of some processes, such as tumor growth, BM transplantation, and graft versus host disease, where NSC can play an important role.

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EXPERIMENTAL GENETICS

Genetic Regulation of Conjugative Properties of pAP18 Plasmid Complex in *E.coli*

E. V. Grishina, V. P. Shchipkov, and A. P. Pekhov

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Cells of natural bacterial populations often harbor complexes of various plasmids providing genetic control over drug resistance, virulence, and other properties of these organisms [1]. However, in many cases the regularities of the relationship between individual plasmids of the complex which determine their most important properties (such as the manifestation of conjugative properties) remain unclear. The objective of the present study was to analyze the interplay between the systems of genetic regulation in the conjugational transfer of plasmids of the pAP18 complex that was found earlier in an *E.coli* strain isolated from an ill animal [2].

Department of Biology and General Genetics, Peoples' Friendship University, Moscow, Russia. (Presented by T. T. Berezov, Member of the Russian Academy of Medical Sciences)

MATERIALS AND METHODS

The plasmids under study were pAP18-1 (TcColV) and pAP18-2 (Sm) comprising the plasmid complex pAP18. As test plasmids we used the standard plasmid Flac and a collection of derepressed F-like plasmids with known types of sensitivity to transfer inhibitors [3]. As host cells or recipient cells we used a serologically untyped *E.coli* strain K-12

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TABLE 1. Ability of the pAP18 Complex Plasmids to Inhibit the Transfer Function in Cells of *E.coli* K12 (14 R525, AP132, AP115, C600)

Plasmid composition of host cells	IPTI		IIPTI		Inhibition of plasmid transfer		
	phage MS2	phage Ike	phage MS2	phage Ike	inhibited plasmid	frequency of plasmid transfer	TII
pAP18	$(1.5-1.8)\times10^4$	-	$(7.3-8.9)\times10^2$	–	Flac	$(2.4-2.6)\times10^{-3}$	$(1.1-1.2)\times10^2$
pAP18-2 Flac							
pAP18-1 Flac	$(2.4-2.7)\times10^4$	–	$(4.6-5.9)\times10^2$	–	Flac	$(2.1-2.4)\times10^{-3}$	$(1.1-1.2)\times10^3$
pAP18-2 Flac	$(1.1-1.3)\times10^7$	–	1.0–1.2	–	Flac	$(2.6-2.8)\times10^{-1}$	1.0–1.1
pAP18-1 pAP18-2	$(0.4-3.6)\times10^3$	$(0.3-3.7)\times10^3$	1.2–1.6	0.9–1.4	pAP18-1	$2.2\times10^{-4}-2.0\times10^{-6}$	0.6–1.0
					pAP18-2	$3.0\times10^{-6}-5.0\times10^{-8}$	$(1.1-1.6)\times10^{-2}$
pAP18-1	$(0.5-5.4)\times10^3$	–	–	–	–	$1.3\text{з}10^{-4}-1.4\times10^{-6}$	–
pAP18-2	–	$(0.4-3.0)\times10^3$	–	–	–	$3.5\times10^{-4}-7.2\times10^{-6}$	–
Flac	$(1.1-1.7)\times10^7$	–	–	–	–	2.9×10^{-1}	–

(14 R525 Nal, AP132 Nal, AP115 Nal, C600 Rif) and serologically typed *E.coli* strains AP15-3 Nal (antigen 0106) and AP70-3 Nal (antigen 0128), selected by us earlier. The sensitivity of plasmid-carrying bacteria to pili-specific phages MS2 and Ike was assessed from the efficacy of phage replication in the reaction of phage titer increase (RPTI), as described previously. The index of phage titer increase (IPTI) was defined as the ratio of the number of phage-lysed zones after a 18-h incubation of the phage-bacterial mixture to the number of zones in the control (prior to incubation). The index of inhibition of phage titer increase (IIPTI) was defined as the ratio of the IPTI value for one-plasmid cells to the corresponding value for the bacteria carrying two or three plasmids. The conjugational transfer of plasmids was accomplished in the standard crossings of bacteria. The transfer inhibition index (TII) was defined as the ratio between the frequencies of plasmid transfer from a one-plasmid donor and from cells carrying two or three plasmids.

RESULTS

Table 1 summarizes the data on the ability of the plasmids in the pAP18 complex to inhibit conjugative functions of one another as well as of the standard plasmid Flac. These functions are associated with the activity of plasmid-specific (sex) pili in the cells of the K12 *E.coli* strain and plasmid transfer into recipient cells of these strains. The functional activity of plasmid- specific pili was assessed from the sensitivity of the corresponding bacteria to pili-specific phages determined in RPTI. Since the pAP18-1 plasmid is F-like [4], the pili-specific activity of the cells carrying this plasmid was determined using F-specific phage MS2. As for the plasmid pAP18-2, we demonstrated its ability to determine synthesis of "sex" pili accounting for the sensitivity of bacteria to the N-specific phage Ike.

As follows from the IIPTI and TII values in Table 1, the pAP18-1 plasmid inhibits the functions of pili formation and conjugational transfer of the standard plasmid Flac and pAP18-2 plasmid. As for

TABLE 2. Inhibition of Genetic Transfer in Cells of Serologically Typed *E.coli* Strains by Plasmids of pAP18 Complex

Host cell	Plasmid composition	IPTI		IIPTI		Inhibition of plasmid transfer		
		phage MS2	phage Ike	phage MS2	phage Ike	inhibited plasmid	frequency of plasmid transfer	TII
E.coli AP15-3	pAP18-1	$(0.8-2.2)\times10^2$	$(4.1-6.6)\times10^2$	1.9–4.9	0.7–1.1	pAP18-1	$(1.6-2.9)\times10^{-6}$	1.1–1.9
	pAP18-2					pAP18-2	$(0.1-9.0)\times10^{-6}$	50–67
	pAP18-1	4.1×10^3	–	–	–	–	3.1×10^{-6}	–
	pAP18-2	–	4.7×10^2	–	–	–	6.0×10^{-4}	–
	pAP18-1	$(4.0-6.0)\times10^4$	$(1.1-2.3)\times10^4$	1.0–1.5	0.5–1.0	pAP18-1	$(1.2-1.4)\times10^{-6}$	0.9–1.1
	pAP18-2					pAP18-2	$(0.2-9.0)\times10^{-6}$	34.1–83
E.coli AP70-3	pAP18-1	6.2×10^4	-	-	-	-	1.3×10^{-6}	–
	pAP18-2	–	1.1×10^4	–	–	–	7.5×10^{-4}	

the pAP18-2 plasmid, it did not display inhibiting activity vis-a-vis Flac and pAP18-1.

On the basis on the results obtained, we are inclined to believe that the ability of the F-like plasmid pAP18-1 to inhibit the conjugational function of Flac may be associated, first, with the presence of a controlling genetic region coding for a transfer inhibitor of Fin V type in the genome of pAP18-1 [4] and, second, with the sensitivity of Flac to an inhibitor of this type [5]. The finding that pAP18-2 can also be inhibited by pAP18-1 may point to its sensitivity to the transfer inhibitor of Fin V type. On the other hand, this self-repressed plasmid is not able to inhibit the transfer of Flac, known to be sensitive to six inhibitors of different types (OP, Q, V, U, W, C) [5], or pAP18-1, which is sensitive to the inhibitors of the V and W types [4]. This allows us to assume that the N-like plasmid pAP18-2 has a transfer genetic regulation system of another type, different from that known for the plasmid F and F-like plasmids. This preliminary assumption was confirmed in further experiments, where a collection of derepressed F-like plasmids with different types of sensitivity to transfer inhibitors was used. We failed to reveal the ability of pAP18-2 to inhibit transfer of any plasmid in this collection.

Since under natural conditions plasmids inhabit serologically typed *E.coli* strains, we thought it of interest to study the functioning of the pAP18 plasmid regulation systems in cells of these bacteria.

The inhibiting properties of these plasmids vis-a-vis to one another in cells of two serologically typed *E.coli* strains is reflected in Table 2. As follows from this table, pAP18-1 displays its inhibiting activity vis-a-vis pAP18-2 in cells of these strains, although the TII values are lower than those in cells of the serologically untyped *E.coli* strain K12.

Thus, the plasmid complex pAP18 in *E.coli* is made up of plasmids with genetic transfer regulation systems of different types. The plasmids reveal their activity in both serologically untyped and serologically typed strains of *E.coli*.

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