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Title: Nrf2 is closely related to enhance bleomycin induced airway inflammatory responses caused by diesel exhaust particles in mice

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Body: Diesel exhaust particles (DEP) induced oxidative stress play an important role in proinflammatory reaction on airway. Nrf2 is involved in the transcriptional regulation of many antioxidant genes. In the present study, we investigated the effect of DEP on an experimental model of bleomycin (BLM)-induced airway inflammatory responses in both of Nrf2+/+ and Nrf2–/– mice. BLM was administered IV to Both Nrf2+/+ and Nrf2–/– C57BL/6J mice at a dosage of 80 mg/kg body weight on day zero. Mice were exposed to 1mg/m^3 DEP for 8 hrs/day and 5 days/week. We designed two experimental groups as follows: group 1, BLM alone, clean air; group 2, BLM plus pre-4wks-DEP exposure. Cell populations in BALF were examined at 10 days after BLM injection. We also examined cytokine level in BALF by ELISA. In the DEP exposed group, the percentage changes from BLM alone group in the total number of cells and macrophages remarkably increased in the both Nrf2+/+ and Nrf2–/– mice. There were DEP-laden alveolar macrophages number were significantly greater in Nrf2-/- than in Nrf2+/+ mice. The percentage changes from BLM alone group in the neutrophils increased in the both Nrf2+/+ and Nrf2–/– mice, the increased neutrophils were significantly greater in Nrf2-/- than in Nrf2+/+ mice. The percentage changes from BLM alone group in the TGF-beta level decreased in the Nrf2-/- than in Nrf2+/+ mice. These findings suggest that DEP might be an important risk factor on the BLM induced lung injury, and Nrf2 might be an important genetic factor in the determination of susceptibility to BLM induced lung injury caused by DEP via regulating the macrophages defense mechanisms in mice.