

Effect of Yeast Superoxide Dismutase Treatment on Some Mediators of Inflammation during Adjuvant-Induced Arthritis in Mice

Tsvetanka H. Stefanova*, Irena Ratcheva, Nadya J. Nikolova, and Hristo O. Neychev

Institute of Microbiology, Bulgarian Academy of Sciences, 26 Acad. G. Bonchev St., 1113 Sofia, Bulgaria. Fax: +++3 59 28 70 01 09. E-mail: tsvetankastefanova@yahoo.com

* Author for correspondence and reprint requests

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The superoxide radical ($O_2^{\cdot-}$), hydrogen peroxide (H_2O_2) and nitric oxide (NO) are pleiotropic inflammatory mediators which play an important role in inflammatory joint diseases. They are overproduced during rheumatoid arthritis and its experimental model – adjuvant-induced arthritis in rodents – and may be detected both systemically and intra-articularly. Their secretion is up-regulated by proinflammatory cytokines such as IFN- γ , IL-12, IL-6 and TNF- α , and they are responsible for the destruction of joint tissue. In this work, the effect of superoxide dismutase (SOD) from a thermotolerant yeast strain, *Kluyveromyces marxianus*, on the production of proinflammatory cytokines, reactive oxygen and nitrogen species was studied. Mice received three intraperitoneal injections of yeast SOD at a dose of 10 mg/kg body weight (30,000 U/kg) on consecutive days starting on the day after arthritic induction. On days 3, 8 and 14 post induction peritoneal macrophages were isolated and both spontaneous and stimulated production of reactive oxygen and nitrogen metabolites were measured. Early in arthritic development yeast SOD treatment did not influence the $O_2^{\cdot-}$ production, but on day 14 both spontaneous and PMA-induced secretion were dramatically reduced. Spontaneous H_2O_2 release was inhibited on day 14, while PMA-stimulated production was decreased from the beginning of the arthritic development. Yeast SOD treatment effectively suppressed the spontaneous and recombinant mouse IFN- γ + LPS induced release of NO as well. Serum levels of proinflammatory cytokines, IL-12, IFN- γ , IL-6 and TNF- α , were also significantly reduced. The obtained results show some of the mechanisms of action of SOD in reducing the severity of arthritic inflammation. Besides direct inhibition of joint tissue destruction exogenous SOD substantially limits the existing positive feedback between secretion of reactive oxygen species and inflammatory cytokine production.

Key words: Adjuvant Arthritis, SOD, Inflammatory Mediators