

## Regulation of Oxidative and Osmotic Stress Response in *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 7,846 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 (Fig. 1, Hahn *et al.*, 2004).

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), NikR (Ni-responsive repressor of Fe-SOD), and OhrR (repressor of organic peroxide reductase). Among these, redox-sensitive modulation of activity has been observed in RsrA, CatR, and OxyR (Fig. 2, 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 osmotic stress is mediated primarily by a sigma factor  $\sigma^B$ , a group 3 sigma factor (Helmann, 2002; Cho *et al.*, 2001). Well above 300 genes are induced by 0.2 M KCl either transiently or persistently over one hour, and induction of more than 90% of these genes are mediated by  $\sigma^B$ , either directly or indirectly. The regulation mechanism and the overlap between oxidative and osmotic stress response will be discussed.

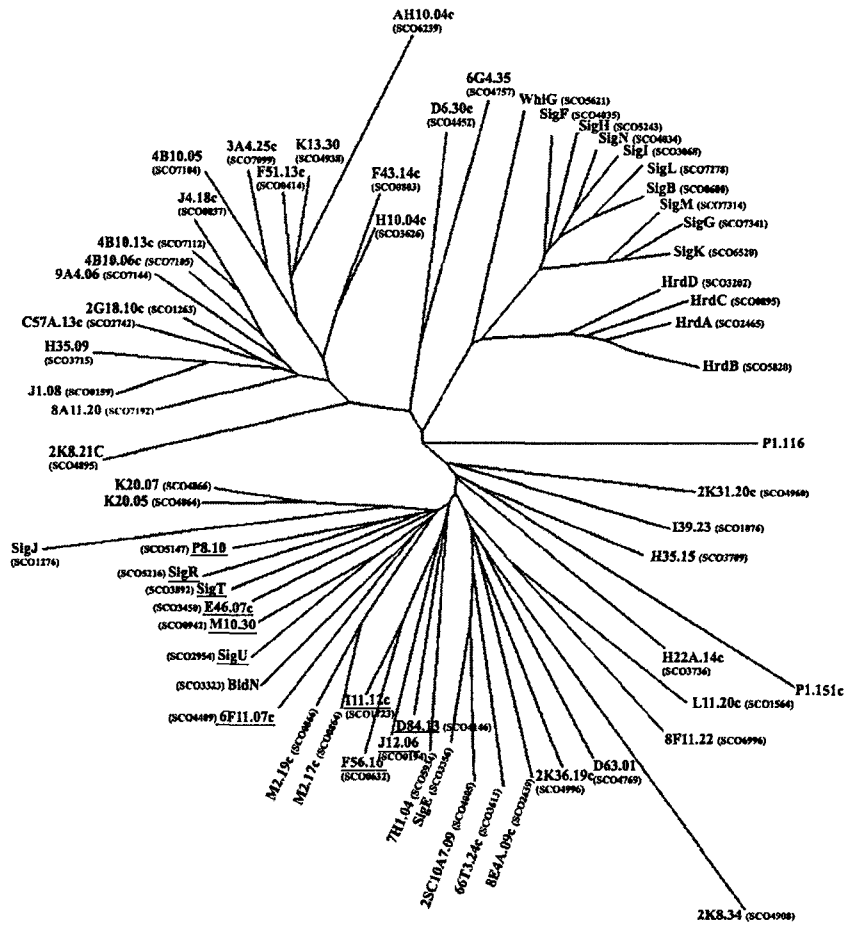


Fig. 1. Phylogenetic relationship among sixty six sigma factors of *S. coelicolor*.

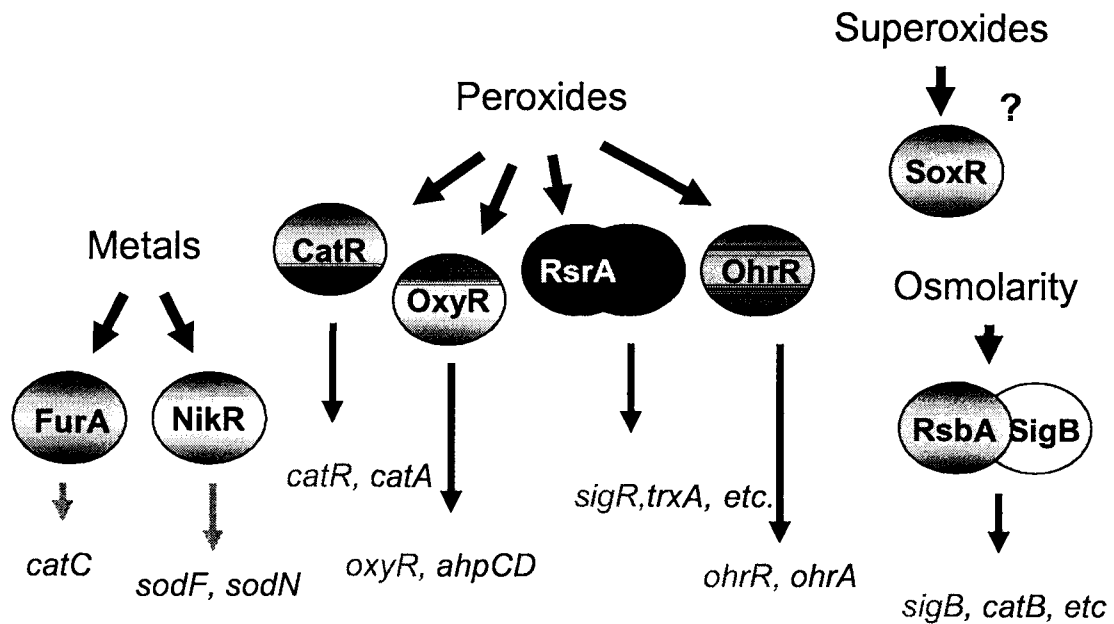


Fig. 2. Anti-Oxidative Regulators in *S. coelicolor*.

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