Communications to the editor

INFECTIOUS RESISTANCE TO CARBENICILLIN IN *PROTEUS RETTGERI*: OCCURRENCE OF TWO DIFFERENT PENICILLINASES IN THE SAME STRAIN

Sir:

Ampicillin, carbenicillin and cephalosporins are beta-lactam antibiotics effective against some gram-negative bacteria. However, they may be neutralized by enzymes, usually beta-lactamases. Different beta-lactamases have been found among enterobacteria[1]. Although ampicillin and carbenicillin are closely related, cross resistance does not always exist. The occurrence of a segregation in the resistance to carbenicillin in a *Proteus rettgeri* population led us to isolate three strains supposed to be three variants of the same strain. These variants LG21, LG22 and LG23 show the following minimal inhibitory concentrations (M.I.C.) (Table 1).

Table 1. M.I.C. in *Proteus rettgeri*

	M.I.C. (mcg/ml)		
	Ampicillin	Carbenicillin	Cephaloridine
LG21	<4	<4	<4
LG22	30~60	<4	250
LG23	1,000	2,000	250

LG21 is sensitive to the three antibiotics. LG22 is sensitive to carbenicillin and resistant to the other two, while LG23 is resistant to all three of them. Through a Millipore membrane LG22 and LG23 secrete a product which neutralizes ampicillin in nutrient agar, thus allowing LG21 to grow on it. It is thought that there are two different enzymes.

Table 2. Segregation frequencies in LG23

	No. tested	No. replicated on		Loss of R to carbenicillin (%)
		Ampicillin (15 mcg)	Carbenicillin (50 mcg)	
Without acriflavine	104	104	88	15
With acriflavine	37	37	18	50

Spontaneously, or after treatment with acriflavine, LG23 is transformed into LG22, but under the same conditions LG22 is not transformed into LG21 (Table 2).

The presence of an R factor was investigated by mating both strains LG22 and LG23 with an *Escherichia coli* K12 variant, resistant to nalidixic acid (G1064). Only with LG23 could transcipient bacteria be obtained, through selection on agar containing nalidixic acid (50 mcg/ml). Transfer frequency (transcipient cells/donorcells, after one hour mating) is about 10^{-5}.

M.I.C. of *E. coli* G 1064 and of the same strain converted either by this R factor or by another R factor found in *Salmonella typhimurium* (EJ 2)[2] are indicated in Table 3. In G1064 this new R factor is not stable. All converted strains present segregation patterns after first isolation.

Table 3. M.I.C. in *Escherichia coli* K12

	M.I.C. (mcg/ml)		
	Ampicillin	Carbenicillin	Cephaloridine
G1064	6	12	3
G1064 (R. LG23)	1,000	>4,000	31~62
G1064 (R. EJ2)	800	125	not tested

These results confirm the occurrence of an R factor developing resistance to carbenicillin and ampicillin in *Proteus rettgeri* in which resistance to ampicillin depends on another mechanism. This R factor is different from the one recently discovered by FULLBROOK *et al.*[3] in *Pseudomonas* where it develops resistance to ampicillin, tetracycline, neomycin and kanamycin.

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(Received January 12, 1971)

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