INDUCTIONS OF SUPEROXIDE DISMUTASE BY ULTRAVIOLET IRRADIATION AND BY MANG. (U) DUKE UNIV MEDICAL CENTER DURHAM NC DEPT OF BIOCHEMISTRY I FRIDOVICH 01 FEB 88
INDUCTIONS OF SUPEROXIDE DISMUTASE BY ULTRAVIOLET IRRADIATION AND BY MANGANESE

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Inductions of Superoxide Dismutase by Ultraviolet Irradiation and by Manganese

We have set out to study the inductions of superoxide dismutase and we have done that and a variety of other related projects. We find that the E. coli MnSOD gene is controlled by a repressor protein which can exist in two states i.e. reduced or oxidized. In the reduced state it blocks transcription of the MnSOD gene and in the oxidized state it does not. In soluble extracts of E. coli the repressor can be reduced by glutathione but not by cysteine and by NADPH but not by NADH. The redox-active component of the repressor could be either a transition metal cation such as iron or a disulfide/thiol couple. This cannot yet be decided. The protein coded for by the MnSOD gene is first released in the form of an inactive precursor, distinct from the apoprotein and is then converted to the apoprotein. Final metal insertion to produce the active holoenzyme occurs much more readily under aerobic than under anaerobic conditions. As a consequence the inactive apoprotein, or a form with a metal other than manganese at the active site, accumulates under anaerobic conditions unless the medium is markedly enriched with Mn(II).
This does not happen in the presence of $O_2$, presumably because the manganese is then oxidized to Mn(III); which is bound to the active site with greater affinity than is Mn(II). Since $O_2^-$ can oxidize Mn(II) and since we think that iron competes with manganese for the active site of the enzyme, we combined iron-chelating agents, with Mn(II) salts in the presence of aerobic paraquat and achieved striking production of MnSOD by E. coli.

Another series of studies bears upon the biological effects of vanadate. We have found that vanadate catalyzes the oxidation of NAD(P)H by $O_2^-$ and that the mechanism involves a free radical chain reaction. Since this chain reaction amplifies the consequences of the initiating event it has allowed the demonstration that plasma, microsomal and mitochondrial membranes produce and release the superoxide radical.

Perusal of the list of publications which acknowledge support from the AROD office will indicate the full range of our work.
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