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Organic Peroxide Sensing by Transcription Factor OhrR from *Bacillus subtilis*

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Reactive oxygen species (ROS), such as superoxide radical anion (O_2•$^-$), peroxide (ROOH), hydroxyl radical (•OH), can damage DNA, proteins, and membranes. Thus, the ability to sense and respond to oxidative stress is critical for survival in an aerobic environment [1]. Cells exposed to ROS upregulate the appropriate defensive systems including detoxification enzymes such as superoxide dismutase, catalase and peroxidases [2].

In *Bacillus subtilis*, the adaptive response to hydrogen peroxide is coordinated by the PerR transcription factor, which senses hydrogen peroxide by Fe-catalyzed histidine oxidation [3]. In contrast, the adaptive response to organic peroxides is controlled by OhrR transcription factor, which senses peroxide by single cysteine oxidation [4].

In the presence of cumene hydroperoxide (CHP), oxidation of OhrR leads to a sulfenic acid intermediate which reacts to form either a mixed disulfide (with a novel 398-Da thiol, cysteine and CoASH) or a protein sulfenamide. These inactive forms of OhrR can be reactivated by thiol–disulfide exchange reactions allowing restoration of repression [4]. However, OhrR is irreversibly oxidized to cysteine sulfinic (and sulfonic) acid even in the presence of low levels of linoleic acid hydroperoxide (LHP), a potent oxidant for OhrR [5]. Kinetic competition experiments indicate that further oxidation of the initial OhrR sulfenate product occurs at least 100-fold more rapidly with LHP than with CHP. These results indicate that OhrR can be either reversibly oxidized or can instead function as a sacrificial regulator depending on the oxidant [5].

References

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