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Title: Resveratrol attenuates cigarette smoke induced oxidative stress: Possible involvement of SIRT1

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Body: Objectives: Cigarette smoke is known to cause oxidative stress in alveolar epithelial cells. In this study, we investigated the effects of resveratrol, a phytoalexin produced by some spermatophytes, on oxidative stress induced by cigarette smoke in airway epithelial cells. Methods: Rats with or without exposure to cigarette smoke were intraperitoneally injected with resveratrol (5,10,20mg/kg·d). TNF- α levels in BALF were determined by ELISA. Total glutathione, SOD and H₂O₂ levels in rat lungs were detected. Human alveolar epithelial cells (A549) were exposed to cigarette smoke extract (CSE), with or without pretreatment of resveratrol (40 μ M). The activity of ROS was detected and the expression of SIRT1 protein was evaluated with western blotting. Results: Cigarette smoke exposure significantly increased TNF- α expression in BALF and this upregulation was significantly attenuated by resveratrol (p<0.05). Meanwhile, the treatment of resveratrol increased the expression of glutathione and SOD in lung homogenates, which were attenuated by cigarette smoke exposure (p<0.05). The expression of H₂O₂ was decreased by resveratrol (p<0.05). Exposure of A549 cells to CSE resulted in the elevated ROS expression, which was inhibited by resveratrol. Meanwhile, SIRT1 protein levels were activated by the pre-treatment of resveratrol. Conclusions: These results suggest that resveratrol attenuated oxidative stress induced by cigarette smoke. The anti-oxidant effect might act through the expression of SIRT1 proteins.