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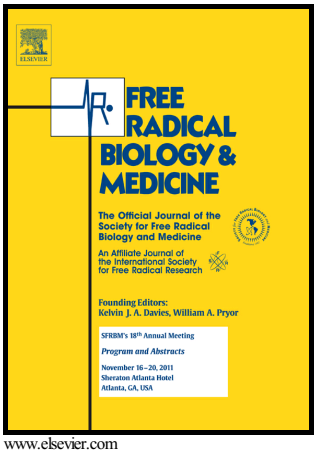

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Extracellular Superoxide Dismutase and its Role in Cancer

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Abstract

Reactive oxygen species (ROS) are increasingly recognized as critical determinants of cellular signaling and a strict balance of ROS levels must be maintained to ensure proper cellular function and survival. Notably, ROS is increased in cancer cells. The superoxide dismutase family plays an essential physiological role in mitigating deleterious effects of ROS. Due to the compartmentalization of ROS signaling, EcSOD, the only superoxide dismutase in the extracellular space, has unique characteristics and functions in cellular signal transduction. In comparison to the other two intracellular SODs, EcSOD is a relatively new comer in terms of its tumor suppressive role in cancer and the mechanisms involved are less well understood. Nevertheless, the degree of differential expression of this extracellular antioxidant in cancer versus normal cells/tissues is more pronounced and prevalent than the other SODs. A significant association of low EcSOD expression with reduced cancer patient survival further suggests that loss of extracellular redox regulation promotes a conducive microenvironment that favors cancer progression. The vast array of mechanisms reported in mediating deregulation of EcSOD expression, function, and cellular distribution also supports that loss of this extracellular antioxidant provides a selective advantage to cancer cells. Moreover, overexpression of EcSOD inhibits tumor growth and metastasis, indicating a role as a tumor suppressor. This review focuses on the current understanding of the mechanisms of deregulation and tumor suppressive function of EcSOD in cancer.

Keywords: EcSOD; SOD3; cancer; reactive oxygen species; heparin binding domain; tumor suppressor; metastasis; recurrence; relapse free survival; epigenetic; loss of heterozygosity; single nucleotide polymorphism; microRNA-21; oxidative tumor microenvironment