Regulation of Bacterial Catalase Synthesis

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All catalases have the common role of dismutating H_2O_2 to O_2 and H_2O, but the activity resides in a structurally diverse group of proteins. *Micrococcus lysodeikticus* (Herbert and Pinsent 1948) and *Proteus mirabilis* (Jouve et al. 1984) produce catalases that closely resemble the classic eukaryotic enzyme with four protoheme IX groups associated with a tetramer of approximately 60-kD subunits. *Escherichia coli* (Loewen and Switala 1986) and *Bacillus subtilis* (Loewen and Switala 1988) produce catalases containing six heme *d*-isomer prosthetic groups in a hexameric structure of larger subunits. *E. coli* (Claiborne and Fridovich 1979) and *Rhodopseudomonas capsulata* (Hochman and Shemesh 1987) produce a bifunctional catalase-peroxidase enzyme with larger than normal subunits. *Lactobacillus plantarum* (Kono and Fridovich 1983) and *Thermoleophilum album* (Allgood and Perry 1986) produce catalases that contain one manganese per subunit rather than a heme prosthetic group associated in hexameric or tetrameric structures, respectively. Finally, one of the three catalases of *Klebsiella pneumoniae* (Goldberg and Hochman 1989a) exists in dimer form. In addition to this diversity in structures, most bacteria produce two catalases, with *K. pneumoniae* (Goldberg and Hochman 1989b) being an exception with three. The two catalases in *E. coli*, labeled hydroperoxidase I (HPI) (Claiborne and Fridovich 1979) and hydroperoxidase II (HPII) (Claiborne et al. 1979), have been most extensively studied and serve as the focus of this review.

HPI is a bifunctional catalase-peroxidase containing two protoheme IX groups associated with a tetramer of identical 80-kD subunits (Claiborne and Fridovich 1979). The deduced

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amino acid sequence of the HPI subunit (Triggs-Raine et al. 1988) has revealed significant similarity with the sequence of a peroxidase from *Bacillus stearothermophilus* (Loprasert et al. 1989) but not to other catalases, suggesting that it may have evolved as a peroxidase rather than a catalase. HPII is a monofunctional catalase with six heme *d* isomers (Chiu et al. 1989) associated in a hexameric structure of 84.2-kD subunits (Loewen and Switala 1986). Despite this dissimilarity in structure from classic catalases, the deduced amino acid sequence of the HPII subunit has revealed significant similarity with the sequences of known eukaryotic catalases (von Ossowski et al. 1991), suggesting that it has evolved as a true catalase.

The presence of two catalases in *E. coli* complicated early studies on the regulation of catalase synthesis because of the inability to ascribe changes in the overall catalase levels to one or the other of the two enzymes. For example, glucose was reported to lower catalase levels (Hassan and Fridovich 1978; Yoshpe-Purer et al. 1977), hydrogen peroxide was reported to induce catalase synthesis (Finn and Codon 1975; Yoshpe-Purer et al. 1977; Richter and Loewen 1981), and catalase levels were reported to increase as cells grew into stationary phase (Finn and Condon 1975), but it was not clear whether one or both of the catalases were changing in response to the stimuli. The isolation of mutants lacking one or the other of the two catalases made it possible to show that it was HPI that responded to H_2O_2 and that HPII was synthesized as the cells entered stationary phase (Fig. 1) (Loewen et al. 1985a). Because the primary role of catalase is to rid the cell of the strong oxidant H_2O_2 before it causes unwanted, possibly destructive, reactions or gives rise to the even more reactive hydroxyl radical $\cdot OH$, the increase in HPI in response to H_2O_2 in the medium is an easily understood protective response to an oxidative stress. On the other hand, the rationale for why catalase HPII synthesis increases as cells enter stationary phase and not in response to H_2O_2 is not as clear but is probably a reflection of the need for protection against H_2O_2 that may arise under nongrowth conditions. Thus, not only are the two enzymes quite different structurally and genetically, but also the systems controlling their synthesis respond to different stimuli and involve different mechanisms.

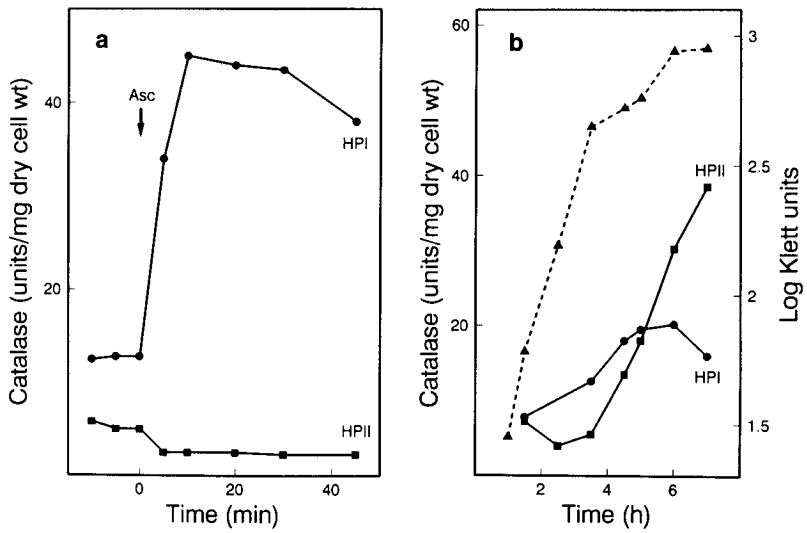

FIGURE 1 Catalase HPI (circle) and HPII (box) synthesis in response to H_2O_2 (from ascorbate added at 0 time) in *a* and to growth through exponential phase into stationary phase in *b*. Strain UM120 (*katE*::Tn*10*) was used for the determination of HPI, and strain UM202 (*katG*::Tn*10*) was used for the determination of HPII. The growth curve in *b* is shown by the dashed line. (Data modified from Loewen et al. 1985a.)

REGULATION OF CATALASE HPI SYNTHESIS

The subunit of HPI is encoded by *katG*, which has been mapped at 89.2 minutes on the *E. coli* chromosome (Loewen et al. 1985b). The gene has been cloned, physically characterized, and sequenced (Loewen et al. 1983; Triggs-Raine and Loewen 1987; Triggs-Raine et al. 1988), revealing an open reading frame of 2181 bp encoding an 80-kD subunit. Putative -10 (TATCGT) and -35 (TTATAA) sequences upstream (Triggs-Raine et al. 1988) of the transcription start site (Tartaglia et al. 1989) differed from the σ^{70} consensus promoter sequence, raising the possibility that an activating protein might be required for transcription initiation.

Cultures of both *E. coli* and *Salmonella typhimurium* treated with low doses of H_2O_2 respond with the synthesis of HPI, as already noted, but also with the synthesis of 33 other proteins that make the cell more resistant to killing by higher, normally

lethal, levels of the same oxidant. Of the 34 proteins induced by H_2O_2, 9, including HPI and an alkyl hydroperoxidase (encoded by *ahpC* and *ahpF*), have been shown to be directly under the control of the *oxyR* gene product (Christman et al. 1985; Morgan et al. 1986). The fact that the levels of *katG* mRNA were increased some 50-fold in a *S. typhimurium oxyR1*-containing mutant that allows constitutive overexpression of the 9 proteins (Morgan et al. 1986) confirmed that the effect of OxyR protein on *katG* was at the level of transcription.

Sequence analysis of *oxyR* revealed an open reading frame encoding a 34-kD protein having significant sequence similarity with a family of bacterial regulator proteins including the *E. coli* LysR, IlvY, CysB proteins; the *S. typhimurium* MetR and CysB proteins; the *Rhizobium* NodD protein; the *Enterobacter cloacae* AmpR protein; and the *Pseudomonas aeruginosa* TrpI protein (Christman et al. 1989). Like OxyR, which activates transcription from *katG* and *ahpC* promoters, members of this family of regulatory proteins act principally as transcriptional activators, although some also act as repressors. Indeed, OxyR was also found to negatively autoregulate its synthesis, with a fivefold higher level of β-galactosidase expression from an *oxyR::lacZ* fusion (Christman et al. 1989) being found in a Δ*oxyR*-containing mutant as compared to a wild-type strain. Identification of the OxyR-binding site in the *oxyR* promoter region showed that it overlapped the +1 to −10 region, thereby preventing RNA polymerase initiation, while at the same time activating a putative promoter oriented in the opposite direction. The sequences of the OxyR-binding sites in the *oxyR*, *katG*, and *ahpCF* promoters have been compared (Tartaglia et al. 1989), revealing too little sequence similarity to allow identification of the OxyR-binding requirements but indicating that OxyR just overlaps part of the −35 regions (ATTA in all three cases), possibly facilitating RNA polymerase binding through a direct protein-protein interaction (Fig. 2). Mutations linked to either *katG* or *ahpC*, which suppress H_2O_2 sensitivity in Δ*oxyR*-containing mutants, have been isolated and characterized (Greenberg and Demple 1988). Those linked to *katG* overproduced catalase HPI to impart peroxide resistance, implicating a change in the *katG* promoter that enhanced RNA polymerase binding in the absence of OxyR. Sur-

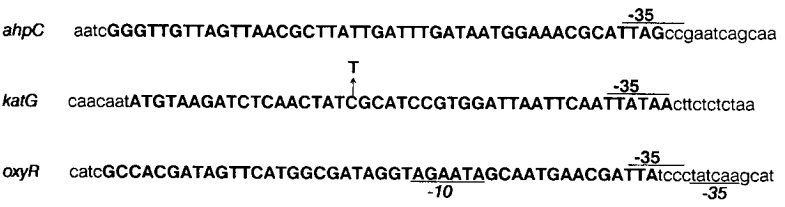

FIGURE 2 Alignment of the OxyR-binding sites in the *ahpC*, *katG*, and *oxyR* promoters. The –35 regions for transcription to the right (away from the *oxyR* gene) are indicated above the sequence, and the –10 for transcription into the *oxyR* gene is shown below. The single C to T change in the *katG* promoter that enhances *oxyR*-independent transcription of *katG* is shown above the *katG* sequence. (Data modified from Tartaglia et al. [1989] and Storz et al. [1990].)

prisingly, all the *katG*-linked mutations were the result of a single C to T change at –58, approximately in the middle of the OxyR-binding site and well removed from the RNA polymerase-binding site (J.T. Greenberg et al., unpubl.). The mutation does not generate an obvious new promoter nor does it change the known RNA polymerase-binding site, suggesting that there may be another activator protein which can activate *katG* expression in the absence of OxyR. One possible source of a candidate for this role might be a putative activator for another, as yet uncharacterized, regulon that enhances the expression of some of the 26 other proteins in response to peroxide (Storz et al. 1990). A more detailed definition of the OxyR-binding sites to be found by studying the interaction in various mutants will help to define the important sites for OxyR-DNA interaction.

The fact that *oxyR* transcription did not increase as a result of H_2O_2 treatment indicated that the inducing effect of OxyR came about as a result of changes in the existing OxyR protein and not as a result of increases in OxyR levels. The oxidation state of OxyR was found to be the determining factor in transcription enhancement, with oxidized OxyR being an effective activator of transcription and the reduced form being ineffective (Storz et al. 1990). Furthermore, the protein could be taken through several reduction-oxidation cycles and still retain the ability to activate transcription. There was little difference in the affinities of reduced and oxidized OxyR for the

promoters, but the binding footprints on the DNA were somewhat different, suggesting that it was a change in conformation brought on by the change in oxidation state that was responsible for enhancing transcription.

OxyR protein is therefore directly activated by the metabolic stimulus, an oxidant, to become the transcriptional activator, making it both the sensor of oxidative stress and the mediator of enhanced transcription of genes whose products are part of the protective response. A reactive species, which is generated from dissolved oxygen in the medium or from the addition of H_2O_2 to the medium, interacts with OxyR to change its oxidation state, causing a conformational change that affects the way in which the protein interacts with its target promoters. Consequently, the *oxyR* regulon response to oxidative stress is one of the few mechanisms for which the translation of an environmental stress into transcriptional control has been defined, and *E. coli* uses this response, in part, to survive the harmful metabolic effects of peroxide and possibly other oxidants in the medium. The importance of catalase HPI in this response is indicated by the fact that overproduction of HPI alone (Greenberg and Demple 1988) was sufficient to impart peroxide resistance. The other 33 proteins, 8 controlled by *oxyR* and 25 by some other mechanism(s), must also have protective roles, but, except for the alkylhydroperoxidase from the *ahp* genes, none has been characterized. The picture is further complicated by the overlap of control mechanisms, with common proteins being among those induced by redox-cycling agents (such as paraquat and menadione), by hydrogen peroxide (Greenberg and Demple 1989), and by heat shock (Morgan et al. 1986). *E. coli* has evolved a very intricate and complex system of overlapping responses to oxidative stresses, and catalase HPI is an important product of this protective response.

REGULATION OF CATALASE HPII SYNTHESIS

The subunit of catalase HPII is encoded by *katE*, which has been mapped at 37.8 minutes on the *E. coli* chromosome (Loewen 1984). The gene has been cloned, physically charac-

terized, and sequenced (Mulvey et al. 1988; von Ossowski et al. 1991), revealing an open reading frame of 2259 bp encoding an 84.2-kD subunit. The pattern of HPII synthesis, including elevated levels in stationary phase and during growth on TCA cycle intermediates, was independent of *oxyR* (Christman et al. 1985) but required an active *katF* gene mapping at 59 minutes on the chromosome (Loewen and Triggs 1984). Cloning and sequence analysis (Mulvey et al. 1988; Mulvey and Loewen 1989) of the *katF* gene revealed a 1086-bp open reading frame encoding a 41.5-kD protein with striking sequence similarity to known sigma transcription factors, suggesting that its role in the activation of expression from *katE* involved facilitating RNA polymerase binding to the *katE* promoter.

It seemed unlikely that a sigma factor would have evolved for the transcription of just one gene, and subsequent work has confirmed that there are a number of other loci controlled by *katF*. The gene, *nur*, was originally identified by its phenotype of conferring resistance to near-ultraviolet (NUV) radiation, and mutants deficient in *nur* were found to be more sensitive to H_2O_2 and to NUV radiation (Sammartano et al. 1986). Genetic analysis revealed that *nur* was an allele of *katF*, and it was confirmed that *katF* mutations were sensitive to NUV (Sammartano et al. 1986) whereas *katE*-containing mutants were not, indicating that *katF* must be influencing the expression of other genes involved in NUV resistance. A number of loci, including several involved in DNA repair, *recA* (Carlsson and Carpenter 1980), *uvrA* (Sammartano et al. 1986), *polA* (Sammartano et al. 1986), and *xthA* (Demple et al. 1983), have been implicated in the repair of NUV damage, and of these, *xthA* has been shown to be under the control of *katF* (Sak et al. 1989) to the extent that mutations in *katF* caused a reduction in *xthA* expression from both chromosomal and plasmid encoded genes. Unexpectedly, the levels of exonuclease III (encoded by *xthA*) increased throughout exponential phase and dropped as the cells entered stationary phase. This is quite unlike the pattern of expression of HPII (Fig. 1), which remains low throughout exponential phase and increases substantially as the cells enter stationary phase. If this pattern of *xthA* expression is confirmed, and *katF* is indeed regulating both *xthA* and *katE* despite the different pat-

terns of in vivo expression, it implies the involvement of additional factors to mediate the effect of the KatF protein on the two promoters. More recently, evidence has been presented that *appR* is very likely an allele of *katF* (Touati et al. 1991), which implies that *appA*, encoding an acid phosphatase, is another gene controlled by *katF*.

The correlation between HPII synthesis and entry into stationary phase has suggested a possible link between *katE-katF* expression and the expression of genes responding to starvation stress. Up to 55 proteins are synthesized as part of the starvation response, and they result in the cell's becoming thermotolerant, resistant to hydrogen peroxide, resistant to osmotic stress, and resistant to acid stress (for a review of the starvation stress response, see Matin 1990). A search for mutations affecting the transition of bacteria to starvation conditions resulted in the identification of a locus named *csi-2* (for carbon-starvation-induced) that controlled the synthesis of at least 16 proteins (Lange and Hengge-Aronis 1991a). Inactivation of the locus by Tn*10* or *lacZ* insertion mutagenesis resulted in reduced glycogen synthesis, an inability to develop thermotolerance or H_2O_2 resistance, and an inability to induce *appA* expression in stationary phase. Like *appR*, *csi-2* was shown to be an allele of *katF*, and growth of a *csi2::lacZ*-containing strain into stationary phase resulted in the induction of β-galactosidase synthesis, confirming that its expression phenotype was very similar to the phenotype of HPII synthesis in wild-type cells (Lange and Hengge-Aronis 1991a). The importance of *katF* in the starvation response has been reinforced with the observation that expression of 32 carbon starvation proteins, including some encoded by *pex* genes, is controlled by *katF* and that starvation-induced cross-protection against heat shock, osmotic shock, oxidative stress, and acid stress did not occur in a *katF* mutant (McCann et al. 1991).

A significant morphological change in cells occurs as they grow into stationary phase. Rod-shaped, exponential phase cells become spherical-shaped as a result of starvation or growth into stationary phase, but the change does not occur in *katF*-containing mutants (Lange and Hengge-Aronis 1991b), thereby implicating *katF* in the regulation of morphological

changes. One gene involved in mediating morphological change is *bolA* (Aldea et al. 1989), which encodes a small regulatory protein required for the synthesis of the penicillin-binding protein PBP6, a carboxy peptidase involved in peptidoglycan synthesis for the cell wall. Like HPII, its synthesis is turned on in wild-type cells growing into stationary phase, and expression from the *bolA* promoter was prevented in a *katF::Tn10*-containing mutant (Lange and Hengge-Aronis 1991b). Because only 32 of a possible 50–80 starvation proteins respond to *katF*, not all proteins turned on in stationary phase are controlled by KatF, and this probably includes the *mcb* operon (Genilloud et al. 1989), which, despite its expression in stationary phase (Connell et al. 1987), is only weakly affected by *katF* (Lange and Hengge-Aronis 1991b).

The sequences from a number of genes expressed in stationary phase and apparently controlled by *katF* are now available, making it possible to search for consensus sequences favored by KatF protein acting as a possible sigma factor (von Ossowski et al. 1991; Lange and Hengge-Aronis 1991b). Included in the comparison shown in Figure 3 are the promoter regions from *katE* (von Ossowski et al. 1991), *xthA* (Saporito et al. 1988), *bolA* (Aldea et al. 1989), *ftsQ* (Aldea et al. 1990), and *mcbA* (Genilloud et al. 1989). The first four have putative –35

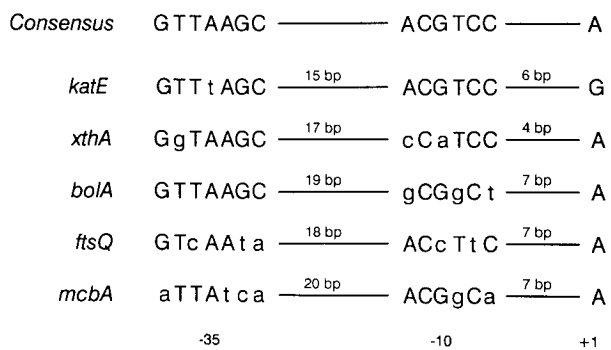

FIGURE 3 Alignment of segments of the promoter regions of *katE*, *xthA*, *bolA*, *ftsQ*, and *mcbA* to provide maximum similarity in the –10 and –35 regions and to provide optimum spacing between the two regions. (Data modified from Connell et al. [1987]; Aldea et al. [1989, 1990]; Genilloud et al. [1989]; Lange and Hengge-Aronis [1991a,b].)

and -10 sequences that are very similar, giving rise to consensus sequences of ACGTCC (-10) and GTTAAGC (-35). The promoter from *mcbA* has least similarity, particularly in the -35 region, consistent with its being controlled by *katF*, only weakly, if at all (Lange and Hengge-Aronis 1991b). The promoter of *ftsQ* has not yet been shown to be controlled by *katF*, but the sequence similarity suggests that it is a strong candidate to be a member of this regulon. Additional similarity that would lengthen the -10 sequence to AACGTCCAGT and the -35 sequence to AnTTGnnGTTAAGC exists but is not included in the figure. There is an alternative alignment for the *xthA* -10 region that is also not shown which would increase the spacing to the start site to a more favorable 8 bp, but which would reduce the spacing between the -10 and -35 regions to a less favorable 13 bp. The significance of these sequences will become clearer as more promoters affected by KatF are sequenced.

It is now evident that *katF* is involved in regulating the expression of a group of genes with very diverse functions, including oxidative protection (*katE*), DNA repair (*xthA*), cell morphology changes (*bolA*), phosphate metabolism (*appA*), starvation protection (*pex*), and possibly cell division (*ftsQ*). Maximal expression of *katF* during stationary phase and starvation (Mulvey et al. 1990; Lange and Hengge-Aronis 1991a) suggests that the primary role of the *katF* regulon is to produce gene products necessary for the adaptation of the cell to conditions of nutrient limitation and survival during periods of dormancy. Indeed, strains lacking KatF protein have been found to die off much more rapidly during incubation in stationary phase (Mulvey et al. 1990) and during starvation (McCann et al. 1991). In view of this role and the apparent sigma-like structure of the protein, it has been proposed that KatF protein be named σ^S, where the S denotes starvation, and that *katF* be renamed *rpoS* (Lange and Hengge-Aronis 1991b). The *katF* terminology has been retained for the remainder of this chapter to avoid confusion.

The lack of an easily assayable activity for KatF protein has made the plasmid-borne *katF::lacZ* fusion an invaluable tool in the study of factors affecting the turn-on of transcription of the *katF* gene (Mulvey et al. 1990; P.C. Loewen et al., in prep.).

Generally, factors that induce expression of *katE* also induce expression of *katF*. However, *katF* expression increased gradually throughout exponential phase to a maximum level in stationary phase, whereas *katE* expression remained very low throughout exponential phase and increased substantially only in stationary phase. Consequently, although KatF protein is required for *katE* expression, its presence in the cell is not sufficient to cause the turn-on of *katE* transcription, suggesting that another factor is involved in controlling *katE* expression. As already noted in the case of *xthA* expression, the exonuclease III levels increased throughout exponential phase, seemingly in parallel with the gradual increase in *katF* expression, but decreased in stationary phase, when *katF* levels increase to their highest, implying that yet another protein is required to mediate the expression of *xthA*. KatF may therefore resemble σ^{54} in its requirement for accessory proteins to modulate its influence on gene expression.

The conditions stimulating *katF* expression, namely growth into stationary phase and starvation, are very closely related phenomena in which nutrient depletion is the probable common factor limiting growth. For *katF* expression to occur under starvation conditions in a simple salts medium, a carbon or energy source and an amino acid supplement, sufficient to support protein synthesis but not growth, were required (Mulvey et al. 1990). Expression under these artificial starvation conditions could be prevented by uncouplers, by inhibitors of electron transport (Fig. 4), and by a reduction in pH of the medium, indicating that the proton motive force had a role in mediating the turn-on of *katF* transcription (P.C. Loewen et al., in prep.). In cells growing in rich medium, the response of *katF* expression was quite different, being turned on when the electron transport process was inhibited (Fig. 4) or the proton motive force was reduced. This has given rise to the hypothesis that an optimally charged membrane as would exist in cells growing in rich medium prevents the expression of *katF*, but as the membrane potential drops because of nutrient depletion or slower metabolism, *katF* expression is turned on. However, if the membrane potential drops too low, as when electron flow is inhibited in starved cells or when a very high concentration of KCN is added to growing cells, the cell is no longer capable

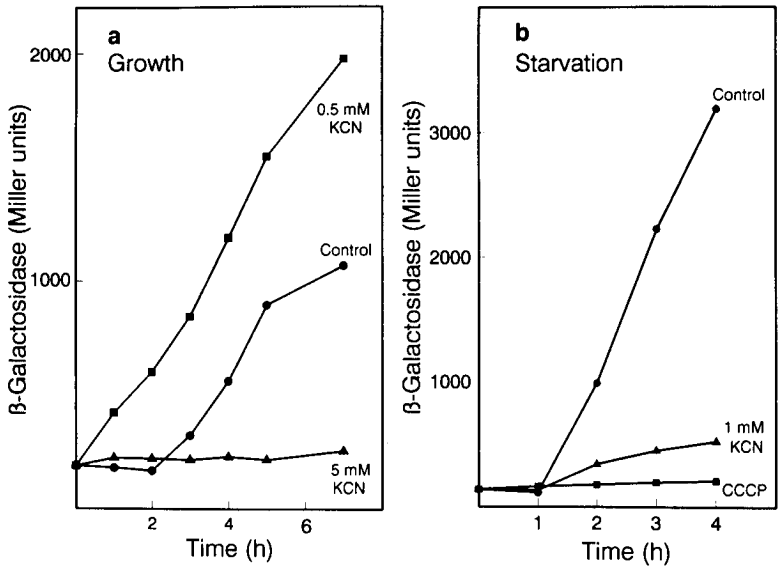

FIGURE 4 Effect of the electron transport inhibitor KCN on *katF* expression in cells growing in LB medium containing 5 g of yeast extract, 10 g of tryptone, and 10 g of NaCl per liter (*a*) and of KCN or the protonophore CCCP on *katF* expression in cells starved for nitrogen and phosphate. Strain NM522 containing plasmid pRSkatF5 (*katF::lacZ* fusion) was used in both experiments. In *a*, growth in the presence of both concentrations of KCN was very slow, whereas the control grew normally. In *b*, no growth occurred in the medium containing 25 mM Tris (pH 8.0), 0.1 M NaCl, 1 mM $MgSO_4$, 16 mM glucose, and 0.006% (w/v) casamino acids.

of supporting the RNA and protein synthesis necessary for expression.

How might changes in the proton motive force be sensed and translated into changes in transcription of *katF*? Several possibilities can be proposed. Because *katF* expression in starved cells is unaffected by valinomycin, it might be the ΔpH component of the membrane potential or the change in activity of proteins involved in the process of pumping protons that is sensed. Alternatively, conformational changes in membrane-associated proteins brought on by changes in membrane potential or proton pumping might be the trigger. Yet another possibility is that changes in the levels of electron carriers such as NAD^+, reflecting changes in electron flow, might serve

as the signal. Regardless of what mechanism is functioning, the involvement of another protein to sense the metabolic changes and affect *katF* transcription is implied by these results. A mutant with a phenotype consistent with the existence of a locus that influences *katF* expression has recently been isolated and is being characterized.

Changes in *katE* expression largely mimic the changes in *katF* expression under all the metabolic conditions so far studied. This is consistent with KatF protein's being required for the initiation of transcription in the *katE* promoter, but it does not explain the fact that *katE* expression may be only partially induced despite the apparent maximal expression from *katF*. Maximum induction of *katF* supports only one third of maximum induction of *katE* (Mulvey et al. 1990), making it very likely that an as yet unidentified accessory protein is required for maximal *katE* expression. As already noted, an additional protein would seem to be required to mediate *xthA* expression, because the synthesis of exonuclease III is not correlated either with the pattern of HPII synthesis or with the pattern of *katF* expression. A few discrepancies have arisen in various studies about what environmental factors do or do not affect the expression of *katE* and the synthesis of HPII. For example, cAMP may (Lange and Hengge-Aronis 1991a) or may not (P.C. Loewen et al., in prep.) inhibit *katF* expression, and anaerobiosis may (Schellhorn and Hassan 1988; Meir and Yagil 1990) or may not (Mulvey et al. 1990) reduce *katE* expression. The possible involvement of cAMP is probably related to the as yet unexplained phenomenon of *katF* mutations acting as *crp* suppressors (Touati et al. 1991). Glucose has been reported to reduce HPII synthesis (Meir and Yagil 1990), which would be inconsistent with cAMP inhibiting *katF* expression, and this was shown to be a result of the high glucose levels delaying the transition to stationary phase with its associated increase in *katF* expression (Mulvey et al. 1990). Ongoing studies of the mechanism controlling *katE* and *katF* expression will address these questions.

The system controlling the synthesis of HPII is part of a regulon that responds to nutrient depletion but which is intricately involved with a number of other regulons, including those imparting thermotolerance and osmotic shock protec-

tion. Another sigma factor, σ^{32}, is involved in the heat shock response; it will be interesting to see how two different sigma factors might affect transcription of the same classes of genes.

SUMMARY

The catalases of *E. coli* are controlled by two different regulons responding to different environmental stimuli. HPI synthesis is controlled by the *oxyR* regulon that responds to oxidative stress by changing the oxidation state of OxyR protein, thereby changing its ability to activate transcription. In this instance, the catalase is serving as one part of a system that protects the cell from reactive oxygen species, including H_2O_2 (Fig. 5). HPII synthesis is controlled by the *katF* regulon (Fig. 5) that responds to nutrient depletion by activating the synthesis of starvation stress proteins, morphological changes, and DNA repair processes, as well as catalase, to prepare the cell for dormancy and to protect it during the dormant state. As just

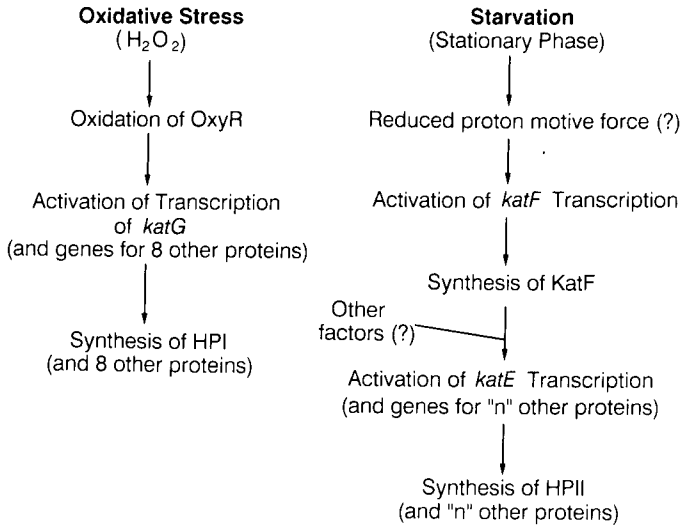

FIGURE 5 Schematic summary of the steps involved in the responses of the two catalases to either oxidative stress or starvation. The designation of "n" for the number of genes and proteins controlled by *katF* was used because the actual number remains uncertain, although it would seem to be in excess of 32.

one enzyme in this very diverse group of proteins, HPII presumably has the role of removing the very reactive H_2O_2 before it can cause cellular damage.

Among other bacterial species, only the catalases from *B. subtilis* have been characterized to provide some limited evidence about factors that affect their synthesis, and the control picture is somewhat similar to that in *E. coli*. Catalase-1 of *B. subtilis* resembles HPI in that it responds to H_2O_2 (Loewen and Switala 1987), but whether or not this is part of an *oxyR*-like regulon response has not been demonstrated. Catalase-2 resembles HPII in several respects: They are structurally and spectrally similar; they both accumulate during nutrient limitation; and the syntheses of both are under the control of an alternate sigma factor (catalase-2 appears only in stage V of the sporulation process [Loewen 1989]). Catalases in other bacterial species have not yet been characterized with respect to their relative levels of expression, preventing any further comparisons.

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