association can be explained by rather narrow group of indicator strains that were used in this study. Nevertheless, we believe that colicinogeny of indigenous *E. coli* should be taken into account both when prescribing and creating a coli-containing probiotics.

A regular increase of the number of small plasmids was found in *E. coli* during the expansion of enterobacterial association in intestinal microflora. Most likely, these plasmids were associated with spreading of the colicin killer activity [11]. However, in this case the source of acquisition or the mechanism for maintaining additional colicinogenic plasmids by indigenous *E. coli* strains was not clear.

The dynamics of changes in the biological features was observed among *E. coli* strains from different age groups of patients. The most significant was high frequency of colicinogenic strains in adult patient (group III) and di-associated *E. coli* containing one large plasmid in the youngest patients (group I). The association with some other opportunistic enterobacteria may reflect the physiological dysbiosis which is often observed in children. In respect to large plasmids, we supposed that they may be involved in the adaptation of *E. coli* to the main type of feeding of this age children.

Until today, it was not clear how antibiotics affect the dynamics of microbes in macroorganism. The common popularity of antibiotics, their frequent uncontrolled application for medicine purposes and food production [17] do not allow to examine patients who have never used them and make it impossible to collect a control group of patients. In this regard we can assume that multiresistant bacteria are typical of the normal microflora of a contemporary human.

Each of the above considered phenotypes is not obligatory for an individual bacterial strain, but their joint consideration allows us to estimate the efficiency of this strain as a component of the healthy intestinal microflora. A detailed study of the plasmid incompatibility, genetic determinants of colicinogeny and phage sensitivity of the gut bacteria at the level of the phage adsorption barrier, restriction/modification systems and others will allow us to understand the population dynamics of enteric bacteria depending on the age and health state of an individual host organism.

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Л.М. Бурова[1], Е.П. Корнейчук[1], А.И. Кушкина[2], Ф.И. Товкач[2]

[1] Львовский национальный медицинский университет им. Данила Галицкого, ул. Пекарская, 69, Львов, 790014, Украина
[2] Институт микробиологии и вирусологии им. Д.К. Заболотного НАН Украины, ул. Академика Заболотного, 154, Киев, ГСП, Д03680, Украина

ПЛАЗМИДНЫЙ ПРОФИЛЬ, КОЛИЦИНОГЕННОСТЬ И ФАГОЧУВСТВИТЕЛЬНСТЬ КАК ИНДИКАТОРЫ ДИНАМИКИ ПОПУЛЯЦИЙ *ESCHERICHIA COLI* В КИШЕЧНИКЕ ЧЕЛОВЕКА

Р е з ю м е

В данной работе рассматривается возможность использовать в качестве показателей динамики популяций кишечных энтеробактерий человека такие бактериальные фенотипы как плазмидный профиль, колициногенность и фагочувствительность. Эти три фенотипа, рассматриваемые совместно с типом ассоциации энтеробактерий и возрастом пациента, могут отражать динамическое состояние индивидуальной популяции *Escherichia coli в* кишечнике человека. Полученные данные относительно структуры плазмидного профиля, колициногенности и фагочувствительности свидетельствуют о значительном количественном и качественном разнообразии генетических элементов *E. coli* и об интенсивном взаимодействии между бактериями в кишечнике. Это разнообразие отражает формирование динамической популяции кишечной палочки, которое, зависит от возраста пациента. Определение трех вышеуказанных фенотипов у *E. coli* показывает, что ее жизнедеятельность тесно скоординирована с другими членами микробной энтеробактериальной ассоциации кишечника. Отмечено, что одновременно с возрастанием количества видов энтеробактерий в кишечнике у *E. coli* увеличивается частота обнаружения плазмид, расширяется спектр активности колицинов и снижается чувствительность к бактериофагам. Динамика изменений биологических свойств наблюдается и среди изолятов *E. coli,* полученных от пациентов из различных возрастных групп. Наиболее значительными из них являются более высокая частота обнаружения колициногенных штаммов у взрослых пациентов и выделение изолятов *E. coli* с одной большой плазмидой у детей до года с дисбиозом кишечника.

Ключевые слова*:* кишечная микрофлора, *Escherichia coli*, плазмиды, колициногенность, фагочувствительность, ассоциация энтеробактерий, возраст пациента.

Л.М. Бурова[1], О.П. Корнейчук[1], А.І. Кушкіна[2], Ф.І. Товкач[2]

[1] Львівський національний медичний університет ім. Данила Галицького, вул. Пекарська, 69, Львів, 790014, Україна
[2] Інститут мікробіології і вірусології ім. Д.К. Заболотного НАН України, вул. Академіка Заболотного, 154, Київ, ДГСП, Д03680, Україна

ПЛАЗМІДНИЙ ПРОФІЛЬ, КОЛІЦИНОГЕННІСТЬ І ФАГОЧУТЛИВІСТЬ ЯК ІНДІКАТОРИ ДИНАМІКИ ПОПУЛЯЦІЙ *ESCHERICHIA COLI* В КИШЕЧНИКУ ЛЮДИНИ

Р е з ю м е

В поданій роботі розглядається можливість використання у ролі показників динаміки популяцій кишкових ентеробактерій людини такі бактеріальні фенотипи як плазмідний профіль, коліциногенність і фагочутливість. Ці три фенотипи разом із типом асоціації ентеробактерій та віком пацієнта можуть відображати динамічний стан індивідуальної популяції *Escherichia coli в* кишечнику людини. Одержані дані стосовно структури плазмідного профілю, коліциногенності й фагочутливості свідчать про значне кількісне та якісне різноманіття генетичних елементів *E. coli* та про інтенсивну взаємодію між бактеріями в кишечнику. Це різноманіття відображає формування динамічної популяції кишкової палички, яке залежить від віку пацієнта. Визначення трьох вищезазначених фенотипів у *E. coli* показує, що її життєдіяльність тісно зкоординована з іншими членами мікробної ентеробактеріальної асоціації кишечнику. Зазначено, що одночасно зі збільшенням кількості видів ентеробактерій в кишечнику у *E. coli* збільшується частота виявлення плазмід, розширюється спектр активності коліцинів та знижується чутливість до бактеріофагів. Динаміка змін біологічних властивостей спостерігається і серед ізолятів *E. coli,* одержаних від пацієнтів різних вікових груп. Найбільш значними з них є більш висока частота виявлення коліциногенних штамів у дорослих пацієнтів та виділення ізолятів *E. coli* з однією великою плазмідою у дітей до року з дисбіозом кишечнику.

К л ю ч о в і с л о в а*:* кишкова мікрофлора, *Escherichia coli*, плазміди, коліциногенність, фагочутливість, асоціація ентеробактерій, вік пацієнта.

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