

## Characterization Of Airway Ormdl3 Expression In Human Asthma And In Relation To The Asthma Gwas Variant Rs7216389

M. E. Lachowicz-Scroggins<sup>1</sup>, E. D. Gordon<sup>1</sup>, C. Urbanek<sup>2</sup>, H. J. MacLeod<sup>1</sup>, S. Yuan<sup>1</sup>, P. G. Woodruff<sup>1</sup>, S. Ramachandran<sup>3</sup>, J. W. Thorner<sup>3</sup>, M. A. Seibold<sup>2</sup>, J. V. Fahy<sup>1, 4</sup>,

<sup>1</sup>University of California, San Francisco, San Francisco, CA, <sup>2</sup>National Jewish Health, Denver, CO, <sup>3</sup>University of California Berkeley, Berkeley, CA, <sup>4</sup>

**Corresponding author's email:** [marrah.lachowicz-scroggins@ucsf.edu](mailto:marrah.lachowicz-scroggins@ucsf.edu)

**RATIONALE:** Genetic variation at the 17q21 locus has been associated with the development of asthma as well as human rhinovirus induced wheezing illnesses in children. An asthma risk SNP in this locus, rs7216389, has been associated with disease and with ORMDL3 gene expression in rhinovirus stimulated peripheral blood mononuclear cells as well as Epstein-Barr virus transformed lymphoblastoid cell lines from children with asthma. The expression of ORLDM3 in airway epithelial cells, which are targets of virus infection in asthma exacerbations, is unknown.

**METHODS:** To determine if ORMDL3 is differentially expressed in airway epithelial cells in asthma, we used qPCR to quantify ORMDL3 expression in airway epithelial brushings collected using standardized methods from mild-moderate stable asthmatics (N=93) and healthy subjects (N=40). We also analyzed ORMDL3 gene expression in airway epithelial cells harvested from 54 human cadaver donors and cultured at air liquid interface for 21 days. These donor cells were genotyped for the rs7216389 variant. To determine if IL-13 regulates ORMDL3 gene expression in airway epithelial cells, we exposed the cultured cells to IL-13 (and to TNF-alpha as a control) for 48 hours.

**RESULTS:** ORMDL3 gene expression is not altered in airway epithelial cells from asthmatic subjects compared to healthy controls. ORMDL3 gene expression is not altered in human airway epithelium in culture following 48 hours of stimulation with IL-13 or TNF-alpha. Genotype at rs7216389 is not associated with altered ORMDL3 gene expression in human airway epithelial cells in culture.

**CONCLUSIONS:** ORMDL3 gene expression is not altered in the airway epithelium in asthma, and its expression in the airway epithelium is not regulated by IL-13 or affected by the rs7216389 SNP.

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