European Respiratory Society
Annual Congress 2012

Abstract Number: 3820

Publication Number: P3724

Abstract Group: 3.2. Airway Cell Biology and Immunopathology

Keyword 1: Asthma - mechanism **Keyword 2:** Molecular pathology **Keyword 3:** Biomarkers

Title: Effect of anti-IgE therapy on microRNAs in the lungs of mice with allergen-driven airway remodeling

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Body: Rationale: Current therapies have had limited effect on structural airway changes in patients with asthma. We recently found that anti-IgE therapy significantly decreased established airway hyperresponsiveness and subepithelial fibrosis in a mouse asthma model (Henderson et al., AJRCCM 183: A4066, 2011). MicroRNA (miRNA or miR)s, small non-coding RNAs, are key regulators of gene expression that may serve as novel biomarkers and therapeutic targets in disease states. Study Aim: Determine the effect of anti-IgE therapy on miRNA expression in a mouse asthma model with airway remodeling. Methods: Mice periodically given OVA (days 14-163) were treated with 100 µg monoclonal rat IgG1 anti-IgE (R35-92, Pharmingen) (OVA/anti-IgE group), rat IgG1 isotype control antibody (OVA/IgG1 group), or saline (OVA/Saline group) days 73-75, and then once weekly until day 163 when lung miRNA was isolated. MiRNA transcriptional profiling was carried out using Affymetrix GeneChip miR 2.0 arrays with data analysis by Bioconductor limma package. MiRNAs whose expression was changed >1.5-fold ($p<0.05$) were considered differentially expressed. Results: 21 miRNAs were significantly changed in the OVA/Saline group vs saline-treated controls including upregulation of profibrotic miR-21 and miR-155. MiRs 467e, 511, and 744* were downregulated and the antifibrotic miR-16* upregulated in the OVA/anti-IgE group vs the OVA/IgG1 group. Conclusions: The ameliorating effect of anti-IgE treatment on established airway remodeling in this asthma model is likely mediated by its differential effects on gene expression in the lung. Our data direct attention to key miRNAs that may serve as biomarkers for this remodeling process.