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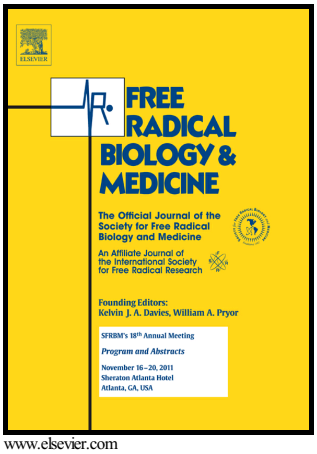

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Tyr42 phosphorylation of RhoA GTPase promotes tumorigenesis through nuclear factor (NF)-κB

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Abstract

Dysregulation of reactive oxygen species (ROS) levels is implicated in the pathogenesis of several diseases, including cancer. However, the molecular mechanisms of ROS in tumorigenesis have not been clearly elucidated. Hydrogen peroxide activated nuclear factor-κB (NF-κB) and RhoA GTPase. In particular, we found that hydrogen peroxide phosphorylated RhoA at Tyr42 *via* Src. P-Ty42 residue of RhoA was a binding site of Vav2, a guanine nucleotide exchange factor (GEF) that activates p-Tyr42 RhoA. P-Tyr42 RhoA then bound to IκB kinase γ (IKKγ), leading IKKβ activation. Furthermore, RhoA WT and Y42E promoted tumorigenesis, whereas RhoA Y42F suppressed it. In addition, hydrogen peroxide induced NF-κB activation, cell proliferation, and expression of c-Myc and cyclin D1 in the presnce of RhoA WT and RhoA Y42E (a phosphomimic), but not of RhoA Y42F (a dephospho-mimic). Indeed, p-Tyr42 Rho, p-Src, and p-65 were significantly increased in human breast cancer tissues and