UDK 578.4:578.81:579.842.1/.2

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EXCLUSION OF POLYVALENT T7-LIKE PHAGES BY PROPHAGE ELEMENTS

The study presents new insights into the process of interaction of T7-like bacteriophages FE44 and BA14 with lysogenic cells. It was demonstrated that single and double lysogens possess Abi-phenotype regardless of genera, species and strain of bacteria that initially had normal phage sensitivity. Efficiency of plating of these phages is reduced by two orders of magnitude on monolysogens, whereas it decreases by 4–6 orders on bilysogens. In the latter case, phage infection leads to formation of more than 60% of aberrant capsids in phage progeny. Abortive phage infection is suggested to be associated with defects in general dynamics of the bacterial chromosome in single and double lysogens of Erwinia "horticola" and Escherichia coli.

Key words: polyvalent T7-like phages, Erwinia, Escherichia coli, lysogens, abortive infection.

Present-day research in the field of microbiology and bacteriophagy involves the extensive use of both genomics and proteomics methods and approaches. However, despite the huge bioinformatics data flow into modern databases, physiological dynamics of such relatively simple systems as phage-bacteria remains largely unknown phenomenon in general, as well as in its particular details and still exists at the level of the "predator-prey" model [15, 16]. It is clear that interaction of phage with bacterial cell is not limited only by molecular genetic parasitism exposed by virus and resistance to it of host bacterium. Abundant evidence proves that exogenous bacteriophage faces the similar genetic elements of the real bacterial cell. They act as active competitive factors and interfere with phage development at all possible levels – from adsorption and to cell lysis [14, 19]. Mechanisms of phage exclusion by endogenous genetic elements of the cell such as prophages, plasmids, restriction-modification (RM) systems, etc. can be diverse and sometimes even unexpected [8, 12, 16, 18, 20]. But the certain result is more or less definitive and consists in alleviation or even arresting of infection, i.e. development of abortive response. It is obvious that to study complex phage-plasmid or phage-prophage relationships in naturally occurring bacterial strains an adequate experiments and relevant molecular genetic tools appliance is required. Recently, we have proposed a two-component model system based on a various, including polyvalent, phages of T7 group, along with broad-host-range temperate bacteriophage P1, which intensively expresses RM-complex EcoP1I in the prophage state. Three groups of bacteriophages were identified due to the extent of their intracellular exclusion by EcoP1I-restriction enzyme and according to the availability of the appropriate cell receptors [10].

Exploration of the influence exposed by lysogenic prophage elements on the development of T7-like virulent broad-host-range phages able to reproduce in a variety of *Enterobacteriaceae* representatives was the aim of the work.

Materials and methods. Common laboratory strains of *Escherichia coli (Eco)* C600, BL21, S/6, C1A, C5201, λ-carrying BL21(DE3), P2-monolysogens C5204 and C339, as well as P2, P4-bilysogen C5651 were used. Two species of phytopathogenic bacteria were selected for phage host range determination: *Erwinia amylovora (Eam)* strains K8 (ATCC 29850), K4, L4 and *Erwinia "horticola" (Eho)* 450, 60-2N, 60-3m, 120, 23a [4]. Strain variants *Eho* 450(P1$^-$)-1 and 450(P1$^-$)-2, denoted hereinafter as 450^{1-} and 450^{2-}, were obtained after spontaneous curing from plasmid P1 [10]. Artificial monolysogens *Eho* 450(49), (59), (120) and bilysogens *Eho* 450(23, 49), (59, 49), (120, 49) were constructed in the course of work or obtained earlier [6].

The objects of the study were phages of T7 group (C1-morphotype, *Podoviridae*) T3, T7 and BA14 from collection of Prof. I.J.Molineux [11]; and FE44 from collection of Dr. F.I. Tovkach [2], adapted to various sensitive bacteria: FE44/C600 – to *Eco* C600, FE44/450 – to *Eho* 450 and to its lysogenic derivatives – FE44/(120), FE44/(23, 49), etc. Erwiniaphages 49 and 59 of B1-morphotype (*Siphoviridae*) [6] and phages 120 and 23, isolated after spontaneous induction of strain *Eho* 120 and *Eho* 23a, were used for lysogenisation of bacterial cultures.

For lysogens construction respective phage was applied on the bacterial lawn. After incubation, cells were picked from the zones of secondary growth, cultivated in the lysogenic broth (LB), and

cloned twice. Bacteria were analysed for lysogenic induction ability and resistance to the phage used for lysogenisation. In case if the results were positive the culture was considered to be lysogenic.

Phage titration was carried out by a standard two-layer agar procedure; extrachromosomal DNA was extracted as described in previous articles without any modifications [10].

Phage obtaining was carried out using fused lysis procedure [7]. Collected phage lysates were clarificated for 1 h by centrifugation at 5000g, 10˚C. The supernatant was centrifuged again at 26 000 rpm for 2 h, 10˚C in rotor SW28, Spinco L7-70. Obtained sediment was resuspended in STM-buffer and further additionally purified by centrifugation at 11 000 rpm for 10 min.

Electron-microscopic studies were carried out using transmission electron microscope JEOL JEM-1400; samples were applied on nitrocellulose-covered copper grids for 20–40 min and contrasted with 2% uranyl acetate.

The kinetics of adsorption was studied according to [7]. Cell suspensions of about 10^8–10^9 cells/ml were mixed with phage in concentration near 10^7 PFU/ml in order to obtain an infection multiplicity of 0.1–0.01. After an incubation at 28˚C for a chosen period of time (from 30 sec to 5 min), chloroform was added (1/50 volume) in order to arrest the process of adsorption. The mixture was immediately centrifuged at 11 000 rpm to sediment the cells together with the adsorbed phage. Supernatant containing unadsorbed phage particles was serially diluted and titrated on *Eco* C600. Plaques were counted after 2.5–3 hours. Obtained data were presented as the curve of logarithm percent of unadsorbed phage dependence on time. The adsorption rate constants were calculated by equation:

$$k = \frac{2,3}{B \bullet t} \lg \frac{P_0}{P},$$

with P_0 and P designating concentration of phage particles at the beginning and the end of period t, respectively; B – concentration of bacterial cells.

Results. The ability of various members of the T7 phage group to infect *E. coli* strains of the three groups, B, K, and C, most commonly used in laboratory practice and modern biotechnology, is well-known [13]. Nevertheless, a little information about these phages' host range among strains of *E. coli*, isolated from natural sources *de novo* exists. Phage FE44, a common representative of this group (GenBank accession no. KF700371) can be regarded as a virus with extended host range among enterobacteria comparing to T7 and T3 phages (Table 1), [2].

Table 1

Efficiency of plating of T7-like phages on enterobacteria species

Phage	Strain											
	E. coli				*E. "horticola"*					*E. amylovora*		
	C600	**BL21**	**BL21 (DE3)**	**S/6**	**450**	**60-2N**	**60-3m**	**23a**	**120**	**K8**	**K4**	**L4**
FE44/ C600	1.00	0.012	0.010	0.017	0.1*	0.25	$2.9 \cdot 10^{-3}$	LS**	$2.1 \cdot 10^{-4}$	$2.1 \cdot 10^{-4}$	$2.9 \cdot 10^{-7}$	–
T3/ C600	1.00	0.62	0.62	1.2	–	–	$9.2 \cdot 10^{-5}$	$2.3 \cdot 10^{-6}$	$6.2 \cdot 10^{-5}$	–	–	–
T7/ C600	1.00	0.93	0.93	1.0	–	–	–	–	–	–	–	–

Note: "*" – reflects the efficiency of plating of FE44/C600 phage population able to form only large negative colonies on *E. "horticola"* 450 (see. text); "**" – on *E. "horticola"* 23a lawn FE44/C600 phage forms lysis spots (LS) that do not appear in subsequent passages.

The results in Table 1 show that FE44 phage is capable of infecting 97% of used enterobacteria of two genera and three species; phage T3 infects 67%, whereas phage T7 reproduces solely in cells of *E. coli* (34%). At the same time, phage FE44 is a subject of considerable restriction by *E. coli* B strains (BL21and S/6). In these cases its efficiency of plating (EOP) decreases by 90% comparing with the reference EOP on *E. coli* C600 (K). As reported earlier, this effect is most likely associated with the intracellular action of EcoB RM-system [5] and virtually, the lack of FE44 gene *ocr* activity. Phage FE44 efficiency of plating is several times lower on parental *Eho* 450 and 60 (60-2N) strains than on *E. coli* C600. However, it is by order of magnitude higher than on the B-strains, and by two orders higher than on the mutant *Eho* 60 (60-3m). In both cases it may be associated with adsorption receptors, but not with the intracellular phage restriction in primary cell infection. FE44 efficiency of

plating reduces to 10^{-4} on *E. "horticola"* strain 120, while on the lawn of sensitive cells *Eho* 23a the phage does not form apparent plaques but the individual inexplicit lysis spots (Table 1). Here a clear correlation between the extrachromosomal elements maintenance in the cells of *Eho* 120 and *Eho* 23a strains is observed. As seen from Fig.1, *Eho*120 strain carries only one plasmid of, most likely, medium copy number, whereas the cells of strain 23a complementary to the analogous plasmid contain small-copy number extrachromosomal DNA, probably, of prophage nature. In our opinion, this alteration of plasmid (prophage) spectrum of strain leads to development of completely abortive response by *Eho* 23a cells to FE44 infection.

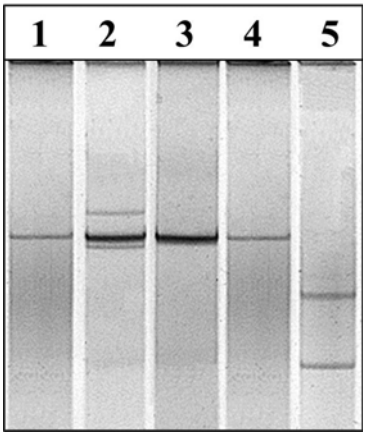

Fig. 1. Electrophoregramm of extrachromosomal DNA extracted from *E."horticola"* 23a (2) and 120 (3) cells; Plasmid F (1, 4) of 100 kb and RP4 (5) of 60 kb were used as controls.

Unlike FE44, phage T3 poorly replicates in *Eho* 60-3m and 120 cells; its efficiency of plating value is reduced by 5–6 orders of magnitude. At the same time, it is able to form distinct plaques on strain 23a lawn instead of lysis spots (Table 1).

In contrast to T3 and T7, FE44 phage is able to reproduce in *E. amylovora* cells, though is characterized by very low value of EOP – 10^{-4}–10^{-7} (Table 1).

Significant interference with phage FE44 and T3 reproduction by the *Eho* and *Eam* strains may be determined by several factors. As noted above, exogenous phage is affected under conditions of interchange of sensitive bacteria. Thus, unlike previous one, the cell surface of a new host may carry different adsorption receptors which do not perfectly fit for phage attachment. Also, it can feature different growth parameters or comprise an individual set of autonomous genetic elements that commonly varies among strains of the same bacterial species and, most certainly, among bacteria of different genera.

In order to show that alongside with extrachromosomes (*Eho* 23a and 120) and RM-systems (e.g., EcoB and EcoP1I [5, 12]) such prophage elements as complete integrated phages can also exert influence on intracellular development of T7-like phages, a set of *E. "horticola"* 450 monolysogens and bilysogens was obtained (see. Materials and methods).

Table 2

Phage FE44 efficiency of plating after its adaptation to *E. "horticola"* 450 lysogens

Phage	Strain						
	Eho 450	*Eho* 450 monolysogen			*Eho* 450 bilysogen		
		(120)	(59)	(49)	(23, 49)	(59, 49)	(120, 49)
FE44/450	1.00	0.014	0.13	0.18	$2.6\cdot10^{-4}$	$4.0\cdot10^{-4}$	$4.6\cdot10^{-5}$
FE44/(120)	0.22	0.035	0.018	0.18	0.11	0.087	$2.2\cdot10^{-3}$
FE44/(23, 49)	0.10	0.023	0.055	0.049	0.072	0.025	0.016
FE44/(59, 49)	$7.3\cdot10^{-3}$	$2.4\cdot10^{-3}$	$1.8\cdot10^{-3}$	$7.3\cdot10^{-3}$	$1.1\cdot10^{-4}$	$3.6\cdot10^{-3}$	$2.6\cdot10^{-3}$
FE44/(120, 49)	0.27	0.063	0.11	0.18	0.044	0.033	0.073

As can be seen from Table 2, adapted to parental strain *Eho* 450 phage FE44 grows on its monolysogens – *Eho* 450(120), (59) and (49) with low efficiency. Lysogen *Eho* 450(120) reduces phage FE44/450 efficiency of plating by 2 orders of magnitude, while the other two lysogenic bacteria, *Eho* 450(59) and (49) maintain its reproduction at approximately similar level reducing the EOP only ten-fold. These data demonstrate that single prophages definitely affect the intracellular development of the FE44 phage. Depending on their nature, the results of the interaction between a prophage and the exogenous phage may vary significantly.

Two-stage phage adaptation to the growth conditions on lysogen *Eho* 450(120) – FE44/(120) – does not lead to recovery of the initial efficiency of plating (Table 2). Since this feature is common for three *Eho* monolysogens 450(120), (59) and (49), it can be suggested that phage reproduction is arrested by the abortive infection. When double lysogens carrying four prophages – 23, 49, 120 and 59 in various combinations were used for phage titration, FE44 variants' infection process was mostly switched to abortive responce (Table 2). In contrast to the parental *Eho* 450 strain and its monolysogens *Eho* 450(120), (59) and (49), the infection level in cells of *Eho* 450 double lysogens (23, 49), (59, 49) and (120, 49) decreases by 4–5 orders of magnitude. Phage reproduction efficiency increases in subsequent passages but still it never reaches the initial value. EOP value constitutes 0.016–0.055 for phage variant adapted to *Eho* 450(23, 49) – FE44/(23, 49), and for phage FE44/(120, 49) it ranges from 0.11 to 0.033. Adapted variant FE44/(59, 49) reveals an unusual reproduction pattern not only in monolysogens and bilysogens, but also in *Eho* 450 cells (Table 2). Its efficiency of plating value lies in the range of $7.3–2.4 \cdot 10^{-3}$, decreasing to $1.1 \cdot 10^{-4}$ on the double lysogen *Eho* 450(23, 49). These results suggest FE44/(59, 49) to be an unusual mutant obtained as a consequence of mild selection of original FE44 phage on bilysogen *Eho* 450(59, 49).

Thus, on the basis of data obtained it can be presumed that phage FE44 falls under a partial exclusion in lysogenic cells, carrying prophage elements, and is not able to accomplish complete adaptation to the isogenic host. The development of abortive infection characterizes the general physiological dynamics of artificial lysogens, as well as phage FE44–*Erwinia* natural systems (Table 1).

In order to prove that abortive infection is specific not only for the mentioned systems, but is a widespread phenomenon phage FE44 and its close relative BA14 were plated on P2-single lysogens and the P2, P4-double lysogens of *E. coli* C [9]. When FE44/450 was propagated on non-lysogenic strains of *E. coli* C1a and C5201, as well as on 2 different strains of C (C5204 and C339) carrying a single P2 prophage and the C5651 double lysogen comprising P2 and P4 prophages, the character of infection didn't significantly differ from that on *E. "horticola"* 450 mono- and bilysogens (Table 3). On P2-monolysogens EOP value is by order of magnitude lower than on isogenic strains C1a and C5201 that serve as P2-indicators since they do not carry this prophage and, hence, are P2-sensitive (Table 3). In addition, we were unable to evaluate FE44/450 efficiency of plating on the double lysogen C5651(P2, P4). Most likely, it is less than 10^{-9} since the appliance of the phage in 10^9 PFU/ml concentration on the lawn of bilysogen does not lead to the formation of visible negative colonies. It is also possible that the phage is not able to adapt to sudden change of the host and requires the gradual passages on appropriate sensitive bacteria. Indeed, in contrast to phage FE44/450 the variant FE44/C1a obtained after one passage on *E. coli* C1a forms negative colonies on the C5651 lawn. Since the phage plaques are heterogeneous in size and efficiency of plating decreases by six orders of magnitude, an abortive response development by the double lysogen (*Abi*-phenotype) can be presumed (Table 3). Similar to *E. "horticola"* 450 double lysogens (Table 2) phage exclusion is systemic since complete productive infection can not be recovered in subsequent passages, or in the successive phage FE44/C1a adaptation to strain C5651 into FE44/C5651 phage variant (Table 3).

Most likely, reversion to productive infection on P2-lysogens using a respective variant (FE44/C1a) is also impossible (Table 3). In this case, however, the efficiency of plating recovery is more essential than for phage FE44–*E. "horticola"* system (Table 2). In order to show that the pattern of *Abi*-exclusion by a defective prophage in the composition of the double lysogen (P2, P4) or complete prophages (P2, 59, 49, 120 and 23) is not only specific to phage FE44, but is common for other phages, we used closely related phage BA14.

Table 3

Efficiency of plating of some FE44 and BA14 variants on lysogenic *E. coli* C strains

Phage	Phage variant			
	FE44/450	**FE44/C1a**	**FE44/C5651**	**BA14/C1a**
E."horticola" 450	1.00	–	–	$1 \cdot 10^{-3}$
E. coli: C1a	0.01	1.0	1.0	1.0
C5201	0.02	0.6	0.22	1.0
C5204(P2)	$2.4 \cdot 10^{-3}$*	0.18	1.0^{i}	1.6
C339(P2)	$2.4 \cdot 10^{-3}$*	0.8	1.0	1.0
C5651(P2,P4)	0	$2 \cdot 10^{-6}$	0.06	$1.8 \cdot 10^{-4}$

Note: "*" – on these strains FE44 forms plaques reduced in size by 2–3 times compared with that on *E. coli* C1a strain; "*i*" – after FE44 plating on *Eco* C5204 lawn sporadic appearance of phage plaques with turbid centers resembling negative colonies of temperate coliphage P2 is observed."–" – not investigated.

As can be seen from Table 3, variant of BA14 adapted to strain *E. coli* C1a (BA14/C1a) in contrast to FE44/C1a is not restricted by P2-monolysogens at all. Its EOP on one of the lysogens, C5204, is 1.6 times higher comparing with that on the reference non-lysogenic strain *E. coli* C1a. This indicates that the exclusion of T7-like phages itself is not associated with specific genetic mechanisms realized by prophages (e.g., *Spi*-system of prophage P2) [14]. It may be associated with the alteration of general physiological state of the cell caused by integration of the prophage with the bacterial genome. On the other hand, the data analysis leads to the following conclusion. Despite the polyvalences exhibited toward various enterobacteria (Table 1, [13]), the phages reveal more affinity to those genera, species and strains of bacteria, which they were initially obtained on. FE44 phage most efficiently replicates in *E. "horticola"* cells, whereas BA14 does in the cells of *E. coli* strains. Phage BA14/C1a, as well as variant FE44/C1a are substantially restricted by the double lysogen C5651 (by approximately 4 orders of magnitude), thus confirming the expression of *Abi*-phenotype by this culture.

Interestingly, BA14/C1a phage significantly reduces its lytic potential on the parental *Eho* 450 strain – by three orders of magnitude (Table 3). Generally, decreasing of the FE44 EOP when plated on *E. "horticola"* strains always occurs after its prior passage on *E. coli* strains K, B and C. However, the subsequent phage passages are effective. Obviously, extrachromosomal elements are not responsible for this phenomenon, since strains *Eho* 450 and 60 do not carry them [10]. It is possible that the indicator strains carry restriction-modification system [1]. Various *E. "horticola"* strains are suspected to be pseudolysogenic since both FE44 and other T7 phages can induce the transition of carried phage (or phages) into genuine prophage state and, subsequently, transition of the ternary complex (exogenous phage FE44 – carried phage – *E. "horticola"*) to the lytic response. This can explain formation of phage colonies of "temperate" type when phage FE44 is titrated on the lawns of sensitive *E. "horticola"* 450 cells (Fig. 2). This phenomenon has a sporadic nature and has been previously designated as "phage-phage induction" [3].

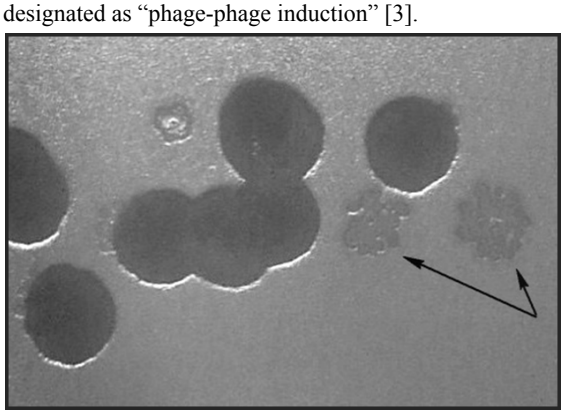

Fig. 2. Phage-phage induction after FE44 plating on *E. "horticola"* 450 lawn. Marked with the arrows are the plaques of "temperate" type.

In the course of the work phage-phage induction was mainly observed when different FE44 variants were titrated on the lawns of *Eho* 450, 450(49) and *E. coli* C5204(P2) cells (Table 3). However, obtaining of temperate phages in preparative quantities and their identification could not be achieved in any of the mentioned cases.

To elucidate the factors responsible for the *Abi*-phenotype development by lysogens carrying one or two prophages the phage adsorption analysis and electron-microscopic studies of phage particles morphology were performed.

The ability of prophages of several *Salmonella typhimurium* temperate phages ϵ^{15}, ϵ^{34}, g_{341} and P22 to convert lysogens for partial or complete resistance to homologous or heterologous phage is well-kown [18, 19]. This conversion is associated with the modification of phage attachment sites which undergo substantial chemical modifications. Consequently the antigenic structure of the outer membrane lipopolysaccharide is significantly altered when prophage state is established. It was shown earlier that temperate phages 59, 49 and E105 also modify the adsorption sites, thereby completely blocking adsorption of a homologous virus [6].

Whether this modification affects the efficiency of phage FE44 adsorption was not established before. To solve this issue the kinetics of FE44/450 adsorption on four isogenic bacteria – *E. "horticola"* 450, 450(49), 450(59) and 450(49, 59) was studied and adsorption rate constants were calculated. As can be seen from Fig. 3 the adsorption curves of non-lysogenic strain variants 450^{1-} and 450^{2-} coincide with that of the double lysogen 450(49, 59). The same is for single lysogens *Eho* 450(49) and 450(59). In 1.5–2 minutes the vast majority of phage particles (more than 90%) is adsorbed in all cases. Afterwards, that adsorption proceeds very slowly and gradually stops. Kinetic curves of phage FE44 adsorption, in general, have the same character as those of T7-like phages [17]. Phage FE44 adsorption rate constants both on the cells of parental strain *Eho* 450 and lysogens 450(49) and 450(49, 59) turned out to be rather similar. They constitute $7.9 \cdot 10^{-9}$, $2.8 \cdot 20^{-9}$ and $8.8 \cdot 10^{-9}$ mL·min^{-1}, respectively. It can be therefore concluded that the restriction of FE44 reproduction on single and double lysogens of *E. "horticola"* is not associated with the adsorption events. Hence, the outer membrane LPS modification by prophage 49 and 59 does not affect the receptors for phage FE44.

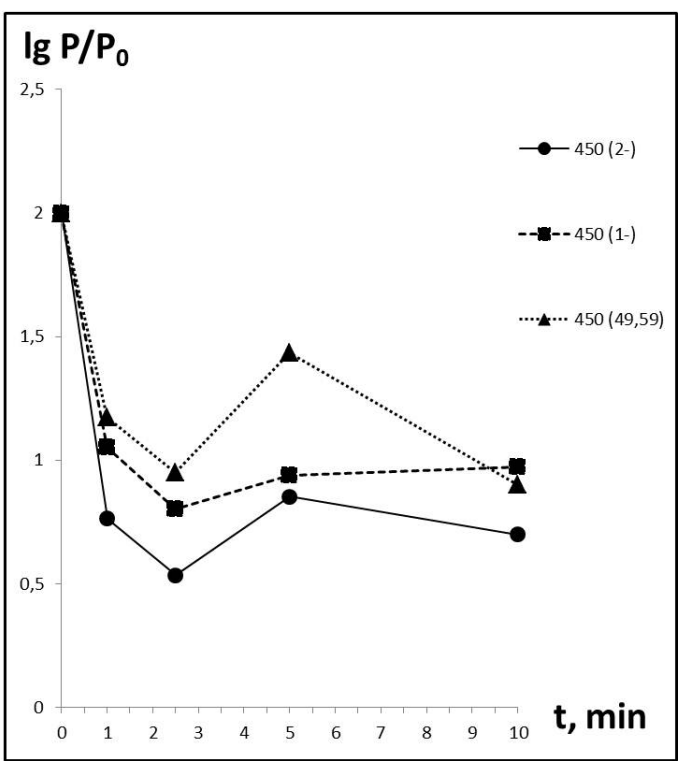

Fig. 3. Kinetics curves of phage FE44/450 adsorption on *E. "horticola"*450^{1-}, 450^{2-} and 450(49, 59) cells.

Electron-microscopic analysis of phage FE44 particles was used to study the consequences of abortive infection involving the phage and lysogenic cells. After fused lysis of the cultures the lysates were collected and purified by a single cycle of ultracentrifugation. Two types of structures of phage nature such as intact particles and proheads were observed in control *E.coli* C600 and *E. "horticola"* 450^{2-} lysates (Fig. 4.A,B). Diameter of intact head is approximately 50 nm; proheads are in general comparably sized though do not reveal well-defined hexagonal structure. The intact heads to proheads ratio in FE44 *E. coli* C600 lysates constitutes 30:1 though it ranges about 10:1 in lysates of *E. "horticola"* 450^{2-} and *E. "horticola"* 450(49, 59) double lysogen. Notably, in 450^{2-} lysates intact particles represent only 70% percent of phage progeny, while near 93% of C600-produced particles are of normal phenotype.

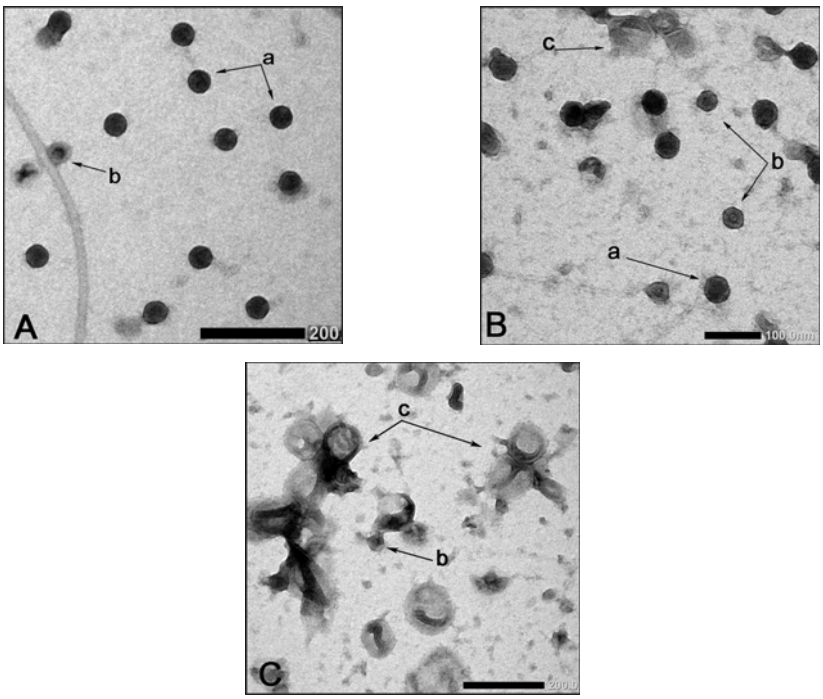

Fig. 4. Electron-microscopic images of phage particles in lysates of *E. coli* C 600 (A), *E. "horticola"*450^{2-} (B), and 450(49, 59) (C). a – intact phage particle, b – prohead, c – aberrant anomalous structure. Scale bars represent 200, 100 and 200 nm, respectively.

In the double lysogen lysate abnormal viral particles are most abundant (67% of the total number of particles compared with 21% for 450^{2-} and 3% for C600). Their detection is of no difficulty (Fig. 4,C). Dimensions of observed anomalous structures are rather larger than the size of intact phage particle. This is indicative for incorrect assembly of capsids. Thus, the EM data clearly show the development of *Abi*-phenotype by double lysogens that blocks one of the intracellular stages of phage virion maturation.

Discussion. We consider a set of T7-group phages to be a reliable genetic tool for studying the various systems of phage exclusion by the bacterial host. In most cases such exclusion can be conceived as a manifestation of a kind of competitive response of cell genetic elements to the introduction of exogenous element into the bacterial cell [14, 15, 16]. On the one hand, endogenous genetic elements have specific mechanisms for the competitive response implementation [8, 12, 14, 18, 19], while exogenous infecting elements carry genes responsible for overcoming defence reaction [15, 16]. Thus, this conception specifies "prey" to be not a complete cell but, most likely, only parity competitor of the "predator." Therefore in this sense the "predator-prey" model is more comprehensive at the level of molecular genetic mechanisms of interaction of simple genetic elements of exogenous and endogenous nature.

Endogenous genetic elements, such as integrated prophages were shown to significantly interfere with exogenous virulent phages of T7 group. The result of this interference depends neither on

the nature of the prophage nor on host bacterium carrying it. The most significant exclusion of T7-phages occurs in the cells maintaining two prophage elements, i.e. double lysogens or bilysogens. They develop complete *Abi*-phenotype which results in abnormal virion assembly of T7-like phages (FE44).

Since *Abi*-phenotype is not associated with any specific exclusion mechanism determined by defined gene or genetic structure, abortive responce is suggested to develop due to defects in general dynamics of bacterial chromosome. Obviously, this defects are caused by integrated prophage elements which alter the rate of host DNA replication.

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ОБМЕЖЕННЯ РОЗВИТКУ ПОЛІВАЛЕНТНИХ ФАГІВ Т7-ГРУПИ ПРОФАГОВИМИ ЕЛЕМЕНТАМИ

Р е з ю м е

В роботі вперше досліджено взаємодію фагів Т7-групи FE44 і BA14 з лізогенними клітинами. Показано, що монолізогени та дилізогени проявляють *Abi*-фенотип незалежно від родової, видової та штамової приналежності вихідних бактерій, фагочутливість яких є нормальною. Ефективність висіву цих фагів на монолізогенах знижується на два порядки, в той час як її падіння сягає 4–6 порядків на подвійних лізогенах. В останньому випадку після інфікування клітин утворюється більше, ніж 60 % аберантних капсидів. Розвиток абортивної фагової інфекції, очевидно, пов'язаний з порушенням загальної динаміки бактеріальної хромосоми в моно- і дилізогенах *Erwinia "horticola"* і *Escherichia coli*.

Ключові слова: полівалентні фаги Т7-групи, *Erwinia, Escherichia coli,* лізогени, абортивна інфекція.

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ОГРАНИЧЕНИЕ РАЗВИТИЯ ПОЛИВАЛЕНТНЫХ ФАГОВ Т7-ГРУППЫ ПРОФАГОВЫМИ ЭЛЕМЕНТАМИ

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В работе впервые исследовано взаимодействие фагов Т7-группы FE44 и BA14 с лизогенными клетками. Показано, что монолизогены и дилизогены обладают Abi-фенотипом вне зависимости от родовой, видовой и штаммовой принадлежности бактерий, которые изначально обладают нормальной фагочувствительностью. Эффективность посева этих фагов на монолизогенах снижается на два порядка, тогда как ее падение достигает 4–6 порядков на двойных лизогенах. В последнем случае после инфекции клеток образуется более 60 % аберрантных капсидов. Предполагается, что абортивная фаговая инфекция связана с нарушением общей динамики бактериальной хромосомы в моно- и дилизогенах *Erwinia "horticola"* и *Escherichia coli*.

Ключевые слова: поливалентные фаги Т7-группы, *Erwinia, Escherichia coli,* лизогены, абортивная инфекция.

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Отримано 22.10.2013