Molecular Diagnosis of Eosinophilic Esophagitis from a Single Esophageal Biopsy

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Introduction: Eosinophilic esophagitis (EoE) is a chronic food-antigen induced allergic inflammatory disease characterized by extensive esophageal eosinophilia. EoE is diagnosed by histological analysis of esophageal biopsies demonstrating at least 15 eosinophils/high-powered-field (EOS/HPF). As a histologically "patchy" disease, characterized by uneven distribution of eosinophils along the esophagus, at least 5 biopsies need to be evaluated for adequate sensitivity. A molecular EoE diagnostic panel (EDP) comprised of 96-genes assessed by Taqman-based PCR was developed as a next-generation diagnostic test with strong merit on esophageal biopsies.

Hypothesis: In this study, we tested the hypothesis that EDP analysis of a single distal esophagus biopsy has diagnostic merit even if inflammation may be present in a different portion of the esophagus.

Methods: We first divided a cohort of 697 subjects into 4 bins with distinct distal (D) and proximal (P) eosinophil counts (D+P+, D+P-, D-P+, D-P-; +/- was defined by ≥/<15 eosinophils/HPF, respectively. For datamining, we used Excel and Prism to compare histology and EDP diagnosis and employ Spearman R for correlation studies.

Results: We report that single distal biopsy derived EDP scores, defined by a reported 77-gene-expression-based algorithm, robustly correlated with distal and proximal eosinophil levels ($R=-0.7461$, $P<0.0001$ and $R=-0.7250$, $P<0.0001$, respectively). With each patchiness bin analyzed as a single unit, their average EDP scores correlated robustly with the peak eosinophil levels for the corresponding bin (Spearman $R = -0.97$), EDP analysis of a histologically negative distal biopsy predicted the presence of a remote proximal esophagitis with high accuracy (85% sensitivity for identifying D-P+ with the EDP). Focusing on the cases with discrepant histological and EDP results, we found that the histological negative individuals (e.g. <15 eosinophils/HPF) had higher rates of EoE relapse when the EDP was positive compared with negative in a 2-year follow-up (Odds Ratio=11, $P=0.003$). To assess the ability of individual genes to overcome histological patchiness, we identified a subset of 16 genes (DxP16) that more precisely reflected the patchy tissue eosinophilia between the 4 disease bins.

Conclusion: In conclusion, EDP analysis of single distal esophageal biopsies predicts remote inflammation in patients with heterogeneous spatial esophageal eosinophilia. As such, molecular transcript analysis of single biopsies has strong diagnostic and predictive medicine capacity for EoE.

Acknowledgements
This study was supported by NIH grant T35DK060444, R37A1045898, U19AI070235 and U54AI117804.