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# Strategies for Survival of an Antibiotic-Producing Bacterium *Streptomyces coelicolor*

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*Streptomyces coelicolor* is a Gram-positive bacterium that undergoes fungus-like morphological differentiation and produces a variety of secondary metabolites including antibiotics. Its linear chromosome of 8,667,507 bp is predicted to encode 7846 proteins, so far the highest number among bacteria whose genome sequencing is completed (Bentley et al., 2002). It devotes more than 12% of its genes (> 900 gene products) as transcriptional regulators. The presence of over 60 sigma factors reflects the complexity of its gene regulation.

The list of regulators that control transcription of these genes include $\sigma^R$/RsrA (sigma/anti-sigma), $\sigma^B$/RsbA/RsbV (sigma/anti-sigma/anti-anti-sigma), OxyR (positive regulator of alkylhydroperoxide reductase system), CatR (Fur-type repressor of catalase A), Nur (Ni-responsive regulator), and OhrR (repressor of organic peroxide reductase). Among these, redox-sensitive modulation of activity has been observed in RsrA, CatR, and OxyR (Kang et al., 1999; Hahn et al., 2000; Hahn et al., 2002). Thiol-disulfide switch mechanism in RsrA has been investigated in detail, revealing a novel way of controlling the activity of zinc-finger protein (Bae et al., 2004).

The division of labor between the two peroxide-sensing regulators, OxyR and CatR, has been suggested. Analysis at both individual gene and genome level reveals how this organism utilizes nearly all the strategies available in bacterial domain to cope with oxidative stress.

Induction of genes in *S. coelicolor* in response to differentiation and osmotic stress is mediated primarily by a sigma factor $\sigma^B$, a group 3 sigma factor, and a functional homologue of $\sigma^S$ from *Escherichia coli* (Helmann, 2002; Cho et al., 2001). Microarray analysis revealed $\sigma^B$-dependent induction of more than 280 genes by 0.2 M KCl. These genes encode several sigma factors, oxidative defense proteins, chaperones, and systems to provide osmolytes, cysteine, mycothiol, and gas vesicle. $\sigma^B$ controlled induction of itself and its two paralogues ($\sigma^L$ and $\sigma^M$) in a hierarchical order of $\sigma^B \rightarrow \sigma^L \rightarrow \sigma^M$, as revealed by S1 mapping and Western blot analyses. The phenotype of each sigma mutant suggested a sequential action in morphological differentiation; $\sigma^B$ in forming aerial mycelium, $\sigma^L$ in forming spores, and $\sigma^M$ for efficient sporulation. $\sigma^B$ was also responsible for the increase in cysteine and mycothiol, the major thiol buffer in actinomycetes, upon osmotic shock, revealing an overlap between protections against osmotic and oxidative stresses.

Proteins in *sigB* mutant were more oxidized (carbonylated) than the wild type. These results support a hypothesis that $\sigma^B$ serves as a master regulator that triggers other related sigma factors in a cascade, and thus regulates differentiation and osmotic and oxidative response in *S.coelicolor*.

## References


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