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Bacteriophage Mu-1-Induced Mutation to *mutT* in *Escherichia coli*

SUSAN E. CONRAD, KARL T. DUSSIK, AND ELI C.. SIEGEL*
Department of Biology, Tufts University, Medford, Massachusetts 02155

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Of approximately 10,000 independent phage Mu-1 lysogens, 3 had a mutator phenotype. One (mutation designated *mut-49*) resembled *mutT1* in the frequency and types of mutations induced. *mut-49* was mapped between *leu* and *ace* and was not separable from the Mu prophage. *mut-49* was recessive and did not complement *mutT1*. *mut-49*, like *mutT1*, did not increase the reversion of the frameshift mutation *lacZ*(ICR48). *mut-49* and *mutT1* induced the same two classes of *trpA78* revertants, indicating that *mut-49* induced adenine-thymine → cytosine-guanine transversions. The results support previous work indicating that the mutational specificity of *mutT* is gene and not allele specific.

Mutations resulting in a mutator phenotype can occur in at least six separate genes in *Escherichia coli*: *mutT* (7, 24), *mutD* (8), *mutS* (6, 18), *mutR* (10), *mutU* (17), and *mutL* (12). The specific functions in deoxyribonucleic acid (DNA) replication or repair of the *mut*$^+$ gene products are not known. No mutation temperature sensitive for DNA replication or affecting any known DNA polymerase, nuclease, or ligase is in the same gene as any of the six mutators. These six loci may code for proteins that have an error-correcting but nevertheless nonessential role in DNA metabolism. R. Hoess (personal communication) has recently shown that the *mutR*$^+$ locus can be deleted, resulting in a viable mutator strain.

We have begun to study this question of essentiality by using phage Mu-1, which inserts at random into the *E. coli* chromosome (2, 3, 14), to induce mutations to the mutator phenotype. The insertion of phage Mu-1 should result in a complete absence of the product of the affected gene. As a result of Mu-1 lysogenization, we induced three mutations that gave the mutator phenotype. One of these had the genetic map location and phenotype of *mutT*, and we chose it for study because of the unusual mutational specificity of *mutT1*, the induction of AT → CG (adenine-thymine → cytosine-guanine) transversions (25). We found no significant differences between the original *mutT1* and the phage Mu-induced mutation.

MATERIALS AND METHODS

Bacterial strains and bacteriophages. Table 1 lists the bacterial strains used and their sources. In the text, the most important markers are sometimes given in parentheses after the strain designation. Transducing phage P1*kc* was from our collection, and phage Mu-1 was a gift from A. L. Taylor. Hereafter, Mu-1 is designated Mu.

Media. Minimal medium, L media, nutrient agar, and Penassay broth were previously described (17). Ace$^+$ transductants were selected on medium containing 0.4% succinate in the form of potassium succinate as the carbon source. For phage Mu growth, assay, and lysogenization, L media were supplemented with 2.5×10^{-3} M $CaCl_2$ and 1.0×10^{-3} M $MgCl_2$ (11).

Lyogenization with phage Mu-1. Phage Mu lysates were prepared by confluent lysis of strain 115. Titers of 10^{10} to 3×10^{10} PFU (plaque-forming units) per ml were usually obtained. For lysogenization, log-phase cells of strain AB3505 (about 3×10^8 cells/ml) were incubated with phage Mu at a multiplicity of infection of about 7 in L broth for 20 min at 37 C. Dilutions of the mixture were then spread on nutrient agar plates that previously had been spread with 10^9 PFU of Mu. This procedure gave about 50% survival of strain AB3505, and about 70% of the survivors were Mu lysogens.

Detection of mutator (Mut$^-$) lysogens and recombinants. The lysogenization with phage Mu and subsequent dilution gave 100 to 200 colonies on the nutrient agar plates. After 2 days of incubation, these plates were replica plated onto nutrient agar + streptomycin (200 μg/ml) to detect possible mutator colonies (17). Recombinants or merodiploids from conjugations or transductions were tested for Mut$^-$ by overnight growth in either Penassay broth or L broth and plating 0.1 ml of the resulting culture on nutrient agar + streptomycin (17).

Test of Trp$^+$ revertants. The quantitative test for sensitivity to 5-methyltryptophan was previously described (6, 19). It was used to distinguish the three classes of *trpA78* revertants.

Genetic procedures. Methods of transduction and conjugation were previously described (17). Tests for complementation between *mutT1* and *mut-49* and for the recessiveness of *mut-49* involved selecting for

TABLE 1. *Bacterial strains*

Strain[a]	Description[b]	Source and/or reference[c]
115	*sup ton* λ^-	S. E. Luria
58-278M*	*bio-1 phe-1 mutT1*	24
AB259	Hfr PO1 *thi-1* λ^-	CGSC
AB1157	*thr-1 leu-6 thi-1 proA2 his-4 argE3 str-31*	CGSC
AB3505	*thi ilvD188 argH1 met-E46 his-4 trp-3 proA2*	CGSC
Hfr 3000 *mutT1*	Hfr PO1 *thi mutT1*	E. C. Cox (5)
JC12	Hfr PO12 *metB1 purF1*	A. J. Clark
KL16-99	Hfr PO45 *recA1* λ^-	CGSC
UH-Ac_2	*aceE1 trp-26 mel-1 sup* λ^+	CGSC
ES644	As AB3505 but Mu-1^+ *mut-49*	Lysogenization with Mu-1 (see text)
ES656	As ES644 but *ilv*$^+$ *arg*$^+$ *met*	JC12 × ES644 conjugation
ES695	Hfr PO1 *leu lacZ* (ICR48)	20
ES751	As ES695 but *leu*$^+$ *mut-49*	ES656 × ES695
ES752	As ES695 but *leu*$^+$	ES656 × ES695
ES755	As AB1157 but *met str*$^+$ *arg*$^+$	JC12 × AB1157 conjugation
ES756	As UH-Ac_2 but *leu*	*leu* EMS induced
ES768	As ES755 but *leu*$^+$ *mut-49*	ES656 × ES755
ES770	As ES768 but *spc-300*	
ES783	As ES770 but *his*$^+$ *recA1*	KL16-99 × ES770 conjugation
ES786	Hfr PO1 *lacZ* (ICR75) *leu trpA78*	
ES797	As ES786 but *leu*$^+$ *mutT1*	58-278M* × ES786
ES798	As ES786 but *leu* $^+$	58-278M* × ES786
ES799	As ES786 but *leu*$^+$ *mut-49*	ES656 × ES786
ES800	As ES786 but *leu*$^+$	ES656 × ES786
ES851	*leu sup mut-49*	Derived by several conjugations from ES656
ES856	As ES752 but Mu-1^+	Lysogenization with phage Mu
ES861	*polA1 mut-49*	Derived from ES751
ES862	*polA1 mut*$^+$ Mu-1^+	Derived from ES856

[a] All strains are derivatives of *E. coli* K-12.

[b] Symbols: λ^+, Phage λ lysogenic; λ^-, phage λ nonlysogenic; Mu-1^+ phage Mu-1 lysogenic; PO, point of origin. All other symbols as given by Taylor and Trotter (22). Genetic descriptions are not complete.

[c] In crosses the donor is listed first. All crosses were transductions unless indicated. Where no source is given, the strain was developed in this laboratory, but its derivation is not relevant to this work. Abbreviations: EMS, ethyl methane sulfonate; CGSC, *E. coli* Genetic Stock Center.

merodiploids from interrupted matings of Hfr donors with F$^-$ *recA* recipients (13). When matings were interrupted by the addition of nalidixic acid (Nal), the donor was Nal^s and the recipient was resistant to 50 μg/ml. This concentration of the drug was added at the time of interruption and was included in the selective medium.

Detection of Mu immunity and Mu release. Mu immunity was detected by plating 0.1 ml of a stationary-phase culture with 0.1 ml of phage Mu (10^5 PFU/ml), using L media. Spontaneous Mu release was determined by treating late-exponential-phase cultures in L broth with chloroform and plating 0.1 ml of the killed culture with 0.1 ml of indicator cells. To verify that the resulting plaques, either normal or minute, actually were phage Mu, we used Mu lysogens and as well as nonlysogens as indicator strains.

Measurement of cell length. Exponential-phase cells growing in L broth were heat fixed and stained with crystal violet. Cell length was measured with an occular micrometer.

Sensitivity to sodium azide and phenethyl alcohol. Inhibition of growth in L broth plus the drug was determined by measurement of optical density, using the method of Yura and Wada (26).

RESULTS

Isolation of the mut-49 strain and genetic mapping. Strain AB3505 was treated with phage Mu as described in Materials and Methods, and the survivors were tested for the Mut$^-$ phenotype. Three of 14,300 survivors, of which about 10,000 were lysogens, were Mut$^-$. The designation ES644 was given to the strain with the greatest mutator activity, and its mutator allele was designated *mut-49*. Strain ES644 was lysogenic for Mu; this was determined by its immunity to the phage and its ability to release Mu PFU spontaneously.

The frequency of spontaneous streptomycin-resistant mutants in strain ES644 varied from 10^{-7} to 20×10^{-7} mutants/cell; we found the same range for strain 58-278M*, the original *mutT1* strain. The frequency of spectinomycin-resistant mutants in these two strains was less than 10^{-9} mutants/cell, as is found with wild-type strains. Since *mutT* increases the frequency of streptomycin but not spectinomycin-resistant mutants (E. C. Cox, personal communication), our results suggested that *mut-49* was an allele of *mutT*.

In a preliminary attempt to map *mut-49*, strain ES644, which is F$^-$, was mated with the Hfr strain JC12, and Ilv$^+$ Arg$^+$ Pur$^+$ recombinants were selected. The results (data not given) indicated that *mut-49* was in the same quadrant of the chromsome as *pro*. Six of 22 recombinants that were tested had become Mut$^+$ and were no longer immune to phage Mu. Five Mut$^-$ recombinants were tested and were Mu immune. The results suggested that strain ES644 was probably a single lysogen and that *mut-49* and the prophage were linked.

mutT is located between *ace* and *leu* on the *E. coli* genetic map and is cotransducible with both markers (5, 7). To determine whether *mut-49* had a similar location, we used strain ES656 (a recombinant from the Hfr × F$^-$ cross previously described) as the donor and strain ES756 (*aceE1 mutT*$^+$ *leu*) as the recipient in a phage

P1*kc*-mediated transduction. Seven of 192 (3.6%) Leu$^+$ transductants and 9 of 193 (4.7%) Ace$^+$ transductants were Mut$^-$. These results placed *mut-49* between *leu* and *ace*, but the frequencies of cotransduction were lower than expected, presumably because of induction of the prophage transferred to the nonlysogenic recipient. All 16 Mut$^-$ transductants were immune to phage Mu and released phage that formed minute plaques on strain ES756. None of several nonmutator transductants from this cross either were Mu immune or released plaque-forming particles. The release of minute plaque-forming phage by Mut$^-$ transductants occurred whenever *mut-49* was transduced into any of several strains by selection for either Leu$^+$ or Ace$^+$. The minute plaques formed on indicator strains other than strain ES756; no plaques appeared when Mu lysogens were used as indicators. It should be pointed out that the original *mut-49* strain ES644 and strain ES656, which was derived from strain ES644 by conjugation, released phage that formed normal plaques.

These results suggested that the original *mut-49* strain ES644 and its derivative ES656 might have two closely linked Mu prophages; one inserted at the *mut-49* site and resulting in minute plaque-forming phage, and the other yielding no phenotypic change and closely linked but separable from *mut-49* by transduction. To test this possibility, we used strain ES851, a *leu mut-49* derivative of strain ES656. Strain ES851 is Mut$^-$ and Mu immune, and it releases Mu that form normal plaques. Strain ES851 was transduced to Leu$^+$, using the *mut*$^+$ strain 115 as the donor. Twenty of 66 transductants tested (30%) lost the mutator phenotype. Nineteen of these were tested; they had lost Mu immunity and did not release plaque-forming particles. Twenty-nine Mut$^-$ transductants were tested; all were Mu immune. Twenty-eight of the 29 released normal phage, and one Mut$^-$ transductant released minute plaque-forming particles. Twenty-seven additional Mut$^-$ transductants from this cross were tested and released normal phage. The results show that the mutator phenotype, Mu immunity, and the ability to release phage Mu are not separable; *mut-49* resulted from the insertion of phage Mu. The ability to release normal phage is separable by transduction from *mut-49*.

Complementation test and recessiveness of mut-49. *mutT1* is recessive (7); before doing a *mutT-mut-49* complementation test, we first had to determine whether *mut-49* was also recessive. The Hfr strain AB259 (*thr*$^+$ *mut*$^+$ *pro*$^+$ *spc*$^+$) was mated with strain ES783 (F$^-$ *thr-4 mut-49 proA2 recA1 spc-300*); the mating was interrupted after 20 min by agitation, and Thr$^+$ Pro$^+$ Spc^r partial diploids were selected. Three of the partial diploids were grown in medium that selected for and maintained the Thr$^+$ Pro$^+$ phenotype and yielded frequencies of streptomycin-resistant mutants of $<3 \times 10^{-8}$ mutants/cell. After the strains were cured of the presumably *thr*$^+$ *mut*$^+$ *pro*$^+$ episome, the mutation frequency increased to 2×10^{-6} mutants/cell. *mut-49* is recessive.

The complementation test was also done by the selection for F-prime recipients in an Hfr $\times$ F$^-$ *recA* cross. Strain Hfr 3000 *mutT1* was crossed to strain ES833 (*thr-4 mut-49 proA2 recA1 spc-300 nal*). The mating was interrupted by the addition of nalidixic acid, and Thr$^+$ Pro$^+$ Spc^r partial diploids were selected. The frequency of streptomycin-resistant mutants in four partial diploids from this cross ranged from 1.2×10^{-7} to 4.4×10^{-7} mutants/cell; the frequencies of streptomycin-resistant mutants of the two parental strains grown under the same conditions as the merodiploids were 8.2×10^{-7} to 12.8×10^{-7} mutants/cell for strain ES833 and 7.8×10^{-7} to 38.6×10^{-7} mutants/cell for strain Hfr 3000 *mutT1*. The results show that *mut-49* and *mutT1* do not complement each other.

Specificity of mut-49. *mutT1* only induces the transversion AT $\rightarrow$ CG (25). Unlike all other *E. coli* mutator genes studied, it does not increase the frequencies of frameshift mutations (9, 10, 20). We transduced *mut-49* into a strain containing the frameshift mutation *lacZ*(ICR48) (15). This frameshift mutation is strongly reverted by *mutS3*, *mutU4*, and *mut-25* (a probable allele of *mutL*), but not by *mutT1* (20). Both strain ES752 [*mut-49 lacZ*(ICR48)] and strain ES751, which is *mut*$^+$ but otherwise co-isogenic with strain ES752, yielded 8.7×10^{-9} Lac$^+$ revertants/cell, a value 40 to 80 times lower than that found with *mut-25*, *mutU4*, or *mutS3*. *mut-49* did not increase the reversion of *lac*(ICR48).

The mutation *trpA78* forms three classes of revertants that can be distinguished by the quantitative test for 5-methyltryptophan sensitivity (6). *mutT1* induces mutants that fall into two of these classes, and *mutS3*, which induces AT $\rightleftarrows$ GC transitions, increases the frequency of the third class. Table 2 shows the frequency of Trp$^+$ revertants in strain ES797 (*mutT1 trpA78*) and the otherwise co-isogenic strain ES798 (*mut*$^+$ *trpA78*), and in strain ES799 (*mut-49 trpA78*) and the otherwise co-isogenic strain ES800 (*mut*$^+$ *trpA78*). The results are given as revertants per cell plated as well as revertants per plate because unwashed cultures were plated on the selective medium. One large

and one small revertant colony from each of several independent strain ES797 and ES799 cultures were purified and tested for sensitivity to 5-methyltryptophan (Fig. 1). Both *mutT1* and *mut-49* induced the same two classes of revertants. As a control to see whether we could detect the third class of revertants that would result from a transition, we grew strain ES800 (*mut*$^+$ *trpA78*) with 2-aminopurine (200 μg/ml), a strong inducer of transitions. 2-Aminopurine increased the reversion of *trpA78* (Table 2), and the revertants clearly fell into the third class (Fig. 1). *mut-49* and *mutT1* induced Trp$^+$ revertants of *trpA78* at approximately the same frequency (Table 2).

Possible polarity effects. The insertion of phage Mu into an operon has a strong polar effect on the expression of genes distal to the insertion (23). Genes affecting cell division (1, 16), resistance to sodium azide and phenethyl alcohol (26), and the level of DNA polymerase II (4) lie near *mutT*. If *mutT* is in the same operon as any of these genes, a polar effect may be detectable in *mut-49* strains. We measured cell length in strain ES751 (*mut-49*) and strain ES856 (*mut*$^+$ Mu$^+$) and found no difference. Sensitivity to sodium azide and phenethyl alcohol was measured by the increase in optical density of cultures of strains ES751 (*mut-49*) and ES856 (*mut*$^+$ Mu$^+$) grown with different concentrations of the drugs. No difference was found between the two strains (data not given). The level of activity of DNA polymerase II was determined in strains ES861 (*polA1 mut-49*) and ES862 (*polA1 mut*$^+$), and no difference was found (R. E. Moses, personal communication).

DISCUSSION

Phage Mu causes mutations by integrating within genes (2, 14). The phage integrates at random into the *E. coli* chromosome (3). We

TABLE 2. *Reversion of trpA78 by mutT1, mut-49, and 2-aminopurine (2-AP)*

Strain	Revertants per cell ($\times 10^{-8}$)	*mut* or 2-AP/ Mut$^+$	Revertants/plate	*mut* or 2-AP/ Mut$^+$
ES797 (*mutT1*)	454	175	1,130	291
ES798 (*mut*$^+$)	2.6		3.9	
ES799 (*mut-49*)	2,300	411	1,620	202
ES800 (*mut*$^+$)	5.6		8	
ES800 + 2-AP[a]	17	8.9	45.6	5.3
ES800 − 2-AP	1.9		8.6	

[a] 200 μg/ml.

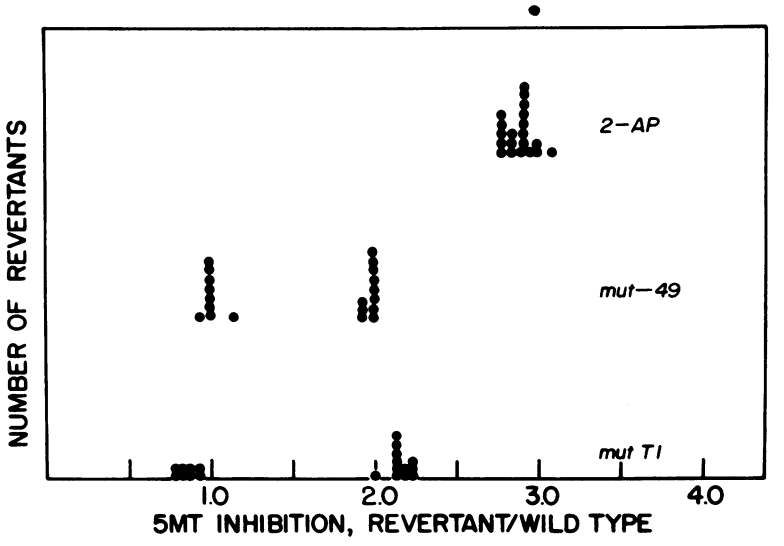

FIG. 1. *5-Methyltryptophan (5MT) sensitivity of trpA78 revertants induced by mutT1, mut-49, and 2-aminopurine (2-AP). The diameter of the zone of inhibition of the revertant was divided by the diameter of the zone obtained with a co-isogenic trp*$^+$ *strain (wild type). This value is shown on the abscissa. Each dot represents one revertant.*

used phage Mu as a mutagen to induce mutations with the expectation that only nonessential genes could be inactivated by the insertion of phage Mu and result in the mutator phenotype. Of three mutations to the mutator phenotype induced in this way, one, *mut-49*, was found by map location and a complementation test to be an allele of *mutT*. The mapping experiments also showed that *mut-49* and the Mu prophage were not separable.

The transduction experiments were able to separate the ability to produce normal phage Mu from *mut-49*. We do not have a complete explanation for the release of wild-type phage Mu by the original *mut-49* lysogen and the release of minute plaque-forming phage by Ace$^+$ or Leu$^+$ transductants that had received *mut-49*. In a cross by transduction of a *leu mut-49* strain that released normal phage with a *leu*$^+$ *mut*$^+$ donor, we found one transductant that was Mut$^-$ and Mu immune and released minute plaque formers. This suggests that a Mu gene or genes essential for normal plaque formation is only weakly linked to the remainder of the prophage integrated at *mutT*. There is, however, no indication from the work of others that separation of Mu genes can result from integration. Our results do show that *mut-49* and the majority of prophage genes are at the same genetic locus.

Cox (5) studied four independent *mutT* mutations induced by the mutagen *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine. All had the same mutational specificity as the original *mutT1*, the induction of the AT → CG transversion, and induced mutations at approximately the same frequency as *mutT1*. Cox pointed out that it was possible but not probable that the four new alleles resulted from an identical mutational event as *mutT1*. *mut-49*, induced by the insertion of phage Mu, is clearly a different mutation from *mutT1* and the four additional *mutT* alleles isolated by Cox. It induces mutations at approximately the same frequency as *mutT1*. The failure of *mut-49* to increase the frequency of *spc* mutations and the induction of the same two classes of *trpA78* revertants as *mutT1* indicate that *mut-49* has the same specificity as *mutT1*. Our results confirm those of Cox (5) that the activity and specificity of *mutT* mutations are characteristic of the gene and not the allele. Our results also suggest that the *mutT*$^+$ gene product is not essential for viability.

The nature of the *mutT*$^+$ gene product is unknown. The *mutT1* allele is not suppressible by several amber and ochre suppressors; other *mutT* alleles were not checked (E. C. Cox, personal communication). *mutT1* is suppressible by *sum-44*, a mutation linked to *dapD*, but it is not known whether *sum-44* is a missense suppressor or is specific for the suppression of *mutT* (5). We do not yet know whether *mutT* has a protein product. Nonsense or missense suppression has been used to show that *mutR* and *uvrE502*, an allele of *mutU*, have protein products (21 R. H. Hoess, personal communication). We tried to determine whether *sum-44* would suppress *mut-49* but were not able to get an answer, presumably because of the instability of *sum-44* (E. C. Cox, personal communication). If *mutT*$^+$ does have a protein product, its loss of activity by either point mutation or insertion results in an identical defect in the accuracy of DNA replication.

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LITERATURE CITED

1. **Allen, J. S., C. C. Filip, R. A. Gustafson, R. G. Allen, and J. R. Walker.** 1974. Regulation of bacterial cell division: genetic and phenotypic analysis of temperature-sensitive, multinucleate, filament-forming mutants of *Escherichia coli*. J. Bacteriol. 117:978–986.
2. **Boram, W., and J. Abelson.** 1971. Bacteriophage Mu integration: on the mechanism of Mu-induced mutations. J. Mol. Biol. 62:171–178.
3. **Bukhari, A., and D. Zipser.** 1972. Random insertion of Mu-1 DNA within a single gene. Nature (London) New Biol. 236:240–243.
4. **Campbell, J. L., H. Shizuya, and C. C. Richardson.** 1974. Mapping of a mutation, *polB100*, affecting deoxyribonucleic acid polymerase II in *Escherichia coli*. J. Bacteriol. 119:494–499.
5. **Cox, E. C.** 1973. Mutator gene studies in *Escherichia coli:* the *mutT* gene. Genetics 73(Suppl.):67–80.
6. **Cox, E. C., G. E. Degnen, and M. L. Scheppe.** 1972. Mutator gene studies in *Escherichia coli:* the *mutS* gene. Genetics 72:551–567.
7. **Cox, E. C., and C. Yanofsky.** 1969. Mutator gene studies in *Escherichia coli*. J. Bacteriol. 100:390–397.
8. **Degnen, G. E., and E. C. Cox.** 1974. Conditional mutator gene in *Escherichia coli:* isolation, mapping and effector studies. J. Bacteriol. 117:477–487.
9. **Fowler, R. G., G. E. Degnen, and E. C. Cox.** 1974. Mutational specificity of a conditional *Escherichia coli* mutator, *mutD5*. Mol. Gen. Genet. 133:179–191.
10. **Hoess, R. H., and R. K. Herman.** 1975. Isolation and characterization of mutator strains of *Escherichia coli* K-12. J. Bacteriol. 122:474–484.
11. **Howe, M. H.** 1973. Prophage deletion mapping of bacteriophage Mu-1. Virology 54:93–101.
12. **Liberfarb, R. M., and V. Bryson.** 1970. Isolation, characterization, and genetic analysis of mutator genes in *Escherichia coli* B and K-12. J. Bacteriol. 104:363–375.
13. **Low, B.** 1968. Formation of merodiploids in matings with a class of Rec$^-$ recipient strains of *Escherichia coli* K-12. Proc. Natl. Acad. Sci. U.S.A. 60:160–167.

14. **Martuscelli, J., A. L. Taylor, D. J. Cummings, V. A. Chapman, S. S. DeLong, and L. Canedo.** 1971. Electron microscopic evidence for linear insertion of bacteriophage Mu-1 in lysogenic bacteria. J. Virol. 8:551-563.
15. **Newton, A.** 1970. Isolation and characterization of frameshift mutations in the *lac* operon. J. Mol. Biol. 49:589-601.
16. **Normark, S.** 1970. Genetics of a chain-forming mutant of *Escherichia coli*. Transduction and dominance of the *envA* gene mediating increased penetration to some antibacterial agents. Genet. Res. 16:63-78.
17. **Siegel, E. C.** 1973. Ultraviolet-sensitive mutator strain of *Escherichia coli* K-12. J. Bacteriol. 113:145-160.
18. **Siegel, E. C., and V. Bryson.** 1967. Mutator gene of *Escherichia coli* B. J. Bacteriol. 94:38-47.
19. **Siegel, E. C., and J. J. Ivers.** 1975. *mut-25*, a mutation to mutator linked to *purA* in *Escherichia coli*. J. Bacteriol. 121:524-530.
20. **Siegel, E. C., and F. Kamel.** 1974. Reversion of frameshift mutations by mutator genes in *Escherichia coli*. J. Bacteriol. 117:994-1001.
21. **Smirnov, G. B., and A. G. Skavronskaya.** 1973. Suppression of ultraviolet sensitivity in *Escherichia coli uvr502* by the *su58* missense suppressor. J. Bacteriol 115:486-489.
22. **Taylor, A. L., and C. D. Trotter.** 1972. Linkage map of *Escherichia coli* strain K-12. Bacteriol. Rev. 36:504-524.
23. **Toussaint, A.** 1969. Insertion of phage Mu.1 within prophage λ: a new approach for studying the control of the late functions in bacteriophage λ. Mol. Gen. Genet. 106:89-92.
24. **Treffers, H. P., V. Spinelli, and N. O. Belser.** 1954. A factor (or mutator gene) influencing mutation rates in *Escherichia coli*. Proc. Natl. Acad. Sci. U.S.A. 40:1064-1071.
25. **Yanofsky, C., E. C. Cox, and V. Horn.** 1966. The unusual mutagenic specificity of an *E. coli* mutator gene. Proc. Natl. Acad. Sci. U.S.A. 55:274-281.
26. **Yura, T., and C. Wada.** 1968. Phenethyl alcohol resistance in *Escherichia coli*. I. Resistance of strain C600 and its relation to azide resistance. Genetics 59:177-190.