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Title: Deletion of peroxiredoxin 6 potentiates OVA-induced asthma epithelial-mesenchymal transition through EGFR pathway

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Body: Background: Epithelial-mesenchymal transition(EMT) has been proposed as an important mechanism for airway remodeling in asthma. Reactive oxygen species have been demonstrated to induce EMT. We aim to investigate the role and signaling pathway of peroxiredoxin 6, a newly identified peroxidase, in ovalbumin(OVA) induced asthma airway remodeling in mice. Methods and results: Prdx6(-/-) and wild-type(WT) mice were immunized on day 1, 8, 15 with OVA 20ug/200uL intraperitoneally(ip) and challenged on day 25-28 with 0.4% OVA 50uL intranasally. Another group of WT mice were treated ip with 10mg/kg AG1478, inhibitor of EGFR tyrosine kinase, 1hr before each challenging. Twenty-four hours after the last OVA challenge, bronchoalveolar lavage fluid(BALF) and lungs were collected. After OVA exposure, leukocyte influx including eosinophils into BALF, IL-4 and IL-13 protein levels in BALF were significantly greater in Prdx6(-/-) mice compared with WT mice, which showed more severe asthma in Prdx6(-/-) mice. Hydrogen peroxide(H2O2) and malondialdehyde levels, matrix metalloproteinase (MMP)-9 mRNA and activity, E-cadherin, and phospho-EGFR expression were markedly increased in lungs of Prdx6(-/-) mice compared with WT mice, which showed more oxidative stress and mesenchymal production in Prdx6(-/-) mice. AG1478 treatment markedly suppressed OVA induced release of cytokines, production of H2O2, MMP-9 and E-cadherin, and phosphorylation of EGFR in WT mice. Conclusions: Deletion of prdx 6 exaggerates OVA-induced asthma and airway remodelling with increased oxidative stress, inflammatory responses and mesenchymal transition, all of which were partially dependent on EGFR pathway.