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Biochemistry

SOS induction and autoregulation of the *him*A gene for site-specific recombination in *Escherichia coli*

(regulation by LexA and RecA/bacteriophage λ integration/gene fusion)

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ABSTRACT **The *him*A gene of *Escherichia coli* controls the lysogenization of bacteriophage λ at the level of catalysis of site-specific recombination and expression of the λ *int* and cI genes required for lysogenic development. We have analyzed the regulation of *him*A by two methods: (*i*) β-galactosidase synthesis from a *lac*Z gene inserted into the *him*A gene and (*ii*) detection of radioactive HimA protein after fractionation by two-dimensional gel electrophoresis. We find that *him*A⁻ mutations produce enhanced expression of the *him*A gene, indicating that HimA protein controls its own synthesis. The *him*A gene is also induced by treatment of cells with UV or mitomycin C, suggesting control by the inducible DNA repair (SOS) system regulated by the LexA and RecA proteins. Regulation of *him*A follows the pattern expected for a typical SOS gene: constitutive high expression in mutants that have inactive LexA or the altered RecA conferred by the *rec*A441 (*tif*1) mutation and low noninducible expression in a mutant that has a deleted *rec*A gene. We conclude that the *him*A gene is a component of the inducible SOS response, repressed by LexA and induced by the capacity of activated RecA to cleave LexA. We suggest that HimA may be subject to SOS induction because it functions as an "acquisitionase" for new genetic material and thus is of special utility under conditions of impaired capacity for growth of the bacterial population.**

The chromosome of *Escherichia coli* specifies gene products active in at least two types of genetic recombination, general (homology dependent) and site specific. The product of the *rec*A gene is a major component of general recombination pathways (1); the *him*A gene specifies a crucial component of site-specific recombination (2). The best studied recombination reaction in which the HimA protein participates is the integration of the DNA of bacteriophage λ into the *E. coli* chromosome (3).

In addition to its catalytic function in general recombination, the RecA protein has a regulatory role in the coupled induced response to DNA damage involving mutagenesis, inhibition of cell division, increased DNA repair capacity, and prophage induction: the "SOS response" (4, 5). One element of the SOS response is induction of the *rec*A gene itself (6–11). This feature probably serves to provide enhanced capacity for recombinational repair (12). A number of other genes are also induced, although the roles of most have not yet been identified (13). Induction of *rec*A (and other SOS genes) occurs by a chain of events in which the first, a signal of DNA damage that activates RecA as a protease, is followed by inactivation of the LexA repressor through RecA-mediated cleavage (5, 11, 13–15). Cleavage of LexA has been demonstrated directly (16). The cI repressor protein for λ is also cleaved by RecA, allowing the phage to escape the damaged cell (15, 17).

HimA protein also has both a catalytic and a regulatory role: It is a subunit of the integration host factor (IHF) required for integrative recombination by λ DNA (18), and it is also needed for efficient expression of the *int* and cI genes specific for the lysogenic response by λ (19, 20). Because of the multiple roles of HimA in prophage insertion, we expected that the *him*A gene might be subject to a variety of cellular control signals. In this paper, we show that *him*A is negatively regulated by its own gene product and is induced as an element of the SOS response. We also consider the possible significance of the SOS regulation.

MATERIALS AND METHODS

Bacteria and Bacteriophage. The basic *E. coli* strains used were K37Sm^{R}Su$^-$ and its *him*A42 derivative K936 (2); K5407, a muc$^+$ lysogen of K37 also *lac*Z deleted; K5070, carrying a *pro lac* deletion (2); and K660, which has the F'148 plasmid that carries the *him*A gene and Tn*10*. Mutations were introduced into the appropriate strains by transduction with phage P1 to tetracycline resistance (Tet^R) from donors containing the Tet^R transposon Tn*10* linked to the mutation. The *rec*A441 (*tif*-1) (21), *rec*AΔ306 (22), and *lex*A3 (23) mutations were from strains JC10257, JC10289, and JC13519, respectively, of A. J. Clark. The *spr*-51 mutation was from DM1187 of D. Mount (24). Tet^S (Tetracycline-sensitive) derivatives were selected by the method of Bochner *et al.* (25). The insertion of the mu-defective *lac*Z phage (mu*d*) (26) is described below. All derivatives containing F'148 mu*d* were tested for the ability to segregate Lac$^-$ ampicillin-sensitive (Ap^S) colonies (≈ 1%) to demonstrate that the mu*d* fusion was maintained solely on the plasmid. Lysogens of muc$^+$ were selected by immunity to superinfecting phage.

Media. Bacteria were propagated in LB medium containing ampicillin at 25 μg/ml where appropriate. P1 transductants to Tet^R were selected on LB agar plates containing 0.01 M sodium pyrophosphate and tetracycline at 15 μg/ml. For assays of β-galactosidase from *lac*Z insertion strains, bacteria were grown in M9 liquid medium (27)/0.1% casamino acids/0.2% glucose containing ampicillin at 25 μg/ml. For control experiments on induction of a normal *lac*Z gene, 0.5% glycerol was substituted for glucose and ampicillin was omitted.

Assay For β-galactosidase. Cultures were assayed for β-galactosidase by hydrolysis of *o*-nitrophenylgalactopyranoside as described (27). One unit produces a change in A_{420} of 0.001/min in the standard reaction. Specific activity is given in units of enzyme per A_{650} unit of the culture. For *lac* operon induction, isopropylthiogalactoside was added to a concentration of 1 mM 20 min prior to assay. Only midlogarithmic phase cultures were assayed.

Radioactive Labeling of Bacterial Cultures and Gel Electrophoresis. Bacteria were grown at 37°C to a density of 2 × 10^8/ml in M9 media/0.2% glucose containing 18 amino acids (no methionine or cysteine) at 10 μg/ml each, at which time 50 μCi of [^{35}S]methionine (Amersham; 1240 Ci/mmol; 1 Ci =

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Abbreviations: IHF, integration host factor; Tet^R, tetracycline resistant.

3.7×10^{10} becquerels) was added to a 2-ml culture. After 2 min, the cultures were chilled, lysed, and subjected to two-dimensional gel electrophoresis and autoradiography by the technique of O'Farrell *et al.* (28) as described (18).

Selection for *him*A-*lac*Z Fusions. We have used the technique of gene fusion to study the transcriptional regulation of the *him*A gene. Bacterial strains in which the promoter for the *him*A gene (*him*AOP) is fused to the *lac*Z structural gene were constructed by using the defective mu phage described by Casadaban and Cohen (26) that carries ampicillin-resistance and *lac*Z genes [mu*d*, (Ap, *lac*)] (Fig. 1). The mu*d* phage is particularly suited for this construction for two reasons: (*i*) it can insert at random into the *E. coli* chromosome to provide for transcription of the *lac*Z gene from the promoter of the target operon and (*ii*) it carries a mutation that confers thermoinducibility and thus high-termperature lethality for the lysogenic bacterium. Because bacterial strains carrying *him*A mutations are able to survive thermal induction of mu (2), selection for a mu*d* lysogen at inducing temperatures selects for mu*d* insertions that inactivate the *him*A gene. Approximately half of the Him$^-$ mu*d* lysogens obtained by this procedure displayed a Lac$^+$ phenotype on indicator media. One representative strain (K5333) of six phenotypically identical insertions was chosen for further tests indicating that transcription of the *lac*Z gene initiates at the *him*A promoter.

The site of the mu*d* insertion was localized to the *him*A gene by two methods: (*i*) the mu*d* prophage was 100% linked by P1 cotransduction to a Tn*10* transposon inserted directly adjacent to the *him*A gene and (*ii*) the Him$^-$ phenotype was converted to Him$^+$ by lysogenization or recombination with λ*him*A, a specialized transducing phage carrying the wild-type *him*A gene and only four other *E. coli* genes (*phe*S, *phe*T, *thr*S, and *inf*C) (2, 18). Because the other four genes present on λ*him*A are essential for growth of *E. coli*, the lesion resulting from mu*d* insertion must be confined to the *him*A gene and thus appears to be a simple insertion of the type shown in Fig. 1.

The chromosomal region containing the mu*d* insertion was transferred, by homogenotization, to an F'148 plasmid, and the resulting episome (F'148*him*A::mu*d*) was transferred by conjugation into a set of isogeneic strains carrying a *lac*Z deletion, a muc$^+$ prophage, and additional mutations of possible regulatory significance.

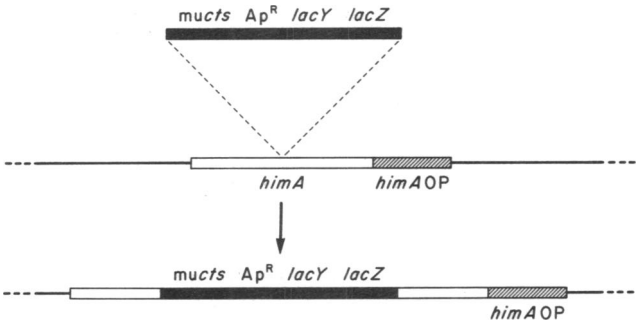

FIG. 1. Construction of a *him*A-*lac*Z fusion. The expected structure is shown for a simple integration of mu*d* (Ap^R, *lac*) into the *him*A gene in the proper orientation such that the *lac*Z and *lac*Y genes are transcribed from the *him*A promoter (*him*AOP). K5070 was grown at 32°C to 2×10^8/ml in LB broth/0.05 M $CaCl_2$/0.01 M $MgSO_4$. The cells were infected at room temperature with a mixed lysate of muc*ts*-62/mu*d* at 1 plaque former per cell. After 60 min of incubation, the infected culture was centrifuged, the cells were suspended in 10 vol of LB broth/0.01 M sodium pyrophosphate containing ampicillin at 25 μg/ml, and the fresh culture was incubated at 32°C overnight. The overnight culture was centrifuged, the pellet was washed with 0.01 M $MgSO_4$, and dilutions were plated at 32°C and 42°C on eosin/methylene blue plates containing ampicillin at 25 μg/ml. Survival at 42°C was 10^{-5}. Colonies surviving at 42°C were screened for λ integration as described (29); clones exhibiting the integration-negative (Him$^-$) phenotype (≈ 5%) were screened for the Lac phenotype on MacConkey lactose indicator plates. One Lac$^+$ Him$^-$ strain, K5333, was chosen for further study.

RESULTS

Autoregulation of the *him*A Gene. The gene fusion system used to study regulation of *him*A gene expression is shown in Fig. 2; we measured β-galactosidase from the *lac*Z gene inserted into the *him*A gene of an F' plasmid. In the standard strain, a wild-type chromosomal *him*A gene is present, producing a Him$^+$ phenotype. Generation of a Him$^-$ phenotype by introduction of a missense, nonsense, or deletion mutation of the *him*A gene into the chromosome results in markedly elevated levels of β-galactosidase (Table 1). From these results, we suggest that HimA is an autoregulatory protein, negatively regulating the *him*A gene. The basal level of expression of *him*A in the Him$^+$ strain is substantial (Table 1), indicating a sensitive balance to the regulatory system (and also that the *him*A gene may be somewhat more repressed in a normal cell in which only one copy of the operator region is present).

The HimA protein is one (IHFα) of two subunits of the IHF (18). The other subunit (IHFβ) is probably specified by an unlinked gene, *him*D (see below); mutations in *him*D produce a similar phenotype to *him*A$^-$ lesions (unpublished work). The *him*D mutations may alter the gene previously defined by the *hip*157 mutation (3). Because of the close functional relationship between the *him*A and *him*D gene products, we studied the effect of a mutation in *him*D on expression of the *him*A gene; β-galactosidase is produced at the same high level found for *him*A$^-$ (Table 1). This result indicates that HimD protein is also a negative regulator of the *him*A gene. HimA and HimD might function separately, as the IHF dimer, or in a more complex fashion.

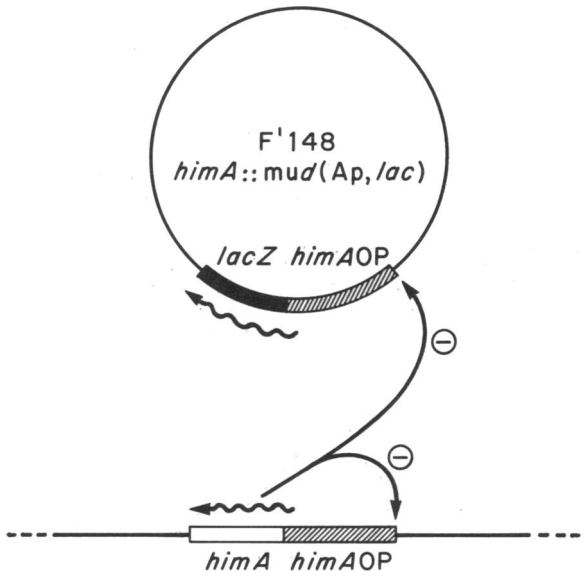

FIG. 2. Schematic representation of the system used for studying himA gene regulation. The basic strain contains an F'148 episome carrying the *him*A::mu*d* fusion. This strain also carries a *lac*Z internal deletion, so that the only source of β-galactosidase is the mu*d* fusion, and a wild-type muc$^+$ prophage, so that experiments can be conducted at temperatures that would induce the thermoinducible repressor of the mu*d* phage. According to the mechanism proposed in this paper, the product of the chromosomal *him*A gene represses both its own promoter and the *him*A promoter controlling *lac*Z transcription. Thus, a mutation inactivating the *him*A gene leads to maximal expression of the *lac*Z gene.

Table 1. Autoregulation of the *him*A gene

Strain	Genotype	β-Galactosidase activity
K5462	*him*$^+$	572
K5466	*him*A42	1719
K5467	*him*A*am*79	1413
K5468	*him*AΔ82	1697
K5469	*him*D63	1752
K37	*him*$^+$	0.9
K37*	*him*$^+$	1192
K936	*him*A42	0.3
K936*	*him*A42	1016

Strain K5462 was constructed as follows. The F'148 plasmid carrying transposon Tn*10* (from K660), was mated into the *Him*A$^-$ mu*d* (Ap, *lac*) strain K5333 [selecting for Tet^R, ampicillin resistance (Ap^R)] to yield K5368. K5368 was mated with the Sm^R*lacZ* deletion K5407, and a Sm^R, Ap^R derivative was selected (K5451). Tn*10* was eliminated from the plasmid by selection for tetracycline sensitivity to yield K5462. The structure of K5462 is shown in Fig. 2. K5466–K5469 are derivatives of K5462 prepared by transduction with phage P1. Bacteria were grown at 37°C to a density of 10^8/ml and assayed for β-galactosidase. Data presented are averages of duplicate determinations. * In the presence of 1 mM isopropylthiogalactoside.

To show that the Him$^-$ phenotype does not generally affect *lacZ* gene expression in some way, we measured β-galactosidase from a *lacZ* gene in the *lac* operon; there is no substantial difference between *him*A$^+$ and *him*A$^-$ (Table 1).

If the *him*A gene is negatively regulated by HimA and HimD, bacterial strains carrying mutations in the *him*A or *him*D genes should exhibit elevated levels of HimA protein. We can establish this point qualitatively because we have identified the migration positions, after fractionation on two-dimensional acrylamide gels, of the *him*A$^+$ and *him*A42 gene products (α and α42) and of the β-subunit of IHF (18). Based on this previous detailed analysis, we can use two-dimensional gel fractionation to estimate the levels of these proteins in cell extracts (Fig. 3). As previously shown, the IHFα and IHFβ synthesized in wild-type *E. coli* is insufficient for detection by this method (18) (Fig. 3*A*); however, the normal migration positions of these proteins are indicated with respect to the position of ribosomal protein S10. The location of S10 can be seen in each gel from its characteristic migration with respect to marker proteins infC, ribosomal protein L5, and an additional ribosomal protein. The sites indicated for IHFα and IHFβ have been confirmed by the use of purified IHFα and IHFβ (18). In contrast to the wild type, fractionation of an extract from a *him*A$^-$ strain shows demonstrable production of IHFα42 and IHFβ (and at least one unidentified third protein; Fig. 3*B*). Thus, we conclude that *him*A$^-$ mutation leads to derepressed synthesis of HimA (IHFα) and IHFβ. The *him*D$^-$ extract exhibits wild-type IHFα and another protein, labeled β63, apparently identical in size to IHFβ but shifted in charge (Fig. 3*C*). The relationship between IHFβ and β63 is shown more clearly in the fractionated mixture of *him*A$^-$ and *him*D$^-$ extracts (Fig. 3*D*); there is a similar molecular weight and charge heterogeneity characteristic of IHFβ in this gel system (18). Thus, the gel analysis suggests that β63 is most likely the missense protein form of IHFβ resulting from the *him*D63 mutation and that *him*D is probably the structural gene for IHFβ. Fig. 3*D* also shows the relationship of α and α42 to ribosomal protein S10.

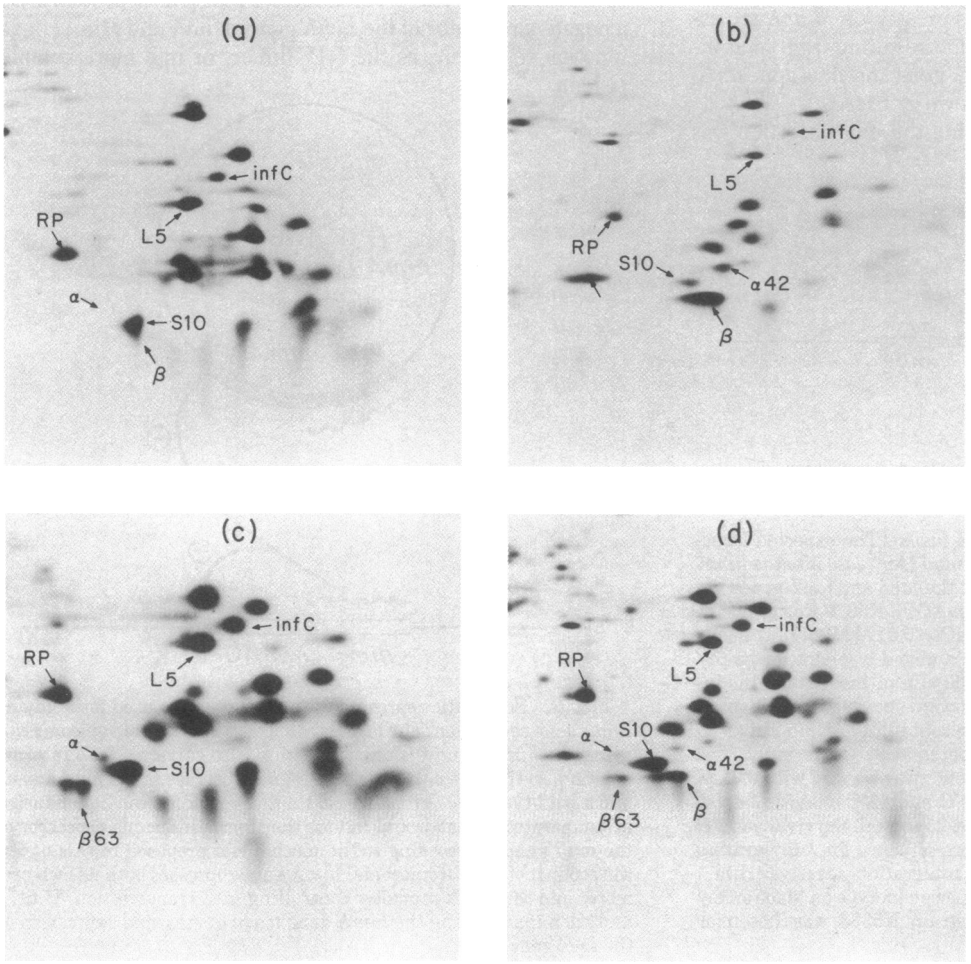

FIG. 3. Two-dimensional gel analysis of proteins from strains carrying *him*A and *him*D mutations. Nonequilibrium two-dimensional gels of [^{35}S]methionine-labeled extracts are shown for the following isogeneic strains: (*a*) wild type (K37), (*b*) *him*A42 (K936), (*c*) *him*D63 (K5283), and (*d*) a mixture of *b* and *c* extracts. Cultures were labeled, lysed, and subjected to electrophoresis and autoradiography. The locations of IHFα; IHFα42; IHFβ; ribosomal proteins S10, L5, and RP; and infC (initiation factor 3) have been described (18, 31). The proteins that we identify as IHFα in *c* and IHFβ in *b* coelectrophorese in two dimensions with IHFα and IHFβ from purified IHF (data not shown). The unlabeled arrow in *b* indicates a protein encoded by an unidentified gene that appears in extracts of *him*A$^-$ strains. The gel analysis was performed several times with qualitatively similar results; representative autoradiograms are shown.

From the qualitative agreement between the measurements of *him*A gene expression by *lac*Z fusion and identification of HimA protein in two-dimensional acrylamide gels, we consider the evidence to be strong that HimA is a negative regulator of the *him*A gene and that the *lac*Z fusion assay provides a valid way to measure *him*A regulation. The results of Fig. 3 also suggest a symmetrical relationship between regulation of *him*A and *him*D in which both HimA and HimD participate in the regulation of the *him*A and *him*D genes. However, this conclusion must be regarded as tentative until the *him*D gene product has been identified more definitively.

SOS Regulation of the *him*A Gene. To analyze the response of the *him*A gene to the SOS induction pathway, we used the *lac*Z fusion shown in Fig. 2 to measure β-galactosidase production in response to agents or mutations known to affect SOS regulation. The regulatory response and essential control experiments are shown in Fig. 4. After treatment with UV, the classical agent for SOS induction, β-galactosidase increases to a level comparable with that in a *him*A$^-$ strain. As for other SOS responses, this induction is blocked by introduction of a *rec*A$^-$ mutation; a *rec*A$^-$ mutation does not prevent β-galactosidase induction from the *lac* operon (in the presence of 1 mM cAMP) after UV irradiation (ref. 13; unpublished work). The induction is specific for the *lac*Z insertion in *him*A and not for the plasmid in general because no increase of β-galactosidase occurs in *rec*A$^+$ bacteria carrying a *lac*Z fusion to a different promoter on the F plasmid.

Other methods of SOS induction show similar responses (Table 2). The *lac*Z fusion is also induced in response to treatment with mitomycin C. As for UV treatment, this increase is inhibited by mutations known to prevent SOS induction: e.g., a *rec*A deletion or a *lex*A3 mutation (5, 23). The SOS pathway will undergo thermal induction in bacteria with the *rec*A441 mutation (*tif*1) (5, 21). The introduction of *rec*A441 into the standard *lac*Z fusion allows thermal induction of β-galactosidase. From the results of Fig. 4 and Table 2, we conclude that the *him*A gene is a component of the induced SOS response to DNA damage.

The induction of SOS-regulated genes is known to occur by at least two different mechanisms. Most appear to be repressed by LexA and derepressed when LexA is cleaved by RecA protease (16). Alternatively, a repressor other than LexA might be cleaved by RecA protease, as for the λ cI repressor (17). To distinguish between these two modes of induction, we measured β-galactosidase from the *lac*Z fusion in strains carrying a mutation that inactivates LexA, with or without an additional deletion mutation of the *rec*A gene (Table 3). The *lex*A$^-$ mutation confers a high level of β-galactosidase synthesis in the presence or absence of the *rec*A441 (*tif*1) mutation, indicating that LexA represses *him*A, either directly or by repression of RecA. The β-galactosidase level remains high for the *lex*A$^-$ *rec*A$^-$ double mutant (*rec*A$^-$ strains generally give slightly lower levels of β-galactosidase; cf. Table 2). From these results, we conclude that derepression of the *him*A gene can occur in the absence of RecA if LexA is inactivated by mutation. Thus, the LexA protein is probably a repressor of the *him*A gene, and the role of RecA is to cleave LexA.

The *him*A gene appears to be repressed, directly or indirectly, by both its own gene product and the LexA repressor. These two repressors might act independently or coordinately. If they act independently, we might observe SOS induction under conditions in which the *him*A gene product is absent. However, UV irradiation of a strain carrying a *him*A deletion does not further increase the level of β-galactosidase above that found prior to induction (Table 3). As *him*A$^-$ strains are not UV sensitive, induction of the SOS pathway presumably occurs normally (2). We suggest that the HimA and LexA proteins probably act coordinately to repress the *him*A gene.

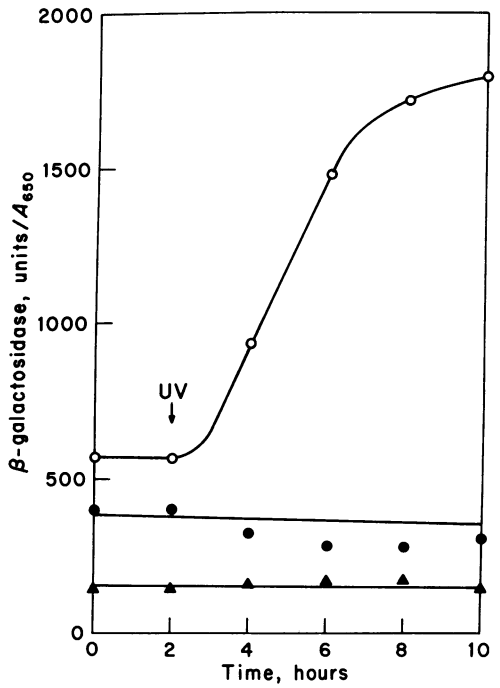

FIG. 4. SOS induction of the *him*A gene. The standard *lac*Z insertion of Fig. 2 is compared with its *rec*A$^-$ derivative and an insertion of *lac*Z under another promoter of the F'148 plasmid (selected as a random transposition of mu*d* into F'148 that was Lac$^+$). Several random *lac*Z fusions were tested; none were UV inducible, although the basal levels of β-galactosidase differed (data not shown). We note that prophage mu is not inducible by the SOS pathway nor is β-galactosidase synthesis from the *lac* operon blocked by UV irradiation of a *rec*A$^-$ strain (see ref. 13 for further discussion). Cells were grown at 37°C to a concentration of 10^8/ml and then exposed to UV light (60 J/m^2) at the indicated time. The cultures were incubated with aeration at 37°C and periodically diluted with fresh medium to maintain the original concentration. At the times shown, samples were assayed for β-galactosidase. ○, Standard *him*A insertion (K5462); ●, *rec*A$^-$ derivative (K5465); △, random insertion (K5523).

DISCUSSION

Autoregulation of the *him*A Gene. We have examined the regulation of the *him*A gene by two methods: (*i*) genetic fusion of the *him*A gene promoter to the *lac*Z gene and (*ii*) identification of radiolabeled *him*A gene product in autoradiograms of two-dimensional gels of cell extracts. Although these two techniques probe different stages in the expression of the *him*A

Table 2. SOS Induction of the *him*A gene

Strain	Genotype	β-Galactosidase activity after treatment			
		None	UV	Mitomycin	43°C
K5462		572	1819	2239	667
K5465	*rec*AΔ306	390	314	363	nt
K5556	*lex*A3	517	580	674	nt
K5504	*rec*A441(*tif*1)	650	nt	nt	1590

Procedures for cell growth and assay are described in the legend to Fig. 4, except for the inducing treatment. For mitomycin or thermal induction of *rec*A441, mitomycin was added to 1 μg/ml or the culture was shifted to and maintained at 43°C, respectively. Assays were performed 6 hr after induction. The *rec*AΔ306, *rec*A441, and *lex*A3 strains were prepared by P1 transduction.

Table 3. Interaction of *recA*, *lexA*, and *himA* in *himA* induction

Strain	Genotype	β-Galactosidase activity
K5462		639
K5534	*lexA*⁻*recA441*	1775
K5555	*lexA*⁻	1937
K5535	*lexA*⁻*recA*⁻	1357
K5468	*himA*⁻	1777
K5468 (UV)	himA⁻ (induced)	1791

Procedures for cell growth and assay are as described in the legend to Table 2. For the assays, strain DM1187, which carries the *lexA*⁻ mutation *spr51* and the recA441 (*tif1*) mutations (24), was converted to *lacZΔ* and a muc⁺ lysogen; the F'148 plasmid, which carries the *lacZ* insertion into *himA* was then introduced by selection for Tet^R and ampicillin resistance to yield K5534. The *recA441* mutation of K5534 was removed by P1 transduction to *recA*⁺ (K5555) or *recAΔ306* (K5535); all these strains carry an additional mutation allowing continued cell division of the *lexA*⁻ bacteria (*sfiA11*) (30).

gene—transcription for the *lacZ* fusion and translation for the gels—their results are in qualitative agreement. Because we infer that both transcription and protein synthesis from the *himA* gene are elevated in *himA*⁻ mutants, we conclude that the *himA* gene is negatively regulated by its gene product. At present, the most likely mechanism seems to be for HimA protein, IHFα, or the IHFα/β complex to repress transcription of *himA*; however, more complicated models are possible at this level of analysis.

We have also found that a mutation in the *himD* gene results in derepression of the *himA* gene. Our data implicate *himD* as the structural gene for the β subunit of IHF, although this point has not been rigorously established. Thus, there may be a symmetrical regulatory interaction in which HimA and HimD each participate in control of both the *himA* and *himD* genes, serving to maintain an appropriate stoichiometry between the two subunits of IHF.

SOS Regulation. Our results indicate that the *himA* gene is a component of the induced SOS response to DNA damage, normally repressed by LexA and induced by cleavage of LexA by activated RecA. The most direct interpretation of the data on auto- and SOS regulation is for HimA and LexA to be joint repressors. However, the apparent regulatory interaction between the *himA* and *himD* genes allows LexA, HimA, and HimD to regulate *himA* in a number of different ways, and further work will be required to clarify the control hierarchy.

Why is the *himA* gene regulated in coordination with genes known or suspected to be active in recovery from DNA damage? Although *himA*⁻ mutants are not UV sensitive (ref. 2; unpublished work), the HimA protein might be involved in some subtle way in repair of damaged DNA. However, we think that a more likely possibility is the capacity of HimA to facilitate the acquisition of completely new genetic material through site-specific recombination. Thus, induction of the *himA* gene increases the likelihood that potentially helpful genes can be acquired by a cell population in distress. Other SOS genes without an identified function might have a similar role (e.g., in transposon mobility). The mutagenic DNA repair associated with the SOS response might have also evolved in response to a need for more varied genetic potential. If present in organisms other than bacteria, an induced capacity for genetic variation might serve in a general way to enhance the rate of evolutionary change under conditions of environmental stress.

In addition to its possible role for the cell, the SOS induction of HimA also presumably helps the phage because it ensures a high level of the host component required for excision of λ DNA during prophage induction.

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1. Clark, A. (1973) *Annu. Rev. Genet.* **7**, 67–86.
2. Miller, H. I. & Friedman, D. I. (1980) *Cell* **20**, 711–719.
3. Miller, H. I., Kikuchi, A., Nash, H. A., Weisberg, R. A. & Friedman, D. I. (1979) *Cold Spring Harbor Symp. Quant. Biol.* **43**, 1121–1126.
4. Radman, M. (1975) in *Molecular Mechanisms for Repair of DNA*, eds. Hanawalt, P. & Setlow, R. (Plenum, New York), pp. 355–368.
5. Witkin, E. (1976) *Bacteriol. Rev.* **40**, 869–907.
6. Gudas, L. J. & Pardee, A. B. (1976) *J. Mol. Biol.* **101**, 459–477.
7. Little, J. W. & Hanawalt, P. C. (1977) *Mol. Gen. Genet.* **150**, 237–248.
8. Little, J. W. & Kleid, D. G. (1977) *J. Biol. Chem.* **252**, 6251–6252.
9. McEntee, K. (1977) *Proc. Natl. Acad. Sci. USA* **74**, 5275–5279.
10. Emmerson, P. T. & West, S. C. (1977) *Mol. Gen. Genet.* **155**, 77–85.
11. McPartland, A., Green, L. & Echols, H. (1980) *Cell* **20**, 731–737.
12. Howard-Flanders, P., Rupp, W. D., Wilkins, B. M. & Cole, R. S. (1968) *Cold Spring Harbor Symp. Quant. Biol.* **33**, 195–205.
13. Kenyon, C. J. & Walker, G. C. (1980) *Proc. Natl. Acad. Sci. USA* **77**, 2819–2823.
14. Mount, D. W. (1977) *Proc. Natl. Acad. Sci. USA* **74**, 300–304.
15. Roberts, J. W., Roberts, C. W. & Mount, D. W. (1977) *Proc. Natl. Acad. Sci. USA* **74**, 2283–2287.
16. Little, J. W., Edmiston, S. H., Pacelli, L. Z. & Mount, D. W. (1980) *Proc. Natl. Acad. Sci. USA* **77**, 3225–3229.
17. Roberts, J. W., Roberts, C. W. & Craig, N. L. (1978) *Proc. Natl. Acad. Sci. USA* **75**, 4714–4718.
18. Miller, H. I. & Nash, H. A. (1981) *Nature (London)* **290**, 523–526.
19. Miller, H. I., Abraham, J., Benedik, M., Campbell, A., Court, D., Echols, H., Fischer, R., Galindo, J. M., Guarneros, G., Hernandez, T., Mascarenhas, D., Montanez, C. Schindler, D., Schmeissner, U. & Sosa, L. (1981) *Cold Spring Harbor Symp. Quant. Biol.* **45**, 439–445.
20. Miller, H. I. (1981) *Cell*, **25**, 269–276.
21. Castellazzi, M., George, J. & Buttin, G. (1972) *Mol. Gen. Genet.* **119**, 139–152.
22. Csonka, L. N. & Clark, A. J. (1979) *Genetics* **93**, 321–343.
23. Mount, D. W., Low, K. B. & Edmiston, S. J. (1972) *J. Bacteriol.* **112**, 886–893.
24. Pacelli, L. Z., Edmiston, S. H. & Mount, D. W. (1979) *J. Bacteriol.* **137**, 568–573.
25. Bochner, B. R., Huang, H.-C., Schieven, G. L. & Ames, B. (1980) *J. Bacteriol.* **143**, 926–933.
26. Casadaban, M. J. & Cohen, S. N. (1979) *Proc. Natl. Acad. Sci. USA* **76**, 4530–4533.
27. Miller, J. H. (1972) *Experiments in Molecular Genetics* (Cold Spring Harbor Laboratory, Cold Spring Harbor, NY).
28. O'Farrell, P. Z., Goodman, H. M. & O'Farrell, P. H. (1977) *Cell* **12**, 1133–1142.
29. Miller, H. I. & Friedman, D. I. (1977) in *DNA Insertion Elements, Plasmids, and Episomes*, eds. Bukhari, A., Shapiro, J. & Adhya, S. (Cold Spring Harbor Laboratory, Cold Spring Harbor, NY), pp. 349–356.
30. George, J., Catellazzi, M. & Buttin, G. (1975) *Mol. Gen. Genet.* **140**, 309–332.
31. Bloch, P. L., Phillips, T. & Neidhardt, F. C. (1980) *J. Bacteriol.* **141**, 1409–1420.