

DNA-mediated redox signaling for transcriptional activation of SoxR

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Abstract

In enteric bacteria, the cellular response to oxidative stress is activated by oxidation of the iron-sulfur clusters in SoxR, which then induces transcription of *soxS*, turning on a battery of defense genes. Here we demonstrate both in vitro and in cells that activation of SoxR can occur in a DNA-mediated reaction with guanine radicals, an early genomic signal of oxidative stress, serving as the oxidant. SoxR in its reduced form is found to inhibit guanine damage by repairing guanine radicals. Moreover, cells treated with a DNA-binding photooxidant, which generates guanine radicals, promotes the expression of *soxS*. In vitro, this photooxidant, tethered to DNA 80 bp from the *soxS* promoter, induces transcription by activating SoxR upon irradiation. Thus, transcription can be activated from a distance through DNA-mediated charge transport. This chemistry offers a general strategy for DNA-mediated signaling of oxidative stress.