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Crystal Structure Determination of SoxR Protein in Oxidative Response Regulation System

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Introduction

The [2Fe-2S] transcription factor SoxR, a member of the MerR family, functions as a sensor of oxidative stress such as superoxide and nitric oxide in bacteria. Under conditions of oxidative stress, the [2Fe-2S] of SoxR is oxidized and then SoxR is activated to enhance the production of various antioxidant proteins through the *soxRS* regulon. In the active state, SoxR and other MerR proteins activate transcription from unique promoters, which have a long 19 or 20 bp spacer between the -35 and -10 operator elements, by untwisting DNA and base-pair breaking. Biochemical and spectroscopic studies have revealed the functional properties of SoxR, but the structural details of the redox sensing and transcriptional activation remains unclear. To obtain further insights into the redox regulation mechanism by SoxR, we have determined the crystal structures of SoxR from *E. coli* and its complex with the *soxS* promoter in the oxidized state at 3.2Å and 2.8Å resolution, respectively [1,2].

Results and Discussion

Crystals of SoxR were obtained using PEG10000 and glycerol as precipitants. The crystals of SoxR belong to the space group $P6_2$ with unit-cell parameters of $a = b = 80.0$ and $c = 88.1$ Å. Crystals of the SoxR-DNA complex were obtained by using a 20 bp DNA fragment from a condition containing PEG10000 and K/Na tartrate. The crystals of the SoxR-DNA complex belong to the space group $P6_122$ with unit cell parameters of $a = b = 53.5$ and $c = 355.6$ Å [1].

The overall structure of SoxR consists of a DNA-binding domain, a dimerization helix and a Fe-S cluster-binding domain (Figure). The dimerization helices form an antiparallel coiled coil stabilizing the SoxR dimer. The overall architecture of the SoxR-DNA complex is similar to those of other MerR family proteins, but the domain arrangement is distinct.

The structures reveal that the [2Fe-2S] cluster of SoxR is completely solvent-exposed and surrounded by an asymmetric environment. The asymmetrically charged environment of the [2Fe-2S] cluster probably causes redox-dependent conformational changes of SoxR and the target promoter.

Compared to the promoter structures with the 19-bp spacer previously studied [3], the DNA structure is more sharply bent, by about 1bp, with the two central base pairs holding Watson-Crick base pairs. Based on comparison of the target promoter sequences of the MerR family, the present structures is shown to be an activated promoter conformation with a 20-bp spacer [2].

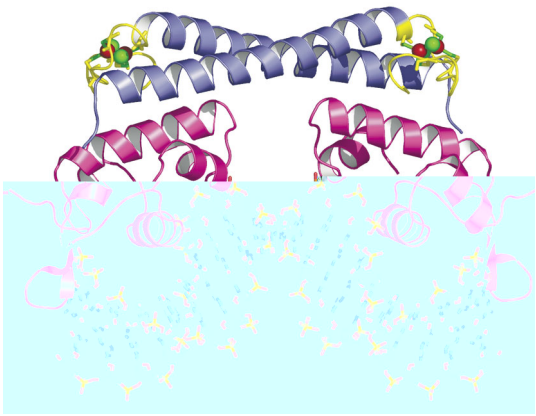

Figure Overall structure of the SoxR-DNA complex. The DNA binding domain, dimerization helix and Fe-S cluster binding domain are shown in magenta, blue and yellow, respectively.

References

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