Title of Dataset

Interleukin-11 Receptor Subunit Alpha-1 is Required for Maximal Airway Responsiveness to Methacholine Following Acute Exposure to Ozone_Dataset

Introduction

Interleukin (IL)-11, a pleiotropic, cationic cytokine, contributes to numerous biological processes, including adipogenesis, hematopoiesis, and inflammation. Asthma, a chronic respiratory disease, is notably characterized by reversible airway obstruction, persistent lung inflammation, and airway hyperresponsiveness (AHR). Nasal insufflation of IL-11 causes AHR in wild-type mice while lung inflammation induced by antigen sensitization and challenge, which mimics features of atopic asthma in humans, is attenuated in mice genetically deficient in IL-11 receptor subunit alpha-1 (IL-11Rα1-deficient mice), a transmembrane receptor that is required along with glycoprotein 130 to transduce IL-11 intracellular signaling. Nevertheless, the contribution of IL-11Rα1 to the manifestation of phenotypic features of non-atopic asthma are not presently known. Thus, based on the aforementioned observations, we hypothesized that genetic deficiency of IL-11Rα1 would attenuate lung inflammation and increases in airway responsiveness following acute inhalation exposure to ozone, a criteria pollutant and non-atopic asthma stimulus.

Methods Collection

- Through this laboratory-based study, we investigated whether mice genetically deficient in IL-11Rα1 (IL-11Rα1-deficient mice) exhibited decreased airway responsiveness to methacholine and lung inflammation induced by acute inhalation exposure to ozone [2 parts/million (ppm)] for three hours as compared to wild-type (C57BL/6J) mice.
- Eight- to twenty-week-old wild-type and IL-11Rα1-deficient mice were exposed for three hours to either filtered room air or ozone (2 ppm) for three hours. Four- or twenty-four-hours following cessation of exposure, one cohort of mice was euthanized so that blood could be collected, a bronchoalveolar lavage (BAL) performed, and lungs harvested. A second cohort of mice was anesthetized twenty-four-hours following cessation of exposure and pressure-volume (PV) curves generated and airway responsiveness to methacholine assessed.
- Endpoint measurements include
    - BAL adiponectin, ciliated epithelial cells, hyaluronan, interleukin (IL)-6, IL-11, keratinocyte chemoattractant (KC), macrophage inflammatory protein (MIP)-3α, macrophages, neutrophils, osteopontin, and soluble tumor necrosis factor receptor (sTNFR) 1 and 2
    - Serum IL-11 and sTNFR1 and 2
    - Expression of lung tissue interleukin 11 receptor, alpha chain 1 (*Il11ra1*) mRNA
    - PV curve parameters: A, an estimate of inspiratory capacity; K, curvature of the upper portion of the expiratory limb of the PV curve; C_{stat}, quasi-static respiratory system compliance; Area, respiratory system hysteresis
    - Airway responsiveness to methacholine indices: R_{aw}, airway resistance; G, coefficient of lung tissue damping; H, coefficient of lung tissue elastance

Citations – Publication Based on the Dataset

Johnston RA, Atkins CL, Siddiqui SR, Jackson WT, Mitchell NC, Spencer CY, Pilkington IV, AW, Kashon ML, and Haque IU. Interleukin-11 receptor subunit alpha-1 is required for maximal airway responsiveness to methacholine following acute exposure to ozone. *Am J Physiol Regul Integr Comp Physiol*. [In clearance].

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