

## The Effects Of Perinatal Exposure To Secondhand Smoke On The Pulmonary Immune Response To Allergens

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**Rational:** Prenatal and early postnatal exposure to secondhand tobacco smoke (TS) in mice enhances allergic airway inflammation by affecting the development of the immune system in the lung, exacerbating airway inflammation and hyper-reactivity. Ambient particulate matter (PM) acts as an adjuvant, enhancing the allergic inflammatory responses, however the combined effects of PM and TS on allergic airway inflammation have not been studied.

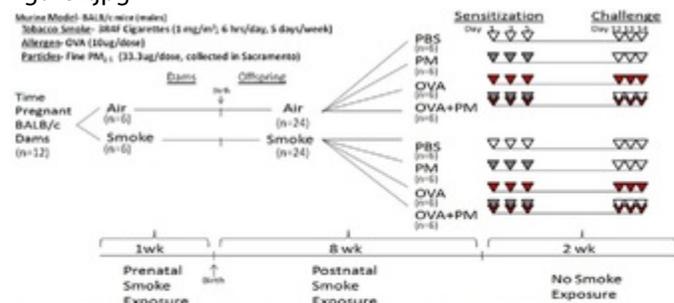
**Objective:** To study how in-utero and postnatal TS exposure in mice shapes the airway immune response to the combined exposure of ovalbumin (OVA) and ambient PM.

**Methods:** Time pregnant BALB/c mice were exposed to filtered air (FA) or 1 mg/m<sup>3</sup> of TS (6 hrs/day, for 5 days). Newborn male offspring from FA exposed mothers were exposed to filtered air for 8 weeks, followed by exposure to PBS (n=6), OVA (n=6), PM (n=6), or OVA+PM (n=6). Newborn male offspring from TS-exposed mothers were further exposed to TS for 8 weeks, followed by exposure to PBS vehicle (n=6), OVA (n=6), PM (n=6), or OVA+PM (n=6). Lung tissue, bronchoalveolar lavage fluid (BALF) and plasma were analyzed for extent of inflammation, cellular infiltrates, cytokine and immunoglobulin E (IgE) levels.

**Results:** In the FA model, OVA+PM significantly increased total cells in BALF compared to OVA alone. Eosinophils recovered in BALF and plasma IgE levels were significantly elevated in FA treatment groups compared to TS groups, indicating smoke suppressed Th2-mediated immune responses in our model. Both IgE and TNF $\alpha$  levels were significantly elevated in OVA and OVA+PM groups over their respective PBS controls in FA exposed mice, whereas OVA and OVA+PM groups were not significantly different from PBS controls in TS exposed mice.

**Conclusion:** Our findings suggest prenatal and postnatal exposure to TS shape the development of the immune system in the lungs at an early age producing an immunosuppressive effect in response to allergic challenge in BALB/c mice.

figure2.jpg



**Figure 1. Experimental design, tobacco smoke, allergen, and particulate matter exposure protocol.** Pregnant BALB/c mice were exposed to filtered air (n=6) or 1 mg/m<sup>3</sup> of tobacco smoke (n=6) (6 hrs/day) 5 days prior to birth. Male offspring mice (n=24) from air-exposed mothers were further exposed to filtered air for 8 weeks whereas male offspring from smoke-exposed mothers (n=24) were further exposed to 8 weeks of smoke (1 mg/m<sup>3</sup>, 6 hrs/day, 5 days/week). After 8 weeks, mice within each air or smoke group were further subdivided into four groups and intranasally administered PBS (vehicle; white triangles), PM (grey triangles), OVA (red triangles), or OVA with PM (overlapping red and grey triangles) during the sensitization period (days 1, 3, and 5). PM is administered at 33  $\mu$ g/dose in 30  $\mu$ l PBS, while OVA is administered at 10  $\mu$ g/dose in 30  $\mu$ l PBS. PBS and PM groups received PBS only during challenge (days 12-14), and both OVA and OVA+PM groups were challenged with OVA.

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