Lung Biology Research & Trainee Day
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Category: Predoc
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Title: INVESTIGATING THE ROLE OF CD4+ T CELLS IN FLAVORINGS-INDUCED BRONCHIOLITIS OBLITERANS
Abstract: Emma House1,2, Soyoung Kim2, Angela M. Groves2, Eric Hernady3, Carl J. Johnston2, Matthew D. McGraw2,3 1Department of Pathology, ¬¬2¬Department of Pediatrics, Division of Pediatric Pulmonology, 3Department of Environmental Medicine, University of Rochester Medical Center, Rochester, NY 14642 Bronchiolitis obliterans (BO) is a fibrotic lung disease characterized by submucosal collagen deposition and concentric narrowing of the small airways. Historically associated with organ transplant, BO has become more recently associated with inhalation exposure to certain volatile chemicals such as the flavoring chemical diacetyl (DA; 2,3-butanedione). Recently, we have shown DA-induced BO develops via an airway epithelial insult, followed by potent neutrophilic inflammation, and subsequent fibrotic airway remodeling. We hypothesize that inflammation resolution in DA-induced BO pathogenesis is primarily modulated by CD4+CD25+FOXP3+ regulatory T cells (Tregs) after DA inhalation injury. To address this, our lab has developed an in vivo pure DA vapor exposure system for modeling BO pathogenesis in Sprague-Dawley rats. In this model, animals undergo whole-body exposures to 200 ppm DA vapor for 5 days, 6 hours/day. Pulse oximetry and weights were measured over the course of 19 days. Animals were sacrificed at various time points during the recovery period after DA exposure including immediately following exposure (Day 5), early inflammation/repair (Day 12), and fibrotic induction (Day 19). Single-cell suspensions from rat whole lung homogenate were prepared for flow cytometry at these time points and stained for CD3, CD8, CD4, CD25, and FoxP3. In DA-exposed rats weight loss and persistent hypoxemia developed during the inflammation/repair phase (Day 12). By Day 19, histology revealed significant airway remodeling consistent with BO pathology. Bronchoalveolar lavage fluid (BALF) from DA-exposed rats showed increased total cell number with significant neutrophilia and elevated albumin at Day12 and 19, supportive of persistent inflammation and impaired barrier function. Proportions of lung CD3+, CD4+ and CD8+ T cells in exposed animals by flow cytometry did not differ significantly from controls with respect to time. However, at Days 12 and 19, the proportion of lung CD4+CD25+ cells increased by 85.4% (p=.0008) and 43.3% (p=.049) from air controls, respectively. Interestingly, this percent increase was inversely correlated with peak weight loss in DA exposed animals (R=0.62; p=0.03) but did not correlate with peak hypoxia measurements by pulse oximetry. This correlation suggests that increased proportions of CD4+CD25+ lung T cells after DA exposure may contribute to injury resolution. Current and future studies are underway validating the expression of FoxP3+ in the CD4+CD25+ T cell population. Our future studies include modulation of the CD4+CD25+FOXP3+ to assess its contribution to lung injury/resolution and/or fibrotic induction in BO pathogenesis.