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UV Mutagenesis in *Salmonella typhimurium* Is *umuDC* Dependent Despite the Presence of *samAB*

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We investigated the role of the *umuDC* and *samAB* operons in the UV mutability of *Salmonella typhimurium*. *umuDC* is located on the chromosome, whereas *samAB* resides on the virulence plasmid pSLT. Using allele replacement and plasmid curing techniques, we found that UV mutability was eliminated when any of three different *umuDC* alleles (*umuD1*, *umuC1*, or *umuD1 umuC1*) were on the chromosome even when *samAB* was present. We conclude that *samAB* normally does not complement *umuDC* function in *S. typhimurium*.

In *Escherichia coli*, efficient UV-induced mutagenesis depends on the inducible products of the chromosomally encoded *umuDC* genes. *Salmonella typhimurium* LT2 strains contain two homologous but different operons akin to *E. coli umuDC*. One operon, also named *umuDC*, appears to be the direct counterpart of the *E. coli* locus. It too is chromosomally situated and shares striking homology with the *E. coli* locus at both the nucleotide (71%) and deduced amino acid (81%) levels (37, 40). Moreover, like the gene products of *E. coli umuDC*, UmuD and UmuC of *S. typhimurium* are expressed, and UmuD is processed to UmuD′ as a function of SOS induction (44).

The other operon, *samAB*, resides on the 90-kb virulence plasmid pSLT, which is present in most *S. typhimurium* LT2 strains. There is more limited homology at both the nucleotide (59 to 60%) and deduced amino acid (60%) levels for *samAB* and its *E. coli* and *S. typhimurium umuDC* homologs (24). At present, little is known about the expression of *samAB* gene products in *S. typhimurium*, although recent studies demonstrated that *samAB*, when contained on a high-copy-number plasmid, complemented *E. coli umuDC* mutants and enhanced UV mutability in *S. typhimurium* (24).

To evaluate the roles of the *S. typhimurium umuDC* and *samAB* operons in UV mutability, we constructed (by allele replacement and plasmid elimination strategies) *S. typhimurium* derivatives that had only one or the other of these operons. Our studies show that the *umuDC* operon is required for UV mutability in *S. typhimurium* and that, normally, *samAB* does not complement *umuDC*.

MATERIALS AND METHODS

Bacterial strains and media. All strains used in these studies are derivatives of *S. typhimurium* LT2; their relevant genotypes are listed in Table 1. LB broth and agar (19) were used for routine propagation of bacterial strains and supplemented, as required, with tetracycline (15 μg/ml) or kanamycin (25 μg/ml). Minimal A medium (8) minus citrate was supplemented with 0.2% D-glucose and, when necessary, 0.3 mM leucine, 0.1 mM tryptophan, or 0.1 mM histidine. Solid media were prepared by adding 15 g of agar (Oxoid) per liter.

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Phage P22-mediated transductions were carried out as previously described (9). For conjugal transfers of F′, plate matings were performed with 20 μl each of donor and recipient strain overnight cultures. For UV mutagenesis and survival measurements, solid minimal A medium with 0.2% D-glucose was supplemented with 0.2% Oxoid no. 2 broth. Logarithmic-phase bacteria (optical density at 650 nm, 0.5 to 0.7) in Oxoid no. 2 broth were washed twice and resuspended in phosphate-buffered saline. Portions of 6 ml were irradiated in 100-mm glass petri dishes at a fluence of 40 $\mu W/cm^2$. Leu^+ revertants and survivors were scored after 48 h at 37°C.

Elimination of plasmid pSLT carrying *samAB*. A P22 lysate was prepared on strain χ3918, containing the virulence plasmid *par* gene inactivated by a Km^r insert (41), and used to transduce strain PM155. A Km^s segregant, strain TW101, was isolated from Km^r transductants after repeated subculturing. Strain TW101 was shown to be devoid of pSLT by pulsed-field gel electrophoresis (data not shown). The absence of *samA* genes in strain TW101 was further confirmed by our inability to amplify *samA* from this strain by the polymerase chain reaction (PCR). PCR primers used to amplify *samA* were 5′-GTTACTGCTTGTAGCACCCG-3′ (position 132, sense) and 5′-CATCAGTCTGTGCTCCGGG-3′ (position 554, antisense); the 5′ nucleotides of primers are identified and numbered as described previously (24). DNA amplification from bacterial lysates was performed with 30 cycles of 1 min each at 94°C for denaturation, 55°C for annealing, and 72°C for extension with *Taq* polymerase (Perkin-Elmer Cetus).

Allele replacement with M13 constructs. Mutant *umu* alleles were constructed in vitro as described below; each *umu* mutant allele described herein possesses unique sequence properties that permit them to be distinguished readily by the PCR. Two primer sets were used to amplify a fragment encompassing *umuD*. The 5′ nucleotides of primers are identified and numbered as described previously (37). Set 1 consisted of 5′-CGATCTTAATGAGTTGCTCG-3′ (position 114, sense) and 5′-GCGATAACGCAGCCATCATTG-3′ (position 538, antisense); set 2 consisted of 5′-GAACTGAG AGAGAAACTTAC-3′ (position −123, sense) and the antisense primer from set 1. Two primer sets were used to amplify a fragment encompassing *umuC*. Set 1 consisted of 5′-CAATGATGGCTGCGTTATCGC-3′ (position 518, sense)

TABLE 1. Bacterial strains

Strain	Relevant genotype	Source or reference
PM155	*leuD21* pSLT$^+$	26
CO109	PM155 *hisG46 zee*::Tn*10*	25
AZ1516	*trp*::Tn*5*	3
AZ1549	*proC90* F'123 (*finP301* Trp$^+$)	3
χ3918	pStSR303 *parA* (89.1-kb *smaI*::Km)	41
χ3385	psLT$^-$ derivative of *S. typhimurium*	41
TT1952	*zea-81*::Tn*10*	32
TT2070	*zea-618*::Tn*10*	32
TT8388	*zea-609*::Tn*10*	32
TW3	CO109 *trp*::Tn*5*	This study
TW103	TW3 F'123 (*finP301* Trp$^+$)	This study
TW1040	TW103 *umuD1*	This study
TW1050	TW103 *umuC1*	This study
TW1060	TW103 *umuD1 umuC1*	This study
TW1041	TW1040 His$^+$ Tet^s	This study
TW101	PM155 (pSLT$^-$ *samAB*)	This study
TW110	TW101 *trp*::Tn*5* F'123 (*finP301* Trp$^+$)	This study
TW111	TW110 *umuD1*	This study
TW112	TW110 *umuC1*	This study
TW114	TW110 *umuD1 umuC1*	This study
TW115	TW101 *zea-618*::Tn*10 umuD1*	This study
TW118	TW101 *zea-618*::Tn*10 umuC1*	This study
TW119	TW101 *zea-618*::Tn*10 umuD1 umuC1*	This study
TW120	PM155 *zea-618*::Tn*10 umuD1*	This study
TW121	PM155 *zea-618*::Tn*10 umuC1*	This study
TW122	PM155 *zea-618*::Tn*10 umuD1 umuC1*	This study

and 5'-CATGGTTAGCCAGCTTGG-3' (position 876, antisense); set 2 consisted of 5'-CGCCTCCTGCGAAACGG-3' (position 455, sense) and the antisense primer from set 1. Set 1 primers were used in the experiment shown in Fig. 1. Set 2 primers were used in the experiment shown in Fig. 2. DNA amplification from bacterial lysates was performed with 30 cycles of 1 min each at 94°C for denaturation, 52°C for annealing, and 72°C for extension by *Taq* polymerase.

Allele replacement via the M13 technique of Blum et al. requires the use of F'-carrying bacteria (3). Strain TW103, an F'123-carrying derivative of strain CO109, was made by introducing a *trp*::Tn*5* allele from strain AZ1516 via P22 transduction and then mating a representative Trp$^-$ transductant (TW3) with strain AZ1549 to introduce F'123 (*finP301* Trp$^+$). Strain TW103 was infected with M13 mp Cam^r phage carrying the various *umu* alleles. Lysogens carrying the M13 vector integrated at the *umuDC* locus were selected on 2× YT plates supplemented with 20 μg of chloramphenicol per ml (21). Recombinants that lost the prophage were selected on LB agar containing 0.2% sodium deoxycholate (3). Ten bile salt-resistant segregants were screened by the PCR for allele replacement; typically 20 to 40% of these were found to carry the desired mutant alleles.

Genetic mapping of *umuDC* locus. P22 phage lysates were prepared on strains TT1952 (*zea-81*::Tn*10*), TT2070 (*zea-618*::Tn*10*), and TT8388 (*zea-609*::Tn*10*). Strain TW1041 (*umuD1* His$^+$ Tet^s), derived from strain TW1040 by selection as described by Bochner et al. (4), was used as the recipient in P22 transductions. From each set of crosses, 33 Tet^r transductants were analyzed by the PCR to determine the frequency of cotransduction of the *umuD1* allele.

P22 lysates for transduction of the *umuD1*, *umuC1*, and *umuD1 umuC1* alleles. P22 lysates prepared on derivatives of strains TW1041, TW112, and TW114 carrying both *zea-618*::Tn*10* and *umu* mutant alleles were used to transduce strains TW101 and PM155. Three Tet^r transductants from each set of crosses were analyzed by the PCR for the presence of *umu* mutant alleles. PCR analyses (see Fig. 2) showed that strains TW115, TW118, and TW119 (derivatives of strain TW101) contained *umuD1*, *umuC1*, and *umuD1 umuC1*, respectively. The pSLT-bearing counterparts, strains TW120, TW121, and TW122, respectively, were constructed and verified (see Fig. 2) in a similar fashion.

Mitomycin C induction of *samAB* expression. Overnight cultures of bacteria grown in minimal A medium minus citrate and supplemented with 0.1% Casamino Acids, 0.5% glucose, and 0.3 mM leucine were diluted 1:50 in fresh minimal medium and grown to an optical density at 650 nm of 0.4 to 0.6. Logarithmic cultures were treated with 2 μg of mitomycin C (Sigma Chemical Co., St. Louis, Mo.) per ml and grown for 30 min at 37°C before harvesting for RNA isolation as described below.

Preparation of RNA and electrophoresis. RNA was isolated by a hot phenol extraction method (1) with the following modification: 10 mM vanadyl ribonucleoside complex (GIBCO BRL, Gaithersburg, Md.) was included in a solution of 0.02 M sodium acetate (pH 5.5), 0.5% sodium dodecyl sulfate, and 1 mM EDTA to resuspend bacteria before phenol (water equilibrated) extraction. The RNA concentration and purity were determined by measuring the ratio of the optical density at 260 nm to that at 280 nm. High-molecular-weight RNAs were resolved by electrophoresis through a 1.2% agarose–formaldehyde gel and visualized by ethidium bromide staining (31).

Northern blot analysis of *samAB*. High-molecular-weight RNAs were resolved as described above, transferred to charge-modified nylon (GeneScreen Plus; NEN Research Products, Boston, Mass.) by capillary elution (31), and UV cross-linked to the membranes with a Stratalinker apparatus (Stratagene, La Jolla, Calif.). A *samA*-specific antisense oligonucleotide (5'-CATCAGTCTGTGCTCCGGG-3'; 5' nucleotide is no. 554 from reference 24) was end labeled (31), and hybridizations were carried out as recommended by the manufacturer for 3 h at 55°C. Filters were washed once at 37°C in 6× SSC (1× SSC is 0.15 M sodium chloride plus 0.015 M sodium citrate) for 20 min and then subjected to a stringent wash at 60°C for 20 min. Filters were dried and exposed to Kodak XAR-2 film for 24 to 72 h at −70°C.

RESULTS

Allele constructions and replacements. The *umuD1* and *umuC1* alleles were constructed by taking advantage of naturally occurring restriction sites in the *umuDC* sequence (Fig. 1). Specifically, *umuD1*, a 185-bp deletion, was made by cutting a *umuDC* clone with *Bst*EII and then religating. *umuC1*, a 4-bp insertion, was produced by restricting a *umuDC* clone with *Xho*I, filling in with DNA polymerase, and religating. The *umuD1 umuC1* double mutant allele was similarly constructed. Mutant alleles contain unique characteristics that permit physical detection by the PCR; the *umuD1* allele is 185 bp smaller than the wild-type allele, and the *umuC1* allele has a *Pvu*I site, rather than the *Xho*I site found in the wild type. We relied on these unique characteristics to identify bacteria in which wild-type *umuDC* had been replaced by mutant alleles. Figure 1 displays results from one such PCR screen, in which 2 of 14 *umuD1* (top half of gel) or 1 of 7 *umuC1* (bottom half of gel) deoxycholate-resistant candidates (see Materials and Methods) carried the desired mutant *umu* alleles.

Strains TW1040, TW1050, and TW1060, containing the *umuD1*, *umuC1*, and *umuD1 umuC1* alleles, respectively,

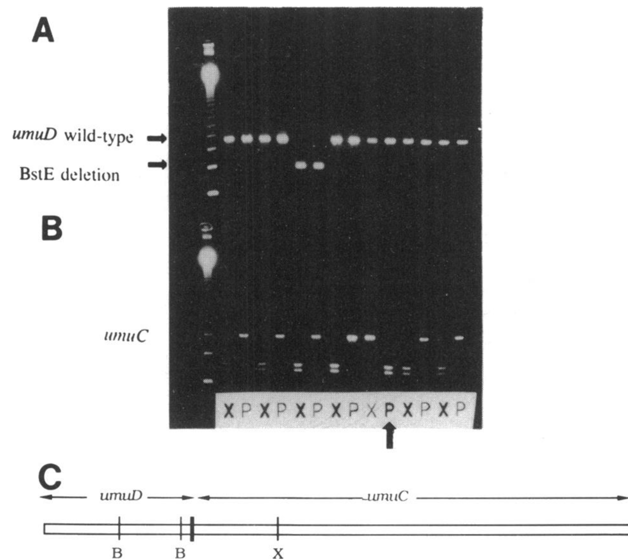

FIG. 1. Screening for *umuD* or *umuC* allele replacements by PCR analysis. The leftmost lanes contain 123-bp ladders (BRL-GIBCO). (A) DNAs from 14 deoxycholate-resistant segregants of TW103 were amplified with *umuD*-specific primers as described in the text. The *umuD1* allele (BstEII deletion) was present in samples in lanes 5 and 6. (B) Seven deoxycholate-resistant segregants of TW103 were amplified with *umuC*-specific primers as described in the text. The *umuC1* allele was present in samples in lanes 9 and 10 (*XhoI* resistant, *PvuI* sensitive). (C) Schematic representation of *umuD1* and *umuC1* allele construction. *umuD1* is a 185-bp deletion between *BstEII* sites (B). *umuC1* is a 4-bp insertion at bp 684 of the *umuDC* coding region (37), which converts an *XhoI* site (X) to a *PvuI* site: bp 684, 5′-CTCGAG→5′-CTCGATCGAG.

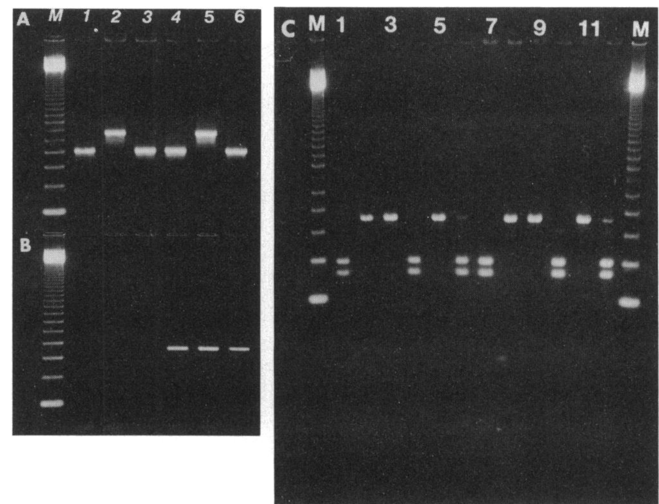

FIG. 2. PCR analyses of *S. typhimurium* strains to confirm *umuDC* and *samAB* genotypes. (A) PCR amplification with *umuD*-specific primers. (B) PCR amplification with *samA*-specific primers. Lanes for panels A and B: M, 123-bp ladder (BRL-GIBCO); 1, TW115 (*umuD1 samAB*); 2, TW118 (*umuD*$^+$ *samAB*); 3, TW119 (*umuD1 samAB*); 4, TW120 (*umuD1 samAB*$^+$); 5, TW121 (*umuD*$^+$ *samAB*$^+$); 6, TW122 (*umuD1 samAB*$^+$). (C) PCR amplification with *umuC*-specific primers. Lanes: M, 123-bp ladder (BRL); 1 and 2, TW115 (*umuC*$^+$ *samAB*); 3 and 4, TW118 (*umuC1 samAB*); 5 and 6, TW119 (*umuC1 samAB*); 7 and 8, TW120 (*umuC*$^+$ *samAB*$^+$); 9 and 10, TW121 (*umuC1 samAB*$^+$); 11 and 12, TW122 (*umuC1 samAB*$^+$).

were made by using M13mp Cam^r bacteriophage constructs as described above and previously (3, 21). In similar fashion, the pSLT-free strains TW111, TW112, and TW114 were prepared via the M13 technique with strain TW101 as the recipient for the *umuD1*, *umuC1*, and *umuD1 umuC1* mutant alleles, respectively. Allele replacements were verified by PCR analysis (data not shown).

Genetic mapping of *umuDC*. To facilitate genetic manipulations of *umu* mutant alleles, we established linkage of a Tn*10* element to *umuDC*. Recently, the *umuDC* locus was localized to a 4.6-min segment, between 35.9 and 40.5 min, of the *S. typhimurium* chromosome (37). Therefore, P22 lysates were prepared on strains containing known Tn*10* insertions in this region of the *Salmonella* chromosome and used to transduce strain TW1041 (carrying *umuD1*). PCR analysis of Tet^r transductants revealed that linkage between *umuD* and the *zea609*::Tn*10*, *zea-81*::Tn*10*, and *zea-618*::Tn*10* alleles was <3, 71, and 81%, respectively. *zea-81*::Tn*10* is 75% linked to H1, and *zea-618*::Tn*10* is 90% linked to *supD* (32). Using a modified form of the Wu equation (31), we estimated a map position of 40.2 ± 0.1 min for the *umuDC* locus in *S. typhimurium*.

We took advantage of the linkage between *umuDC* and *zea*::Tn*10* and used P22 transduction to construct a set of *S. typhimurium* strains containing the different *umu* alleles with or without the pSLT plasmid. The genotypes of these constructs were verified by PCR analysis (Fig. 2). The fragment amplified by the *umuD*-specific primers when *umuD1* is present (Fig. 2A, lanes 1, 3, 4, and 6) is shorter (by the expected amount) than that amplified when the wild-type *umuD* allele is present (lanes 2 and 5). The fragment amplified by the *umuC*-specific primers is cut by *PvuI* but not by *XhoI* (Fig. 2C, lanes 3 and 4, 5 and 6, 9 and 10, 11 and 12), whereas the wild-type *umuC* fragment is cut by *XhoI* but not by *PvuI* (lanes 1 and 2, 7 and 8). Figure 2B also shows the results of a PCR amplification of DNA from strains missing (lanes 1 through 3) or bearing (lanes 4 through 6) the *samAB* locus.

UV mutagenesis and UV sensitivity. To address the roles of *umuDC* and *samAB* in UV mutability and UV sensitivity, we examined strains that contained either wild-type or mutant *umu* alleles and that carried or lacked the virulence plasmid pSLT. Since *samAB* is located on plasmid pSLT, a comparison of pSLT-bearing strains, PM155 (*umuD*$^+$ *umuC*$^+$), TW120 (*umuD1 umuC*$^+$), TW121 (*umuD*$^+$ *umuC1*), and TW122 (*umuD1 umuC1*), with strains devoid of pSLT, strains TW101 (*umuD*$^+$ *umuC*$^+$), TW115 (*umuD1 umuC*$^+$), TW118 (*umuD*$^+$ *umuC1*), and TW119 (*umuD1 umuC1*), should delineate the contributions of *umuDC* and *samAB* to the lethal and mutagenic effects of UV.

In strains containing wild-type alleles of *umu*, over the dose range examined, the presence or absence of plasmid pSLT had no effect on UV mutability or UV sensitivity (Fig. 3). Since, upon SOS induction, UmuD and UmuC proteins of *S. typhimurium* are expressed and UmuD is processed to UmuD′ (44), this experiment provides evidence that the *samAB* gene products do not attenuate or potentiate UV mutagenesis in the presence of UmuD and UmuC. In contrast, a *umuD1 umuC1*-bearing strain was nonmutable by UV, whether *samAB* was present or not (Fig. 3). Identical results were obtained with strains carrying either the *umuD1* or *umuC1* allele (data not shown). These findings demonstrate that *umuDC* is essential for UV mutagenesis in *S. typhimurium* and that *samAB* normally does not contribute to the UV mutability phenotype of *S. typhimurium*.

DNA damage-inducible *samAB* expression. Since *samAB*

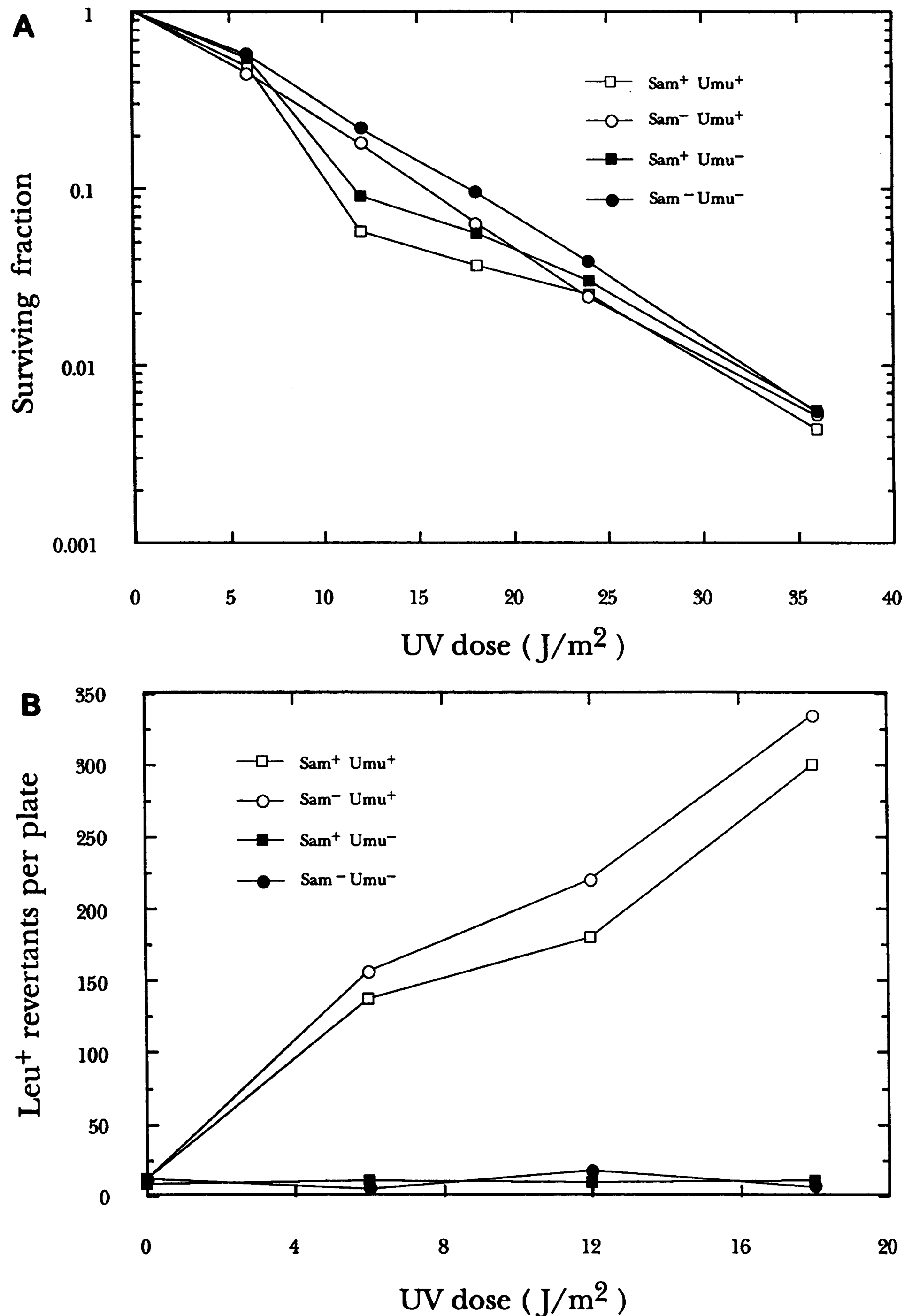

FIG. 3. Effect of *umuD1 umuC1* and loss of plasmid pSLT carrying *samAB* on survival after UV irradiation (A) and on Leu+ reversion (B) induced by UV irradiation in *S. typhimurium* PM155 (□), TW101 (Sam−) (○), TW122 (Umu−) (■), and TW119 (Sam− Umu−) (●).

provides a mutagenic repair function when expressed from a multicopy plasmid (24), we asked whether *samAB* genes on pSLT are expressed in response to DNA damage induction. Northern blots were probed with a *samA* antisense oligonucleotide, providing a facile means of examining *samAB*-specific transcripts in the presence of *umuDC* (Fig. 4). *samAB* transcripts were not observed in strain TW101 (lacking pSLT) or in untreated control bacteria. However, *samAB* transcripts were observed within 30 min of exposure to mitomycin C, indicating that *samAB* expression is induced by DNA-damaging agents, most likely as part of the SOS regulon. It is interesting that, in addition to a full-length transcript of about 2 kb, hybridization of mRNA with an antisense oligonucleotide probe complementary to the carboxyl terminal portion of *samA* revealed two shorter transcripts of about 1.25 and 0.95 kb.

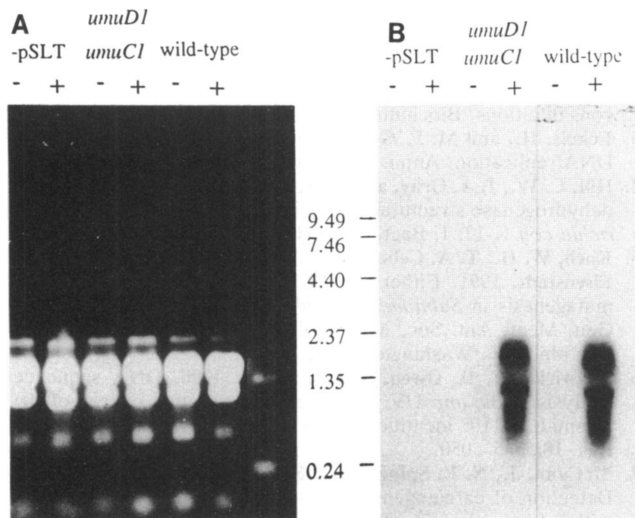

FIG. 4. Northern analysis of mitomycin C-inducible *samAB* expression. RNA from strain TW101 (−pSLT), TW122 (*umuD1 umuC1*), or PM155 (wild type) was extracted from cultures treated (+) or not treated (−) with mitomycin C. (A) Ethidium bromide-stained gel before transfer. (B) Autoradiograph of the blotted gel after hybridization with an end-labeled *samA*-specific antisense oligonucleotide and washing. An RNA ladder (0.24 to 9.5 kb; BRL-GIBCO) was used for size markers.

DISCUSSION

Map position of *umuDC*. The genetic maps of the *E. coli* and *S. typhimurium* chromosomes are congruous. One notable exception is the large rearrangement of gene sequences involving approximately 15% of *E. coli* and *S. typhimurium* genomes. Relative to that of *E. coli*, the *S. typhimurium* map order is inverted in a region designated the segment 51 inversion (7, 29). Our present studies help define the junctions of this massive chromosomal inversion. In *E. coli*, the *icd* locus is at 25 min with *umuDC* situated approximately 38 kb clockwise from *icd* (14, 30). In *S. typhimurium*, the *icd* locus is also positioned near 25 min (37), but, as shown here, the *umuDC* locus is located at 40.2 ± 0.1 min, approximately 675 kb (45 kb/min) removed from *icd*.

***umuDC* and *samAB* are not essential genes.** The observation that *S. typhimurium* strains lacking pSLT-borne *samAB* and chromosomal *umuDC* can readily be constructed provides evidence that the *umuDC* operon is not essential for bacterial viability. This finding corroborates recent observations made with *E. coli umuDC* deletion mutants constructed by allele replacement (43).

***S. typhimurium* UV mutagenesis.** The experiments described here demonstrate that UV mutagenesis in *S. typhimurium* LT2 cannot normally occur in the absence of *umuDC*, despite the presence of *samAB*. This finding is surprising, given the amino acid sequence similarity of SamAB and other known UmuDC homologs (24). In *E. coli*, processing of the UmuD protein to the mutagenically active carboxyl-terminal UmuD′ cleavage product via RecA-mediated proteolysis is essential for SOS mutagenesis (5, 23, 35). The deduced amino acid sequence of SamA includes Ala-24 and Gly-25, the known cleavage site found in MucA (34, 39), and a putative cleavage site in ImpA (16). Additionally, SamA retains the highly conserved Ser-61 and Lys-98 residues, which are thought to play a catalytic role in the RecA-mediated processing of LexA and of UmuD and its homologs (23, 24, 36). Further, because *samAB* promotes UV mutagenesis in *E. coli umuDC* strains as well as *S. typhimurium* when present on a multicopy plasmid, it is unlikely that SamA is defective for RecA-mediated cleavage (24).

It has been conjectured that the ability of *samAB* to promote UV mutagenesis might, in some unknown way, be suppressed by the product(s) of a gene(s) residing on the *S. typhimurium* cryptic plasmid (24). Indeed, suppression of plasmid-borne mutagenic repair genes is well known. For example, the mutagenic activity of *mucAB* is suppressed by a region of the R46 plasmid that was deleted in the construction of pKM101 (10, 17, 22). Additionally, the *impC* gene of the TP110-borne *imp* operon appears to regulate the *impAB* genes (16). The results presented in Fig. 4 demonstrate that the *samAB* genes are expressed in response to DNA damage. Therefore, the apparent inability of SamAB to promote mutagenesis at UV lesions when expressed from single-copy genes may reflect that SamA and SamB are intrinsically less active than UmuD and UmuC in promoting UV mutagenesis. One wonders why *S. typhimurium* carries and regulates the expression of a *umuDC*-like operon that, by itself, conveys no obvious phenotype.

We previously reported that *umuDC* strains TW1040, TW1050, and TW1060 (Table 1) were UV mutable, and we concluded that UV mutability in these strains was a consequence of *samAB* activity (15). We were surprised to find in subsequent experiments that the mutable phenotype of these *umuDC samAB*$^+$ strains did not disappear when *samAB* was eliminated. Thus, there is no fundamental contradiction between the results reported in reference 15 and those reported here; i.e., *samAB* alone does not complement *umuDC*. The genetic basis for the UV mutability of these strains is being investigated.

Biological role of *umu*-like operons. SOS mutagenesis in *S. typhimurium* has been variously described as poor, weak, and defective as compared with that in *E. coli*; however, a recent survey of mutagenesis and SOS repair in enterobacteria showed that even a collection of *E. coli* strains may vary in UV-induced mutagenesis and UV sensitivity by a factor of 200 (33). In fact, some of these *E. coli* isolates were less mutable than *S. typhimurium*. Chromosomally encoded genetic elements of the SOS regulon including *lexA* (6, 28), *recA* (for a review, see reference 20), and *umuDC* (33) and analogous plasmid-borne *umu*-like operons (38) are widespread and conserved in prokaryotes, which exhibit little or no SOS mutagenesis (42). These observations underscore the notion that *umu*-like operons may confer on bacterial cells some evolutionary advantage that is unrelated to their mutagenic activities (33). Thus, although *samAB* genes clearly do not contribute significantly to UV-induced SOS mutagenic repair in *S. typhimurium*, they may function in some as yet unknown way to confer a selective advantage to *S. typhimurium*. Similarly, although *S. typhimurium* UmuDC-dependent mutagenesis is less efficient than that of *E. coli*, the high degree of conservation between these proteins suggests that they provide some benefit for *S. typhimurium* populations.

The notion that SOS-inducible DNA repair provides bacterial populations with a selective advantage in responding to severe environmental stress is not new (11–13, 27). However, there is no direct support for the idea. Recently it was observed that a bleomycin resistance (Bm^r) gene (*ble-333*), derived from the transposon Tn*5*, confers a survival advantage to *E. coli* during the phase of decline in resting bacterial cultures (2). Since the presence of the *ble-333* gene also

enhances survival upon exposure to the alkylating agent ethyl methanesulfonate and provides a growth advantage, it was hypothesized that the improved fitness of Bm^r cells is associated with DNA repair functions encoded by *ble* (2). By analogy, an intriguing possibility is that *umu*-like genes provide enhanced fitness to starving bacterial cells that are accumulating DNA damage. Amino acid deprivation has been shown to induce lambda prophage in a *recA*-dependent fashion (18). Since prophage induction requires repressor cleavage by activated *recA*, it is conceivable that some cleavage of LexA also occurs during starvation conditions. Although this situation would not lead to a fully induced SOS response, it might allow sufficient expression of *umu*-like genes to enhance bacterial survival. This hypothesis can be tested by asking whether the presence of *umuDC* and/or *samAB* enhances survival of *S. typhimurium* during the phase of decline associated with starvation.

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