749 Microarray Analysis and Transcriptional Phenotypes in Pediatric Patients with Eosinophilic Esophagitis

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RATIONALE: Currently patients with eosinophilic esophagitis (EoE) are treated empirically to resolve esophageal eosinophilia. Our objective was to compare gene expression profiles in EoE patients at baseline and after treatment to characterize transcriptional phenotypes and identify molecular pathways involved in the disease.

METHODS: We collected blood samples at baseline and after 6-8 weeks of treatment from EoE patients treated with cow's milk elimination diet or swallowed fluticasone. We extracted RNA and analyzed whole genome expression using Illumina Beadstation, GeneSpring software and a modular transcriptional analysis tool.

RESULTS: We compared 20 age-matched healthy controls with 40 EoE patients at baseline. Thirty patients were also studied after treatment. Among EoE patients, 159 genes were differentially expressed with a minimum of two-fold expression change compared with healthy controls. By comparison with controls, EoE patients had over expression of genes involved in cell cycle and inflammation and under expression of cytotoxic/NK cell and platelets/red blood cell related genes. In EoE treated patients, a high proportion of cytotoxic/NK cell genes were over expressed. Although the signature was faint, hierarchical clustering revealed two groups of EoE patients with distinct transcriptional profiles.

CONCLUSIONS: EoE patients showed differences in gene expression patterns compared with healthy controls that are modified following treatment suggesting that they may be functionally significant. Further studies are needed to understand the significance of two distinct groups of EoE patients.

750 Differences in CD4IL-17+ in Children and Adults with Eosinophilic Esophagitis

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RATIONALE: Eosinophilic esophagitis (EoE) is an atopic disease defined by eosinophilic infiltration greater than 15 eosinophils per high power field in the esophagus. The clinical manifestations of the disease are known to vary with age, however it is not known if local inflammation changes with age. CD4Th17 cells produce the pro-inflammatory cytokine, IL-17, which has been implicated in the pathogenesis of a variety of atopic and autoimmune diseases. Variations in Th17 in patients with EoE have not been previously reported.

METHODS: Peripheral blood mononuclear cells (PBMCs) from 10 children with active EoE, 4 children with controlled EoE, 10 healthy pediatric controls, 7 adults with active EoE and 4 healthy adult controls were collected. CD4IL-17+ cells were quantified at baseline. The PBMCs were incubated with or without anti-CD3/CD28 beads and CD4IL-17+ levels were assessed after 7 days via flow cytometry.

RESULTS: Children with EoE had lower levels of CD4IL-17+ compared to healthy controls (median $\pm$ standard error (SE): 0.061 $\pm$ 0.168 vs 1.49 $\pm$ 0.443 respectively $p<0.02$). Children with active EoE had lower levels of CD4IL-17+ compared to adults with active disease (0.052 $\pm$ 0.012 vs 0.4 $\pm$ 0.067, $p<0.02$). PBMCs that were cultured with anti-CD3/CD28 beads displayed an increase in CD4 IL-17+ compared to untreated cultures, but only in adult controls (14.10 $\pm$ 11.53 vs 0.0790 $\pm$ 0.1023, $p<0.03$).

CONCLUSIONS: This data suggests that Th17 cells are involved in the pathogenesis of EoE. Expression of IL-17 varies between children and adults with active disease, which may contribute to the age-related variation seen in EoE.

751 Aeroallergen and Food Sensitization Patterns in Adults with Eosinophilic Esophagitis

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RATIONALE: Eosinophilic esophagitis (EoE) is diagnosed in patients with symptoms of esophageal dysfunction associated with predominant eosinophilic inflammation. Traditionally, attention has been directed toward IgE-mediated immediate-type food allergies, but environmental allergies may also play an important role. Th2 inflammation, implicated in EoE immunopathogenesis, is shared by many atopic conditions. The objective of this project was to contribute to the limited literature on the prevalence of environmental sensitization in adults with EoE.

METHODS: We conducted a retrospective chart review from multiple allergy clinics in five Canadian cities for patients diagnosed with EoE. Demographics, skin prick tests (SPT), and treatment data were collected and reviewed.

RESULTS: A total of 182 patients (male:female ratio of 2:1, p-value<0.01; 35$\pm$16 years) were diagnosed with EoE. Food sensitization was identified on SPTs in 47% of patients (peanuts=22%, tree nuts=27%, milk=12%, soy=12%, seafood=11%, egg=9%, vegetables=8%, wheat=5%, meat=6%, seeds=5%, fruits=4%, oats=2%). Environmental sensitization was detected in 85% of patients (tree=66%, grass=62%, ragweed=62%, dust mites=59%, cat=56%, mould=32%, dog=21%, cockroach=16%). Most patients had both environmental and food sensitization (43%) or environmental sensitization only (42%). Few had food sensitization only (8%) and some were negative to both food and environmental allergens (18%). Most patients were on PPIs (77%) or inhaled/swallowed corticosteroids (73%).

CONCLUSIONS: Environmental allergies had a significantly higher prevalence than food sensitization. Comorbid atopic conditions like environmental allergies should be optimized, as there are trends in early clinical and basic research which suggest environmental allergies may contribute to EoE. The mechanism of EoE requires further study.