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Structural and functional analysis of the global transcriptional regulator SdrP from *Thermus thermophilus* HB8

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The stationary phase-dependent regulatory protein (SdrP) is a CRP/FNR family transcriptional activator from an extremely thermophilic bacterium *Thermus thermophilus* HB8, whose expression increases in the stationary growth phase. By the differential expression analysis using DNA microarray, we identified 14 SdrP-controlled genes which are involved in nutrient and energy supply, redox control, and nucleic acid metabolism. *E. coli* CRP, a prototype of the CRP family protein, undergoes conformational change upon cAMP binding, and the CRP-cAMP complex interacts with DNA and RNA polymerase to regulate transcription. Interestingly, the crystal structure of SdrP is similar to that of the DNA-binding form of *E. coli* CRP, even though SdrP does not contain any effector molecule. This result supports that the transcriptional activation by SdrP *in vitro* occurs independently of any added effector molecule [1]. Recently, we found that expression of the *sdrP* gene was enhanced by various stresses such as oxidative, heavy metal ion, high-salt, antibiotics, and organic-solvent stresses, even in the logarithmic growth phase, among which oxidative stress was the most effective. The genome-wide expression pattern analysis using 306 DNA microarray data from 117 experimental conditions revealed that the expression of many genes related to redox control, DNA repair, and turnover and repair of protein, were highly positively correlated with that of *sdrP* gene. Among them, we identified eight novel genes which were directly regulated by SdrP. These results suggest that SdrP is a transcriptional activator which manages an oxidative stress response.

In the case of the oxidative stress responsive transcriptional regulators of the other bacteria, such as OxyR, PerR, and SoxRS, formation of inter-molecular disulfide-bonds or oxidation of effecter molecules trigger structural changes to DNA-binding or -unbound form, resulting in the expression of the target genes being controlled (Fig. 1). As for the SdrP

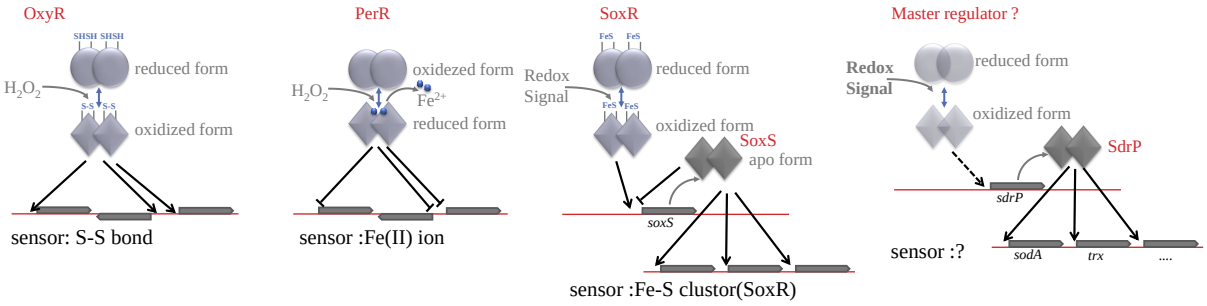

Fig. 1 Oxidative stress response regulators in bacteria

regulon, the expression may be controlled by the amount of SdrP, because SdrP has no cystein residue, any effector molecule is not necessary to the transcriptional activation, and the expression pattern of the target genes positively correlates with that of *sdrP* gene.

Reference

[1] Agari *et al.* (2008) *Mol. Microbiol.* **70**, 60-75