Lung Biology Research & Trainee Day
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Category: Predoc
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Title: Perfluorooctane sulfonic acid (PFOS) disrupts protective tight junction proteins in lung epithelial cells
Abstract: Recent epidemiological evidence suggests that perfluorooctane sulfonic acid (PFOS) may be associated with the development of atopic asthma. Rodent studies indicate that PFOS exposure results in asthma related outcomes such as increased type 2 inflammation and eosinophilic infiltration, but no studies have examined the impact of PFOS on the lung epithelial barrier. The respiratory epithelium plays a crucial role in modulating the body's response to environmental allergens and is maintained by protective tight junction proteins. Disruption of tight junction proteins may facilitate allergen translocation and type 2 immune responses. In addition, deficiencies in the barrier forming capacity of bronchial epithelial cells from asthmatic patients has been observed and is correlated with disease severity, further supporting a role of the lung epithelial barrier in asthma. Studies have demonstrated that PFOS exposure results in perturbations to the blood-brain and intestinal barriers in rodent models, suggesting that tight junction proteins may be sensitive to PFOS exposure. However, the effects of PFOS on pulmonary tight junctions is not well-understood. Thus, we hypothesized that PFOS exposure would compromise lung epithelial barrier integrity by downregulating tight junction proteins. To address this question, we exposed human bronchial epithelial cells (16HBE14o-) to PFOS (5-25 μM). We observed a dose and time dependent decrease in transepithelial electrical resistance (TEER) and increased permeability to 4 kDa FITC-dextran at 15 μM PFOS following 72 hours exposure. Cell viability was unchanged as assessed by lactate dehydrogenase (LDH) release in the conditioned media. Alterations in barrier function were accompanied by a reduction in the tight junction proteins, occludin and zonula occludens 1 (ZO-1). Furthermore, disrupted tight junction protein localization was observed by immunofluorescence. Our results demonstrate that lung barrier proteins may be targets of PFOS toxicity, possibly by disrupting the production and distribution of protective tight junction proteins to cell-cell contacts. Additional studies will be needed to determine the mechanisms underlying PFOS induced barrier dysfunction, whether these effects are reproduced in vivo, and if they modulate the risk of developing chronic lung diseases such as asthma.