Global transcriptional profiling reveals a link between regulation by IscR and regulation by oxygen

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IscR (iron-sulfur cluster regulator) is an Fe-S cluster-containing transcription factor in *Escherichia coli* that represses transcription from a promoter governing its own gene and the *iscSUA-hscBA-fdx* genes, whose products are involved in Fe-S cluster biogenesis. To enhance our understanding of the role of IscR in *E. coli* physiology and in Fe-S cluster stress, we investigated whether IscR regulates genes in addition to *iscRSUA-hscBA-fdx* with the use of DNA microarrays. We examined the global transcriptional changes in a strain lacking *iscR* and found 38 candidate genes representing 18 operons regulated by IscR under aerobic growth conditions. Many of the candidate promoters for IscR regulation were previously shown to be regulated by oxygen and have well-established roles in *E. coli* physiology. To determine whether IscR has an effect on expression of these genes under anaerobic growth conditions, global transcriptional profiling experiments were also carried out on cells grown under anaerobic conditions. Surprisingly, only three operons were common to both the aerobic and anaerobic data sets, and three additional genes appear to be regulated by IscR only under anaerobic growth conditions. The promoter regions responsible for *in vivo* regulation by IscR have been identified for half of the candidate genes. In addition, *in vitro* assays of these promoter regions have shown that IscR directly regulates the *hyaA*, *hybO*, *iscR*, *mqo*, *napF*, and *sufA* promoters driving the expression of hydrogenase-1, hydrogenase-2, the Isc system of Fe-S cluster biogenesis, malate:quinone oxidoreductase, periplasmic nitrate reductase, and the Suf system of Fe-S cluster biogenesis, respectively. Finally, the IscR binding site has been mapped for the *iscR* and *sufA* promoters. The findings presented here indicate that the role of IscR extends beyond that of regulation of Fe-S cluster biogenesis and that IscR contributes to the oxygen regulation of several promoters.