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Bacteriophage-Induced Antigenic Conversion and Transduction of Drug Resistance in Group E Salmonellas

By

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In previous papers Uetake and his associates (1954; 1955)[25),26)] reported that all type strains of E_2 group Salmonella, so far tested, were found to be lysogenic and the bacteriophages obtained from the same were capable of infecting E_1 group organisms, resulting in lysogenization and antigenic alteration from 3, 10 to 3, 15 in 0 antigenic structure. It has also been pointed out that this phenomenon is slightly different from transduction (Zinder and Lederberg, 1952[27)]; Lederberg and Edwards, 1953[20)]; Stocker, Zinder and Lederberg, 1953[24)]; Baron, Formal and Spilman, 1953[5)]), being quite similar to the relationship of bacteriophage to toxigenicity in Corynebacterium diphtheriae (Freeman, 1951[11)]; Parsons and Frobisher, 1951[21)]; Freeman and Mores, 1952[12)]; Groman, 1953[14)], 1955[15)]; Barksdale and Pappenheimer, 1954[4)]; Groman and Eaton, 1955[16)]), phage to colony type transformation in Bacillus megaterium (Ionesco, 1953[17)]), phage to change in phage adsorption ability in Salmonella (Boyd, 1954[6)]) and phage to changes in phage type in Salmonella (Anderson, 1951[1)], 1955[2)]; Felix and Anderson, 1951[9)]; Sholtens, 1955).

The experiments in this report were conducted in order to compare the actual phage-induced antigenic alterations with transduction, in detail.

Materials and Methods

1. Salmonella strains

S. anatum 293, S. butantan, S. vejle, S. simi, S. kinshasa, S. cambridge and S. canoga are all international standard strains which were donated by F. Kauffmann to the Japan Enterobacteriaceae Committee, the donor. Streptomycin (to be referred to as SM, henceforth, to facilitate description) sensitivity of these strains in synthetic fluid medium are shown in table 1. Though it would appear that the level of natural resistance to streptomycin is very high, it is considered to be due to the medium used, since the level is within ranges of levels reported hitherto (Florey et al. 1949[10)]; Fukui, 1952[13)]) when tested in nutrient broth.

2. Streptomycin-resistant strains

S. kinshasa and S. cambridge of E_2 group were serially subcultured in synthetic fluid medium containing SM, and SM-resistant strains, capable of growing in medium containing 100 mg of SM per mℓ, were obtained from each strain respectively. The fluid medium consists of NaCl 2.5 g, $(NH_4)H_2PO_4$ 0.5 g, K_2HPO_4 0.5 g, glucose 1 g, $MgSO_4 \cdot 7H_2O$ 0.1 g, and distilled water 250 mℓ, and pH was adjusted to 7.2–7.4 using sodium hydroxide solution.

3. Preparation of O and H antisera

Both O and H antisera were prepared using standard procedures (Kojima and Hatta, 1941[16)]; Edwards and Bruner, 1942[8)]; Kauffmann 1951[18)]; Denken-Gakuyukai, 1951[7)]).

4. Determination of O and H antigens

O and H antigens were determined by slide agglutination, tube agglutination and agglutinin absorption, using monofactor sera and/or un-

Table 1. *Streptomycin Sensitivity of Salmonella Strains of Group E_1 and E_2*

Group	Strain	Concentration of streptomycin (μg/mℓ)				
		250	167	125	100	50
E_1	S. anatum 293	−	+	+	+	+
	S. butantan	−	−	−	+	+
	S. vejle	−	−	−	+	+
	S. simi	−	+	+	+	+
E_2	S. kinshasa	−	−	−	+	+
	S. cambridge	−	−	−	+	+
	S. canoga	−	−	−	−	+

One loopful (3 mm in diameter) of culture grown in synthetic fluid medium at 37°C for 20 hours was inoculalted into 1 mℓ of SM-containing medium.
+ : growth after 20 hours incubation at 37°C
− : no growth

absorbed sera.

5. Phages

Phages were obtained by autolysis or broth culture of lysogenic cells or by mixed cultivation of lysogenic and susceptible cells.

i) Autolysate: Bacterial cells grown on agar medium at 37°C for 20 hours were suspended in physiological saline solution with density at approximately 3×10^{10} cells per mℓ, kept at 37°C for 48 hours, further centrifuged to remove the bacterial cells and the resultant supernatant was filtered through Chamberland L_3. The filtrate was used as autolysate, containing approximately 10^6 phage particles per mℓ. Phage titration of autolysate should be conducted using E_1 strain which possesses the same structure in H antigens as that of the strain from which autolysate was prepared, since host-controlled variation must be taken into consideration.

ii) Filtrate of mixed culture: Lysogenic and susceptible cells were cultured in nutrient broth at 37°C for 20 hours. A part of the supernatant after centrifuging was added to new nutrient broth. The broth was inoculated with susceptible cells, incubated at 37°C for 20 hours and centrifuged to remove the cells. The above procedures were repeated several times, and the supernatant of the resulting broth culture was filtered through Chamberland L_3. Phage suspensions were tested for sterility at the time of preparation and when used.

6. Optical density was determined by electrophotometer with wave length at 6430A.

7. Plaque count was carried out by agar-layer method (Denken-Gakuyukai, 1951[7]).

8. Antigenic alteration by antisera

Anti-15 monofactor serum was prepared by absorbing anti-S. newington or anti-S. newbrunswick O serum with S. london or S. anatum. Antigenic variants, possessing O antigenic factor 15, were cultured in nutrient broth containing anti-15 monofactor serum and, when nessessary, serially subcultured. At appropriate intervals the culture was plated out on nutrient agar plate and resulting colonies were tested by monofactor sera.

9. Test for lysogenicity of induced variant cells

i) After soaking in phage antiserum, pure culture of respective induced variant strain was obtained. From each pure culture, autolysate was prepared and its lytic activity to E_1 grous organisms was tested by plaque formation

and by densitometric determination of broth culture. As indicator strains, respective parent strain and S. anatum 293 were generally employed.

ii) Each autolysate was additionally tested for its activity of inducing antigenic conversion in E_1 group organisms, generally using S. anatum 293 as an indicator strain.

iii) Further tests were conducted to determine whether each pure culture was immune or susceptible to the phages obtained from E_2 group organisms.

10. As a desoxyribonuclease preparation, varidase (Lederle),

a commercial preparation, containing streptokinase and streptodornase, was used. Lytic activity and SM-resistance inducing activity of phage suspension were tested after keeping the mixture of phages and varidase at 30°C for 5 hours. Varidase is a white, lyophilized enzyme preparation, containing 20,000 units of streptokinase and at least 5,000 units of streptodornase (desoxyribonuclease), prepared from culture filtrate of group C hemolytic streptococcus. Enzymatic activity was verified using thymus nucleic acid as a substrate.

Results

1. Induction of streptomycin-resistance by autolysate

Autolysate prepared from SM-resistant S. kinshasa was mixed aseptically with nutrient broth in proportions of 3 and 7. After the mixture was tested for sterility, S. anatum, S. butantan, S. vejle and S. simi of E_1 group were inoculated separately and serially subcultured. Each of the 4 th subcultures was plated on agar plates containing SM, at the rate of 0.1 mℓ per plate. SM-resistant colonies appeared in S. anatum, S. vejle and S. simi, with the

Table 2. *Induction of Streptomycin-resistance in E_1 Group Organisms by Autolysate of Streptomycin-resistant Strain of Kinshasa*

Nutrient broth mixed with	Recipient strain	No. of colonies on nutrient agar containing streptomycin (mg/mℓ1)									
		100	40	20	10	5	2.5	1.25	0.625	0.3	0.15
Autolysate of SM-resistant S. kinshasa	S. anatum 293	11 (10)	19 (1)	16 (1)	4 (1)	6 (1)	11 (2)				
	S. butantan	0	4 (4)	0	0	0	0				
	S. vejle	0	0	0	2 (2)	0	0				
	S. simi	2 (2)	1 (1)	2 (1)	1	1 (1)	1 (1)				
None	S. anatum 293			0				0	0	0	0
	S. butantan							0	0	0	0
	S. vejle							0	0	0	0
	S. simi			0				0	0	0	0
Heated autolysistant of SM-resistant S. kinshasa	S. anatum 293			0*	0*						
	S. simi			0*	0*						
Autolysate of SM-sensitive S. kinshasa	S. anatum 293			0*							
	S. batantan			0*							

Figures indicate number of colonies.

* 3 plates were used, on each of which 2 times as many cells as those on test plate were inoculated.

exception of S. butantan, in which, however, SM-resistant colonies appeared in the 8 th subculture.

The above findings are summarized in table 2, which shows that autolysate of SM-resistant S. kinshasa was capable of inducing SM-resistance in all four recipient strains. When autolysate was not added to nutrient broth, SM-resistant colonies could not be detected even on agar plate containing less than 1.25 mg of SM per mℓ. Moreover, when autolysate was heated at 100°C for 30 minutes and also when autolysate of SM-sensitive S. kinshasa was used instead of that of SM-resistant strain, SM-resistant cells were not detected.

Among the SM-resistant colonies, 16 strains of S. anatum, 4 of S. butantan, 2 of S. vejle and 6 of S. simi (which correspond to the figures in parentheses in table 2) were picked at random and tested for grade of SM-resistance. All of the above were found to be capable of growing in synthetic fluid medium containing 100 mg of SM per mℓ.

Similar results were also obtained in S. anatum and S. simi, using autolysate of SM-resistant S. cambridge.

2. *O antigenic structure and lysogenicity of induced streptomycin-resistant strains*

All SM-resistant strains obtained from S. simi and S. vejle were found agglutinable by anti-15 serum but not by anti-10 serum, which findings were confirmed by tube agglutination and by agglutinin absorption. Thus, it can be said that in these strains O antgens were converted from 3, 10 to 3, 15.

Contrary to the above, SM-resistant strains of S. butantan were found to possess 3, 10 as O antigens, the same structure as that of parent strain.

Among SM-resistants of S. anatum, only one of 16 strains was found to possess 3, 15 antigens and the remaining 15 strains were found antigenically unaltered.

The above indicates that in some strains induction of SM-resistance is associated with antigenic alteration from 3, 10 to 3, 15, while in others the former is not associated with the latter. Taking the antigenic change into consideration, two kinds of SM-resistant variant cells were tested for their lysogenicity, with the following results.

i) It has been found that the autolysates of antigenically altered SM-resistant strains, which were obtained from S. anatum, S. simi and S. vejle, contained phages capable of infecting S. anatum 293, resulting in antigenic alteration from 3, 10 to 3, 15 in a limited number of the cells.

ii) It has also been confirmed that the antigenically altered SM-resistant strains were resistant to lytic activity of the phages obtained from S. canoga of E_2 group.

iii) Contrary to the above, in the anigenically unaltered SM-resistant strains of S. anatum and S. butantan, neither phages infecting E_1 group organisms nor activity of inducing antigenic conversion in E_1 group organisms could be detected in the autolysates of the respective strains and/or in the mixed broth culture of SM-resistant variant and E_1 group orgnisms (S. anatum or S. butantan). These SM-resistant strains were also susceptible to the lytic action of the phages of S. canoga.

iv) Among SM-resistant antigenically unaltered strains of S. anatum and S. butantan, two strains were picked at random respectively (S. antum S^r-6; S^r-7 and S. butantan S^r-1; S^r-2). Four hours broth culture of each strain, was mixed with phages of S. canoga, and was incubated at 37°C for 18 hours and plated out on agar plates. Resulting colonies were examined serologically. In S. anatum S^r-6 5 out of 15 colonies, in S. anatum S^r-7 6 of 15, in S. butantan S^r-1 3 of 15, and in S. butantan S^r-2 1 of 15 were agglutinable by antiserum but not by 10 antiserum. Seven of the antigenically altered colonies were picked at random and were further confirmed to be capable of growing in synthetic fluid medium containing 100 mg

of SM per mℓ and to be lysogenic.

v) Each single strain of SM-resistant antigenically altered S. anatum and S. simi was selected at random and cultured in broth containg anti-15 serum. From both strains antigenic variants, possessing 3, 10 instead of 3, 15, were obtained. Antigenic variants were also confirmed to be non-lysogenic, while remaining SM-resistant.

3. Necessity of phage

In order to prove the neceasity of phages for transmission of SM-resistance the following additional experiments were carried out.

i) SM-resistant S. anatum S^r-6, which was obtained in experiment 1 and possessing 3, 10 antigenic factors, was cultured in nutrient broth at 37°C overnight. After removing the cells by centrifuge, a small amount of supernatant was added to nutrient broth and in it S. anatum S^r-6 was cultured at 37°C for 20 hours and the supernatant was obtained by removing cells by centrifuge. The above procedures were repeated through 10 passages, and the supernatant of the 10th broth culture was filtered through Chamberland L_3. The filtrate was added to nutrient broth and S. anatum 293 was serially subcultured in the above medium through 5 passages. SM-resistant cell, however, could not be detected.

ii) Phage suspension was made from S. anatum S^r-6 and added to nutrient broth. Though in this phage-broth mixture S. anatum was serially subcultured through 10 passages, SM-resistant cell could not be detected.

It is evident from the above that phage is a necessary factor for transmission of SM-resistance.

4. Frequency of occurrence of streptomycin-resistant cells

The cells of S. anatum, grown on agar medium at 37°C for 20 hours, were suspended in physiological saline solution with the density at 9.8×10^8 cells per mℓ, and phage suspension containing 6.8×10^9 lytic particles per mℓ was prepared from SM-resistant S. kinshasa. The cell suspension was mixed with the phage suspension in equal volume (5 mℓ), kept at room temperature for 30 min., and centrifuged at 4,000 R.P.M. for 30 min.. The sedimented cells were resuspended in a small amount (2 mℓ) of saline solution, and 0.1 mℓ of this suspension was seeded on each one of 10 agr plates. Five of them were overlayered with agar medium containing 10 mg of SM per mℓ immediately (Group A) and the remaining five plates were after standing at 37 °C for 5 hours (Group B).

Table 3 shows the results. In both groups A and B SM-resistant colonies developed on every plate while in control groups C and D, in which the bacterial cells were not treated with the phage, no or only a very few SM-resistant colonies appeared in spite of the fact that each plate was inoculated with 2 times as many cells as in groups A and B.

Table 3. *Frequency of Occurrence of SM-resistant Cells*

Group	Recipient strain		S. anatum 293				
	Treated with	Phenomic lag	plate No.				
			1	2	3	4	5
A	Phage	−	4	3	14	12	17
B		+	21	23	84	57	60
C	None	−	0	0	0		
D		+	0	1	0		

Figures indicate number of colonies.

The second point which should be mentioned is the effect of phenomic lag, which was observed in groups B and D. The number of SM-resistant colonies increased definitely when phage-treated or non-treated cells were incubated for 5 hours prior to exposure to streptomycin. The findings in groups C and D support Newcomb's statement that a phenomic lag also occurrs in spontaneous mutation.

Thus, the frequency of transmission of SM-resistance to group E_1 cells by the phages seems to be about 1 out of 10^6 to 10^7 cells. This order of magnitude of the frequency is

Table 4. *Transduction of SM-resistance in E_1 Group Organisms by Phages, Which Were Obtained from SM-sensitive S. canoga and Propagated on SM-resistant S. anatum S^r-6, S^r-7 and/or S. butantan S^r-1*

Recipient strain	S. anatum 293							S. butantan					
Donor strain	Plate No.												
	1	2	3	4	5	6	7	1	2	3	4	5	6
S. anatum S^r-6	12	14	6	7	13	15	27						
None	0*	0*											
S. anatum S^r-7	17	27	9	15	9	14	19	8	13	16	22	30	9
None	0*	0*						0*	0*				
S. butantan S^r-1	2	1	1	0				Confl.	Confl.	Confl.	Confl.		
None	0*	0*						0*	0*				
SM-sensitive S. anatum 293	0*	0*	0*					0*	0*	0*			
SM-sensitive S. butantan	0*	0*	0*					0*	0*	0*			

Figures indicate number of colonies.

* 0.1 mℓ of broth culture alone containing 2 times as many bacterial cells as those test plate weare was plated out.

Confl.: Confluent colonies.

consistent with that in transduction.

5. Transduction of streptomycin-resistance

Since the data of the above experiments suggested that the transmission of SM-resistance is due to transduction and is slightly different from antigenic conversion by phage, transduction of SM-resistance was tested by using the phages of E_2 group organisms and by adhering strictly to the procedures described in references. And while in most of the above experiments phages used were originated from SM-resistant strain, in this experiment phages originated from SM-sensitive strain of S. canoga were employed.

Six hours broth culture of SM-resistant antigenically unaltered S. anatum (S^r-6 and S^r-7) or S. butantan S^r-1 was mixed with phages obtained from SM-sensitive S. canoga and incubated at 37°C for an additional 18 hours. The bacterial cells were removed by centrifugation and the supernatant was filtered through Chamberland L. One mℓ of this filtrate was added to 5 mℓ of nutrient broth, to which SM-sensitive S. anatum or S. butantan was inoculated and further incubated at 37°C for 18 hours. The cultures were plated on agar plates containing 20 mg of SM per mℓ at the rate of 0.05 mℓ per plate and the plates were incubated at 37°C. The results are shown in table 4.

Regardless of the donor strain, S. anatum S^r-6 S. anatum S^r-7 or S. butantan S^r-1 SM-resistance was transmited to both of the recipient strains, SM-sensitive S. anatum and S. butantan. When phages were not added or when phages propagated on SM-sensitive strains, S. anatum 293 or S. butantan, were added to the recipient strains, no colonies appeared. And also no colonies were formed when the filtrate, heated at 100°C for 1 hour, was added.

Among SM-resistant colonies, 8 colonies of S. anatum and 14 of S. butantan were picked at random and were submitted to serological and SM-sensitivity tests. The entire number was found to be capable of growing in synthetic medium containing 100 mg of SM per mℓ and

to possess 3, 15 factors as O antigens instead of 3, 10. These findings also indicate that conversion of O antigens occur even when phages are propagated on strains possessing 3, 10, while SM-resistance can be transferred only when donor strain is SM-resistant but not when it is SM- sensitive.

6. Effect of desoxyribonuclease

It has been reported that transduction is not affected by DNAase (Zinder, and Lederberg, 1952[27]) while the transforming principle is inactivated rapidly by DNAase (Austrian, 1952[3]). In the authors' experiments there remains a possibility that DNA may have been released in large amounts from phagelysed SM-resistant bacterial cells and DNA may have played the role of transforming principle in transmission of SM-resistance to SM-sensitive cells. To test this point DNAase was employed. 0.6 mℓ of phage suspension (5×10^9 particles per mℓ), which was obtained from SM-sensitive S. canoga and propagated on SM-resistant S. anatum S^r–7, was mixed with 0.4 mℓ of varidase solution (5,000 u per mℓ), incubated at 30°C for 5 hours, then further mixed with 0.5 mℓ of bacterial suspension of SM-sensitive strain of S. anatum (6×10^9 cells per mℓ) and kept standing at 37°C for hour. Then 0.1 mℓ of the phage-bacterium mixture was plated on each agar plate containing 20 mg of SM per mℓ. As control, phage suspension, mixed with nutrient broth in equal volume, was kept at 30°C for 5 hours, mixed with SM-sensitive cells of S. anatum, kept at 37°C for 1 hour and 0.1 mℓ were plated on each SM-agar plate. As the second control, 0.1 mℓ of recipient cell suspension alone was plated on each of 4 SM-agar plates. The results are shown in table 5 and 6. Table 5 shows that phages were not inactivated by varidase-treatment. Table 6 shows that phage suspension was still capable of transmitting SM-resistance to recipient cells after varidase treatment. The number of SM-resistant colonies was almost the same in varidase-treated and in non-treated phage group (control 1). In control 2 no SM-resistant colonies appeared in spite of the fact that the number of cells seeded per plate was 3 times as many as in the other two groups. In addition, it was also confirmed that all the resulting colonies in both groups were capable of growing in synthetic fluid medium containing 100 mg of SM per mℓ and that 6 of the colonies had 3, 15 factors as O antigens.

Table 5. *Effect of Varidase on Lytic Activity of Phage*

Dilution	Number of plaques	
	Phages	Varidase-treated phages
$1:10^7$	340	296
$1:10^8$	29	31
$1:10^9$	2	5

Table 6. *Effect of Varidase on Transmission of SM-resistance*

Recipient strain	S. anatum 293					
	Plate No.					
	1	2	3	4	5	6
Phage varidase	1	1	3	0	0	0
Phage alone (control 1)	1	1	0	0		
Bacterial cells (control 2)	0	0	0	0		

Figures indicate number of SM-restsiant colonies.

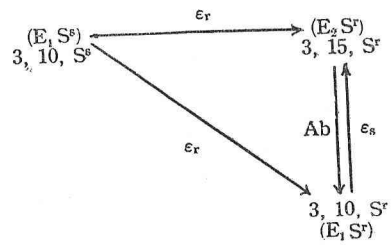
The above experiments indicate that the transmission of SM-resistance was not inhibited by DNAase.

Discussion

The above experimental results are summarized below.

The transmission of SM-resistance by phage, observed in the above experiments, is considered to be a transduction, for the following reasons: that it required active phages, that it is not prevented by DNAase, that it occurrs at the same rate as that reported in transduction and that it depends on SM-resistance of donor strains.

Antigenic alteration by phage differs from



S^r: Sterptomycin resistant
S^s: Streptomycin sensitive
ε : Phages obtained from E_2 group organisms
ε_r: Phages obtained by autolysis of SM-resistant cells of E_2 group or phages propagated on SM-resistant cells of E_1 group
ε_s: Phages obtained by autolysis of SM-sensitive cells of E_2 group or phages propagated on SM-sensitive cells of E_1 group
$\vec{\varepsilon}$= Direction of variation (SM-resistance and antigenic structure) by phage
$\vec{Ab}$= Direction of antigenic alteration after exposure to antiserum

transmission of SM-resistance in the following points.

i) For transmission of SM-resistance, phages were required to be propagated on SM-resistant cells, while recipient cells could be altered from 3, 10, to 3, 15 in their O antigenic structure, even when phages were propagated on E_1 group cells, possessing 3, 10, but not 3, 15 factors.

ii) In transmission of SM-resistance, phage was not always transmitted to all the progeny of cells showing a transduced character (SM-resistance), while antigenic alteration, phage was always transmitted to all the progeny of cells, showing antigenic structure of 3, 15.

iii) In transmission of SM-resistance the order of magnitude of frequency was very low (approxmately only one per 10^6 to 10^7 recipient cells acquired SM-resistance), while in antigenic alteration it has been reported in previous paper (Uetake et al., 1955) that about 2 to 3 per cent of recipient cells could be altered antigenically from 3, 10 to 3 15.

As evident from the order of magnitude of the frequency, in transduction it has been reported that the simultaneous transduction of two characters to a single cell has not been demonstrated as yet, except in particular cases in which two characters are related to one definite character, e.g. flagella, and the genes concerned are assumed to be located near one another, perhaps on short pieces of chromosome (Stocker, Zinder and Lederberg, 1953[24]).

In the authors' experiments, however, the simultaneous transmission of two characters, SM-resistance and antigenic structure of 3, 15, was readily demonstrated. This could hardly be expected if both transmissions were transductions.

While the authors' experiments were being conducted, it was reported that autolysate of SM-resistant S. newington was capable of transmitting SM-resistance to SM-sensitive cells of S. anatum which were simultaneously altered from 3, 10 to 3, 15 in O antigens and that phages seem to play a role of passive carrier of filtrable agnt (Sakai and Iseki, 1955[22]). Though the frequency rate of occurrence of SM-resistance cells was not described, their observations seem to be similar to the authors'. It was also pointed out that even after SM-resistant variant cells were converted antigenically from 3, 15 to 3, 10 by being cultivated in broth containing phage antiserum and accompanied by simultaneous loss of lysogenicity, the cells still remained SM-resistant. This is also consistent with the author's findings.

The above 3 points constitute the main differences existing between 'phage-induced antigenic conversion' and 'phage-induced transmission of SM-resistance'. These are also the differences between 'phage-induced antigenic convenrsion in group E Salmonellas' and 'transduction'. The nature of the transmission of SM-resistance can not be distinguished from transduction. It therefore can not be anything but transduction itself.

Though the comparison of table 1 with table 2 may appear to suggest there would be some

correlation between level of natural SM-resistance of E_1 strains and the ease with which they can be transduced, this is not conclusive for the following reasons; first, no difference can be noticed between S. anatum and S. butantan in table 4; second, the difference of natural SM-resistance among E_1 strains are not so great; third, it is difficult to make numerical comparison in experiments shown in table 2, since bacterial cells were allowed to multiply freely in phage-containing broth, irrespective of SM-sensitivity.

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Summary

It has been demonstrated that the phages obtained from SM-resistant cells of group E_2 or propagated on SM-resistant cells of group E_1 were capable of transducing SM-resistance in SM-sensitive cells of group E_1. In some instances, the transmission of drug resistance was associated with antigenic change in recipient cells, while in others the former was not associated with the latter. It was also confirmed that antigenic conversion was associated with lysogenization of recipient cells, while the transmission of drug resistance was not associated with lysogenization unless being associated with antigenic conversion.

The differences were discussed between the transmission of SM-resistance or the transduction and the phage-induced antigenic conversion.

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