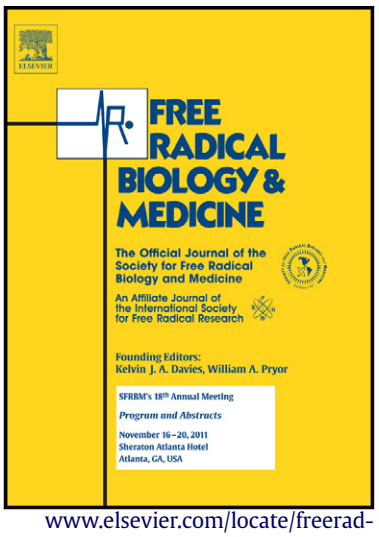

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Original Research Communication

Redox Regulation of Rac1 by Thiol Oxidation

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Abstract

The Rac1 GTPase is an essential and ubiquitous protein that signals through numerous pathways to control critical cellular processes, including cell growth, morphology, and motility. Rac1 deletion is embryonic lethal, and its dysregulation or mutation can promote cancer, arthritis, cardiovascular disease, and neurological disorders. Rac1 activity is highly regulated by modulatory proteins and post-translational modifications. While much attention has been devoted to guanine nucleotide exchange factors that act on Rac1 to promote GTP loading and Rac1 activation, cellular oxidants may also regulate Rac1 activation by promoting guanine nucleotide exchange. Herein, we show that Rac1 contains a redox-sensitive cysteine (Cys^{18}) that can be selectively oxidized at physiological pH due to its lowered pK_a. Consistent with these