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**Title:** Estrogen protects against airway inflammation via upregulation of SLPI and downregulation of IL-33

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**Body:** Airway epithelium (AE) can modify airway responses through production of anti-inflammatory mediators like secretory leukoprotease inhibitor (SLPI) and pro-inflammatory mediators like IL-33. Estrogen can modulate AE responses and we therefore investigated how estrogen affects severity of airway inflammation and SLPI and IL-33 production in mice. Female balb/c mice were ovariectomized (OVX) or sham-treated and received a 0.1 mg estrogen (E2) pellet at OVX or not (all groups n=8). Four weeks after OVX, mice were sensitized i.p. with OVA and alum on days 1 and 7 and challenged with 1% OVA on days 14-20. On day 21, allergic inflammation (OVA-specific IgE, eosinophils) and production of IL-33 and SLPI were assessed. Ablating estrogen significantly increased airway inflammation as compared to sham-treated mice. Treating OVX mice with E2 significantly reduced the higher airway inflammation induced by OVX as judged from lower eosinophil numbers in lung and lower OVA-specific IgE levels in serum. In the parenchyma of E2-treated OVX mice we found more type II alveolar epithelial cells (AECII) expressing SLPI than in nontreated OVX mice, which correlated with higher SLPI levels in lung. The number of AECII producing IL-33 on the other hand was lower in E2-treated OVX mice as compared to nontreated OVX mice. This study shows that estrogen protects female mice against the development of airway inflammation and this is associated with higher SLPI and lower IL-33 production by AECII. We therefore postulate that estrogen has a protective effect on asthma development through induction of anti-inflammatory SLPI production and inhibition of pro-inflammatory IL-33 production by AECII.