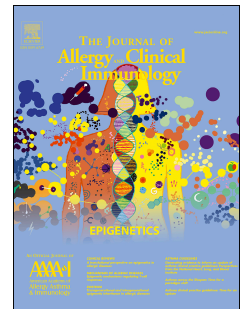


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Molecular, Endoscopic, Histologic and Circulating Biomarker-Based Diagnosis of Eosinophilic Gastritis: Multi-Site Study

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PII: S0091-6749(19)31519-2

DOI: <https://doi.org/10.1016/j.jaci.2019.11.007>

Reference: YMAI 14260

To appear in: *Journal of Allergy and Clinical Immunology*

Received Date: 14 August 2019

Revised Date: 3 November 2019

Accepted Date: 6 November 2019

Please cite this article as: Shoda T, Wen T, Caldwell JM, Collins MH, Besse JA, Osswald GA, Abonia JP, Arva NC, Atkins D, Capocelli KE, Dellon ES, Falk GW, Gonsalves N, Gupta SK, Hirano I, Mikkada VA, Putnam PE, Sheridan RM, Spergel AK R, Spergel JM, Wechsler JB, Yang G-Y, Aceves SS, Furuta GT, Rothenberg ME, on behalf of the Consortium of Eosinophilic Gastrointestinal Disease Researchers (CEGIR), Molecular, Endoscopic, Histologic and Circulating Biomarker-Based Diagnosis of Eosinophilic Gastritis: Multi-Site Study, *Journal of Allergy and Clinical Immunology* (2019), doi: <https://doi.org/10.1016/j.jaci.2019.11.007>.

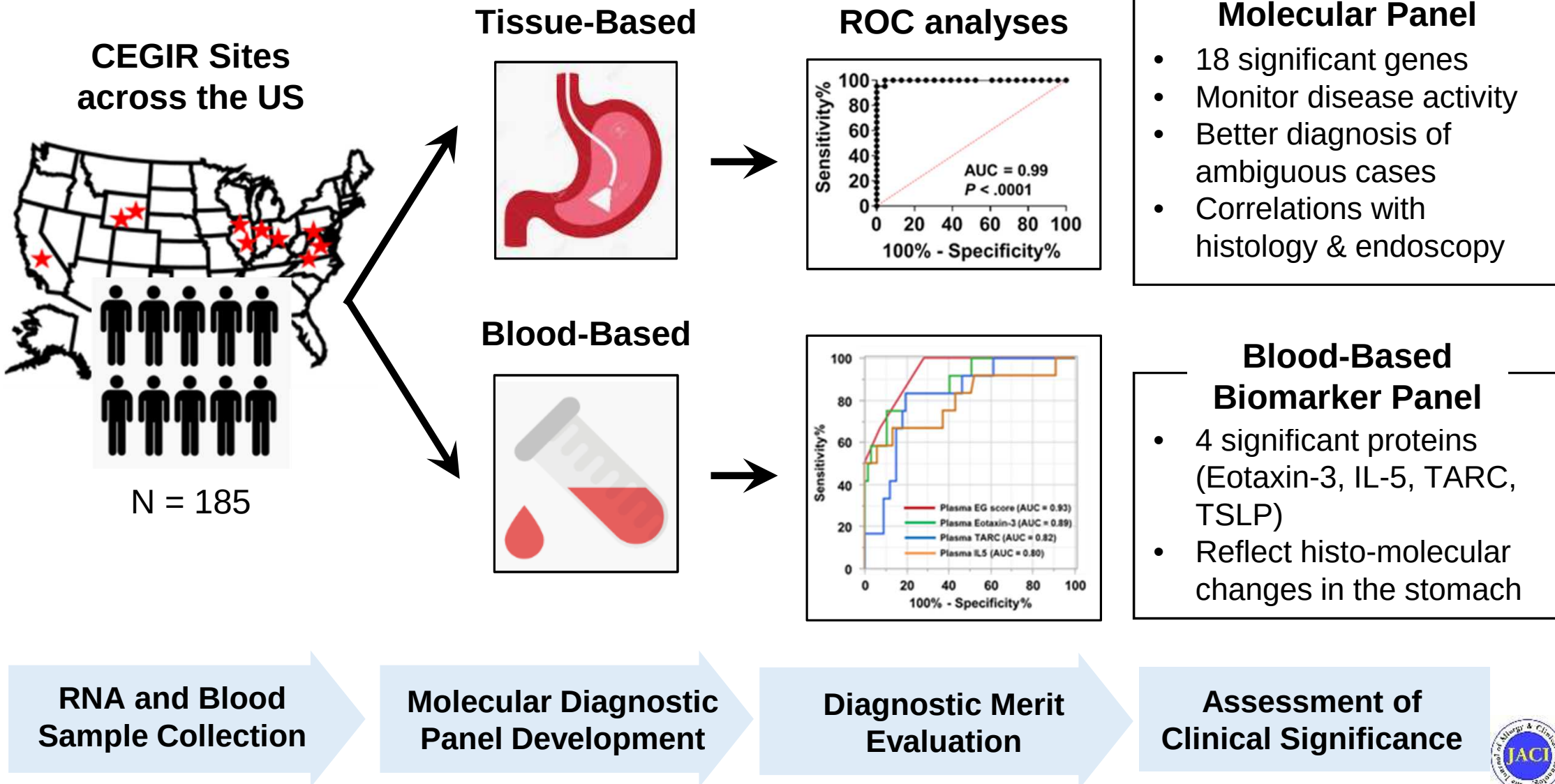
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Original article**Molecular, Endoscopic, Histologic and Circulating Biomarker-Based Diagnosis of Eosinophilic Gastritis: Multi-Site Study**

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Acknowledgments

The authors would like to thank all patients who participated in the study. The authors are also grateful to their colleagues and clinical support staff for procuring biopsies, blood samples, and clinical data.

Grant Support

This study was supported by CEGIR (U54 AI117804), which is part of the Rare Diseases Clinical Research Network (RDCRN), an initiative of the Office of Rare Diseases Research (ORDR), National Center for Advancing Translational Sciences (NCATS), and is co-funded by National Institute of Allergy and Infectious Diseases (NIAID), National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), and NCATS. CEGIR is also supported by patient advocacy groups including the American Partnership for Eosinophilic Disorders (APFED), Campaign Urging Research for Eosinophilic Disease (CURED), and Eosinophilic Family Coalition (EFC).

Conflicts of Interest

M.E.R. is a consultant for Pulm One, Spoon Guru, Celgene, Shire, Astra Zeneca, GlaxoSmithKline, Allakos, Adare, Regeneron, and Novartis and has an equity interest in Pulm One, and ClostaBio, and Spoon Guru and royalties from reslizumab (Teva Pharmaceuticals). M.E.R. is an inventor of patents, owned by Cincinnati Children's. G.W.F. has received research support from Celgene/Receptos, Regeneron, Takeda/Shire, and Adare and is a consultant for Adare and Takeda/Shire. M.H.C. is a consultant for Shire, Regeneron, Receptos, and Esocap and has received research funding from Shire, Regeneron, and Receptos. S.K.G. is a consultant for Abbott, Adare, Allakos, QOL, and Receptos/Celgene and receives research support from Shire. V.A.M. is a consultant for Shire and has received research funding from Shire. N.G. is a consultant for Allakos. E.S.D. is a consultant for Adare, Alivio, Allakos, AstraZeneca, Banner, Biorasi, Calypso, Enumeral, EsoCap, Gossamer Bio, GlaxoSmithKline, Receptos/Celgene, Regeneron, Salix, and Shire; has received research funding from Adare, Allakos, GlaxoSmithKline, Meritage, Miraca, Nutricia, Receptos/Celgene, Regeneron, and Shire; and has received educational grants from Allakos, Banner, and Holoclara. S.S.A. is a consultant for Regeneron, AImmune Therapeutics, and Gossamer; is an inventor of oral viscous budesonide, patented by UCSD and licensed by Shire/Takeda; and has research funding from the Ferring Research Institute. J.M.S. is a consultant for Regeneron and DBV Technology, and his research is supported by the NIH, Everbody Eats (EATS) foundation, AImmune Therapeutics, Food Allergy Research & Education (FARE), and DBV Technology. I.H. is a consultant for Regeneron, Receptos, Shire, Allakos, and Adare and has received research funding from Regeneron, Receptos, Shire, and Adare. G.T.F. is a consultant for Shire and a co-founder of EnteroTrack. J.B.W. is a consultant for Allakos. All other authors declare that they have no competing interests.

Writing assistance

Shawna Hottinger provided editorial assistance as a medical writer funded by Cincinnati Children's Hospital Medical Center.

Author Contributions

T.S., T.W., and M.E.R. conceived the study and design. T.S. performed the laboratory work. J.M.C., J.A.B., G.A.O., provided technical support. T.S. contributed to the statistical analysis. TW provided analytical and bioinformatic support. M.H.C., N.C.A., K.E.C., R.M.S., and G.Y. performed the pathologic assessments. J.P.A., D.A., E.S.D., G.W.F., N.G., S.K.G., I.H., V.A.M., P.E.P., R.S.A., J.M.S., J.B.W., S.S.A., and G.T.F. provided administrative, clinical, or material support through CEGIR. T.S. and M.E.R. drafted the paper. M.E.R. obtained funding and led the study. All of the authors discussed the results and commented on the manuscript.

Clinical Implications:

We have developed tissue- and blood-based platforms for diagnosing and monitoring eosinophilic gastritis and uncovered likely molecular pathogenesis that accounts for the distinct endoscopic and histological features of the disease.

Capsule summary:

We have developed molecular diagnostic platforms for EG, validated their utility for disease diagnosis and monitoring, and assessed their clinical significance by concurrent analysis of histological and endoscopic findings, providing insight into disease pathogenesis.

Abbreviations used

APFED, American Partnership for Eosinophilic Disorders; AUC, area under the curve; CCED, Cincinnati Center for Eosinophilic Disorders; CCHMC, Cincinnati Children's Hospital Medical Center; CEGIR, Consortium of Eosinophilic Gastrointestinal Disease Researchers; CURED, Campaign Urging Research for Eosinophilic Disease; DMCC, Data Management and Coordinating Center; EDP, EoE diagnostic panel; EFC, Eosinophilic Family Coalition; EG, eosinophilic gastritis; EGDP, EG Diagnostic Panel; EGID, eosinophilic gastrointestinal disorders; EMT, epithelial-mesenchymal transition; EoE, eosinophilic esophagitis; DEG, differentially expressed genes; FDR, false-discovery rate; GO, gene ontology; GAPDH, glyceraldehyde-3-phosphate dehydrogenase; GI, gastrointestinal; GOI, gene of interest; HPF, high-power field; IQR, interquartile range; NPV, negative predictive value; OMEGA, Outcomes Measures in Eosinophilic Gastrointestinal disorders Across the ages; ORDR, Office of Rare Diseases Research; PCA, principal component analysis; PPI, proton pump inhibitor; PPV, positive predictive value; RDCRN, Rare Diseases Clinical Research Network; ROC, receiver operating characteristic; RPKM, reads per kilobase of exon per million reads mapped; TARC/CCL17, thymus and activation-regulated chemokine/chemokine ligand 17; TSLP, thymic stromal lymphopoietin.

ABSTRACT

Background: Eosinophilic gastritis (EG) is a clinicopathologic disorder with marked gastric eosinophilia and clinical symptoms. There is an unmet need in EG for more precise diagnostic tools.

Objective: We aimed to develop tissue- and blood-based diagnostic platforms for EG.

Methods: Patients with EG and non-EG controls were enrolled across 9 Consortium of Eosinophilic Gastrointestinal Disease Researchers (CEGIR)-associated sites. An EG Diagnostic Panel (EGDP; gastric transcript subset) and EG blood biomarker panel (protein multiplex array) were analyzed. The EGDP₁₈ scores were derived from the expression of 18 highly dysregulated genes and Blood EG scores from dysregulated cytokines/chemokine levels.

Results: Gastric biopsies and blood samples from 185 subjects (EG 74, non-EG 111) were analyzed. The EGDP a) identified patients with active EG ($P < .0001$, AUC ≥ 0.95); b) effectively monitored disease activity in longitudinal samples ($P = .0078$); c) highly correlated in same-patient samples (antrum vs. body, $r = 0.85$, $P < .0001$); and d) inversely correlated with gastric peak eosinophil levels ($r = -0.83$, $P < .0001$), periglandular circumferential collars ($r = -0.73$, $P < .0001$), and endoscopic nodularity ($r = -0.45$, $P < .0001$). For blood-based platforms, eotaxin-3, TARC, IL-5, and TSLP levels were significantly increased. Blood EG scores a) distinguished patients with EG from non-EG controls ($P < .0001$, AUC ≥ 0.91); b) correlated with gastric eosinophil levels (plasma $r = 0.72$, $P = .0002$; serum $r = 0.54$, $P = .0015$); and c) inversely correlated with EGDP₁₈ scores (plasma $r = -0.64$, $P = .0015$; serum $r = -0.46$, $P = .0084$). Plasma eotaxin-3 strongly associated with gastric *CCL26* expression ($r = 0.81$, $P < .0001$).

Conclusion: We developed tissue- and blood-based platforms for assessment of EG and uncovered robust associations between specific gastric molecular profiles and histologic and endoscopic features, providing insight and tools for this emerging rare disease.

Keywords: biomarker, diagnostic panel, eosinophil, eosinophilic gastritis, transcriptome

INTRODUCTION

Eosinophilic gastritis (EG) is one of the eosinophilic gastrointestinal disorders (EGIDs) characterized by marked eosinophil accumulation into the gastrointestinal tract^{1, 2} with an estimated prevalence of about 6.3 patients per 100,000 individuals, which is likely rising.^{3, 4} Although studies of eosinophilic esophagitis (EoE) have elucidated specific molecular, cellular, and immune mechanisms involved in its pathogenesis,⁵ EG is more rare than EoE and thus less well understood, with few publications even addressing diagnostic criteria, genetics, biomarkers, or disease pathogenesis. Unlike in the esophagus, eosinophils normally reside in gastric mucosa during homeostasis,^{6, 7} adding complexity to disease diagnosis and monitoring.

Substantial progress has been made using whole-genome transcript expression profiling (transcriptome) of tissue biopsies from patients with EGIDs, particularly EoE.⁸⁻¹⁵ We previously developed a molecular EoE diagnostic panel (EDP), a set of 96 informative transcripts that can distinguish, monitor, and endotype EoE;^{16, 17} however, such molecular diagnostic profiles are lacking for the other EGIDs. To date, EG studies have identified a prominent and conserved gastric transcriptome that is largely distinct from the EoE transcriptome.^{10, 13} In this context, we hypothesized that a tissue-based diagnostic platform based on the EG transcriptome would provide more clarity to EG diagnosis than would isolated eosinophil counts, would correlate with gastric endoscopic and pathologic parameters, and would align with specific clinical findings.

EGID diagnosis and management requires procuring tissue biopsies during endoscopy, an invasive procedure that adds costs and risk. Two unmet needs are to more precisely and

objectively diagnose EG and to develop monitoring tools for disease management.^{18, 19}
Circulating biomarkers have the potential to facilitate non-invasive disease diagnosis and
monitoring and represent a pressing need in the field. Previous studies suggest that EG has
potential systemic markers, for example concurrent peripheral blood eosinophilia.^{10, 20, 21}
However, the peripheral expression of EG-related inflammatory markers and their potential to
function as surrogate disease markers in EG has not been examined.

Herein, we aimed to develop tissue and blood-based diagnostic platforms for EG; validate their
utility for diagnosis, monitoring, and management; assess their clinical significance by
concurrent analysis of histologic and endoscopic findings; and provide insight into disease
pathogenesis. To approach this aim, we examined patients with EG across multiple sites
associated with the Consortium of Eosinophilic Gastrointestinal Disease Researchers (CEGIR)²²
and an independent replication cohort from a single center.

METHODS

Study design and participants

This study was conducted within the context of CEGIR,²² a national collaborative network of 16 academic centers caring for adults and children with EGIDs. The CEGIR clinical study, Outcomes Measures in Eosinophilic Gastrointestinal disorders Across the ages (OMEGA), is a longitudinal cohort study aimed at understanding the natural history of EoE, EG, and eosinophilic colitis during routine clinical care. Demographic, clinical, endoscopic, and histologic data, as well as gastrointestinal and blood samples, were prospectively collected starting from 2015; all samples from any CEGIR site that contributed patients with EG were used (n = 9 sample-providing institutions). The clinical features of subjects were determined during a standard-of-care evaluation using standardized intake forms (see Supplementary Materials for details). All subjects' clinical data were stored at the Data Management and Coordinating Center (DMCC) at the University of South Florida in Tampa, FL. Data were systematically extracted from the databases. Pediatric subjects were defined as having an age of less than 18 years. Atopy was defined on the basis of self-report of allergic rhinitis, dermatitis, asthma, or food allergy. For the validation cohort of the tissue-based platform and the plasma cohort of the blood-based platform, children and adults with EG presenting for standard care between 2007–2016 were enrolled in an independent cohort at Cincinnati Children's Hospital Medical Center (CCHMC) using the same disease definitions. This study was approved by the institutional review boards of the participating institutions via a central institutional review board at CCHMC.

Patients were defined as having EG if they had ≥ 30 eosinophils/high-power field (HPF) in ≥ 5 HPFs.²³ There were no other known causes of gastric mucosal eosinophilia as defined by standard of care, such as negative testing for other potential causes including stool culture for pathogenic bacteria or parasites, viral antibody titers and/or PCR, celiac and inflammatory bowel disease serology, and staining for *H. pylori* infection. Active EG was defined as gastric biopsies that showed ≥ 30 eosinophils/HPF in ≥ 5 HPFs, intermediate EG was defined as gastric biopsies that showed ≥ 30 eosinophils in 1-4 of 5 HPFs, and inactive EG was defined as < 30 eosinophils/HPF in all HPFs in patients with a previous history of EG. Patients with EG were allowed to be included if they had gastrointestinal eosinophilia outside of the stomach.

Non-EG control subjects, from the Cincinnati Center for Eosinophilic Disorders (CCED) EGID database between 2015–2018, included children and adults who had undergone endoscopy, had no history of EG, had no pathologic evidence of EG surveyed during the index endoscopy, were not taking systemic glucocorticoid treatments in the period immediately prior to the index endoscopy, and had gastric biopsies and/or blood samples collected for research purposes during the index endoscopy. For the tissue-based platform and blood-based platform, control subjects included those with atopic comorbidities, chronic gastritis, and concurrent active EoE since these controls, with different T_H2 baseline levels, would aid in identifying transcriptional changes that are specific to EG. Controls were selected with an effort of closely matching the gender and age. Gastric biopsies in the discovery and validation cohorts did not overlap.

RNA sequencing analysis

Fresh biopsy specimens collected from patients with EG and non-EG controls were stored in RNAlater until they were subjected to RNA isolation using the miRNeasy kit (Qiagen, Valencia, Calif) per the manufacturer's instructions. Samples for RNA sequencing were selected from the total cohort on the basis of RNA quality and quantity. RNA sequencing acquired 20 million mappable, 75–base-pair reads from paired-end libraries and was performed at the DNA Sequencing and Genotyping Core Facility at CCHMC. Data were aligned to the GRCh37 build of the human genome using the Ensembl annotations as a guide for TopHat. Expression analysis was performed using DESeq2 in CLC Genomics Workbench software (CLC bio, Waltham, MA, USA). Reads per kilobase of exon per million reads mapped (RPKM) were assessed for statistical significance using a Welch *t* test with Benjamini–Hochberg false-discovery rate (FDR) and a threshold of $P < .05$ and a 2-fold–change cut-off filter. Gene ontology enrichment analysis was performed with the ToppGene suite (<https://toppgene.cchmc.org/>).

Tissue-based diagnostic platform

RNA from fresh gastric biopsies (from antrum and/or body) was isolated from patients with EG and non-EG controls as described above. RNA was reverse transcribed using the iScript cDNA Synthesis Kit (170-8891; Bio-Rad Laboratories, Hercules, CA) according to the manufacturer's protocol. The transcriptomic signature of gastric biopsy samples was obtained using an EG diagnostic panel (EGDP) comprising a set of 48 gastric transcripts (including 2 housekeeping

transcripts) (Table E1 in this article's Online Repository at www.jacionline.org). In addition to the significantly dysregulated gene transcripts highly reproducible by microarrays and RNA sequencing, we considered the magnitude of dysregulation, the direction of dysregulation and cell type tissue origins to optimize the diagnostic algorithm. Moreover, we aimed to reveal the presence and function of different biological processes and cell types that are known to be involved in GI T_H2 allergic disorders, so that we would be able to diagnose EG using a personalized medicine approach. TaqMan reagents for amplification of major EG signature genes were obtained from Applied Biosystems (Foster City, CA), and TaqMan real-time PCR amplification was performed on the Quant Studio 7 (Life Technologies). Glyceraldehyde-3-phosphate dehydrogenase (*GAPDH*) was used as an expression control for all analyzed genes. Samples with a *GAPDH* value of <30 CT value were considered acceptable for analysis. The expression CT value of the housekeeping gene *GAPDH* was subtracted from each EG gene of interest (GOI) CT value to acquire the Δ CT. The EGDP score was calculated by summing Δ CT values of the most highly dysregulated genes ($\Sigma\Delta$ CT), as described previously¹⁶ and expanded upon later.

Blood-based diagnostic platform

Peripheral blood samples were collected prior to the endoscopy, separated into serum and/or plasma, and aliquots were frozen and stored at -80°C . The major difference between plasma and serum is the depletion of the coagulation components present in the blood, a process that might alter the detection of cytokine profiles in the blood. The levels of blood cytokines/chemokines — eotaxin-1 (CCL11), eotaxin-2 (CCL24), eotaxin-3 (CCL26), IL-1 α , IL-4, IL-5, IL-13, IL-33, thymus- and activation-regulated chemokine/chemokine ligand 17 (TARC/CCL17), and thymic

stromal lymphopoietin (TSLP) were assayed by customized immunoassays, quantified on a Sector Imager 6000 (Meso Scale Discovery, Gaithersburg, MD, USA), according to the manufacturer's instructions. Scoring systems for plasma and serum were established separately by their respective dysregulated biomarker levels. One point was added to a score for upregulation of specific cytokines (upregulation, having a value higher than the cut-off value [pg/mL] based on the comparison between active EG and non-EG [cut-off values (plasma: eotaxin-3 > 168, IL-5 > 1.4, and TARC > 87; serum: eotaxin-3 > 32, IL-5 > 1.5, and TSLP > 6.7)] (see Fig E8 in this article's Online Repository at www.jacionline.org). A plasma or serum EG score is the sum of the assigned scores for each biomarker assessed, ranging from 0 to 3.

Endoscopic and histologic data

Endoscopic features were prospectively recorded in real-time using a classification and grading system specifically developed for EG by CEGIR, including erosion/ulceration, granularity, raised lesions nodularity, erythema, friability/bleeding, and fold thickness. These findings were scored (erosion/ulceration: 0–6; granularity: 0–2; raised lesions nodularity: 0–2; erythema: 0–2; friability/bleeding: 0–2; fold thickness: 0–1) for the fundus, body, and antrum. The total score for each feature was calculated as the sum of the scores for the three anatomical sites. The overall global assessment of endoscopic severity for the stomach, ranging from 0 to 10, was evaluated for each patient.

Gastric biopsies were assessed by the peak eosinophil counts and the histologic features of EG. These features included lamina propria eosinophil sheets (LPES), periglandular circumferential

collars (PCC), eosinophils in surface epithelium (EoSE), eosinophil glandulitis (EoG), eosinophil gland abscess (EoGA), eosinophils in muscularis mucosa (EoM), lamina propria fibroplasia (LPF), lamina propria smooth muscle hyperplasia (LPSMH), reactive epithelial changes (REC), acute inflammatory cells (AIC), and surface erosion/ulceration (SEU) (Table E2 in this article's Online Repository at www.jacionline.org). Each feature was scored using a 3-point scale (0 = absent, 1 = mild/moderate, 2 = marked). The maximum score for each biopsy is 22, as it is the summation of the 11 feature scores if each feature were to be scored at 2. The final score of the histologic severity, which ranges from 0–1, is the ratio of the sum of the assigned scores for each evaluated feature (0–22) divided by the maximum possible score for that biopsy (22). For example, if all 11 features have maximum scores of 2, the final score is $22/22 = 1$. If a feature were not evaluated, the maximum possible score was reduced by 2 per feature not evaluated; most score reductions occurred because gastric muscularis mucosa was not present in the biopsy.

Statistical analysis

Statistical analyses were performed using the JMP v13.1 (SAS Institute, Cary, NC), CLC Genomics Workbench software (CLC bio, Waltham, MA, USA), GeneSpring GX 12.6 (Agilent Technologies, Santa Clara, CA), and GraphPad Prism 8 (GraphPad Software, Inc., San Diego, CA). Data are n (%) or median (interquartile range [IQR]) unless otherwise stated. Missing data were excluded from all formal statistical analyses. Sample size was estimated to provide 90% power to conclude that 0.8 of the area under the curve (AUC) for an individual marker was significantly greater than 0.5 while controlling the type I error rate at 1% for multiplicity. Statistical significance comparing 2 different groups was determined by the Mann-Whitney *U* test (nonparametric test, 2 groups), the Kruskal-Wallis test followed by a Dunn multiple-

comparison test (nonparametric test, 3 groups or more), or a paired t test (for quantification of longitudinal data and different site of biopsies in the same patients). Nonparametric correlations were calculated using Spearman correlations. Receiver operating characteristic (ROC) curves were constructed, and AUC were calculated to determine the utility of the developed platforms for distinguishing patients with EG from non-EG controls. The optimal cut-off points were determined by Youden's index. We measured sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) to assess the diagnostic accuracy of the scoring systems. A significant P value was defined as less than 0.05.

RESULTS

Patient characteristics

A total of 185 subjects (patients with EG n = 74; non-EG controls n = 111) provided 201 gastric biopsies (RNA sequencing n = 21; EGDP discovery n = 104; EGDP validation n = 76) and 155 blood samples (plasma n = 81; serum n = 74) for analyses. A flow chart of the analysis is shown in Fig 1, A. Demographic and clinical characteristics of the study cohort and subsets, including patients with EG and clinically relevant non-EG controls, are detailed in Table I.

Among all of the study subjects, the age ranged from 1 year to 67 years, with 124 pediatric (67%) and 61 adult (33%) subjects. There was a similar proportion of both genders, with 90 male (48.6%) and 95 female (51.4%) subjects; the majority of subjects were white (91.4%). Peak gastric eosinophil counts ranged from 0 to 352 eosinophils/HPF (active EG: 36–352; inactive EG: 2–29; non-EG controls: 0–28 eosinophils/HPF). Non-EG controls (n = 111) included subjects with atopic comorbidities (n = 47, 42.3%), chronic gastritis (n = 44, 39.6%), and active EoE without EG (n = 20, 18.0%).

There were no significantly different baseline demographic features among the cohorts for the tissue (n = 124) and blood-based (n = 108) platforms. Focusing on patients with EG (n = 74), 46 (62%) had concurrent eosinophilia in the esophagus, 2 (3%) had concurrent eosinophilia in the colon, and 3 (4%) had concurrent eosinophilia in both the esophagus and colon. In tissue- and blood-based platforms, active EG did not reveal any significant differences from non-EG controls in age, gender, race, atopic status, or proton pump inhibitor (PPI) therapy at time of

biopsy, whereas active EG showed significantly higher levels in the disease parameters (peak/average gastric eosinophil counts, endoscopic severity, and histologic severity [$P < .01$, respectively]) and a higher rate of treatment (ongoing diet therapy, topical steroid therapy, and systemic steroid therapy).

RNA sequencing of gastric tissue for identifying representative biomarkers

In order to obtain the molecular foundation for developing the EGDP, we aimed to identify a gene set that was conserved across multiple experimental platforms. Accordingly, we generated an RNA sequencing data set of gastric tissue from active EG ($n = 9$) and non-EG control ($n = 12$) individuals. Unsupervised principal component analysis (PCA) demonstrated robust separation of the two groups (Fig 1, B) defined by 1,226 differentially expressed genes (DEG) (≥ 2 -fold change, FDR $P < .05$) (Fig 1, C and see Fig E1, in this article's Online Repository at www.jacionline.org). We then overlapped this gene signature with two recently published, microarray-based expression profiles (Fig 1, D and Supplementary Fig E1 in this article's Online Repository at www.jacionline.org). Upregulated genes (≥ 10 -fold change, FDR $P < .05$) were markedly enriched in cytokine/chemokine-associated pathways (Fig 1, E), notably including the IL-13 pathway.

Development of tissue-based platform (EGDP) and EGDP₁₈ score based on differentially expressed genes

We manually curated the EG transcriptome with the aim of selecting 48 informative genes that could be embedded into a multiplex PCR-based panel for serially diagnosing and probing

clinical samples. Accordingly, an EG Diagnostic Panel (EGDP) was generated based on the following considerations: dysregulation between EG and non-EG defined by *P* value and fold change, bi-directional changes of gene expression, and inclusion of genes in pathways that were likely to be involved, such as type 2 immunity. The major functional categories represented included those associated with antimicrobial defense, cell adhesion, cytokines and chemokines, epithelial-to-mesenchymal transition, hypoxia, eosinophils, epithelium, fibrosis, inflammatory response, ion transportation, mast cells, neurosensory, neutrophils, and stomach-related processes (Table E1 in this article's Online Repository at www.jacionline.org).

Using this set of 48 informative genes, we aimed to determine the minimal number that would successfully distinguish patients with active EG (*n* = 21) from control individuals (*n* = 23) in a discovery cohort (Table E3 in this article's Online Repository at www.jacionline.org). Using relatively stringent criteria (≥ 10 -fold change, FDR *P* < .01), 18 differentially expressed genes completely separated the two groups (Fig 2, A and B). Among the 18 genes, 8 were upregulated genes related to cytokine/chemokines (*CCL26*, *CCL18*, *IL13RA2*, and *IL5*), eosinophilia (*CLC*), cell adhesion (*CDH26*), antimicrobial defense (*KLK7*), and epithelial-related (*MUC4*), and 10 were downregulated genes related to antimicrobial defense (*DEFB1*), fibrosis (*BMP3* and *COL2A1*), ion transportation (*SLC26A7*), neurosensory activity (*GABRA1*, *GLDN*, *NPY*, and *TAC1*), and stomach-related processes (*ATP4A* and *SST*).

With the goal of developing a quantitative diagnostic cut-off, the EGDP₁₈ score was developed to distinguish EG versus non-EG and to quantify the severity of EG. On the basis of the 18

significant and reproducible differential genes, we made CT sums of the upregulated genes and downregulated genes separately, and then combined the two sums considering their different direction of dysregulation. The EGDP₁₈ score was significantly decreased in patients with active EG compared to non-EG patients in the discovery cohort ($P < .0001$) and similarly decreased in the validation cohort ($P < .0001$) (Fig 2, C). ROC analysis demonstrated an excellent diagnostic merit ($P < .0001$, AUC ≥ 0.95) in both cohorts (Fig 2, D). After investigation by setting the optimal cut-off points, a score of less than 0 resulted in PPV of 100% and NPV of >94% (Fig 2, D). Of note, the EGDP₁₈ score is inversely correlated with disease severity as defined by eosinophil counts when analyzed cross sectionally ($r = -0.83$, $P < .0001$) (Fig 2, E) and longitudinally ($P = .0078$) (Fig 2, F). The EGDP₁₈ score showed comparable levels and high correlation between the gastric antrum and body ($n = 8$, $r = 0.85$, $P < .0001$) (Fig 2, G). Among patients with active EG, the EGDP₁₈ score showed consistency across geographically diverse sites (see Fig E2 in this article's Online Repository at www.jacionline.org) and comparable levels across ages (pediatric vs. adult patients), atopic status (atopy vs. no atopy), co-existence with EoE (EG only vs. EG with EoE), and treatment status at biopsy (ongoing therapy including diet and steroids vs. no therapy) (see Fig E3 in this article's Online Repository at www.jacionline.org).

Interestingly, the EGDP₁₈ score was able to classify patients with intermediate tissue eosinophil levels (i.e., the number of HPFs with ≥ 30 eosinophils, $n = 1-4$ HPFs). When these patients were analyzed by the EGDP₁₈ score ($n = 8$, all of them were clinically symptomatic), 5 patients (63%) were molecularly equivalent to active EG (Fig 2, H and see Fig E4 in this article's Online Repository at www.jacionline.org).

Gastric transcript associations with histologic and endoscopic features

Significant correlations were noted between specific genes within the EGDP and the peak gastric eosinophil level, histologic severity, and overall global assessment of endoscopic severity (Fig 3, A and Table E4 in this article's Online Repository at www.jacionline.org). The top 10 genes that tracked with tissue eosinophilia were *CCL26*, *CLC*, *IL13RA2*, *BMP3*, *IL5*, *CDH26*, *CCL18*, *NPY*, *HPGDS*, and *SST*; with histologic severity were *CCL26*, *IL13RA2*, *CLC*, *SST*, *BMP3*, *IL5*, *CDH26*, *GLDN*, *ANXA1*, and *DEFB1*; and with endoscopic severity were *CCL26*, *GLDN*, *IL13RA2*, *SST*, *DEFB1*, *GABRA1*, *IL5*, *TAC1*, *CLC*, and *IL13*. Notably, these gene groups included genes that overlapped between tissue eosinophilia, histologic severity, and endoscopic severity (i.e., *CCL26*, *CLC*, *IL13RA2*, *IL5*, and *SST*).

Individual components of the histologic and endoscopic features associated with the EGDP₁₈ score. Associations were noted between the EGDP₁₈ score and several histologic features (Spearman *r* range: -0.05 – -0.73; Fig 3, *B left panel*) with periglandular circumferential collars showing the highest magnitude of correlation with the EGDP₁₈ score (*r* = -0.73, FDR *P* < .0001). Associations were also observed between the EGDP₁₈ score and several endoscopic features (Spearman *r* range: -0.22 – -0.45; Fig 3, *B right panel*). The EGDP₁₈ score inversely correlated the most with granularity (*r* = -0.45, FDR *P* < .0001) and nodularity (*r* = -0.45, FDR *P* < .0001).

Three histologic features (lamina propria eosinophil sheets, periglandular circumferential collars, and eosinophil glandulitis) showed higher correlations, based on hierarchical clustering of

Spearman correlations (Fig 3, *C left panel*), suggesting that they might be more effective than other features at capturing biological processes underlying the EGDP. At the gene level, *CCL26* showed the strongest correlation with the histologic features, most notably periglandular circumferential collars ($r = 0.74$, $P = 7.0E-21$) and eosinophil glandulitis ($r = 0.68$, $P = 2.0E-16$); in correlation strength, *CCL26* was followed by *IL13RA2*, which correlated most notably with periglandular circumferential collars ($r = 0.67$, $P = 7.0E-16$) and lamina propria eosinophil sheets ($r = 0.67$, $P = 5.0E-16$). Interestingly, though muscularis mucosa eosinophilia showed relatively weak associations compared with epithelial and lamina propria changes, *DUOX2* and *DUOXA2* showed unique association with muscularis mucosa eosinophilia ($r = 0.32$, $P = 3.8E-3$) (see Fig E5 and Table E5 in this article's Online Repository at www.jacionline.org). Some features, such as acute inflammation and erosion/ulcer, were uncommon and, possibly for that reason, did not show gene correlations.

In contrast to histology, for which gene transcripts showed association with only a limited set of histologic features, all recorded endoscopic features correlated with specific gastric transcripts (Fig 3, *C right panel*). *CCL26* showed the strongest correlation with any endoscopic features, most notably nodularity ($r = 0.55$, $P = 2.8E-5$) and granularity ($r = 0.53$, $P = 4.9E-5$), followed by *IL33*, which inversely correlated most notably with granularity ($r = -0.46$, $P = 6.1E-4$) and friability and bleeding ($r = -0.39$, $P = 3.9E-3$). Interestingly, clustering separated endoscopic features into 2 general groups, one was associated with endoscopic changes, including friability/bleeding and erythema, and the other was associated with endoscopic changes, including nodularity and granularity. Endoscopic changes, including friability/bleeding and erythema, were associated with downregulation of molecular signatures (*ATP4A*, *IL33*, and

SLC26A7), whereas endoscopic changes, including nodularity and granularity, were associated with upregulation of type 2 immunity and eosinophil-associated pathways (*CCL26*, *IL13RA2*, and *IL5*) (see Fig E6 and Table E6 in this article's Online Repository at www.jacionline.org). A heat map showing $-\log_{10}$ FDR P value determined by differential expression between patients with EG with or without a specific endoscopic feature by the Mann-Whitney U test also supported this finding (see Fig E7 in this article's Online Repository at www.jacionline.org).

Development of blood-based platforms and blood EG score based on significantly increased biomarkers

We explored the possibility that systemic levels of cytokines/chemokines might be elevated in EG. Focusing on plasma and serum samples from patient cohorts with and without EG, we designed a multiplex immunoassay containing 10 EG-relevant cytokines/chemokines, particularly those based on type 2 immunity as reflected in the functional predictions found in the EG transcripts (Fig 1, *E*). Notably, patients with active EG showed significantly higher levels of 3 cytokines in the plasma and 3 cytokines in the serum (plasma eotaxin-3/*CCL26*, IL-5, and TARC/*CCL17*; serum TSLP, eotaxin-3/*CCL26*, and IL-5) (Fig 4, *A* and *B*, and Table E7 in this article's Online Repository at www.jacionline.org), suggesting that the activity of the disease consistently affects these cytokines systemically.

On the basis of the levels of these dysregulated cytokines and chemokines, we developed a circulation-based EG biomarker scoring system for plasma and serum (see Fig E8 in this article's Online Repository at www.jacionline.org). The blood-based EG score differentiated patients

with active EG from non-EG controls in both the plasma and serum cohorts ($P < .0001$) (Fig 4, C and D). Notably, patients with active EG showed significantly higher scores than did patients with inactive EG (plasma EG score $P < .0001$, serum EG score $P = .0012$) (Fig 4, E and F). To determine their diagnostic performances, ROC analyses were constructed to investigate the use of blood EG scores and cytokine/chemokine levels alone (Fig 4, G and H). The plasma EG score yielded an AUC of 0.93, whereas levels of eotaxin-3 alone yielded an AUC of 0.89, levels of TARC alone yielded an AUC of 0.82, and levels of IL-5 alone yielded an AUC of 0.80. The serum EG score yielded an AUC of 0.91, whereas levels of TSLP alone yielded AUC of 0.86, levels of eotaxin-3 alone yielded an AUC of 0.80, and levels of IL-5 alone yielded an AUC of 0.77.

Associations among the local and systemic molecular expressions

We were interested in exploring the association between the tissue local gene expressions and circulating systemic molecular expressions. Notably, plasma eotaxin-3 exhibited a higher magnitude of correlation with the EGDP than any other protein ($P < .01$) (Fig 5, A, *upper panel*). Using Spearman r for the correlation between the EGDP gene expressions and plasma and serum protein biomarkers, a Spearman r -based heat diagram for the correlation at the gene level was generated (Fig 5, A, *lower panel*). Focusing on the plasma eotaxin-3, we observed that plasma eotaxin-3 correlated with genes related to gastric cytokine/chemokines (*CCL26*, *IL13RA2*, *IL1RL1*, *IL4*, and *IL5*), eosinophilia (*CLC* and *CCR3*), cell adhesion (*CDH26*), mast cells (*CPA3* and *HPGDS*), inflammatory response (*ANXA1*), other (*ITLN1*), neurosensory features (*GLDN*), fibrosis (*BMP3*), and antimicrobial defense (*DEFB1*).

516

517 The blood EG score—the circulation-based biomarker—showed significant correlations with
518 gastric eosinophil counts (plasma $r = 0.72$, $P = .0002$; serum $r = 0.54$, $P = .0015$) (Fig 5, *B*) and
519 EGDP₁₈ score (plasma $r = -0.64$, $P = .0015$; serum $r = -0.46$, $P = .0084$) (Fig 5, *C*), suggesting
520 that the systemic circulating biomarker levels reflect the local gastric inflammatory process
521 defined by the eosinophil levels and transcript expression profiles.

522

DISCUSSION

In this study, we have established molecular diagnostic criteria for EG by utilizing gastric mRNA transcript and circulating protein levels. We have 1) developed a set of EG transcripts, composed of 48 genes, that robustly distinguishes EG from non-EG and whose expression is equivalent across independent and geographically diverse sites and across patient ages (including children and adults) and medical therapy; 2) determined that a diagnostic score limited to changes in a subset of 18 genes, referred to as the EGDP₁₈ score, is sufficient to allow EG diagnosis relative to controls (sensitivity of 88–95% in discovery and validation cohort and specificity of 100%), including individuals with non-EG and patients with EGID limited to the esophagus; 3) determined that the EGDP₁₈ score can robustly separate patients with active EG from those with inactive EG, strongly correlates with gastric eosinophil levels ($r = -0.83$, $P < .0001$), and potentially aids in diagnostic classification of patients with intermediate eosinophil levels; 4) determined that expression of specific genes tracks with tissue eosinophilia, namely expression of *CCL26*, *CLC*, *IL13RA2*, *BMP3*, *IL5*, *CDH26*, *CCL18*, *NPY*, *HPGDS*, and *SST*; 5) linked the magnitude of molecular changes to endoscopic changes, most notably associating nodularity and granularity with a subset of type 2 inflammatory genes, including *CCL26* and *IL13RA2*, respectively; 6) linked the magnitude of molecular changes to histologic changes; most notably, the levels of *CCL26* strongly associated with periglandular circumferential collars ($r = 0.74$, $P = 7.0E-21$) and eosinophil glandulitis ($r = 0.68$, $P = 2.0E-16$), whereas *IL13RA2* correlated most notably with periglandular circumferential collars ($r = 0.67$, $P = 7.0E-16$) and lamina propria eosinophil sheets ($r = 0.67$, $P = 5.0E-16$); 7) identified circulating biomarkers that reflect local changes in the stomach, most notably gastric eosinophilia; and 8) demonstrated that the

combined levels of plasma eotaxin-3, TARC, and IL-5 have the capacity to diagnose EG disease and monitor disease activity with high sensitivity and specificity (100% and 72%, respectively).

Herein, we analyzed more than 200 gastric tissue samples and assessed the overlap among molecular profiles. Although it is conceivable that EG and EoE share a common T_H2 molecular pathogenesis, as we published earlier,¹⁰ the EG and EoE transcriptomes (as assessed by microarray analysis) only overlap by 7% despite a common IL-13 induced signature. In this study, using independent methods of RNA sequencing and qPCR arrays, we confirmed our previous observation that the overall gene expression profiles of EoE and EG are distinct at a transcription level. Previous histopathologic studies indicate that the eosinophilic infiltration in EG can be patchy and that the minimum threshold number of gastric eosinophils required for the diagnosis of EG varies, ranging from 20 eosinophils in 1 HPF to 70 eosinophils per HPF in at least 3 HPFs.^{21, 24} Our results were obtained by using only 1 RNA sample per patient, suggesting that molecular diagnosis is a relatively promising and sensitive method for disease diagnosis and monitoring. The EGDP₁₈ score algorithm indicated that 63% of the histologically intermediate patients were molecularly equivalent to patients with active EG, providing evidence that 30 eosinophils/HPF in less than 5 HPFs is still associated with robust molecular inflammatory processes. These data suggest that analysis of less than 5 HPFs may be sufficient for diagnosis.

Beyond diagnostic merits, in order to understand disease pathogenesis, we also assessed correlations between molecular profiles and histologic and endoscopic features. For EG histologic features, regardless of the distribution, eosinophilic features (periglandular

circumferential collars, eosinophil glandulitis, lamina propria eosinophil sheets, and eosinophils in surface epithelium) were highly associated with the EG transcriptome (especially the EGDP core 18 genes), with the strongest association occurring in periglandular circumferential collars. Not all histologic features showed strong associations with the EGDP, possibly due to the insufficient depth of biopsies resulting in many of them not including muscularis mucosa and/or to the low occurrence of some histologic features (lamina propria fibroplasia, surface erosion/ulceration, eosinophil gland abscess, and acute inflammatory cells). Moreover, certain features of endoscopic changes, such as nodularity and granularity, were notable as features uniquely related to transcript changes, particularly those enriched in inflammatory responses involving upregulation of type 2 immunity and eosinophil-related pathways (*IL13RA2*, *CCL26*, and *IL5*). Both *CCL26* and *IL13RA2* are IL-13-inducible genes;²⁵ controversy exists as to whether the latter is an activating or possibly inhibitory signaling molecule (including a potential inhibitor role of soluble IL-13R α 2). The prominent role of type 2 immunity-related responses provides the scientific basis for therapeutic intervention with dupilumab (anti-IL-4R α , which inhibits IL-4R α /IL-13R α 1), anti-IL-13R α 1, and/or anti-IL-13 (e.g., RPC4046 inhibiting IL-13 interactions with both IL-13R α 1 and IL-13R α 2).²⁶ Increased expression levels of type 2 immune/eosinophil associated pathways can be seen in other atopic disorders associated with nodularity, such as chronic rhinosinusitis with nasal polyps, suggesting that they were not to be EG-specific but might function to generate these histological features in certain tissue/conditions. Interestingly, endoscopic changes, such as friability and erythema, were associated with downregulation of *IL33* (epithelium-derived, pro-inflammatory alarmin), *SLC26A7* (anion exchange transporter), and *ATP4A* (proton pump; gastric H, K-ATPase alpha subunit). Decreased expression levels of these genes may suggest injured mucosa due to tissue inflammation. Our

current findings only showed minimal overlap (e.g. *AREG*, *CXCL8*, *SST*, and *TGFBR1*) compared to a prior report limited to 8 patients with EG from a single site,¹³ probably due to the differences in sample size, molecular platform, and definition of endoscopic features. However, in this large, cross-sectional cohort of EG, we could identify specific findings with differences in potential pathways.

Biopsy procurement is currently required to establish definitive diagnosis of EGID. The field urgently calls for developing non-invasive biomarkers. Prior findings suggested that EG is more systemic than EoE on the basis of the co-occurrence of EG with circulating eosinophilia;¹⁰ therefore, we hypothesized that circulating biomarkers may be present in patients with EG. Indeed, eotaxin-3 and IL-5 were significantly upregulated in both serum and plasma of patients with EG compared to non-EG controls, and circulating levels of eotaxin-3 were particularly correlative with tissue expression of *CCL26*. Of note, the plasma eotaxin-3 levels in EG were not reflective of an atopic state in general, as they were not elevated in patients with EoE. Furthermore, average circulating eotaxin-3 levels in EG appear to be substantially higher than levels reported in other atopic diseases, such as chronic rhinosinusitis with high-eosinophil mucosal infiltration (plasma 122.6 pg/mL vs. 481.2 pg/mL seen in our study),²⁷ but in the same range for serum as seen for another rare eosinophilic disease, eosinophilic granulomatosis with polyangiitis.²⁸ We speculate that the stomach (related disease EG) may contribute to higher circulating eotaxin-3 levels than does the esophagus (related disease EoE) due to differences in the underlying tissue architecture, with the gastric mucosa having relatively increased proximity to the vasculature, a relatively large surface area, and resident eosinophil populations during

homeostasis. The reasons for the selective increase in circulating eotaxin-3 levels in EG compared with other EGIDs deserves further attention.

To our knowledge, this is the first EGID study simultaneously addressing tissue signature and circulating cytokine profiles in the same disorder with autologous samples across different collecting centers. This study was not intended to replace the histologic method but rather to provide at least two alternative platforms to more precisely and sensitively diagnose EG. It is conceivable that the circulating markers could serve as an early non-invasive test during EGID/EG screening, whereas the tissue signature profiling (EGDP) could be used for definitive diagnostic confirmation. The combination of both would provide molecular tools to diagnose, monitor, and potentially further subtype (e.g., endotype) knowledge of EG. Future studies should examine the utility of the blood-based platform to identify disease remission with treatment, which would prevent the need for repeat endoscopy.

Our study has several strengths. First, we analyzed samples from multiple sites across the USA, which increases the generalizability of the results. Second, participants were assessed with several diagnostic assessments, allowing us to examine associations between gene expressions, endoscopic, and histologic parameters. Third, we assessed not only gene expression, but also circulating blood protein. Fourth, we validated gene expression differences between EG diagnoses in an independent cohort. Our study also has limitations. First, our findings include patients with active EG with mixed treatment status or who have disease that is refractory to treatment, which might potentially influence the results. However, patients still exhibited signs

of disease clinically, histologically, and molecularly. Second, most of the analyses for gene expression and biomarker were restricted to 48 genes included in the EGDP and 10 blood biomarkers. Unbiased, genome-wide transcriptome and proteome approaches would likely reveal additional genes of interest, biomarkers, and optimal combinations. Finally, the data are limited by the cross-sectional approach, highlighting the importance of additional replication, particularly in prospective and longitudinal studies.

In conclusion, we have developed and validated diagnostic panels that can diagnose EG using biopsy and blood samples. *CCL26/eotaxin-3* emerged as the strongest single tissue and circulating disease biomarker. We have uncovered robust associations among the EG molecular profile, periglandular circumferential collars, and endoscopic granularity/nodularity, providing insight into the better understanding of the pathogenesis for EG. Further work is required to apply these platforms to a prospective trial in a different clinical setting, explore the feasibility and further validation, and optimize platforms for disease stratification.

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TABLE I. Demographic and clinical characteristics of study subjects*

		Tissue-based platform				Blood-based platform				
		All study subjects (n = 185)	All study subjects in tissue-based platform (n = 124)	Non-EG (n = 55)	Active EG (n =39)	P value	All study subjects in blood-based platform (n = 108)	Non-EG (n = 67)	Active EG (n =27)	P value
Demographics										
Age at biopsy (years)		15.2 (11.0 – 20.0)	15.5 (11.2 – 20.5)	14.2 (8.4 – 18.0)	16.5 (12.3 – 21.2)	0.06	15.4 (11.2 – 19.5)	14.6 (10.5 – 19.1)	17.7 (12.5 – 20.6)	0.11
Gender	Pediatric subjects	124 (67.0%)	81 (65.3%)	40 (72.7%)	23 (59.0%)	0.19	74 (68.5%)	48 (71.6%)	15 (55.6%)	0.15
	Male	90 (48.6%)	65 (52.4%)	24 (43.6%)	21 (53.8%)	0.40	51 (47.2%)	28 (41.8%)	14 (51.9%)	0.49
Race	White	169 (91.4%)	111 (89.5%)	52 (94.5%)	34 (87.2%)	0.27	100 (92.6%)	65 (97.0%)	24 (88.9%)	0.14
History of EGID										
	EG only	22 (11.9%)	22 (17.7%)	-	12 (30.8%)	-	14 (13.0%)	-	8 (29.6%)	-
	EG and EoE	47 (25.4%)	46 (37.1%)	-	27 (69.2%)	-	20 (18.5%)	-	16 (59.3%)	-
	EG and EC	2 (1.1%)	1 (0.8%)	-	-	-	2 (1.9%)	-	2 (7.4%)	-
	EG, EoE, and EC	3 (1.6%)	3 (2.4%)	-	-	-	3 (2.8%)	-	1 (3.7%)	-
	EoE only	20 (10.8%)	10 (8.1%)	10 (18.2%)	-		10 (9.3%)	10 (14.9%)	-	-
Clinical symptoms at biopsy										
	Symptomatic (any)	130 (70.3%)	85 (68.6%)	30 (54.6%)	39 (100%)	< 0.01	90 (83.3%)	53 (79.1%)	27 (100%)	< 0.01
	Abdominal pain	91 (49.2%)	52 (41.9%)	19 (34.6%)	22 (56.4%)	0.04	66 (61.1%)	41 (61.2%)	18 (66.6%)	0.62
	Heartburn	66 (35.7%)	37 (29.8%)	13 (23.6%)	12 (30.8%)	0.44	45 (44.4%)	30 (44.8%)	9 (33.3%)	0.31
	Nausea/vomit	88 (47.6%)	54 (43.6%)	23 (41.8%)	19 (48.7%)	0.51	60 (55.6%)	40 (59.7%)	14 (51.9%)	0.49
	Other	33 (17.8%)	33 (26.6%)	20 (36.4%)	16 (41.0%)	0.65	14 (13.0%)	19 (28.4%)	11 (40.7%)	0.24
Atopic status										
	Atopy (any)	129 (69.7%)	84 (67.7%)	36 (65.5%)	31 (79.5%)	0.17	76 (70.4%)	51 (76.1%)	19 (70.4%)	0.61
	Asthma	74 (40.0%)	49 (39.5%)	14 (25.5%)	19 (48.7%)	0.03	40 (37.0%)	25 (37.3%)	11 (40.7%)	0.82
	Allergic rhinitis	80 (43.2%)	55 (44.4%)	25 (45.5%)	18 (46.2%)	1.00	48 (44.4%)	30 (44.8%)	14 (51.9%)	0.65
	Eczema	52 (28.1%)	33 (26.6%)	11 (20.0%)	13 (33.3%)	0.16	30 (27.8%)	20 (29.9%)	9 (33.3%)	0.81
	Food allergy	60 (32.4%)	58 (46.8%)	12 (21.8%)	28 (71.8%)	< 0.01	18 (16.7%)	1 (1.5%)	11 (40.7%)	< 0.01
Treatment at biopsy										
	Ongoing diet therapy	54 (29.2%)	44 (35.5%)	13 (23.6%)	22 (56.4%)	< 0.01	29 (26.9%)	10 (14.9%)	13 (48.1%)	< 0.01
	Proton pump inhibitor	93 (50.3%)	48 (38.7%)	19 (34.5%)	19 (48.7%)	0.29	67 (62.0%)	48 (71.6%)	15 (55.6%)	0.15
	Topical steroids	50 (27.0%)	49 (39.5%)	13 (23.6%)	19 (48.7%)	0.03	19 (17.6%)	0 (0%)	12 (44.4%)	< 0.01
	Systemic steroids	10 (5.4%)	8 (6.5%)	0 (0%)	5 (12.8%)	0.01	6 (5.6%)	0 (0%)	2 (7.4%)	0.08
Disease parameters in stomach										
	Peak eosinophil	16 (10 – 65)	16 (10 – 63)	11 (6 – 15)	124 (68 – 192)	< 0.01	56 (10 – 127)	7 (5 – 9)	123 (77 – 183)	< 0.01

counts									
Average eosinophil counts	11.8 (6.0 – 53.7)	11.8 (5.9 – 51.1)	6.6 (3.8 – 10.0)	88.2 (61.2 – 142.6)	< 0.01	33.8 (5 – 77.2)	4.3 (1.9 – 5.0)	72.6 (62.0 – 128.6)	< 0.01
Endoscopic severity	0 (0 – 3)	0 (0 – 3)	0 (0 – 0)	4 (0 – 7)	< 0.01	2 (0 – 5)	0 (0 – 0)	6 (3 – 7)	< 0.01
Histologic severity	0.14 (0.09 – 0.35)	0.14 (0.09 – 0.35)	0.09 (0.05 – 0.14)	0.41 (0.35 – 0.55)	< 0.01	0.35 (0.10 – 0.46)	0.10 (0.06 – 0.10)	0.35 (0.29 – 0.50)	< 0.01

*Data pertains to the time at biopsy/blood procurement. Data are n (%) or median (IQR). EGID, eosinophilic gastrointestinal disorders; EG, eosinophilic gastritis; EoE, eosinophilic esophagitis; EC, eosinophilic colitis; EGDP, eosinophilic gastritis diagnostic panel.

FIGURE LEGENDS

FIG 1. Schematic illustration of the study and genome-wide screening of gastric tissue for identifying representative biomarkers

A, Flow chart of the study design and strategy. **B**, The gastric transcriptome data on non-EG controls (*blue*) and patients with EG (*red*) were reduced to 3-dimensional presentation by multidimensional scaling analysis at the whole-genome level for visual presentation of the expression distance between samples. **C**, Heat map (*red*, *upregulated*; *blue*, *downregulated*) of 1,226 differentially dysregulated genes' expression profiles (FDR $P < .05$, ≥ 2 -fold change). Clustering analysis was performed; each column represents an individual patient or control. **D**, Venn diagram comparing the number of genes identified as dysregulated in EG across different platforms. **E**, Functional enrichment gene ontology analysis of the strongly upregulated genes (FDR $P < .01$, ≥ 10 -fold change). The x-axes represent the negative log₁₀ FDR P value. Red bars indicate cytokine/chemokine-associated terms and pathways. *EG*, eosinophilic gastritis; *EGDP*, eosinophilic gastritis diagnostic panel; *FDR*, false-discovery rate; *GO*, gene ontology.

FIG 2. Development of tissue-based platform (EGDP) and EGDP₁₈ score on the basis of differentially expressed genes

A, Heat map (*yellow*, *upregulated*; *blue*, *downregulated*) based on the 18 core genes (FDR $P < .01$ and fold change ≥ 10 -fold change) in the discovery cohort. **B**, Three-dimensional presentation by PCA between samples on the basis of the 18 core genes (*blue*, *non-EG controls*; *red*, *patients with EG*). **C**, Comparison of the EGDP₁₈ score between EG and non-EG in discovery and validation cohort. **D**, ROC curve analysis showing the utility of the EGDP₁₈ score for the diagnosis of EG. **E**, Correlation between peak gastric eosinophil counts and EGDP₁₈ score. **F**, Longitudinal changes of peak gastric eosinophil counts and EGDP₁₈ score in patients with EG at active and inactive state. **G**, Correlation of EGDP₁₈ score between the gastric antrum and body mucosa from the same subjects. **H**, EGDP₁₈ score as a function of different patient groups, including patients with EG with involvement of 1-5 HPFs. *AUC*, area under the curve; *EG*, eosinophilic gastritis; *EGDP*, eosinophilic gastritis diagnostic panel; *FDR*, false-discovery rate; *HPF*, high-power field; *NPV*, negative predictive value; *PCA*, principal component analysis; *PPV*, positive predictive value; *ROC*, receiver operating characteristic.

FIG 3. Gastric transcript associations with histologic and endoscopic features

A, Associations between the individual genes of EGDP and diagnostic parameters. Negative log₁₀ FDR P value of the Spearman correlation between the individual genes of EGDP and peak gastric eosinophil counts (*left*), histologic severity (*middle*), and the overall assessment of endoscopic severity (*right*). Red indicates a positive correlation and blue indicates a negative correlation. The dashed line indicates an FDR P value of .05. The top genes and features are

labeled. **B**, Associations between the EGDP₁₈ score and the individual components of histology (left) and endoscopy (right). **C**, Associations between the EGDP and the histologic (left) and endoscopic (right) features. Clustering tree with Spearman r-based heat diagram for the correlation at the gene level were generated. Darker red shades indicate stronger positive correlations, whereas darker blue shades indicate stronger negative correlations. The shorter the distance (*tree-branch length*) the more similar the expression correlation is for each feature. *EG*, eosinophilic gastritis; *FDR*, false-discovery rate; *AIC*, acute inflammatory cells; *EoG*, eosinophil glandulitis; *EoGA*, eosinophil gland abscess; *EoM*, eosinophils in muscularis mucosa; *EoSE*, eosinophils in surface epithelium; *LPES*, lamina propria eosinophil sheets; *LPF*, lamina propria fibroplasia; *LPSMH*, lamina propria smooth muscle hyperplasia; *PCC*, periglandular circumferential collars; *REC*, reactive epithelial changes; *SEU*, surface erosion/ulceration.

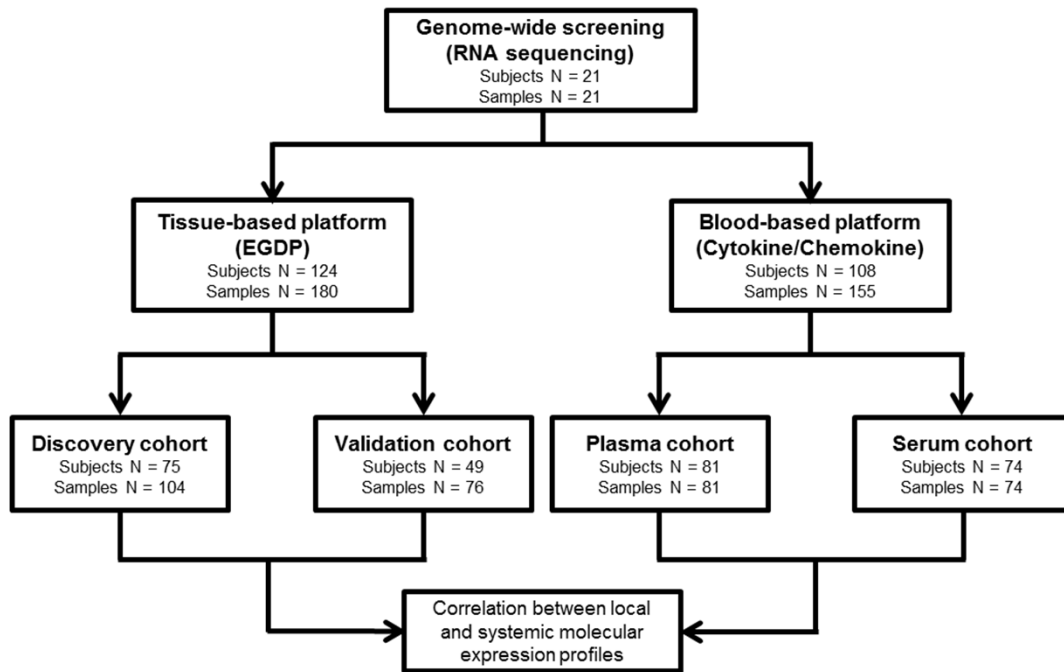
FIG 4. Development of blood-based platforms via a multiplex protein array

A and **B**, Among the 10 biomarkers embedded in the platform, a statistical screening was performed between the non-EG subjects and patients with EG in the (A) plasma and (B) serum cohort, separately, resulting in 3 biomarkers (red) with adjusted $P < .05$ (Bonferroni correction). **C** and **D**, Levels of blood EG scores in patients with active EG (C, plasma; D, serum). **E** and **F**, Blood EG scores in patients with active EG and inactive EG (E, plasma; F, serum). **G** and **H**, ROC curves and performance of blood EG scores. The AUC was calculated for 4 conditions: (G) Plasma cohort; plasma EG score, eotaxin-3, IL-5, and TARC. (H) Serum cohort; serum EG score, eotaxin-3, IL-5, and TSLP. *AUC*, area under the curve; *EG*, eosinophilic gastritis; *NPV*, negative predictive value; *PCA*, principal component analysis; *PPV*, positive predictive value; *ROC*, receiver operating characteristic.

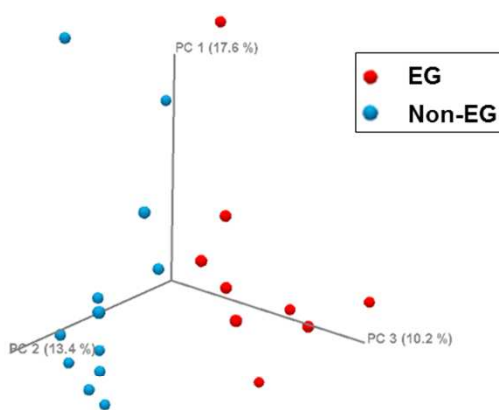
FIG 5. Associations among the local and systemic features

A, Associations between the EGDP and the blood cytokine/chemokines. Using Spearman r for the correlation between the EGDP gene expressions and (left) plasma and (right) serum cytokine/chemokines, the magnitudes of correlation with the EGDP are shown (upper). A Spearman r-based heat diagram for the correlation at the gene level are shown (lower). Genes shown on the y axis are organized within functional groupings. Darker red shades indicate stronger positive correlations, whereas darker blue shades indicate stronger negative correlations. **B**, Correlation between blood EG score (left, plasma; right, serum) and peak gastric eosinophil counts, with Spearman r and P values shown. **C**, Correlation between blood EG scores (left, plasma; right, serum) and the EGDP₁₈ score, with Spearman r and P values shown. *EG*, eosinophilic gastritis; *EGDP*, eosinophilic gastritis diagnostic panel; *EMT*, epithelial-mesenchymal transition; *HPF*, high-power field. $*P < .01$ vs. all other proteins.

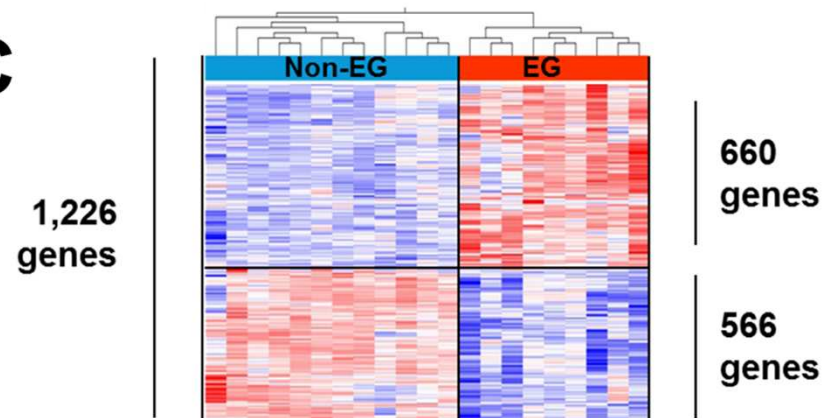
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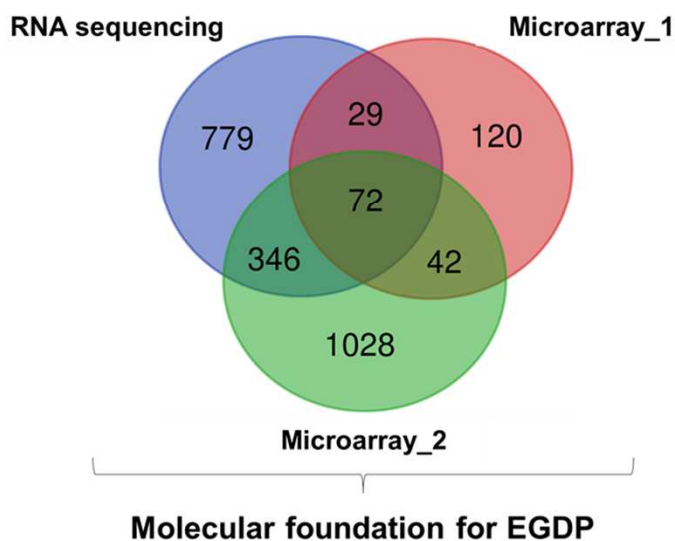
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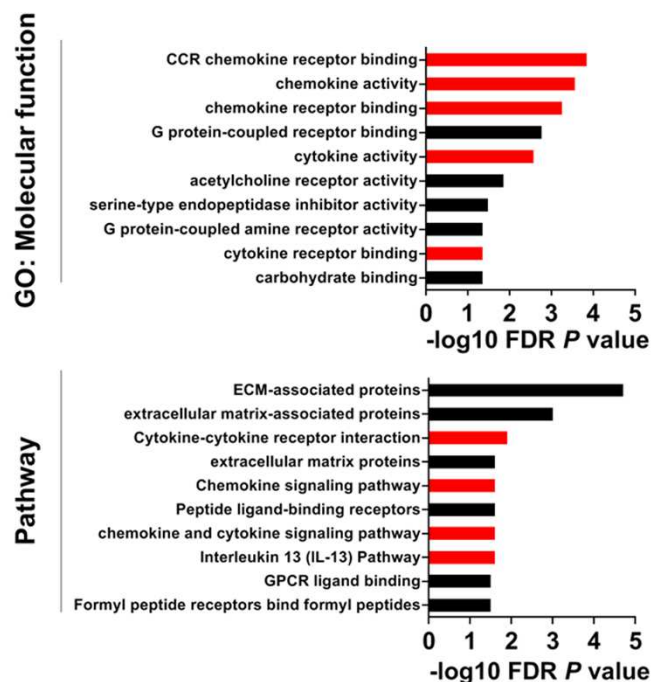


Figure 1

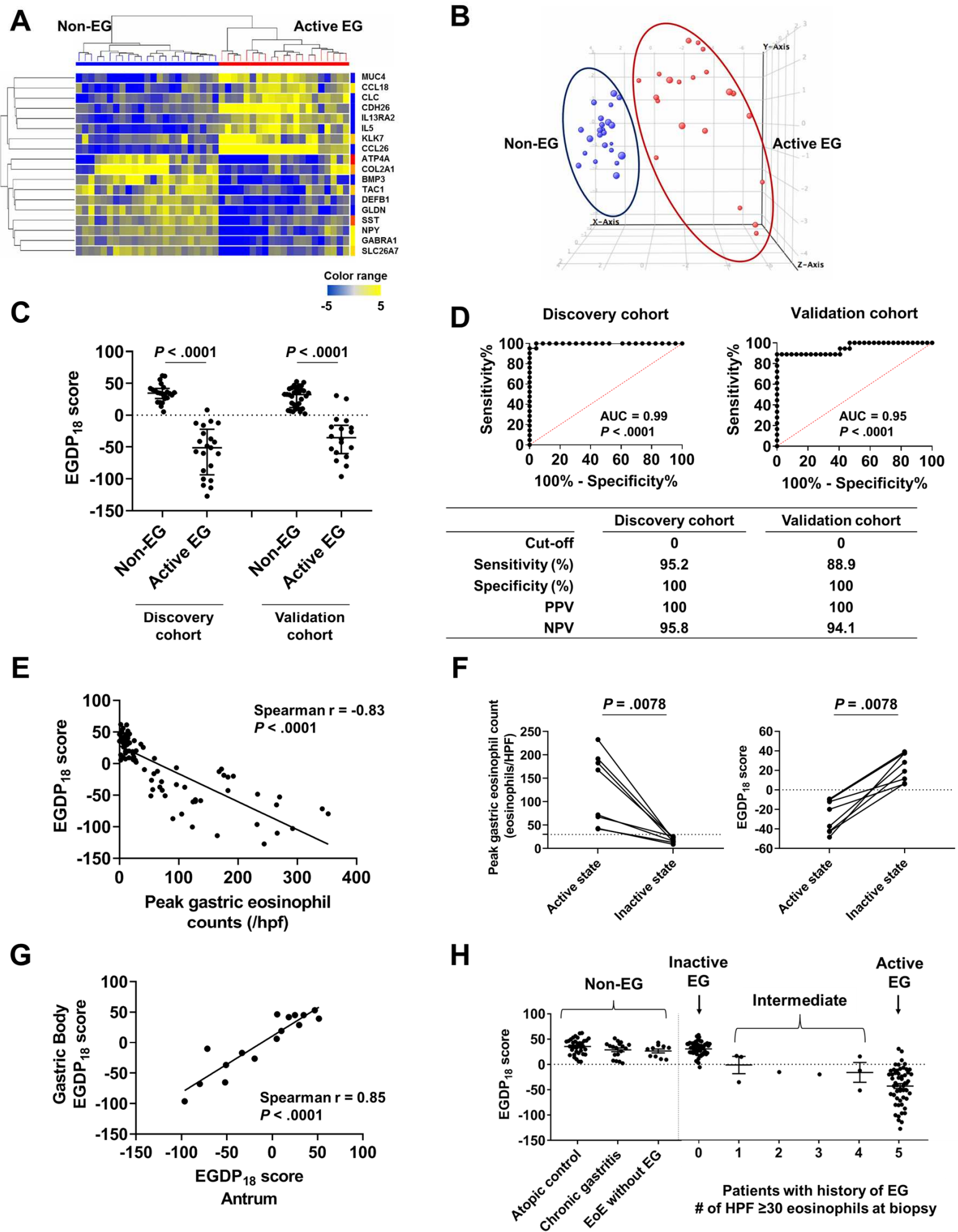
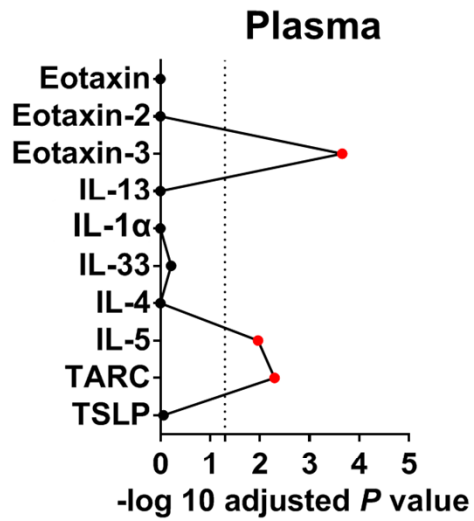
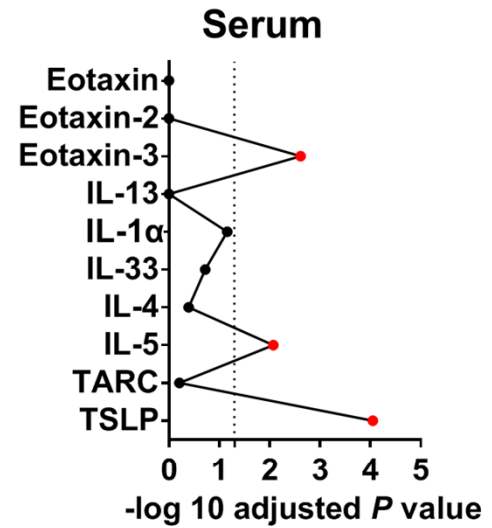
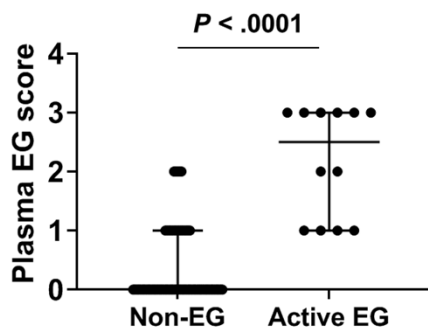
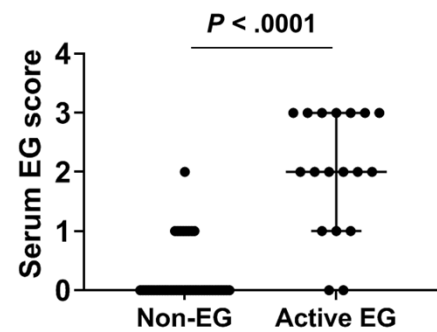
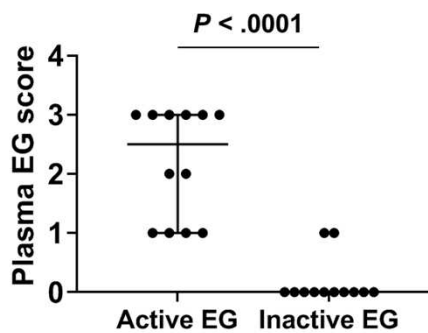
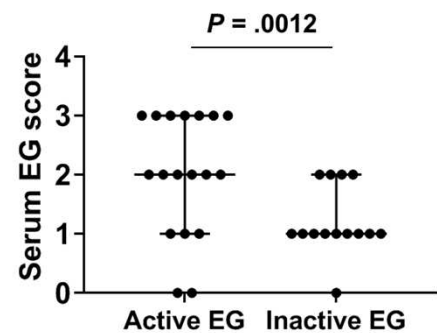
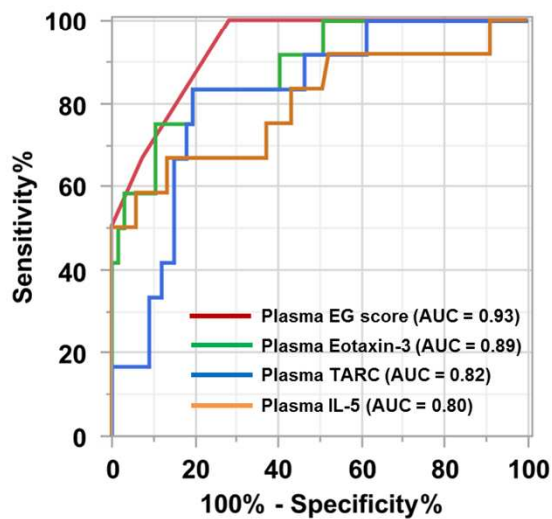
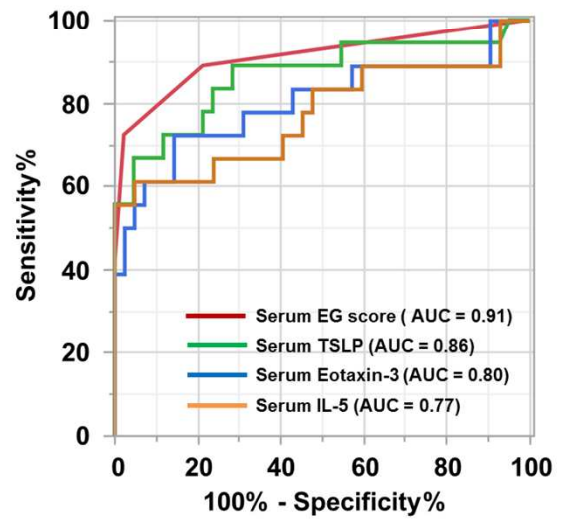
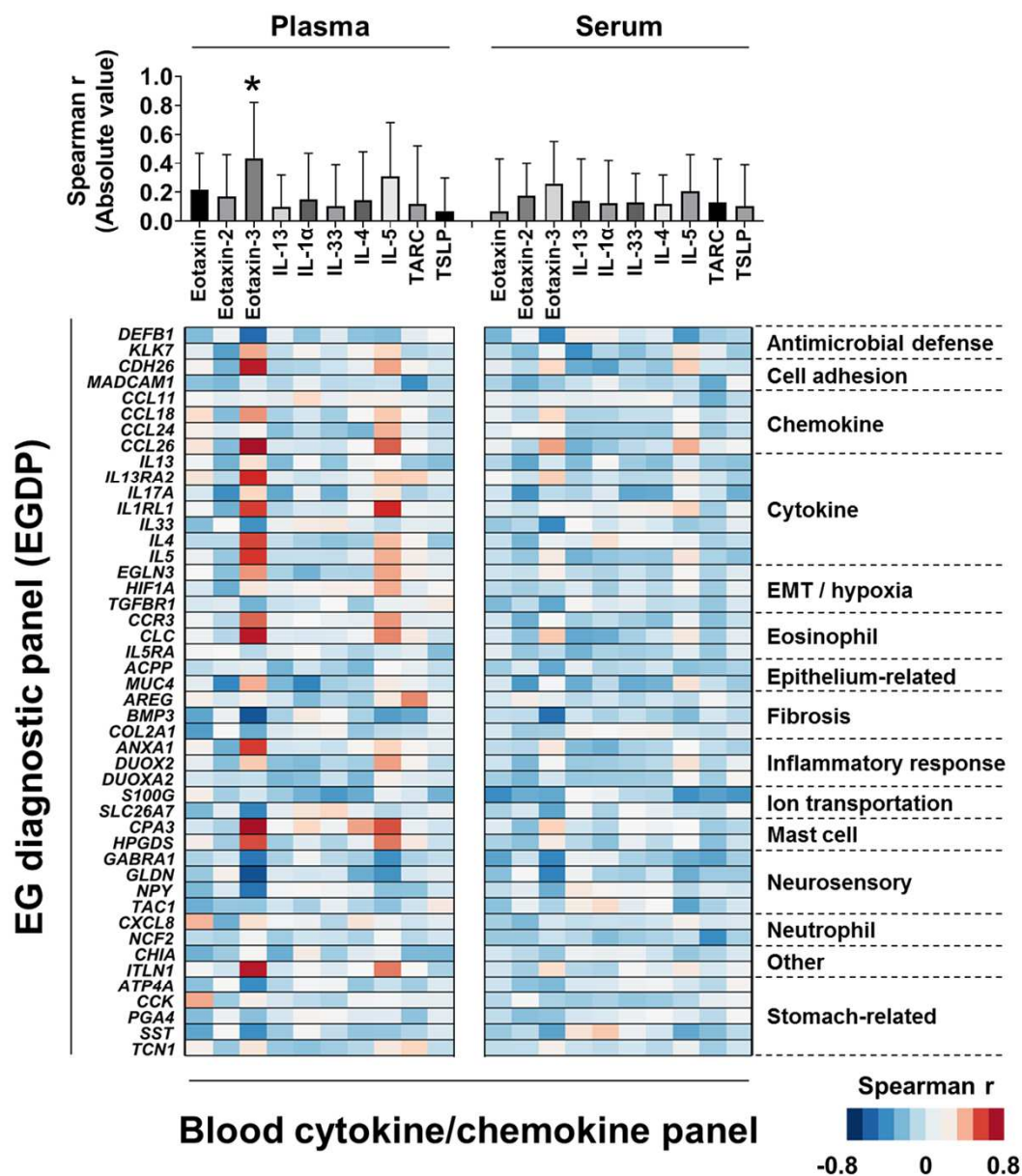


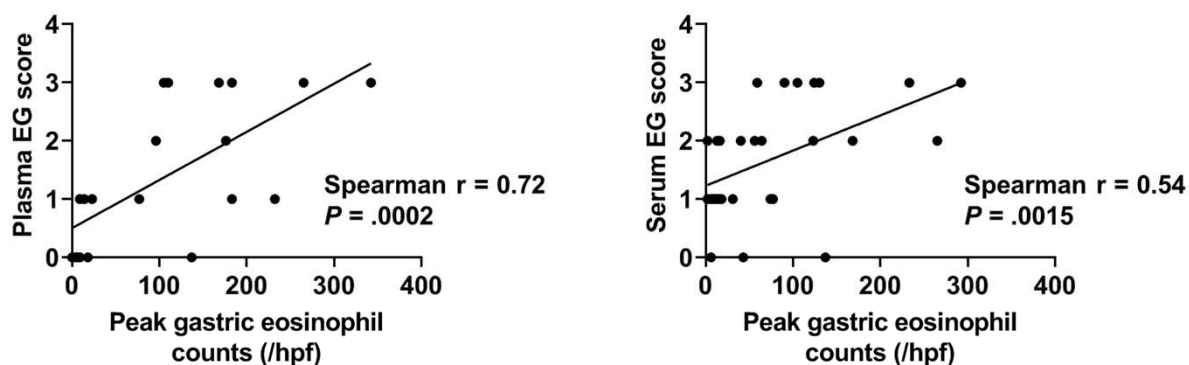
Figure 2

A**B****C****D****E****F****G****H****Figure 4**

A



B



C

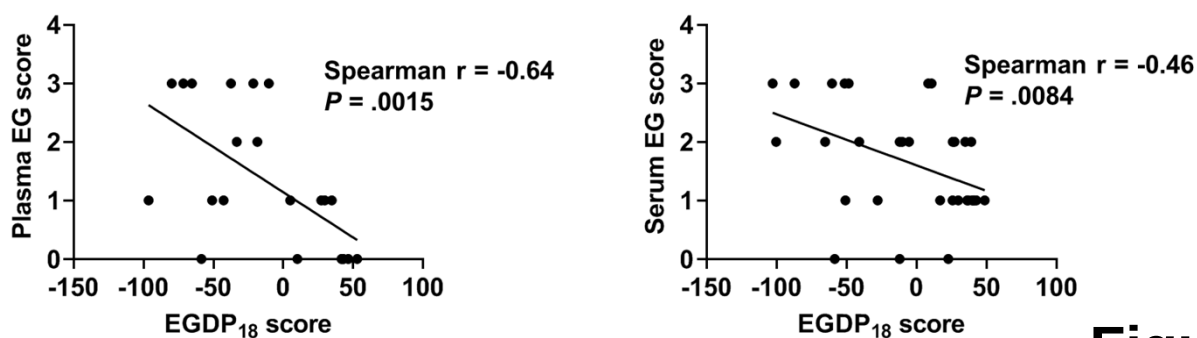


Figure 5

Online Repository Materials**Molecular, Endoscopic, Histologic, and Circulating Biomarker-Based Diagnosis of Eosinophilic Gastritis: Multi-Site Study**

Tetsuo Shoda^a, Ting Wen^a, Julie M. Caldwell^a, Margaret H. Collins^b, John A. Besse^a, Garrett A. Osswald^a, J. Pablo Abonia^a, Nicoleta C. Arva^c, Dan Atkins^d, Kelley E. Capocelli^e, Evan S. Dellon^f, Gary W. Falk^g, Nirmala Gonsalves^h, Sandeep K. Guptaⁱ, Ikuo Hirano^h, Vincent A. Mikkada^j, Philip E. Putnam^j, Rachel M. Sheridan^b, Rudman Spergel AK^k, Jonathan M. Spergel^l, Joshua B. Wechsler^m, Guang-Yu Yangⁿ, Seema S. Aceves^o, Glenn T. Furuta^p and Marc E. Rothenberg^a on behalf of the Consortium of Eosinophilic Gastrointestinal Disease Researchers (CEGIR)*

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*The list of participants is provided in this article's Supplementary Material

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Consortium of Eosinophilic Gastrointestinal Disease Researchers (CEGIR) questionnaires

Registry for Eosinophilic Gastrointestinal Diseases (REGID) Provider Questionnaire

CEGIR Outcomes Measures in Eosinophilic Gastrointestinal disorders Across the ages

(OMEGA) Patient Intake Questionnaire

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Sandeep	Gupta
Frank	Hamilton
Kirk	Harris
Jennifer	Harris
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Kaitlin	Keeley
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Barry	Wershil
Lisa	Wheatley
Leah	Wilkey
Guang-Yu	Yang
Angelika	Zalewski
Amy	Zicarelli

Supplementary Table 1. List of EGDP genes

Gene Symbol	Description	Fold Change (EG vs. Non-EG)	Representative Functionality	AssayID
<i>ACPP</i>	acid phosphatase, prostate	1.2	Epithelium-related	Hs00173475_m1
<i>ANXA1</i>	annexin A1	2.2	Inflammatory response	Hs00167549_m1
<i>AREG</i>	amphiregulin	-1.0	Fibrosis	Hs00950669_m1
<i>ATP4A</i>	ATPase H ⁺ /K ⁺ transporting subunit alpha	-5.4	Stomach-related	Hs00167575_m1
<i>BMP3</i>	bone morphogenetic protein 3	-13.8	Fibrosis	Hs00609638_m1
<i>CCK</i>	cholecystokinin	-1.0	Stomach-related	Hs00174937_m1
<i>CCL11</i>	C-C motif chemokine ligand 11	-1.0	Cytokine/Chemokine	Hs00237013_m1
<i>CCL18</i>	C-C motif chemokine ligand 18	8.6	Cytokine/Chemokine	Hs00268113_m1
<i>CCL24</i>	C-C motif chemokine ligand 24	3.2	Cytokine/Chemokine	Hs00171082_m1
<i>CCL26</i>	C-C motif chemokine ligand 26	210.3	Cytokine/Chemokine	Hs00171146_m1
<i>CCR3</i>	C-C motif chemokine receptor 3	2.4	Eosinophil	Hs99999027_s1
<i>CDH26</i>	cadherin 26	14.2	Cell adhesion	Hs00375371_m1
<i>CHIA</i>	chitinase, acidic	1.3	Other	Hs00253976_m1
<i>CLC</i>	Charcot-Leyden crystal galectin	10.7	Eosinophil	Hs00171342_m1
<i>COL2A1</i>	collagen type II alpha 1 chain	-3.6	Fibrosis	Hs01064869_m1
<i>CPA3</i>	carboxypeptidase A3	1.7	Mast cell	Hs00157019_m1
<i>CXCL8</i>	C-X-C motif chemokine ligand 8	2.1	Neutrophil	Hs99999034_m1
<i>DEFB1</i>	defensin beta 1	-12.3	Antimicrobial defense	Hs00608345_m1
<i>DUOX2</i>	dual oxidase 2	3.2	Inflammatory response	Hs00204187_m1
<i>DUOX2</i>	dual oxidase maturation factor 2	3.8	Inflammatory response	Hs01595312_g1
<i>EGLN3</i>	egl-9 family hypoxia inducible factor 3	2.0	EMT/Hypoxia	Hs00222966_m1
<i>GABRA1</i>	gamma-aminobutyric acid type A receptor alpha1 subunit	-7.3	Neurosensory	Hs00971228_m1
<i>GAPDH</i>	glyceraldehyde-3-phosphate dehydrogenase	-	Aux. housekeeping control	Hs99999905_m1
<i>GAPDH</i>	glyceraldehyde-3-phosphate dehydrogenase	-	Main housekeeping control	Hs03929097_g1
<i>GLDN</i>	gliomedin	-18.5	Neurosensory	Hs00738960_m1
<i>HIF1A</i>	hypoxia inducible factor 1 subunit alpha	1.4	EMT/Hypoxia	Hs00153153_m1
<i>HPGDS</i>	hematopoietic prostaglandin D synthase	1.8	Mast cell	Hs00183950_m1
<i>IL13</i>	interleukin 13	4.7	Cytokine/Chemokine	Hs99999038_m1
<i>IL13RA2</i>	interleukin 13 receptor subunit alpha 2	9.6	Cytokine/Chemokine	Hs00152924_m1
<i>IL17A</i>	interleukin 17A	1.3	Cytokine/Chemokine	Hs00174383_m1
<i>IL1RL1</i>	interleukin 1 receptor like 1	2.1	Cytokine/Chemokine	Hs00249384_m1
<i>IL33</i>	interleukin 33	-2.0	Cytokine/Chemokine	Hs04931857_m1
<i>IL4</i>	interleukin 4	1.9	Cytokine/Chemokine	Hs00174122_m1

<i>IL5</i>	interleukin 5	12.8	Cytokine/Chemokine	Hs00174200_m1
<i>IL5RA</i>	interleukin 5 receptor subunit alpha	1.1	Eosinophil	Hs00236871_m1
<i>ITLN1</i>	intelectin 1	6.2	Other	Hs00914745_m1
<i>KLK7</i>	kallikrein related peptidase 7	11.0	Antimicrobial defense	Hs00192503_m1
<i>MADCAM1</i>	mucosal vascular addressin cell adhesion molecule 1	-1.5	Cell adhesion	Hs00175533_m1
<i>MUC4</i>	mucin 4, cell surface associated	7.3	Epithelium-related	Hs00366414_m1
<i>NCF2</i>	neutrophil cytosolic factor 2	1.5	Neutrophil	Hs00166416_m1
<i>NPY</i>	neuropeptide Y	-38.3	Neurosensory	Hs00173470_m1
<i>PGA4</i>	pepsinogen 4, group I pepsinogen A	-1.2	Stomach-related	Hs01029048_m1
<i>S100G</i>	S100 calcium binding protein G	-7.8	Ion transportation	Hs00187854_m1
<i>SLC26A7</i>	solute carrier family 26 member 7	-4.6	Ion transportation	Hs01104163_m1
<i>SST</i>	somatostatin	-14.4	Stomach-related	Hs00356144_m1
<i>TAC1</i>	tachykinin precursor 1	-11.6	Neurosensory	Hs00243225_m1
<i>TCN1</i>	transcobalamin 1	3.1	Stomach-related	Hs01055538_m1
<i>TGFBR1</i>	transforming growth factor beta receptor 1	-1.1	EMT/Hypoxia	Hs00610320_m1

EG, eosinophilic gastritis; *EGDP*, eosinophilic gastritis diagnostic panel; *EMT*, epithelial-mesenchymal transition.

Supplementary Table 2. Definitions of EG histologic features

Features	Definition	Mild/moderate	Marked
Lamina propria eosinophil sheets	Contiguous eosinophils that form masses in the lamina propria and may increase interglandular distance	Contiguous eosinophil masses without increased interglandular distance	Contiguous eosinophil masses with increased interglandular distance
Periglandular circumferential collars	At least one layer of eosinophils that surround $\geq 3/4$ of circumference of gland cut in cross section, or entire base of a gland cut	Single layer of eosinophils forms collar	More than 1 layer of eosinophils forms collar
Eosinophils in surface epithelium	Eosinophils in surface epithelium	1-5 eosinophils/HPF	>5 eosinophils/HPF or a group of eosinophils of any size
Eosinophil glandulitis	Eosinophils in glandular epithelium, $\pm$ eosinophils in lumen	1-5 eosinophils/HPF	>5 eosinophils/HPF or a group of eosinophils of any size
Eosinophil gland abscess	Dilated gland lined by attenuated epithelium with eosinophils in periglandular lamina propria, gland epithelium, and gland lumen	$\leq 10\%$ of glands	>10% of glands
Eosinophils in muscularis mucosa		Found in ≤ 5 HPF	Found in >5 HPF
Lamina propria fibroplasia	Acellular pink fibrous tissue in lamina propria	Found in ≤ 5 HPF	Found in >5 HPF
Lamina propria smooth muscle hyperplasia	Strands of smooth muscle perpendicular to the lumen	Found in ≤ 5 HPF	Found in >5 HPF
Reactive epithelial changes	reduced mucin, increased nuclear:cytoplasmic ratio, increased mitotic activity, apoptosis, intestinal metaplasia, etc.	Found in ≤ 5 HPF	Found in >5 HPF
Acute inflammatory cells	Acute inflammatory cells in lamina propria and/or intraepithelial	Found in ≤ 5 HPF	Found in >5 HPF
Surface erosion/ulceration	Denuded surface with fibrin deposits in denuded area, with or without lamina propria acute inflammation, necrosis, granulation tissue, etc.	Found in ≤ 5 HPF	Found in >5 HPF

HPF, high-power field.

Supplementary Table 3. Screening of differentially expressed gene sets for EGDP*

Fold-change cut-off	Statistical cut-off		
	None	FDR $P < .05$	FDR $P < .01$
None	48	31	25
2 fold	36	31	25
5 fold	23	21	19
10 fold	20	19	18

*Number of genes that pass various filter cut-offs following comparison of the expression level of all genes between non-EG controls (n = 12) and patients with active EG (n = 9). *EG*, eosinophilic gastritis; *EGDP*, eosinophilic gastritis diagnostic panel; *FDR*, false-discovery rate.

Supplementary Table 4. Spearman correlations between EG diagnostic parameters and a diagnostic subset of the EG transcriptome

Representative Functionality	EGDP Genes	Gastric Peak Eosinophil Counts	Histologic Severity	Endoscopic Severity
Antimicrobial defense	<i>DEFB1</i>	-0.49	-0.48	-0.39
Antimicrobial defense	<i>KLK7</i>	0.30	0.36	0.28
Cell adhesion	<i>CDH26</i>	0.59	0.52	0.29
Cell adhesion	<i>MADCAM1</i>	-0.10	-0.12	-0.07
Cytokine/Chemokine	<i>CCL11</i>	0.21	0.17	0.14
Cytokine/Chemokine	<i>CCL18</i>	0.58	0.46	0.20
Cytokine/Chemokine	<i>CCL24</i>	0.32	0.34	0.20
Cytokine/Chemokine	<i>CCL26</i>	0.76	0.69	0.44
Cytokine/Chemokine	<i>IL13</i>	0.30	0.40	0.34
Cytokine/Chemokine	<i>IL13RA2</i>	0.67	0.64	0.41
Cytokine/Chemokine	<i>IL17A</i>	0.21	0.09	0.11
Cytokine/Chemokine	<i>IL1RL1</i>	0.33	0.32	0.30
Cytokine/Chemokine	<i>IL33</i>	-0.39	-0.37	-0.22
Cytokine/Chemokine	<i>IL4</i>	0.27	0.24	0.23
Cytokine/Chemokine	<i>IL5</i>	0.62	0.54	0.39
EMT/Hypoxia	<i>EGLN3</i>	0.35	0.30	0.12
EMT/Hypoxia	<i>HIF1A</i>	0.18	0.21	0.15
EMT/Hypoxia	<i>TGFBR1</i>	-0.19	-0.10	-0.05
Eosinophil	<i>CCR3</i>	0.34	0.29	-0.02
Eosinophil	<i>CLC</i>	0.71	0.59	0.35
Eosinophil	<i>IL5RA</i>	0.05	0.07	0.05
Epithelium-related	<i>ACPP</i>	0.03	0.00	0.13
Epithelium-related	<i>MUC4</i>	0.53	0.45	0.17
Fibrosis	<i>AREG</i>	0.06	0.03	0.05
Fibrosis	<i>BMP3</i>	-0.63	-0.55	-0.27
Fibrosis	<i>COL2A1</i>	-0.32	-0.31	-0.17
Inflammatory response	<i>ANXA1</i>	0.52	0.49	0.28

Inflammatory response	<i>DUOX2</i>	0.42	0.32	0.14
Inflammatory response	<i>DUOXA2</i>	0.19	0.17	0.08
Ion transportation	<i>S100G</i>	-0.15	-0.08	-0.19
Ion transportation	<i>SLC26A7</i>	-0.37	-0.34	-0.15
Mast cell	<i>CPA3</i>	0.46	0.40	0.20
Mast cell	<i>HPGDS</i>	0.53	0.45	0.26
Neurosensory	<i>GABRA1</i>	-0.52	-0.46	-0.39
Neurosensory	<i>GLDN</i>	-0.50	-0.50	-0.43
Neurosensory	<i>NPY</i>	-0.56	-0.45	-0.28
Neurosensory	<i>TAC1</i>	-0.35	-0.34	-0.35
Neutrophil	<i>CXCL8</i>	0.28	0.23	0.18
Neutrophil	<i>NCF2</i>	0.24	0.25	0.16
Other	<i>CHIA</i>	-0.04	-0.05	0.04
Other	<i>ITLN1</i>	0.42	0.33	0.16
Stomach-related	<i>ATP4A</i>	-0.35	-0.34	-0.17
Stomach-related	<i>CCK</i>	0.14	0.05	-0.07
Stomach-related	<i>PGA4</i>	-0.16	-0.15	-0.04
Stomach-related	<i>SST</i>	-0.53	-0.55	-0.40
Stomach-related	<i>TCN1</i>	0.46	0.36	0.07

Correlations by functional groupings of genes are shown. The text within the cell indicates the Spearman r value. Values in boldface indicate the top 10 genes with nominal statistical significance ($P < .05$). *EG*, eosinophilic gastritis; *EGDP*, eosinophilic gastritis diagnostic panel; *EMT*, epithelial-mesenchymal transition.

Supplementary Table 5. Spearman correlations between EG histologic features and a diagnostic subset of the EG transcriptome

Representative Functionality	EGDP Genes	AIC	EoGA	SEU	LPF	EoM	LPSMH	EoG	LPES	PCC	EoSE	REC
Antimicrobial defense	<i>DEFB1</i>	-0.01	-0.15	-0.15	0.02	-0.19	-0.19	-0.50	-0.55	-0.59	-0.46	-0.51
Antimicrobial defense	<i>KLK7</i>	0.15	0.07	0.07	0.15	0.07	0.32	0.37	0.28	0.40	0.34	0.25
Cell adhesion	<i>CDH26</i>	0.00	0.16	0.16	0.14	0.22	0.40	0.48	0.60	0.59	0.39	0.41
Cell adhesion	<i>MADCAM1</i>	-0.02	0.01	0.01	-0.02	0.09	-0.12	-0.07	-0.12	-0.12	-0.02	-0.11
Cytokine/Chemokine	<i>CCL11</i>	-0.13	0.07	0.07	0.00	0.28	-0.01	0.15	0.14	0.15	0.09	0.18
Cytokine/Chemokine	<i>CCL18</i>	-0.02	0.15	0.15	-0.03	0.30	0.28	0.47	0.51	0.52	0.30	0.42
Cytokine/Chemokine	<i>CCL24</i>	0.15	0.13	0.13	0.13	0.24	0.16	0.35	0.39	0.43	0.31	0.26
Cytokine/Chemokine	<i>CCL26</i>	0.14	0.16	0.16	0.06	0.38	0.41	0.68	0.67	0.74	0.57	0.62
Cytokine/Chemokine	<i>IL13</i>	-0.12	0.14	0.14	0.20	0.08	0.30	0.38	0.35	0.37	0.44	0.31
Cytokine/Chemokine	<i>IL13RA2</i>	0.01	0.14	0.14	0.04	0.19	0.52	0.57	0.67	0.67	0.46	0.53
Cytokine/Chemokine	<i>IL17A</i>	-0.02	-0.15	-0.15	-0.16	0.15	-0.03	0.17	0.11	0.13	0.16	0.17
Cytokine/Chemokine	<i>IL1RL1</i>	-0.08	0.13	0.13	0.07	0.26	0.07	0.38	0.40	0.41	0.37	0.30
Cytokine/Chemokine	<i>IL33</i>	-0.19	-0.15	-0.15	-0.10	-0.01	-0.34	-0.33	-0.40	-0.42	-0.26	-0.25
Cytokine/Chemokine	<i>IL4</i>	-0.22	0.14	0.14	0.02	0.12	0.08	0.29	0.26	0.23	0.18	0.16
Cytokine/Chemokine	<i>IL5</i>	-0.03	0.15	0.15	0.00	0.25	0.39	0.61	0.61	0.64	0.53	0.47
EMT/Hypoxia	<i>EGLN3</i>	-0.08	0.14	0.14	0.08	0.15	0.26	0.25	0.36	0.37	0.20	0.21
EMT/Hypoxia	<i>HIF1A</i>	-0.10	0.06	0.06	0.08	0.19	0.10	0.17	0.16	0.18	0.19	0.14
EMT/Hypoxia	<i>TGFBR1</i>	-0.08	-0.09	-0.09	0.11	0.20	-0.16	-0.11	-0.14	-0.16	-0.05	-0.12
Eosinophil	<i>CCR3</i>	-0.10	0.10	0.10	0.06	0.08	0.22	0.36	0.33	0.35	0.22	0.16
Eosinophil	<i>CLC</i>	-0.02	0.15	0.15	0.04	0.29	0.27	0.62	0.59	0.64	0.47	0.56
Eosinophil	<i>IL5RA</i>	0.04	0.06	0.06	0.13	0.01	0.02	0.14	0.13	0.06	-0.01	0.03
Epithelium-related	<i>ACPP</i>	0.00	-0.09	-0.09	0.08	0.03	-0.04	0.06	-0.02	-0.04	-0.03	0.02
Epithelium-related	<i>MUC4</i>	0.19	0.08	0.08	0.13	0.16	0.35	0.45	0.50	0.52	0.36	0.31
Fibrosis	<i>AREG</i>	-0.05	0.03	0.03	0.00	-0.04	0.13	0.02	-0.01	-0.03	-0.06	-0.01
Fibrosis	<i>BMP3</i>	-0.10	-0.10	-0.10	-0.01	-0.24	-0.40	-0.55	-0.57	-0.64	-0.48	-0.46
Fibrosis	<i>COL2A1</i>	-0.21	-0.15	-0.15	-0.08	-0.05	-0.31	-0.24	-0.32	-0.34	-0.22	-0.21
Inflammatory response	<i>ANXA1</i>	0.11	0.10	0.10	0.06	0.23	0.45	0.39	0.44	0.46	0.34	0.38
Inflammatory response	<i>DUOX2</i>	-0.07	0.11	0.11	0.04	0.32	0.18	0.34	0.38	0.37	0.20	0.20
Inflammatory response	<i>DUOX2</i>	-0.01	0.14	0.14	0.09	0.32	-0.01	0.21	0.20	0.19	0.13	0.10
Ion transportation	<i>S100G</i>	-0.16	-0.15	-0.15	0.06	0.01	0.01	-0.06	-0.12	-0.09	-0.25	-0.19
Ion transportation	<i>SLC26A7</i>	-0.13	-0.14	-0.14	-0.04	-0.04	-0.36	-0.33	-0.40	-0.42	-0.24	-0.21
Mast cell	<i>CPA3</i>	-0.04	0.00	0.00	-0.01	0.24	0.19	0.40	0.39	0.43	0.30	0.38
Mast cell	<i>HPGDS</i>	-0.01	0.09	0.08	0.08	0.28	0.19	0.43	0.45	0.49	0.36	0.42

Neurosensory	<i>GABRA1</i>	-0.12	-0.14	-0.14	0.04	-0.10	-0.27	-0.44	-0.49	-0.50	-0.41	-0.49
Neurosensory	<i>GLDN</i>	-0.08	-0.12	-0.12	0.01	-0.10	-0.28	-0.57	-0.59	-0.62	-0.57	-0.51
Neurosensory	<i>NPY</i>	-0.11	-0.16	-0.16	-0.11	-0.06	-0.23	-0.43	-0.55	-0.59	-0.39	-0.43
Neurosensory	<i>TAC1</i>	-0.02	-0.08	-0.08	-0.06	-0.11	-0.11	-0.40	-0.35	-0.39	-0.38	-0.38
Neutrophil	<i>CXCL8</i>	0.27	0.09	0.09	0.05	0.24	0.15	0.22	0.18	0.22	0.24	0.17
Neutrophil	<i>NCF2</i>	0.18	-0.10	-0.10	0.08	0.29	0.09	0.30	0.27	0.25	0.21	0.25
Other	<i>CHIA</i>	-0.14	-0.15	-0.15	-0.12	0.06	-0.08	0.03	-0.09	-0.09	-0.01	-0.02
Other	<i>ITLN1</i>	-0.25	0.14	0.14	-0.07	0.11	0.16	0.40	0.45	0.47	0.33	0.33
Stomach-related	<i>ATP4A</i>	-0.11	-0.10	-0.10	-0.05	-0.01	-0.36	-0.28	-0.37	-0.37	-0.24	-0.25
Stomach-related	<i>CCK</i>	-0.02	0.12	0.12	0.02	0.16	0.10	0.02	0.01	0.04	0.00	-0.03
Stomach-related	<i>PGA4</i>	-0.15	-0.02	-0.02	-0.04	0.04	-0.24	-0.06	-0.14	-0.14	-0.03	-0.07
Stomach-related	<i>SST</i>	-0.09	-0.14	-0.14	-0.06	-0.12	-0.29	-0.53	-0.56	-0.60	-0.52	-0.57
Stomach-related	<i>TCN1</i>	0.01	0.14	0.14	0.00	0.26	0.26	0.34	0.39	0.41	0.20	0.30

Correlations by functional groupings of genes are shown. The text within the cell indicates the Spearman r value. Values in boldface indicate absolute Spearman $r > 0.3$ with nominal statistical significance ($P < .05$). Red shading indicates positive correlations, whereas blue shading indicates negative correlations. *EG*, eosinophilic gastritis; *EGDP*, eosinophilic gastritis diagnostic panel; *EMT*, epithelial-mesenchymal transition; *AIC*, acute inflammatory cells; *EoG*, eosinophil glandulitis; *EoGA*, eosinophil gland abscess; *EoM*, eosinophils in muscularis; *EoSE*, eosinophils in surface epithelium; *LPES*, lamina propria eosinophil sheets; *LPF*, lamina propria fibroplasia; *LPSMH*, lamina propria smooth muscle hyperplasia; *PCC*, periglandular circumferential collars; *REC*, reactive epithelial changes; *SEU*, surface erosion/ulceration.

Supplementary Table 6. Spearman correlations between EG endoscopic features and a diagnostic subset of the EG transcriptome

Representative Functionality	EGDP Genes	Nodularity	Granularity	Folds	Friability Bleeding	Erythema	Erosion Ulceration
Antimicrobial defense	<i>DEFB1</i>	-0.41	-0.38	-0.26	-0.18	-0.10	0.00
Antimicrobial defense	<i>KLK7</i>	0.17	0.21	0.26	0.17	0.22	0.15
Cell adhesion	<i>CDH26</i>	0.45	0.49	0.35	0.31	0.28	0.23
Cell adhesion	<i>MADCAM1</i>	-0.14	-0.07	-0.15	-0.12	-0.12	-0.09
Cytokine/Chemokine	<i>CCL11</i>	-0.09	-0.18	0.02	-0.30	-0.10	-0.16
Cytokine/Chemokine	<i>CCL18</i>	0.44	0.38	0.25	0.24	0.11	-0.02
Cytokine/Chemokine	<i>CCL24</i>	0.48	0.49	0.30	0.15	0.22	0.06
Cytokine/Chemokine	<i>CCL26</i>	0.55	0.53	0.39	0.30	0.36	0.13
Cytokine/Chemokine	<i>IL13</i>	0.19	0.26	0.20	0.02	0.05	0.05
Cytokine/Chemokine	<i>IL13RA2</i>	0.49	0.51	0.31	0.32	0.24	0.14
Cytokine/Chemokine	<i>IL17A</i>	0.11	0.02	0.08	-0.02	-0.27	0.05
Cytokine/Chemokine	<i>IL1RL1</i>	0.32	0.30	0.03	0.09	-0.02	-0.12
Cytokine/Chemokine	<i>IL33</i>	-0.36	-0.46	-0.18	-0.39	-0.41	-0.24
Cytokine/Chemokine	<i>IL4</i>	-0.15	-0.16	0.01	-0.16	-0.23	-0.06
Cytokine/Chemokine	<i>IL5</i>	0.47	0.47	0.33	0.21	0.17	0.17
EMT/Hypoxia	<i>EGLN3</i>	0.26	0.28	0.15	0.26	0.20	0.00
EMT/Hypoxia	<i>HIF1A</i>	0.11	0.04	0.26	-0.08	-0.06	-0.14
EMT/Hypoxia	<i>TGFB1</i>	-0.11	-0.14	-0.15	-0.18	-0.28	-0.24
Eosinophil	<i>CCR3</i>	0.23	0.20	0.15	0.19	0.10	0.11
Eosinophil	<i>CLC</i>	0.40	0.32	0.29	0.17	0.12	0.05
Eosinophil	<i>IL5RA</i>	-0.06	-0.10	0.05	-0.16	-0.01	0.01
Epithelium-related	<i>ACPP</i>	-0.12	-0.13	-0.24	-0.34	-0.22	-0.09
Epithelium-related	<i>MUC4</i>	0.46	0.43	0.27	0.22	0.26	0.19
Fibrosis	<i>AREG</i>	0.03	-0.02	-0.09	0.13	0.18	0.00
Fibrosis	<i>BMP3</i>	-0.42	-0.40	-0.21	-0.28	-0.32	-0.19
Fibrosis	<i>COL2A1</i>	-0.46	-0.38	-0.25	-0.29	-0.43	-0.11
Inflammatory response	<i>ANXA1</i>	0.36	0.35	0.23	0.35	0.35	0.24
Inflammatory response	<i>DUOX2</i>	0.35	0.27	0.32	0.14	0.04	-0.05
Inflammatory response	<i>DUOX2</i>	0.35	0.22	0.19	0.09	0.00	-0.06
Ion transportation	<i>S100G</i>	-0.34	-0.35	-0.18	-0.20	-0.21	-0.02
Ion transportation	<i>SLC26A7</i>	-0.41	-0.47	-0.22	-0.38	-0.38	-0.22
Mast cell	<i>CPA3</i>	-0.08	-0.04	0.19	-0.13	-0.02	-0.03
Mast cell	<i>HPGDS</i>	0.09	0.06	0.20	-0.02	0.09	0.02

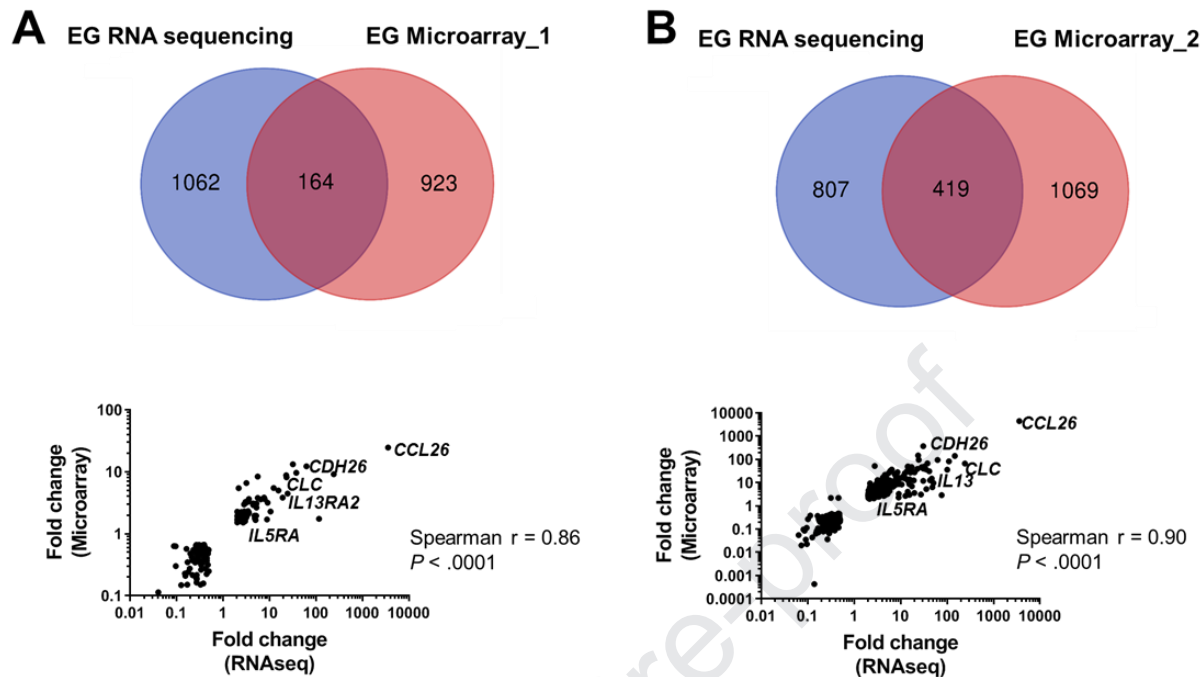
Neurosensory	<i>GABRA1</i>	-0.31	-0.33	-0.25	-0.33	-0.35	-0.37
Neurosensory	<i>GLDN</i>	-0.35	-0.41	-0.27	-0.16	-0.29	-0.14
Neurosensory	<i>NPY</i>	-0.50	-0.41	-0.20	-0.30	-0.32	-0.11
Neurosensory	<i>TAC1</i>	-0.30	-0.34	-0.12	-0.07	-0.08	-0.12
Neutrophil	<i>CXCL8</i>	0.46	0.32	0.08	0.39	0.20	0.10
Neutrophil	<i>NCF2</i>	0.30	0.20	0.04	0.03	0.05	-0.05
Other	<i>CHIA</i>	-0.34	-0.29	-0.16	-0.37	-0.27	-0.21
Other	<i>ITLN1</i>	0.04	0.05	0.24	-0.07	0.01	-0.08
Stomach-related	<i>ATP4A</i>	-0.35	-0.39	-0.19	-0.45	-0.33	-0.15
Stomach-related	<i>CCK</i>	0.14	0.12	-0.11	0.17	0.06	-0.15
Stomach-related	<i>PGA4</i>	-0.23	-0.27	-0.16	-0.34	-0.31	-0.13
Stomach-related	<i>SST</i>	-0.46	-0.38	-0.28	-0.19	-0.30	-0.18
Stomach-related	<i>TCN1</i>	0.30	0.25	0.22	0.12	0.06	-0.12

Correlations by functional groupings of genes are shown. The text within the cell indicates the Spearman r value. Values in boldface indicate absolute Spearman $r > 0.3$ with nominal statistical significance ($P < .05$). Red shading indicates positive correlations, whereas blue shading indicates negative correlations. *EG*, eosinophilic gastritis; *EGDP*, eosinophilic gastritis diagnostic panel; *EMT*, epithelial-mesenchymal transition.

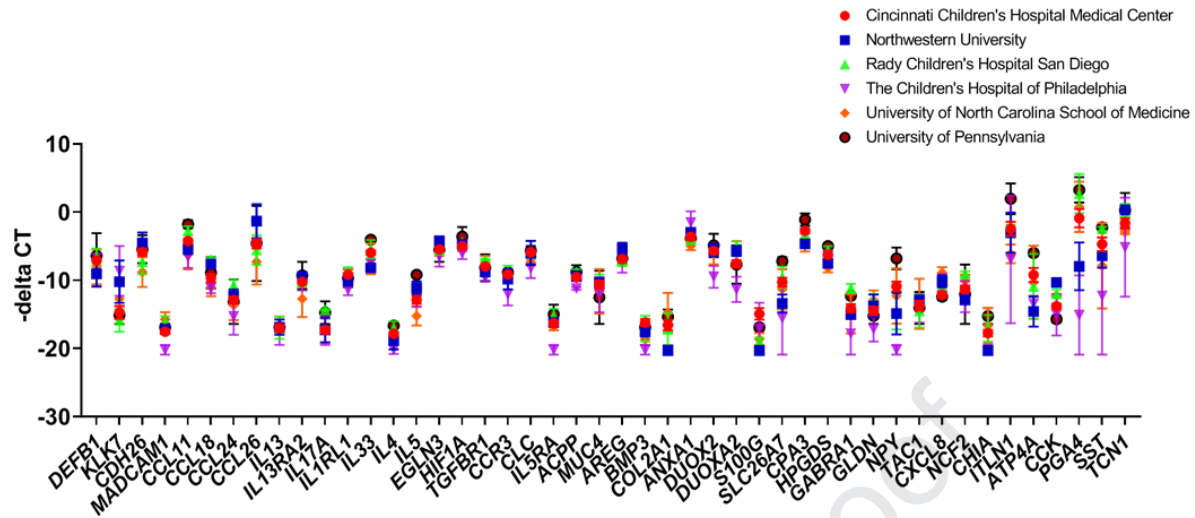
Supplementary Table 7. Circulating biomarker levels of non-EG and active EG groups

	Plasma		Adjusted <i>P</i> value	Serum		Adjusted <i>P</i> value
	Non-EG	Active EG		Non-EG	Active EG	
Eotaxin	629.2 ± 31.2	659.7 ± 76.8	5.2980	169.3 ± 8.0	219.5 ± 25.3	1.5110
Eotaxin-2	1434.2 ± 160.1	1139.1 ± 173.6	9.2383	2644.4 ± 380.9	2721.2 ± 484.8	5.7235
Eotaxin-3	103.6 ± 5.9	481.1 ± 175.6	< 0.0001	23.5 ± 2.4	738.0 ± 543.7	0.0024
IL-13	3.3 ± 0.2	3.7 ± 1	9.7238	3.2 ± 0.3	2.7 ± 0.4	6.4881
IL-1 α	0.1 ± 0	0.1 ± 0.1	7.4777	0.4 ± 0.2	0.1 ± 0.1	0.0688
IL-33	1.9 ± 0.2	3.3 ± 1.1	0.6035	0.9 ± 0.1	3.0 ± 0.9	0.1891
IL-4	0.1 ± 0	0.2 ± 0	3.4244	0.1 ± 0	0.1 ± 0	0.4048
IL-5	0.7 ± 0.1	3.6 ± 1.3	0.0107	0.6 ± 0.1	3.7 ± 1.1	0.0084
TARC	74.1 ± 5.1	135.3 ± 25.8	0.0050	311.4 ± 34.7	603.4 ± 141.3	0.6132
TSLP	4.7 ± 0.3	7.8 ± 2.1	0.8648	3.6 ± 0.3	8.0 ± 0.8	< 0.0001

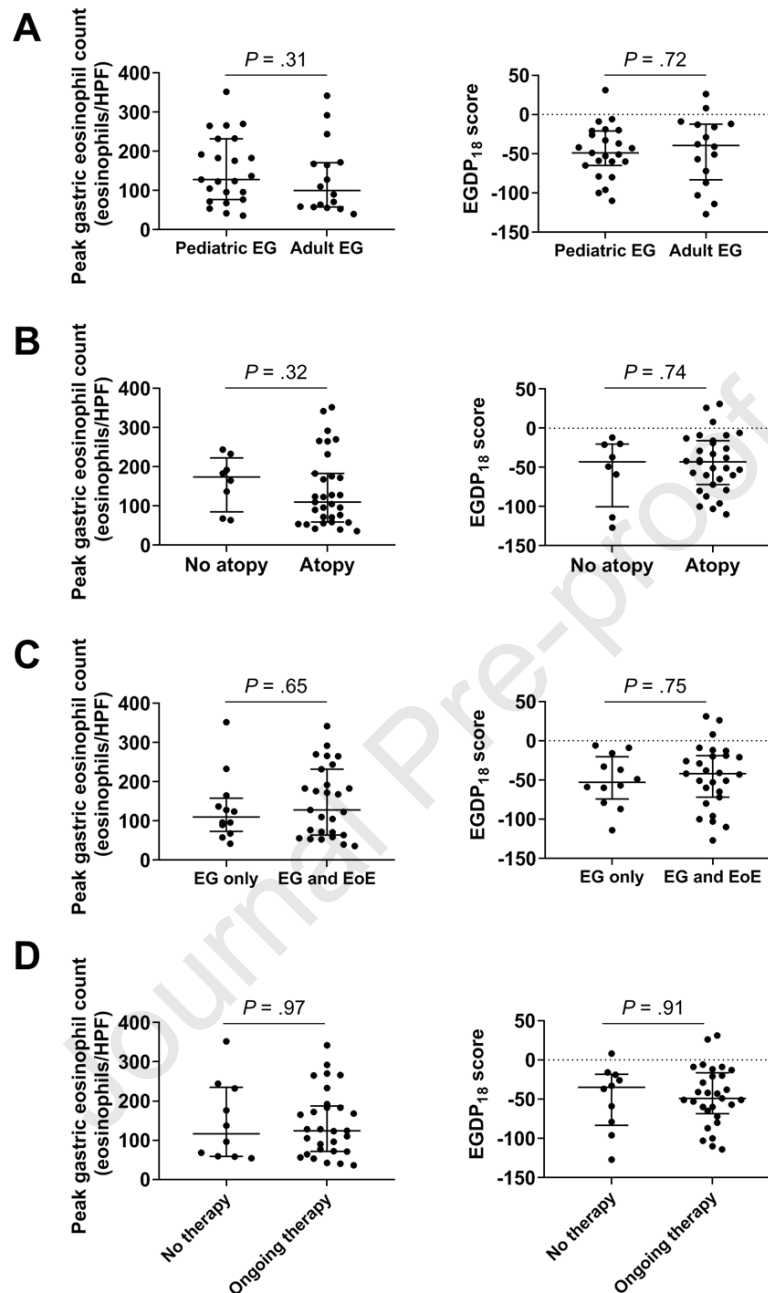
Data are mean ± SEM. *EG*, eosinophilic gastritis; *FDR*, false-discovery rate; *SEM*, standard error of the mean; *TARC*, thymus- and activation-regulated chemokine; *TSLP*, thymic stromal lymphopoietin.



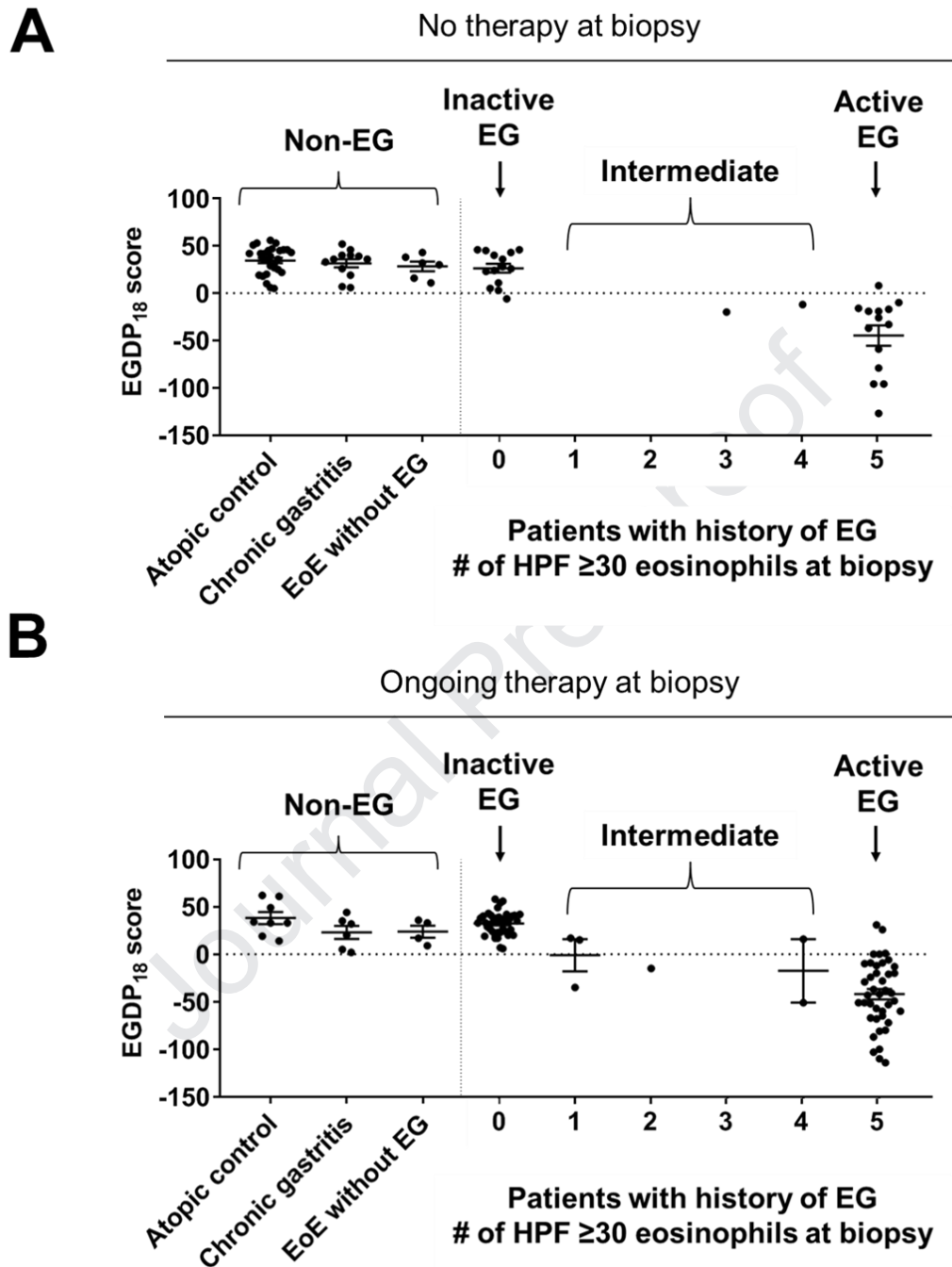
Supplementary Figure 1. Comparison between EG transcriptome genes identified by RNA sequencing and previously published microarray data. Venn diagrams comparing the number of genes identified as dysregulated in EG (FDR $P < .05$, ≥ 2 -fold change) across different studies (A, Microarray_1; B, Microarray_2, upper panels). Spearman correlations comparing fold-change values for the overlapping genes identified as dysregulated by each datasets (A, Microarray_1; B, Microarray_2, lower panels). Microarray_1 was from *J Allergy Clin Immunol.* 2014 and Microarray_2 was from *J Allergy Clin Immunol Pract.* 2017. EG, eosinophilic gastritis; FDR, false-discovery rate.



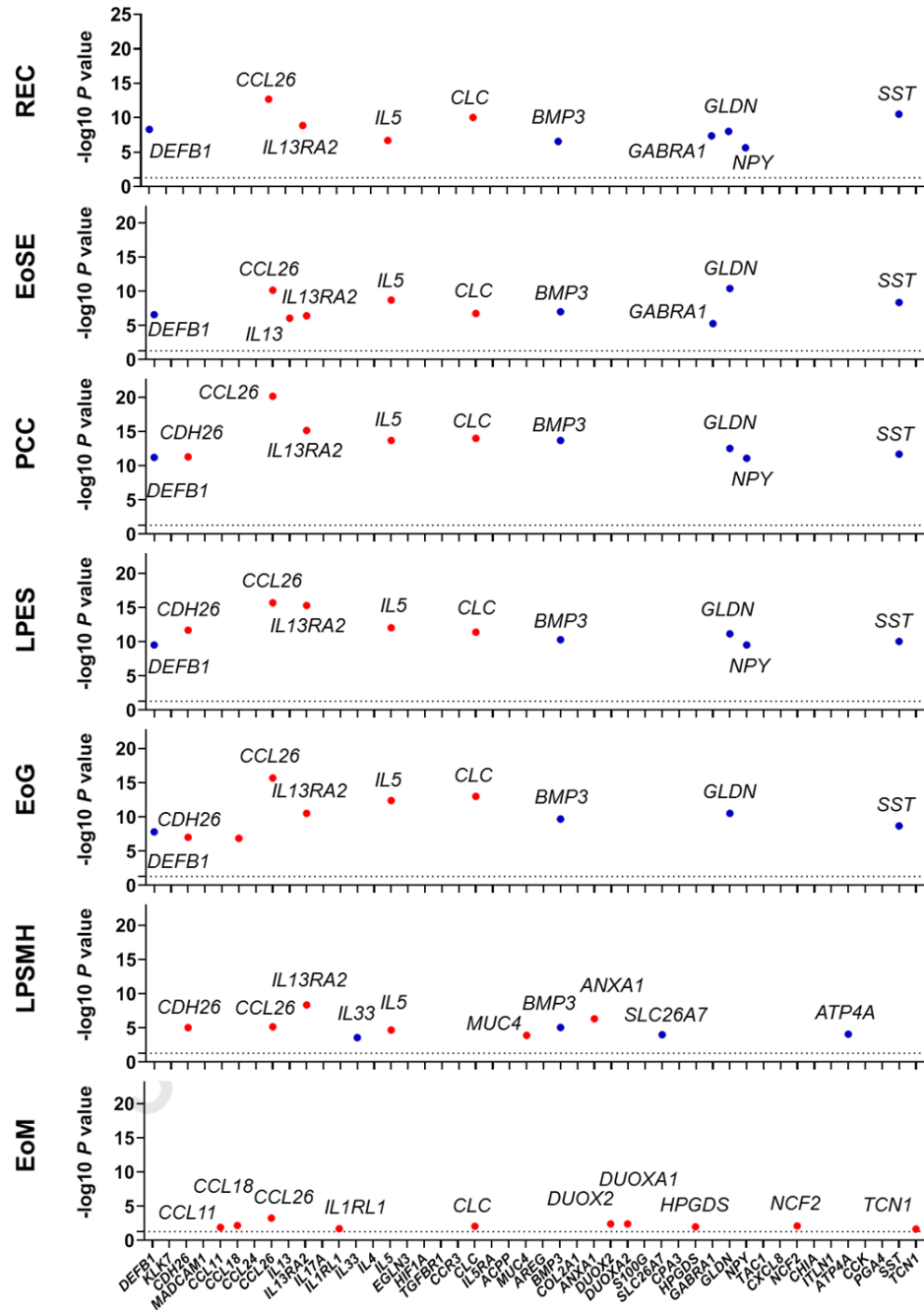
Supplementary Figure 2. EGDP performance across the sites in the discovery cohort. Distributions of individual gene expressions among patients with active EG from various sites were graphed. Data points represent median of subject data by site; error bars show interquartile range. *EG*, eosinophilic gastritis; *EGDP*, eosinophilic gastritis diagnostic panel.



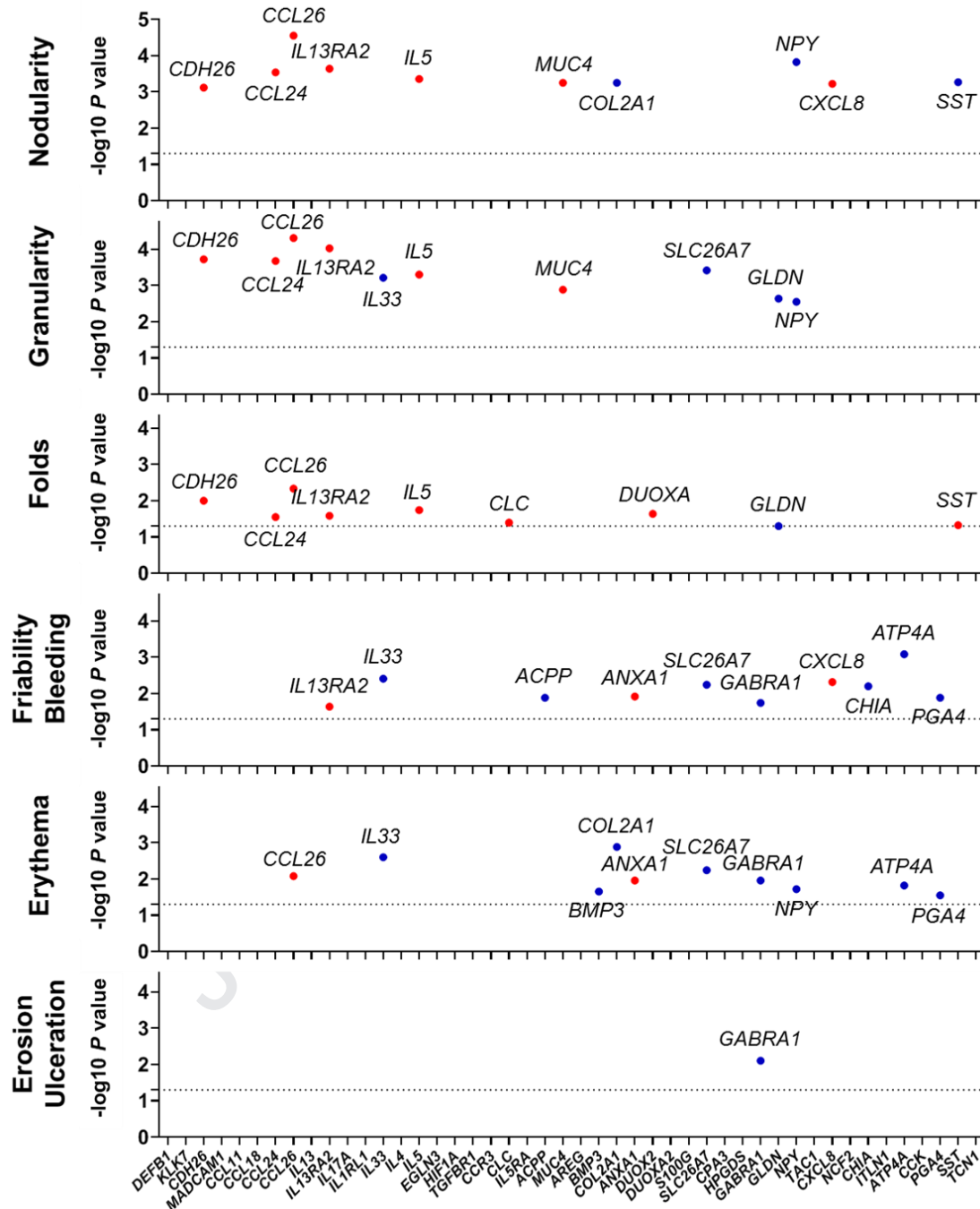
Supplementary Figure 3. Comparison of EGDP₁₈ score across clinically stratified patients with active EG. **A - D**, Comparison of peak gastric eosinophil counts (*left*) among patients with active EG when stratified by clinical characteristics (age, atopic status, co-existence of EoE, and treatment status at biopsy). Comparison of the EGDP₁₈ score (*right*) across age groups (pediatric vs. adult patients) (A), atopic status (atopy vs. no atopy) (B), co-existence of EoE (EG only vs. EG and EoE) (C), and treatment status at biopsy (ongoing therapy including diet and steroids vs. no therapy) (D). Line and error bars show the median and interquartile range, respectively. Data points represent individual subjects. EG, eosinophilic gastritis; EGDP, eosinophilic gastritis diagnostic panel; EoE, eosinophilic esophagitis.



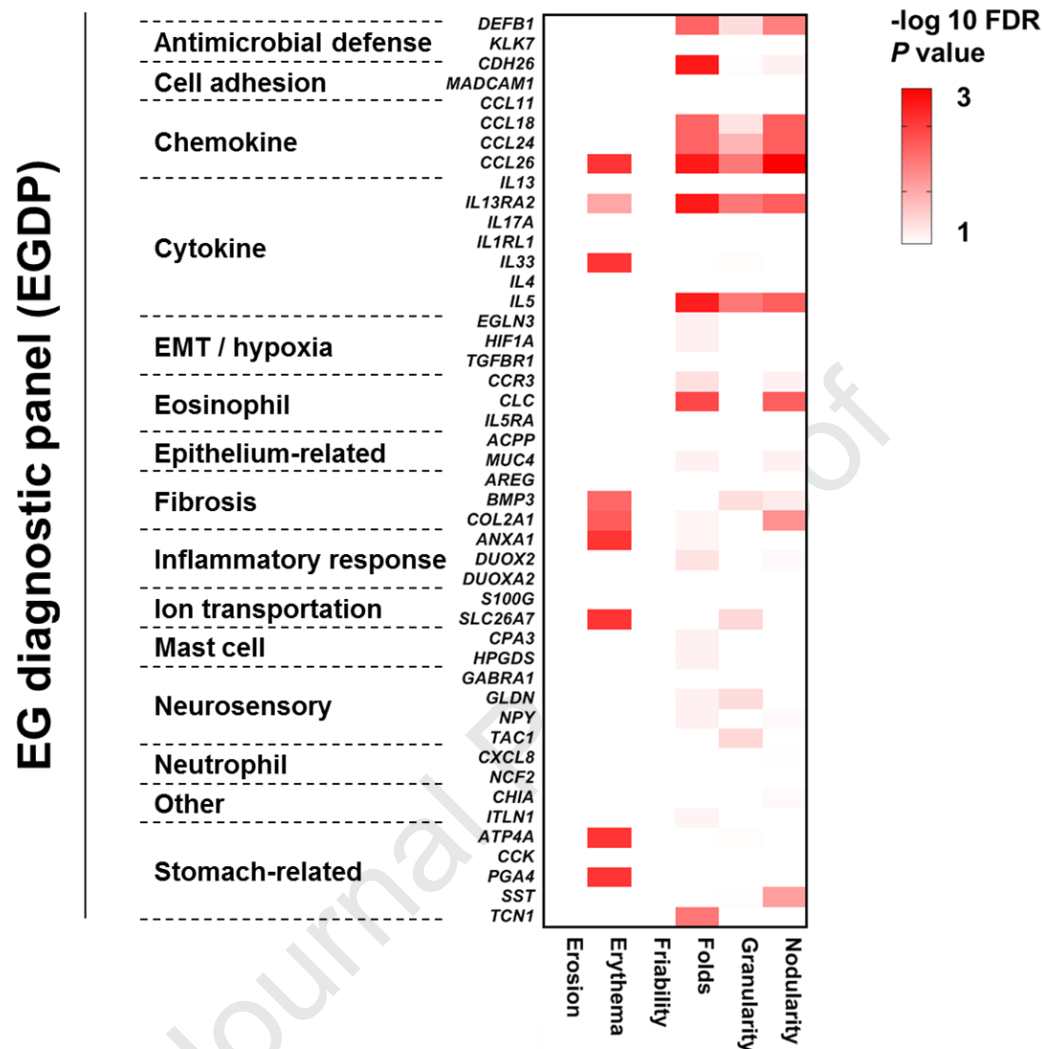
Supplementary Figure 4. EGD₁₈ score as a function of patient groups stratified by the treatment status at biopsy (A, no therapy; B, ongoing therapy). Line and error bars show the median and interquartile range, respectively. Data points represent individual subjects. EG, eosinophilic gastritis; EGD₁₈, eosinophilic gastritis diagnostic panel; EoE, eosinophilic esophagitis.



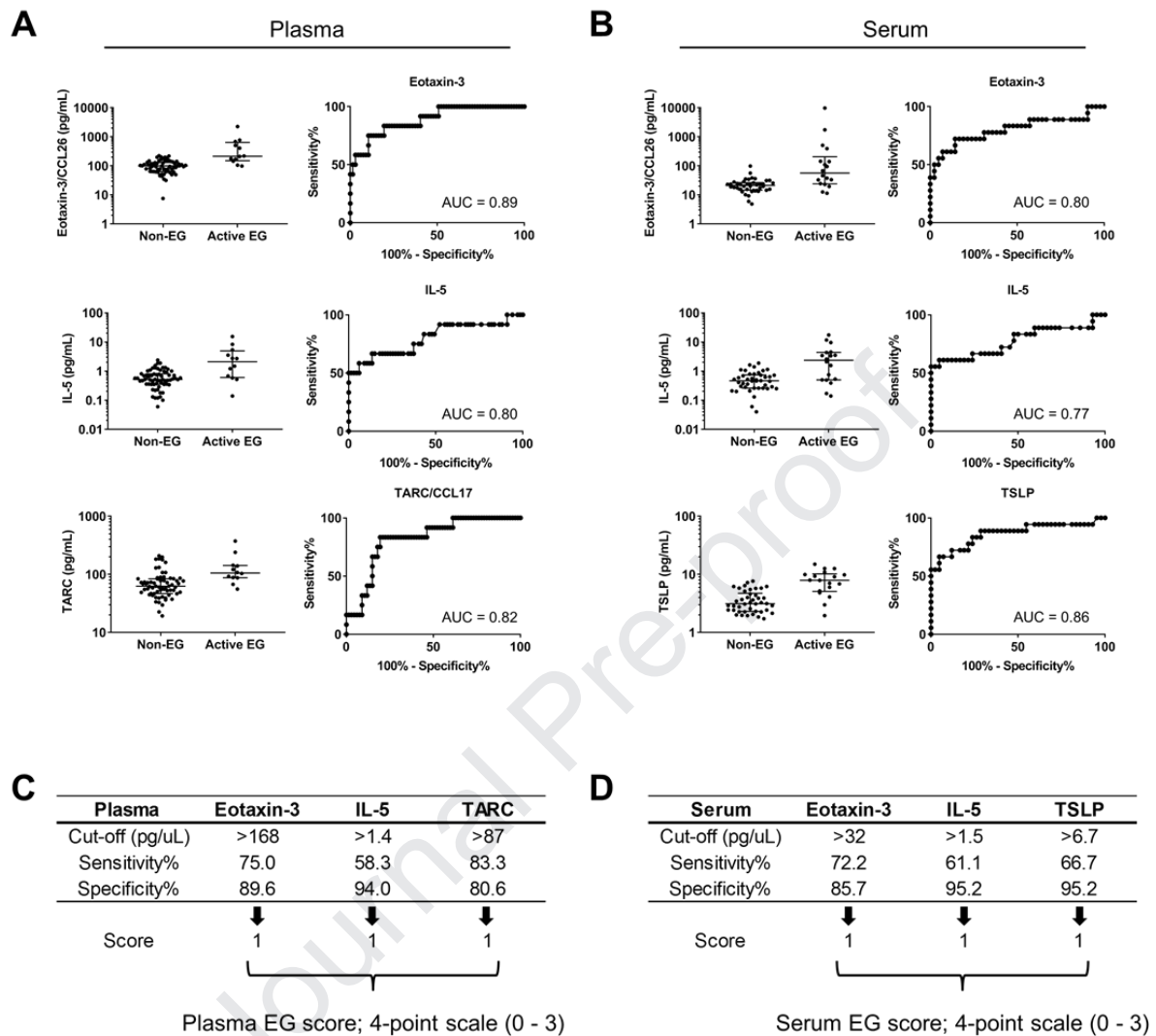
Supplementary Figure 5. Correlations between EG histologic features and a diagnostic subset of the EG transcriptome. The y axis represents the negative log₁₀ P value of the Spearman correlation between 7 eosinophilic gastritis (EG) histologic features and a diagnostic subset of genes from the EG transcriptome (eosinophilic gastritis diagnostic panel [EGDP]). The x axis represents the top 10 genes for each feature ($P < .05$). A red dot indicates a positive correlation, and a blue dot indicates a negative correlation. The dashed line indicates $P < .05$. *EoG*, eosinophil glandulitis; *EoM*, eosinophils in muscularis mucosa; *EoSE*, eosinophils in surface epithelium; *LPES*, lamina propria eosinophil sheets; *LPSMH*, lamina propria smooth muscle hyperplasia; *PCC*, periglandular circumferential collars; *REC*, reactive epithelial changes.



Supplementary Figure 6. Correlations between EG endoscopic features and a diagnostic subset of the EG transcriptome. The y axis represents the negative $\log_{10} P$ value of the Spearman correlation between 6 eosinophilic gastritis (EG) endoscopic features and a diagnostic subset of genes from the EG transcriptome (eosinophilic gastritis diagnostic panel [EGDP]). The x axis represents the top 10 genes for each feature ($P < .05$). A red dot indicates a positive correlation, and a blue dot indicates a negative correlation. The dashed line indicates $P < .05$.



Supplementary Figure 7. Heat map showing $-\log_{10}$ FDR P value determined by differential expression between patients with EG with or without a specific endoscopic feature by the Mann-Whitney U test. A tile is displayed if the FDR P value $< .05$ for each gene in the 46-gene panel (y axis), as distributed among endoscopic features (x axis). The darker the color is, the stronger the differential gene expression. EG, eosinophilic gastritis; EGDP, eosinophilic gastritis diagnostic panel; EMT, epithelial-to-mesenchymal transition; FDR, false-discovery rate.



Supplementary Figure 8. Development of blood EG score based on significantly increased biomarkers. **A** and **B**, Levels of 3 biomarkers between the non-EG patients and patients with EG in the (A) plasma and (B) serum cohort (*left panels*). Line and error bars show the median and interquartile range, respectively. Data points represent individual subjects. ROC curves and performances of each biomarkers in the (A) plasma and (B) serum cohort (*right panels*). **C** and **D**, Scoring systems for plasma (C) and serum (D) established by dysregulated biomarker levels. AUC, area under the curve; EG, eosinophilic gastritis; ROC, receiver operating characteristic.

List of EG transcriptome genes identified by RNA sequencing

Name	Ensembl annotation	Fold change	FDR p-value
<i>CCL26</i>	ENSG00000006606	3590.94	1.00E-15
<i>ITLN1</i>	ENSG00000179914	243.47	1.00E-15
<i>SNORD3D_1</i>	ENSG00000277947	233.86	1.24E-05
<i>SH2D1B</i>	ENSG00000198574	146.87	1.00E-15
<i>LINC02577</i>	ENSG00000228742	133.06	2.94E-09
<i>HSD3B2</i>	ENSG00000203859	116.93	1.00E-15
<i>C8B</i>	ENSG00000021852	110.09	3.47E-05
<i>TREML2</i>	ENSG00000112195	100.99	1.00E-15
<i>TNFRSF6B</i>	ENSG00000243509	77.00	4.65E-04
<i>KLK7</i>	ENSG00000169035	68.34	4.86E-07
<i>CDH26</i>	ENSG00000124215	62.79	1.00E-15
<i>TBC1D3E</i>	ENSG00000278599	56.19	3.47E-03
<i>ADAMTS20</i>	ENSG00000173157	51.27	1.52E-06
<i>SERPINB2</i>	ENSG00000197632	50.92	1.00E-15
<i>ALOX15</i>	ENSG00000161905	48.33	1.00E-15
<i>AC092892.1</i>	ENSG00000242770	47.63	1.31E-07
<i>WDR72</i>	ENSG00000166415	47.08	1.00E-15
<i>AL157815.1</i>	ENSG00000282865	44.51	1.29E-04
<i>AC015563.2</i>	ENSG00000264982	43.97	4.44E-03
<i>AC079062.1</i>	ENSG00000263711	43.39	9.97E-05
<i>PRB1</i>	ENSG00000251655	43.30	8.12E-08
<i>AL159152.1</i>	ENSG00000283097	43.00	4.19E-03
<i>PSG3</i>	ENSG00000221826	42.16	2.30E-03
<i>IL13</i>	ENSG00000169194	41.46	3.19E-07
<i>AL132780.3</i>	ENSG00000259132	40.61	1.00E-02
<i>GPC5</i>	ENSG00000179399	39.06	1.00E-15
<i>MS4A3</i>	ENSG00000149516	38.61	6.18E-05
<i>CLC</i>	ENSG00000105205	37.91	1.00E-15
<i>C4BPA</i>	ENSG00000123838	37.61	2.73E-07
<i>GNAT3</i>	ENSG00000214415	35.76	2.19E-09
<i>CEBPE</i>	ENSG00000092067	35.24	9.18E-11
<i>DUOXA2</i>	ENSG00000140274	31.88	1.00E-15
<i>BPIFB1</i>	ENSG00000125999	31.86	1.00E-15
<i>PADI4</i>	ENSG00000159339	31.43	8.89E-07
<i>AL356118.1</i>	ENSG00000282864	31.30	1.31E-10
<i>VSTM1</i>	ENSG00000189068	30.99	1.54E-07
<i>CCL13</i>	ENSG00000181374	30.89	1.00E-15
<i>PRB2</i>	ENSG00000121335	30.81	2.85E-09
<i>LINC02300</i>	ENSG00000258175	29.94	1.00E-02
<i>PGA4</i>	ENSG00000229183	29.62	1.56E-04
<i>SAA1</i>	ENSG00000173432	28.33	1.37E-06
<i>HIST1H4K</i>	ENSG00000273542	28.17	5.20E-04

<i>GSDMC</i>	ENSG00000147697	27.53	4.18E-10
<i>ADGRG3</i>	ENSG00000182885	26.82	1.00E-15
<i>AC020895.2</i>	ENSG00000280091	26.44	4.85E-06
<i>SNORA50A_2</i>	ENSG00000281910	25.07	5.00E-02
<i>TCN1</i>	ENSG00000134827	24.59	1.00E-15
<i>SLC4A1</i>	ENSG00000004939	24.53	2.40E-04
<i>OLFM4</i>	ENSG00000102837	23.94	1.35E-05
<i>REG1B</i>	ENSG00000172023	23.83	2.81E-03
<i>ADGRG7</i>	ENSG00000144820	23.83	2.25E-05
<i>CCDC190</i>	ENSG00000185860	23.79	1.21E-06
<i>MUC4</i>	ENSG00000145113	23.44	1.00E-15
<i>CCL18</i>	ENSG00000275385	23.04	1.00E-15
<i>LINC02431</i>	ENSG00000248872	22.31	3.31E-04
<i>ADGRE3</i>	ENSG00000131355	21.02	1.00E-15
<i>CCR3</i>	ENSG00000183625	20.03	2.17E-12
<i>LINP1</i>	ENSG00000223784	19.96	1.00E-02
<i>LGALS12</i>	ENSG00000133317	19.88	4.24E-08
<i>LINC02418</i>	ENSG00000214039	19.59	4.26E-05
<i>HBD</i>	ENSG00000223609	19.46	3.35E-05
<i>IL13RA2</i>	ENSG00000123496	19.26	1.00E-15
<i>AC126564.1</i>	ENSG00000280217	19.17	4.00E-02
<i>OLIG2</i>	ENSG00000205927	18.45	3.40E-05
<i>AC016866.3</i>	ENSG00000280335	18.29	2.52E-09
<i>CCL23</i>	ENSG00000274736	17.62	5.84E-05
<i>ADGRE1</i>	ENSG00000174837	17.44	1.00E-15
<i>CASC19</i>	ENSG00000254166	17.40	1.00E-15
<i>SERPINA3</i>	ENSG00000196136	17.35	2.95E-10
<i>HMX3</i>	ENSG00000188620	17.32	4.00E-02
<i>AP001150.1</i>	ENSG00000259541	17.31	7.01E-07
<i>AC016168.3</i>	ENSG00000280122	17.24	8.48E-04
<i>SLC28A3</i>	ENSG00000197506	16.97	1.00E-15
<i>TAT</i>	ENSG00000198650	16.96	9.83E-09
<i>CCDC129</i>	ENSG00000180347	16.95	1.00E-15
<i>AC025278.1</i>	ENSG00000268845	16.55	5.00E-02
<i>OLIG1</i>	ENSG00000184221	16.42	1.51E-04
<i>CHI3L1</i>	ENSG00000133048	16.19	3.31E-09
<i>CCL24</i>	ENSG00000106178	15.88	1.00E-15
<i>AC097478.1</i>	ENSG00000251095	15.83	3.60E-05
<i>DUOX2</i>	ENSG00000140279	15.71	1.00E-15
<i>HRH4</i>	ENSG00000134489	15.56	5.08E-10
<i>PTPRO</i>	ENSG00000151490	15.38	1.00E-15
<i>AB015752.1</i>	ENSG00000254180	15.17	3.00E-02
<i>PI3</i>	ENSG00000124102	14.82	1.38E-12
<i>SAA2</i>	ENSG00000134339	14.52	6.22E-05

<i>HBE1</i>	ENSG00000213931	14.27	2.00E-02
<i>HTR3C</i>	ENSG00000178084	14.26	2.03E-05
<i>GF11B</i>	ENSG00000165702	14.26	1.26E-08
<i>SERPINB4</i>	ENSG00000206073	13.69	3.98E-04
<i>SH2D7</i>	ENSG00000183476	13.68	1.00E-15
<i>LINC01630</i>	ENSG00000227115	13.27	4.49E-03
<i>PSG7</i>	ENSG00000221878	13.24	3.98E-03
<i>AL162456.1</i>	ENSG00000282997	13.01	4.88E-03
<i>TREML4</i>	ENSG00000188056	12.91	2.00E-02
<i>CCDC60</i>	ENSG00000183273	12.75	1.82E-05
<i>LINC02042</i>	ENSG00000240893	12.53	1.74E-03
<i>BMX</i>	ENSG00000102010	12.36	1.00E-15
<i>PIWIL1</i>	ENSG00000125207	12.29	5.44E-06
<i>AP000904.1</i>	ENSG00000273415	12.20	2.00E-02
<i>HKDC1</i>	ENSG00000156510	12.16	4.46E-10
<i>CDH3</i>	ENSG00000062038	11.99	1.00E-15
<i>C6orf58</i>	ENSG00000184530	11.93	8.35E-06
<i>AC139749.1</i>	ENSG00000254872	11.77	1.00E-15
<i>ACTC1</i>	ENSG00000159251	11.68	3.15E-08
<i>NRK</i>	ENSG00000123572	11.64	1.11E-04
<i>AC111000.4</i>	ENSG00000250696	11.62	6.24E-07
<i>PROK1</i>	ENSG00000143125	11.60	1.36E-03
<i>AP005137.2</i>	ENSG00000272703	11.57	1.66E-03
<i>AC012321.1</i>	ENSG00000260772	11.40	8.33E-04
<i>CELA1</i>	ENSG00000139610	11.34	5.00E-02
<i>TBC1D3C</i>	ENSG00000278299	11.25	2.55E-03
<i>SLCO1B3</i>	ENSG00000111700	10.92	1.00E-02
<i>AMY1C</i>	ENSG00000187733	10.75	4.00E-02
<i>CCK</i>	ENSG00000187094	10.63	1.48E-09
<i>HTR3E</i>	ENSG00000186038	10.45	7.43E-11
<i>AC097478.3</i>	ENSG00000276542	10.29	1.00E-02
<i>LINC02073</i>	ENSG00000267452	10.11	2.89E-03
<i>WFDC21P</i>	ENSG00000261040	10.06	1.48E-08
<i>AL034397.3</i>	ENSG00000274536	10.00	7.24E-11
<i>UCN2</i>	ENSG00000145040	9.85	4.00E-02
<i>PRSS33</i>	ENSG00000103355	9.84	6.60E-05
<i>ABCA12</i>	ENSG00000144452	9.81	4.82E-05
<i>KRT2</i>	ENSG00000172867	9.75	2.00E-02
<i>HK3</i>	ENSG00000160883	9.56	6.65E-13
<i>CLEC4G</i>	ENSG00000182566	9.49	4.73E-06
<i>ALKAL1</i>	ENSG00000196711	9.36	1.74E-03
<i>AL355916.1</i>	ENSG00000250548	9.31	2.16E-06
<i>CHAT</i>	ENSG00000070748	9.28	7.26E-03
<i>LY6D</i>	ENSG00000167656	9.26	1.00E-02

<i>ERBB4</i>	ENSG00000178568	9.18	1.72E-06
<i>MUC5B</i>	ENSG00000117983	9.17	1.98E-13
<i>DDX53</i>	ENSG00000184735	9.16	4.03E-03
<i>NLRP12</i>	ENSG00000142405	9.14	5.41E-05
<i>C6orf223</i>	ENSG00000181577	9.08	3.01E-06
<i>TRPM5</i>	ENSG00000070985	9.08	2.91E-13
<i>PRSS2</i>	ENSG00000275896	8.87	6.13E-03
<i>ALAS2</i>	ENSG00000158578	8.77	2.10E-03
<i>CT83</i>	ENSG00000204019	8.76	3.00E-02
<i>ZPLD1</i>	ENSG00000170044	8.75	1.00E-04
<i>SFTPA2</i>	ENSG00000185303	8.67	1.00E-02
<i>AL583785.1</i>	ENSG00000226197	8.64	3.23E-03
<i>NFE2</i>	ENSG00000123405	8.58	4.37E-07
<i>CD200R1L</i>	ENSG00000206531	8.44	3.00E-02
<i>UNC5D</i>	ENSG00000156687	8.43	5.32E-10
<i>LTF</i>	ENSG00000012223	8.40	2.12E-07
<i>CHURC1-FNTB</i>	ENSG00000125954	8.37	3.00E-02
<i>TRIM15</i>	ENSG00000204610	8.35	4.21E-11
<i>AMY2A</i>	ENSG00000243480	8.29	2.00E-02
<i>GABRA4</i>	ENSG00000109158	8.21	7.19E-08
<i>PSG1</i>	ENSG00000231924	8.16	8.32E-04
<i>VNN3</i>	ENSG00000093134	8.11	9.89E-05
<i>AL158064.2</i>	ENSG00000284196	8.09	2.00E-02
<i>AL033397.1</i>	ENSG00000231683	8.05	1.00E-02
<i>OR52K1</i>	ENSG00000196778	7.97	7.04E-03
<i>PLA2G2A</i>	ENSG00000188257	7.96	2.37E-03
<i>WFDC2</i>	ENSG00000101443	7.89	1.00E-15
<i>ANXA13</i>	ENSG00000104537	7.82	1.18E-09
<i>GUCA1A</i>	ENSG00000048545	7.81	5.76E-03
<i>TRIM7</i>	ENSG00000146054	7.65	1.48E-11
<i>AC243829.4</i>	ENSG00000277089	7.53	4.28E-05
<i>C8A</i>	ENSG00000157131	7.50	2.56E-06
<i>MMP12</i>	ENSG00000262406	7.48	3.80E-06
<i>PSG5</i>	ENSG00000204941	7.46	3.00E-02
<i>PSG8</i>	ENSG00000124467	7.39	8.81E-03
<i>LINC00443</i>	ENSG00000230156	7.34	2.67E-04
<i>RNU5F-1</i>	ENSG00000199377	7.32	1.89E-04
<i>RNASE2</i>	ENSG00000169385	7.31	1.00E-02
<i>CAPN14</i>	ENSG00000214711	7.29	2.00E-02
<i>AC011511.5</i>	ENSG00000267607	7.29	5.00E-02
<i>C1QTNF1-AS1</i>	ENSG00000265096	7.28	4.00E-02
<i>RNU5A-8P</i>	ENSG00000200972	7.25	9.86E-04
<i>SPSB4</i>	ENSG00000175093	7.24	3.50E-03
<i>C1QTNF1</i>	ENSG00000173918	7.21	1.00E-15

<i>MLC1</i>	ENSG00000100427	7.21	1.40E-07
<i>IL19</i>	ENSG00000142224	7.09	4.77E-05
<i>HRK</i>	ENSG00000135116	7.03	5.47E-03
<i>PSG6</i>	ENSG00000170848	6.92	7.74E-03
<i>AC090753.1</i>	ENSG00000254000	6.91	4.83E-04
<i>LIPG</i>	ENSG00000101670	6.91	1.00E-15
<i>AC009163.2</i>	ENSG00000260092	6.88	5.27E-06
<i>AC079298.2</i>	ENSG00000280005	6.85	2.00E-02
<i>DSCAM</i>	ENSG00000171587	6.83	3.63E-03
<i>GLB1L3</i>	ENSG00000166105	6.79	3.59E-05
<i>SHD</i>	ENSG00000105251	6.79	1.00E-02
<i>AC025524.2</i>	ENSG00000254119	6.73	2.00E-02
<i>AL359095.1</i>	ENSG00000230001	6.69	2.81E-05
<i>CTRB2</i>	ENSG00000168928	6.69	4.00E-02
<i>AL049839.2</i>	ENSG00000273259	6.63	2.00E-02
<i>AC044839.2</i>	ENSG00000255226	6.51	2.00E-02
<i>EGLN3</i>	ENSG00000129521	6.51	1.00E-15
<i>CLDN2</i>	ENSG00000165376	6.49	5.58E-06
<i>LINC02009</i>	ENSG00000283646	6.43	2.72E-07
<i>CXCL5</i>	ENSG00000163735	6.42	1.92E-03
<i>HIF1A-AS2</i>	ENSG00000258667	6.36	6.56E-05
<i>GCGR</i>	ENSG00000215644	6.36	2.00E-02
<i>SH2D6</i>	ENSG00000152292	6.12	3.21E-11
<i>RN7SKP266</i>	ENSG00000222164	6.11	4.00E-02
<i>L1TD1</i>	ENSG00000240563	6.09	1.00E-02
<i>AC078789.1</i>	ENSG00000257880	6.06	1.00E-02
<i>RETREG1</i>	ENSG00000154153	6.05	1.00E-15
<i>LINC01235</i>	ENSG00000270547	6.05	2.69E-04
<i>AC108463.3</i>	ENSG00000271590	6.04	2.67E-03
<i>NPTX1</i>	ENSG00000171246	6.00	7.03E-04
<i>AP000873.3</i>	ENSG00000254551	5.99	2.00E-02
<i>ST3GAL4</i>	ENSG00000110080	5.91	1.00E-15
<i>AC011389.3</i>	ENSG00000279752	5.85	3.00E-02
<i>AL031283.3</i>	ENSG00000236045	5.84	6.30E-05
<i>SELP</i>	ENSG00000174175	5.80	1.00E-15
<i>CAPN13</i>	ENSG00000162949	5.80	1.00E-15
<i>HBA1</i>	ENSG00000206172	5.77	2.19E-03
<i>HPDL</i>	ENSG00000186603	5.74	1.00E-15
<i>CD300LF</i>	ENSG00000186074	5.74	3.41E-07
<i>SEMG1</i>	ENSG00000124233	5.71	4.00E-02
<i>KCNE1</i>	ENSG00000180509	5.70	3.93E-05
<i>GP2</i>	ENSG00000169347	5.69	1.48E-05
<i>UTS2</i>	ENSG00000049247	5.68	9.25E-03
<i>LINC01665</i>	ENSG00000235343	5.65	6.90E-03

<i>ANXA1</i>	ENSG00000135046	5.62	1.95E-12
<i>EREG</i>	ENSG00000124882	5.61	2.71E-04
<i>RGS13</i>	ENSG00000127074	5.60	5.05E-11
<i>KYAT1</i>	ENSG00000171097	5.55	1.00E-15
<i>ADAMDEC1</i>	ENSG00000134028	5.53	2.12E-09
<i>TMIGD3</i>	ENSG00000121933	5.51	1.29E-06
<i>IL11</i>	ENSG00000095752	5.51	1.00E-02
<i>SLC9B2</i>	ENSG00000164038	5.49	1.00E-15
<i>RAB44</i>	ENSG00000255587	5.49	1.17E-06
<i>MDFI</i>	ENSG00000112559	5.48	2.59E-07
<i>TNFRSF10C</i>	ENSG00000173535	5.45	1.76E-06
<i>CRISP2</i>	ENSG00000124490	5.39	3.00E-02
<i>HPR</i>	ENSG00000261701	5.30	4.53E-03
<i>NCF2</i>	ENSG00000116701	5.28	5.43E-11
<i>GAPT</i>	ENSG00000175857	5.26	1.08E-06
<i>FAM155A-IT1</i>	ENSG00000227248	5.23	2.00E-02
<i>PLA2G3</i>	ENSG00000100078	5.22	7.14E-06
<i>GCNT3</i>	ENSG00000140297	5.20	1.00E-15
<i>HDAC9</i>	ENSG00000048052	5.18	1.45E-09
<i>CD300LB</i>	ENSG00000178789	5.17	1.23E-05
<i>AC068491.3</i>	ENSG00000270190	5.13	3.00E-02
<i>DAB1</i>	ENSG00000173406	5.10	5.43E-07
<i>SNCA</i>	ENSG00000145335	5.10	4.74E-06
<i>CLNK</i>	ENSG00000109684	5.08	9.84E-09
<i>RN7SL471P</i>	ENSG00000263426	5.08	2.09E-03
<i>IL1RL1</i>	ENSG00000115602	5.04	1.88E-10
<i>CHST6</i>	ENSG00000183196	5.02	1.84E-03
<i>AL162727.1</i>	ENSG00000233817	5.01	2.00E-02
<i>CHST5</i>	ENSG00000135702	5.01	1.65E-08
<i>RHOXF2B</i>	ENSG00000203989	5.01	3.00E-02
<i>HOXB7</i>	ENSG00000260027	4.94	1.65E-03
<i>AC084048.1</i>	ENSG00000249334	4.93	2.00E-02
<i>DLGAP1-AS5</i>	ENSG00000261520	4.93	4.36E-03
<i>CFI</i>	ENSG00000205403	4.92	9.08E-09
<i>CP</i>	ENSG00000047457	4.91	4.06E-06
<i>GATA1</i>	ENSG00000102145	4.90	1.00E-02
<i>RNU5E-1</i>	ENSG00000199347	4.89	2.00E-02
<i>AL355312.3</i>	ENSG00000273132	4.89	7.43E-04
<i>ALDH1A2</i>	ENSG00000128918	4.89	1.79E-05
<i>ACOXL</i>	ENSG00000153093	4.88	1.00E-02
<i>SRARP</i>	ENSG00000183888	4.87	2.00E-02
<i>SMIM33</i>	ENSG00000283288	4.85	6.98E-05
<i>IL5RA</i>	ENSG00000091181	4.84	4.38E-07
<i>INO80C</i>	ENSG00000153391	4.78	1.00E-15

<i>ALDH3B2</i>	ENSG00000132746	4.77	5.23E-03
<i>ITGA2B</i>	ENSG00000005961	4.76	1.13E-03
<i>ADH6</i>	ENSG00000172955	4.75	9.04E-08
<i>STAB2</i>	ENSG00000136011	4.74	1.56E-04
<i>CD274</i>	ENSG00000120217	4.72	1.17E-12
<i>SLC6A14</i>	ENSG00000268104	4.64	7.95E-07
<i>TRIM10</i>	ENSG00000204613	4.63	2.47E-05
<i>TNS4</i>	ENSG00000131746	4.63	1.37E-07
<i>CXCL8</i>	ENSG00000169429	4.62	1.00E-02
<i>AL603840.1</i>	ENSG00000234810	4.61	3.51E-03
<i>AC011603.2</i>	ENSG00000258017	4.60	4.06E-03
<i>HCK</i>	ENSG00000101336	4.58	3.57E-12
<i>RD3</i>	ENSG00000198570	4.56	2.00E-02
<i>CLDN4</i>	ENSG00000189143	4.54	6.41E-06
<i>AREG</i>	ENSG00000109321	4.53	4.28E-05
<i>DCLK3</i>	ENSG00000163673	4.52	5.00E-02
<i>CD55</i>	ENSG00000196352	4.50	1.00E-15
<i>AC007998.5</i>	ENSG00000279074	4.50	5.80E-03
<i>AC013549.2</i>	ENSG00000254688	4.49	5.00E-02
<i>ST3GAL6</i>	ENSG00000064225	4.47	1.00E-15
<i>TNFSF11</i>	ENSG00000120659	4.47	2.22E-03
<i>SLC28A2</i>	ENSG00000137860	4.47	3.30E-04
<i>AL138752.2</i>	ENSG00000255872	4.45	3.00E-02
<i>GLYATL2</i>	ENSG00000156689	4.45	2.00E-02
<i>LINC01013</i>	ENSG00000228495	4.44	2.85E-03
<i>INHBA</i>	ENSG00000122641	4.43	9.45E-05
<i>FAM95C</i>	ENSG00000283486	4.42	2.92E-10
<i>GPR87</i>	ENSG00000138271	4.41	2.00E-02
<i>MMP1</i>	ENSG00000196611	4.40	5.43E-11
<i>RN7SL449P</i>	ENSG00000242889	4.38	2.00E-02
<i>NOXO1</i>	ENSG00000196408	4.37	1.00E-02
<i>NABP1</i>	ENSG00000173559	4.34	1.32E-12
<i>AC004990.1</i>	ENSG00000232756	4.34	1.00E-02
<i>PKHD1L1</i>	ENSG00000205038	4.34	2.44E-07
<i>AC007906.2</i>	ENSG00000277639	4.31	1.15E-05
<i>FGFBP1</i>	ENSG00000137440	4.26	2.62E-03
<i>CDA</i>	ENSG00000158825	4.25	2.00E-02
<i>FAM3D</i>	ENSG00000198643	4.22	4.10E-11
<i>UPP1</i>	ENSG00000183696	4.22	1.75E-10
<i>AP001453.2</i>	ENSG00000256940	4.22	4.47E-04
<i>CALHM1</i>	ENSG00000185933	4.21	2.00E-02
<i>LCN2</i>	ENSG00000148346	4.19	4.33E-06
<i>AL390726.3</i>	ENSG00000272904	4.18	1.42E-04
<i>RNU5E-6P</i>	ENSG00000202444	4.16	2.00E-02

<i>ADGRF4</i>	ENSG00000153294	4.15	2.00E-02
<i>AP005131.2</i>	ENSG00000267366	4.11	1.88E-03
<i>LINC00839</i>	ENSG00000185904	4.10	4.00E-02
<i>SIGLEC10</i>	ENSG00000142512	4.10	1.65E-05
<i>AVIL</i>	ENSG00000135407	4.07	2.50E-12
<i>CXCR2</i>	ENSG00000180871	4.06	1.60E-03
<i>FCGBP</i>	ENSG00000275395	4.03	1.42E-08
<i>UGT2B11</i>	ENSG00000213759	3.99	2.00E-02
<i>CLDN7</i>	ENSG00000181885	3.97	1.79E-05
<i>AC007998.3</i>	ENSG00000267583	3.97	1.00E-02
<i>AC017002.3</i>	ENSG00000240350	3.96	4.00E-03
<i>CEACAM6</i>	ENSG00000086548	3.96	5.64E-05
<i>LRRC4</i>	ENSG00000128594	3.94	4.35E-08
<i>AC008149.1</i>	ENSG00000258177	3.93	4.00E-02
<i>HPGDS</i>	ENSG00000163106	3.92	1.03E-09
<i>AC026740.1</i>	ENSG00000271781	3.92	3.41E-03
<i>OR2AG2</i>	ENSG00000188124	3.92	2.00E-02
<i>AP005131.7</i>	ENSG00000272746	3.91	2.43E-04
<i>HIST1H1A</i>	ENSG00000124610	3.90	8.61E-06
<i>NOTUM</i>	ENSG00000185269	3.90	2.00E-02
<i>SIRPB1</i>	ENSG00000101307	3.88	7.92E-03
<i>LINC00342</i>	ENSG00000232931	3.87	3.71E-05
<i>HRASLS</i>	ENSG00000127252	3.87	2.00E-02
<i>MFSD2A</i>	ENSG00000168389	3.85	2.72E-05
<i>PTCHD1</i>	ENSG00000165186	3.79	5.12E-03
<i>AC004009.3</i>	ENSG00000279655	3.77	2.00E-02
<i>STAC</i>	ENSG00000144681	3.76	1.00E-02
<i>TPO</i>	ENSG00000115705	3.73	4.60E-04
<i>FAP</i>	ENSG00000078098	3.73	6.08E-04
<i>SERPINA1</i>	ENSG00000197249	3.69	9.76E-06
<i>PIK3R6</i>	ENSG00000276231	3.67	5.30E-05
<i>CD101</i>	ENSG00000134256	3.64	4.23E-05
<i>GPAT3</i>	ENSG00000138678	3.63	5.43E-11
<i>AC005725.1</i>	ENSG00000264727	3.63	3.60E-05
<i>AP000547.3</i>	ENSG00000283633	3.63	1.90E-04
<i>CD1A</i>	ENSG00000158477	3.62	2.03E-03
<i>FMO3</i>	ENSG00000007933	3.62	3.62E-04
<i>ZNF385D</i>	ENSG00000151789	3.62	5.04E-05
<i>SOCS3</i>	ENSG00000184557	3.62	1.49E-07
<i>SIGLEC8</i>	ENSG00000105366	3.62	2.80E-04
<i>FOSB</i>	ENSG00000125740	3.61	3.00E-02
<i>ADGRE2</i>	ENSG00000127507	3.60	1.64E-06
<i>WISP1</i>	ENSG00000104415	3.59	4.70E-04
<i>MELTF</i>	ENSG00000163975	3.57	6.15E-07

<i>PSTPIP2</i>	ENSG00000152229	3.57	3.79E-07
<i>ANKRD18A</i>	ENSG00000180071	3.56	2.03E-09
<i>F3</i>	ENSG00000117525	3.54	9.18E-11
<i>AC051619.5</i>	ENSG00000259520	3.52	5.09E-03
<i>APOL1</i>	ENSG00000100342	3.52	1.18E-09
<i>RN7SL3</i>	ENSG00000278771	3.50	5.70E-12
<i>AC007319.1</i>	ENSG00000224063	3.49	1.33E-03
<i>ENKUR</i>	ENSG00000151023	3.49	4.39E-04
<i>PYGL</i>	ENSG00000100504	3.47	1.25E-06
<i>SOCS1</i>	ENSG00000185338	3.47	1.14E-03
<i>AL031283.2</i>	ENSG00000233485	3.45	1.00E-02
<i>PCSK9</i>	ENSG00000169174	3.45	1.00E-02
<i>LIF</i>	ENSG00000128342	3.45	1.97E-06
<i>SLC5A1</i>	ENSG00000100170	3.44	2.56E-06
<i>AC021483.1</i>	ENSG00000259548	3.43	3.42E-03
<i>MIR3142HG</i>	ENSG00000253522	3.42	6.69E-03
<i>CRYBG2</i>	ENSG00000176092	3.41	1.69E-04
<i>PHEX</i>	ENSG00000102174	3.41	8.88E-03
<i>SMIM25</i>	ENSG00000224397	3.40	3.00E-02
<i>NTRK1</i>	ENSG00000198400	3.39	1.31E-03
<i>NWD2</i>	ENSG00000174145	3.38	1.00E-02
<i>AL512306.2</i>	ENSG00000240219	3.36	6.57E-03
<i>AC099329.1</i>	ENSG00000235288	3.36	2.00E-02
<i>SPP1</i>	ENSG00000118785	3.36	7.42E-03
<i>RAPSN</i>	ENSG00000165917	3.36	4.00E-02
<i>ADAMTS18</i>	ENSG00000140873	3.36	2.00E-02
<i>CYSLTR2</i>	ENSG00000152207	3.35	3.03E-03
<i>AP000688.2</i>	ENSG00000233393	3.35	1.00E-02
<i>PLEKHS1</i>	ENSG00000148735	3.34	5.04E-04
<i>CATSPERB</i>	ENSG00000133962	3.34	2.18E-07
<i>HIF1A</i>	ENSG00000100644	3.33	9.14E-13
<i>ST3GAL6-AS1</i>	ENSG00000239445	3.32	1.00E-02
<i>MUC17</i>	ENSG00000169876	3.32	9.78E-03
<i>FPR1</i>	ENSG00000171051	3.32	1.00E-02
<i>FCAMR</i>	ENSG00000162897	3.31	2.00E-02
<i>TRABD2A</i>	ENSG00000186854	3.29	8.68E-04
<i>AC021683.2</i>	ENSG00000267506	3.29	2.00E-02
<i>AP005131.1</i>	ENSG00000267136	3.28	1.46E-04
<i>AL133373.2</i>	ENSG00000279286	3.26	1.00E-02
<i>TIMP1</i>	ENSG00000102265	3.25	9.18E-11
<i>ANKRD36C</i>	ENSG00000174501	3.24	9.38E-05
<i>SMIM31</i>	ENSG00000248771	3.24	9.51E-03
<i>TCTEX1D1</i>	ENSG00000152760	3.23	1.00E-02
<i>AC068491.4</i>	ENSG00000279191	3.21	1.39E-03

<i>PCDH7</i>	ENSG00000169851	3.21	1.54E-05
<i>PIGR</i>	ENSG00000162896	3.19	2.27E-08
<i>PDZK1IP1</i>	ENSG00000162366	3.18	1.19E-10
<i>AP005131.4</i>	ENSG00000267529	3.18	4.51E-03
<i>CR1</i>	ENSG00000203710	3.17	1.00E-02
<i>GLIS3</i>	ENSG00000107249	3.16	3.56E-10
<i>GAREM2</i>	ENSG00000157833	3.15	6.72E-05
<i>AC083949.1</i>	ENSG00000224875	3.15	4.63E-03
<i>CDX1</i>	ENSG00000113722	3.15	4.00E-02
<i>LAMC2</i>	ENSG00000058085	3.14	2.70E-10
<i>GABRR2</i>	ENSG00000111886	3.14	1.00E-02
<i>OIT3</i>	ENSG00000138315	3.14	1.07E-03
<i>AC007614.6</i>	ENSG00000280189	3.14	5.00E-02
<i>ANGPTL4</i>	ENSG00000167772	3.14	6.97E-04
<i>FFAR2</i>	ENSG00000126262	3.14	2.55E-03
<i>KRT80</i>	ENSG00000167767	3.13	4.00E-02
<i>SPIB</i>	ENSG00000269404	3.13	2.00E-02
<i>TFAP2C</i>	ENSG00000087510	3.13	2.54E-03
<i>CACNB4</i>	ENSG00000182389	3.12	1.24E-03
<i>TFPI</i>	ENSG00000003436	3.12	5.06E-10
<i>S100A10</i>	ENSG00000197747	3.10	9.89E-08
<i>AC003991.1</i>	ENSG00000228113	3.10	2.00E-02
<i>FUT6</i>	ENSG00000156413	3.10	3.18E-03
<i>LINC00639</i>	ENSG00000259070	3.07	2.00E-02
<i>AL512662.2</i>	ENSG00000283913	3.06	2.00E-02
<i>LDLRAD4-AS1</i>	ENSG00000267690	3.06	4.00E-02
<i>ACPP</i>	ENSG00000014257	3.05	4.64E-07
<i>PTAFR</i>	ENSG00000169403	3.01	1.54E-08
<i>MALL</i>	ENSG00000144063	3.01	6.06E-05
<i>FAM124B</i>	ENSG00000124019	3.01	4.42E-03
<i>CXCL1</i>	ENSG00000163739	3.01	7.95E-03
<i>AMOT</i>	ENSG00000126016	3.01	3.94E-09
<i>F12</i>	ENSG00000131187	3.00	2.00E-02
<i>CLRN3</i>	ENSG00000180745	3.00	8.75E-04
<i>OSCAR</i>	ENSG00000170909	2.99	5.00E-02
<i>AOC1</i>	ENSG00000002726	2.96	1.25E-05
<i>COL17A1</i>	ENSG00000065618	2.96	1.23E-05
<i>CPXM2</i>	ENSG00000121898	2.96	4.78E-04
<i>MADCAM1</i>	ENSG00000099866	2.96	1.00E-02
<i>COCH</i>	ENSG00000100473	2.95	6.15E-04
<i>GRHL3</i>	ENSG00000158055	2.93	1.31E-03
<i>HS3ST1</i>	ENSG00000002587	2.92	2.92E-09
<i>PIK3CG</i>	ENSG00000105851	2.92	1.29E-06
<i>AADAC</i>	ENSG00000114771	2.90	4.30E-08

<i>GRM8</i>	ENSG00000179603	2.90	2.00E-02
<i>AK8</i>	ENSG00000165695	2.89	6.29E-04
<i>AC108134.3</i>	ENSG00000262370	2.89	1.00E-02
<i>SIPA1L2</i>	ENSG00000116991	2.88	8.00E-10
<i>KRT15</i>	ENSG00000171346	2.88	2.07E-03
<i>ADAM23</i>	ENSG00000114948	2.86	3.36E-04
<i>COL23A1</i>	ENSG00000050767	2.86	8.57E-04
<i>CD9</i>	ENSG00000010278	2.86	5.06E-10
<i>DUOXA1</i>	ENSG00000140254	2.86	2.20E-03
<i>SLC6A8</i>	ENSG00000130821	2.85	1.89E-04
<i>DPEP2</i>	ENSG00000167261	2.83	2.07E-03
<i>AP003355.2</i>	ENSG00000272321	2.81	4.00E-02
<i>ZG16B</i>	ENSG00000162078	2.81	2.81E-05
<i>PLCG2</i>	ENSG00000197943	2.81	8.89E-09
<i>SNTG2</i>	ENSG00000172554	2.80	2.00E-02
<i>LST1</i>	ENSG00000204482	2.80	4.80E-03
<i>CPZ</i>	ENSG00000109625	2.79	3.00E-02
<i>AC015871.4</i>	ENSG00000279394	2.79	7.72E-04
<i>LRP8</i>	ENSG00000157193	2.78	1.36E-03
<i>AC017002.1</i>	ENSG00000224959	2.78	2.00E-02
<i>TNC</i>	ENSG00000041982	2.78	3.48E-07
<i>TFF3</i>	ENSG00000160180	2.78	4.00E-02
<i>TREM2</i>	ENSG00000095970	2.77	1.00E-02
<i>MMP13</i>	ENSG00000137745	2.77	3.00E-02
<i>HCN4</i>	ENSG00000138622	2.76	3.60E-03
<i>ALOX5AP</i>	ENSG00000132965	2.75	4.93E-04
<i>KRT7</i>	ENSG00000135480	2.73	9.65E-04
<i>CISH</i>	ENSG00000114737	2.72	1.54E-05
<i>C18orf15</i>	ENSG00000279020	2.72	3.00E-02
<i>SIRPB2</i>	ENSG00000196209	2.71	1.00E-02
<i>ADH1C</i>	ENSG00000248144	2.70	9.15E-04
<i>CILP</i>	ENSG00000138615	2.70	8.69E-03
<i>AP001043.1</i>	ENSG00000205622	2.70	3.00E-02
<i>TRPV4</i>	ENSG00000111199	2.69	6.97E-03
<i>SHISA6</i>	ENSG00000188803	2.69	1.27E-05
<i>RHOA-IT1</i>	ENSG00000235908	2.68	3.00E-02
<i>AC106791.1</i>	ENSG00000250159	2.68	2.70E-03
<i>AL359532.1</i>	ENSG00000272914	2.68	5.00E-02
<i>CALML4</i>	ENSG00000129007	2.68	5.27E-06
<i>LBH</i>	ENSG00000213626	2.67	1.49E-07
<i>ELF5</i>	ENSG00000135374	2.67	3.00E-02
<i>RHOD</i>	ENSG00000173156	2.67	7.62E-06
<i>C11orf53</i>	ENSG00000150750	2.67	5.24E-04
<i>SLC4A11</i>	ENSG00000088836	2.67	4.81E-03

<i>FCGR3A</i>	ENSG00000203747	2.66	3.00E-02
<i>CEP72</i>	ENSG00000112877	2.66	3.20E-03
<i>C3</i>	ENSG00000125730	2.66	3.00E-02
<i>TNFRSF12A</i>	ENSG00000006327	2.65	5.41E-03
<i>AP005131.6</i>	ENSG00000267702	2.65	3.35E-03
<i>CPA3</i>	ENSG00000163751	2.64	4.45E-06
<i>ANKRD18B</i>	ENSG00000230453	2.64	3.00E-02
<i>FAM19A2</i>	ENSG00000198673	2.63	1.18E-03
<i>LINC01504</i>	ENSG00000225434	2.62	1.00E-02
<i>MMP3</i>	ENSG00000149968	2.62	2.00E-02
<i>CARD14</i>	ENSG00000141527	2.61	2.39E-03
<i>ASRGL1</i>	ENSG00000162174	2.60	4.01E-07
<i>MIR4435-2HG</i>	ENSG00000172965	2.59	4.66E-05
<i>COL6A3</i>	ENSG00000163359	2.59	1.18E-09
<i>C10orf128</i>	ENSG00000204161	2.59	1.23E-04
<i>LINC00941</i>	ENSG00000235884	2.59	3.00E-02
<i>CEMIP</i>	ENSG00000103888	2.59	1.00E-02
<i>LRRN2</i>	ENSG00000170382	2.58	2.00E-02
<i>ITGAM</i>	ENSG00000169896	2.57	1.69E-03
<i>IL9R</i>	ENSG00000124334	2.57	2.00E-02
<i>ORC6</i>	ENSG00000091651	2.56	2.29E-05
<i>KIAA1644</i>	ENSG00000138944	2.56	1.34E-03
<i>FHAD1</i>	ENSG00000142621	2.54	2.07E-06
<i>CFB</i>	ENSG00000243649	2.54	1.16E-08
<i>C4B</i>	ENSG00000224389	2.54	1.05E-03
<i>AL139353.1</i>	ENSG00000203546	2.54	3.00E-02
<i>CRIP2</i>	ENSG00000182809	2.54	9.59E-06
<i>GLCE</i>	ENSG00000138604	2.54	5.23E-08
<i>TOE1</i>	ENSG00000132773	2.52	3.37E-06
<i>AC025539.1</i>	ENSG00000251152	2.52	4.00E-02
<i>C4A</i>	ENSG00000244731	2.52	6.85E-03
<i>AC025580.1</i>	ENSG00000259342	2.52	2.00E-02
<i>MMRN1</i>	ENSG00000138722	2.51	9.65E-04
<i>FGR</i>	ENSG00000000938	2.50	3.00E-02
<i>HABP2</i>	ENSG00000148702	2.50	1.69E-04
<i>FADS2</i>	ENSG00000134824	2.49	1.00E-02
<i>AC020656.2</i>	ENSG00000274979	2.49	1.70E-03
<i>ADAMTS4</i>	ENSG00000158859	2.48	3.00E-02
<i>ATP1B3</i>	ENSG00000069849	2.48	2.97E-07
<i>FOXC1</i>	ENSG00000054598	2.48	9.90E-03
<i>PFKP</i>	ENSG00000067057	2.48	1.68E-06
<i>AC016542.2</i>	ENSG00000279502	2.48	2.00E-02
<i>CDRT1</i>	ENSG00000241322	2.48	2.54E-03
<i>AC090229.1</i>	ENSG00000267397	2.48	2.00E-02

<i>IQCA1</i>	ENSG00000132321	2.47	4.00E-02
<i>CADM3-AS1</i>	ENSG00000225670	2.46	2.00E-02
<i>MEOX1</i>	ENSG00000005102	2.46	2.55E-03
<i>NCF1</i>	ENSG00000158517	2.45	5.89E-03
<i>DOC2B</i>	ENSG00000272636	2.45	1.00E-02
<i>NRXN3</i>	ENSG00000021645	2.43	2.00E-02
<i>MME</i>	ENSG00000196549	2.42	5.00E-02
<i>SLC39A8</i>	ENSG00000138821	2.42	1.73E-04
<i>CXCL2</i>	ENSG00000081041	2.41	4.00E-02
<i>ANXA2</i>	ENSG00000182718	2.41	4.73E-06
<i>ATF3</i>	ENSG00000162772	2.40	1.07E-04
<i>MUC6</i>	ENSG00000184956	2.39	6.85E-03
<i>RGS18</i>	ENSG00000150681	2.38	1.00E-02
<i>HRH1</i>	ENSG00000196639	2.38	1.79E-06
<i>GABRP</i>	ENSG00000094755	2.38	4.00E-02
<i>AC083837.1</i>	ENSG00000261618	2.38	2.00E-02
<i>LINC00857</i>	ENSG00000237523	2.38	8.42E-03
<i>NNMT</i>	ENSG00000166741	2.38	6.41E-03
<i>OSBPL3</i>	ENSG00000070882	2.37	3.33E-09
<i>IL3RA</i>	ENSG00000185291	2.37	3.20E-03
<i>AL031283.1</i>	ENSG00000228140	2.35	2.00E-02
<i>GNA14</i>	ENSG00000156049	2.35	1.00E-02
<i>LDHA</i>	ENSG00000134333	2.35	1.77E-07
<i>TM4SF1</i>	ENSG00000169908	2.34	1.49E-04
<i>KIAA1211</i>	ENSG00000109265	2.34	4.20E-03
<i>AC006064.4</i>	ENSG00000269968	2.34	3.00E-02
<i>MYOF</i>	ENSG00000138119	2.33	5.43E-07
<i>RAB31</i>	ENSG00000168461	2.33	5.61E-08
<i>SNORA80B</i>	ENSG00000206633	2.32	3.00E-02
<i>AC005062.1</i>	ENSG00000243004	2.32	3.00E-02
<i>IQCH</i>	ENSG00000103599	2.31	8.73E-04
<i>ITGAX</i>	ENSG00000140678	2.31	7.38E-03
<i>AC016542.3</i>	ENSG00000280166	2.30	3.00E-02
<i>NFIL3</i>	ENSG00000165030	2.29	1.10E-04
<i>CIDEB</i>	ENSG00000136305	2.29	1.33E-03
<i>AC092718.8</i>	ENSG00000284512	2.29	5.00E-02
<i>SLC38A1</i>	ENSG00000111371	2.27	4.78E-05
<i>FAM155A</i>	ENSG00000204442	2.27	1.00E-02
<i>LILRB2</i>	ENSG00000131042	2.27	1.00E-02
<i>PLA2G7</i>	ENSG00000146070	2.26	4.00E-02
<i>NIPA1</i>	ENSG00000170113	2.26	3.32E-06
<i>AC021483.2</i>	ENSG00000261229	2.26	2.00E-02
<i>HAS3</i>	ENSG00000103044	2.26	1.00E-02
<i>ATP2C2-AS1</i>	ENSG00000261286	2.25	2.00E-02

<i>BTK</i>	ENSG00000010671	2.25	5.24E-03
<i>AC239798.4</i>	ENSG00000273213	2.24	2.00E-02
<i>ITGA10</i>	ENSG00000143127	2.24	9.53E-03
<i>CCL11</i>	ENSG00000172156	2.24	2.00E-02
<i>APOL2</i>	ENSG00000128335	2.24	1.54E-04
<i>CARD11</i>	ENSG00000198286	2.23	1.02E-03
<i>TPST1</i>	ENSG00000169902	2.23	6.31E-06
<i>PDCD1LG2</i>	ENSG00000197646	2.23	3.00E-02
<i>GPRC5A</i>	ENSG00000013588	2.23	9.79E-06
<i>CSF2RB</i>	ENSG00000100368	2.23	3.85E-03
<i>PKM</i>	ENSG00000067225	2.22	4.06E-06
<i>SEMA7A</i>	ENSG00000138623	2.22	2.00E-02
<i>SERTAD4-AS1</i>	ENSG00000203706	2.21	2.00E-02
<i>TNFRSF11A</i>	ENSG00000141655	2.21	1.01E-04
<i>MASP1</i>	ENSG00000127241	2.20	5.00E-02
<i>ZC3H12D</i>	ENSG00000178199	2.20	2.00E-02
<i>AC007364.1</i>	ENSG00000231969	2.19	4.00E-02
<i>BDNF</i>	ENSG00000176697	2.19	2.00E-02
<i>SLFN11</i>	ENSG00000172716	2.19	9.05E-05
<i>CYSLTR1</i>	ENSG00000173198	2.19	7.96E-03
<i>KCNAB1</i>	ENSG00000169282	2.18	3.36E-03
<i>GSN</i>	ENSG00000148180	2.18	8.57E-04
<i>OSMR</i>	ENSG00000145623	2.17	3.79E-06
<i>AHCYL2</i>	ENSG00000158467	2.17	2.81E-05
<i>LINC00896</i>	ENSG00000236499	2.17	2.00E-02
<i>ALPL</i>	ENSG00000162551	2.16	5.00E-02
<i>CYR61</i>	ENSG00000142871	2.16	5.00E-02
<i>ACKR1</i>	ENSG00000213088	2.16	2.00E-02
<i>TBC1D1</i>	ENSG00000065882	2.16	1.37E-07
<i>GPRIN1</i>	ENSG00000169258	2.16	4.00E-02
<i>MEIS1-AS2</i>	ENSG00000230749	2.15	5.00E-02
<i>SSFA2</i>	ENSG00000138434	2.15	2.02E-04
<i>VEPH1</i>	ENSG00000197415	2.15	4.00E-02
<i>ANKDD1B</i>	ENSG00000189045	2.15	9.08E-03
<i>SAMSN1</i>	ENSG00000155307	2.15	2.10E-03
<i>SHC3</i>	ENSG00000148082	2.14	5.00E-02
<i>AL390774.2</i>	ENSG00000230826	2.14	5.00E-02
<i>ARNTL</i>	ENSG00000133794	2.14	5.03E-04
<i>EMP1</i>	ENSG00000134531	2.14	1.09E-03
<i>MTHFS</i>	ENSG00000136371	2.14	1.79E-06
<i>AP001625.2</i>	ENSG00000235772	2.14	4.00E-02
<i>UBXN10</i>	ENSG00000162543	2.13	3.00E-02
<i>ALOX5</i>	ENSG00000012779	2.13	1.09E-03
<i>SORD</i>	ENSG00000140263	2.13	2.80E-05

<i>AC090181.2</i>	ENSG00000269951	2.13	1.00E-02
<i>ENO1</i>	ENSG00000074800	2.12	7.02E-05
<i>MIR34AHG</i>	ENSG00000228526	2.12	3.28E-03
<i>DGKA</i>	ENSG00000065357	2.12	1.09E-03
<i>DUSP10</i>	ENSG00000143507	2.11	1.19E-03
<i>AGT</i>	ENSG00000135744	2.11	1.00E-02
<i>C15orf48</i>	ENSG00000166920	2.11	5.86E-04
<i>SIGLEC6</i>	ENSG00000105492	2.11	3.00E-02
<i>SNPH</i>	ENSG00000101298	2.11	4.02E-04
<i>LSAMP</i>	ENSG00000185565	2.10	1.00E-02
<i>TLL1</i>	ENSG00000038295	2.10	2.00E-02
<i>TBXAS1</i>	ENSG00000059377	2.10	1.36E-04
<i>PRSS3</i>	ENSG00000010438	2.10	3.29E-03
<i>ZNF438</i>	ENSG00000183621	2.10	5.04E-04
<i>KYNU</i>	ENSG00000115919	2.09	3.00E-02
<i>AKR1C1</i>	ENSG00000187134	2.09	3.63E-03
<i>CD209</i>	ENSG00000090659	2.09	3.00E-02
<i>STN1</i>	ENSG00000107960	2.08	1.24E-05
<i>CAVIN3</i>	ENSG00000170955	2.08	6.93E-04
<i>CD44</i>	ENSG00000026508	2.08	1.32E-04
<i>P2RY2</i>	ENSG00000175591	2.08	4.00E-02
<i>SMOX</i>	ENSG00000088826	2.08	3.00E-02
<i>S100A16</i>	ENSG00000188643	2.07	1.35E-04
<i>COL7A1</i>	ENSG00000114270	2.07	2.14E-03
<i>TPK1</i>	ENSG00000196511	2.07	2.96E-03
<i>KRT19</i>	ENSG00000171345	2.07	2.00E-02
<i>ETS2</i>	ENSG00000157557	2.07	5.94E-08
<i>SLC22A3</i>	ENSG00000146477	2.06	6.08E-04
<i>FMNL2</i>	ENSG00000157827	2.05	6.72E-05
<i>F2R</i>	ENSG00000181104	2.05	1.40E-03
<i>AGPAT4</i>	ENSG00000026652	2.05	3.74E-03
<i>LRMP</i>	ENSG00000118308	2.05	4.06E-03
<i>MUC13</i>	ENSG00000173702	2.04	1.00E-02
<i>HK1</i>	ENSG00000156515	2.04	4.05E-04
<i>AC025569.1</i>	ENSG00000258168	2.04	4.00E-02
<i>DOCK9</i>	ENSG00000088387	2.04	1.11E-04
<i>AC090181.3</i>	ENSG00000278991	2.04	1.00E-02
<i>BCL2L15</i>	ENSG00000188761	2.03	1.65E-05
<i>KIAA0513</i>	ENSG00000135709	2.03	1.38E-03
<i>G6PD</i>	ENSG00000160211	2.03	4.73E-03
<i>BCYRN1</i>	ENSG00000236824	2.02	2.00E-02
<i>TCIM</i>	ENSG00000176907	2.02	2.00E-02
<i>AFAP1-AS1</i>	ENSG00000272620	2.01	5.00E-02
<i>CCND3</i>	ENSG00000112576	2.01	6.98E-04

<i>LPCAT1</i>	ENSG00000153395	2.00	1.14E-03
<i>PLEKHB1</i>	ENSG00000021300	2.00	2.67E-04
<i>CSRNP3</i>	ENSG00000178662	-2.00	3.85E-03
<i>GPX3</i>	ENSG00000211445	-2.00	5.12E-03
<i>FAM135B</i>	ENSG00000147724	-2.01	4.00E-02
<i>BARX1</i>	ENSG00000131668	-2.01	5.00E-02
<i>TM7SF2</i>	ENSG00000149809	-2.01	2.00E-02
<i>PTMS</i>	ENSG00000159335	-2.01	2.91E-03
<i>PDZK1</i>	ENSG00000174827	-2.02	3.00E-02
<i>CYFIP2</i>	ENSG00000055163	-2.02	5.00E-02
<i>KLHL32</i>	ENSG00000186231	-2.02	5.00E-02
<i>NFIX</i>	ENSG00000008441	-2.02	2.69E-04
<i>ZNF512B</i>	ENSG00000196700	-2.02	1.38E-03
<i>FAHD2B</i>	ENSG00000144199	-2.03	2.03E-03
<i>ZAP70</i>	ENSG00000115085	-2.03	2.00E-02
<i>PSD</i>	ENSG00000059915	-2.03	5.00E-02
<i>MS4A8</i>	ENSG00000166959	-2.03	3.00E-02
<i>MAP6</i>	ENSG00000171533	-2.03	3.00E-02
<i>SSTR1</i>	ENSG00000139874	-2.03	4.21E-03
<i>GDPD1</i>	ENSG00000153982	-2.03	1.11E-04
<i>ZNF677</i>	ENSG00000197928	-2.03	2.13E-04
<i>TMEM47</i>	ENSG00000147027	-2.03	1.33E-03
<i>NR2F1</i>	ENSG00000175745	-2.04	2.00E-02
<i>CDKN1C</i>	ENSG00000129757	-2.04	3.00E-02
<i>IL2RB</i>	ENSG00000100385	-2.04	4.00E-02
<i>AL031587.5</i>	ENSG00000278948	-2.04	4.00E-02
<i>OBSCN</i>	ENSG00000154358	-2.05	1.00E-02
<i>AAMDC</i>	ENSG00000087884	-2.05	2.05E-04
<i>HSPA2</i>	ENSG00000126803	-2.05	2.00E-03
<i>CD2</i>	ENSG00000116824	-2.06	6.08E-03
<i>CD247</i>	ENSG00000198821	-2.06	4.00E-02
<i>RNF150</i>	ENSG00000170153	-2.06	2.00E-02
<i>CD3E</i>	ENSG00000198851	-2.06	3.00E-02
<i>AC004656.1</i>	ENSG00000260822	-2.06	2.85E-03
<i>BEX2</i>	ENSG00000133134	-2.06	3.00E-02
<i>RAB9B</i>	ENSG00000123570	-2.06	9.90E-03
<i>LINC00865</i>	ENSG00000232229	-2.07	2.35E-03
<i>IRS2</i>	ENSG00000185950	-2.07	2.60E-03
<i>ZNF626</i>	ENSG00000188171	-2.07	3.47E-05
<i>AP001062.1</i>	ENSG00000184441	-2.07	2.00E-02
<i>WASF3</i>	ENSG00000132970	-2.09	8.46E-03
<i>ASPG</i>	ENSG00000166183	-2.09	2.00E-02
<i>SEC14L5</i>	ENSG00000103184	-2.09	4.83E-03
<i>CU633906.1</i>	ENSG00000275496	-2.09	1.00E-02

<i>NR1D2</i>	ENSG00000174738	-2.10	2.30E-03
<i>IGSF10</i>	ENSG00000152580	-2.10	4.00E-02
<i>FUT9</i>	ENSG00000172461	-2.10	3.92E-03
<i>SLITRK6</i>	ENSG00000184564	-2.10	2.66E-03
<i>GNG2</i>	ENSG00000186469	-2.10	3.78E-04
<i>SEPT5</i>	ENSG00000184702	-2.10	2.00E-02
<i>ZNRF3</i>	ENSG00000183579	-2.10	3.84E-03
<i>RIMS3</i>	ENSG00000117016	-2.11	2.00E-02
<i>NPIPA2</i>	ENSG00000254852	-2.11	3.00E-02
<i>SYT17</i>	ENSG00000103528	-2.11	5.15E-03
<i>KLHL13</i>	ENSG00000003096	-2.11	8.46E-03
<i>GRIN2A</i>	ENSG00000183454	-2.12	2.00E-02
<i>MSH5-SAPCD1</i>	ENSG00000255152	-2.14	4.73E-03
<i>MAMDC2</i>	ENSG00000165072	-2.14	2.00E-02
<i>ZNFX26</i>	ENSG00000213967	-2.14	2.00E-02
<i>NCMAP</i>	ENSG00000184454	-2.15	2.00E-02
<i>DGKG</i>	ENSG00000058866	-2.16	1.00E-02
<i>CSPG4</i>	ENSG00000173546	-2.16	7.10E-04
<i>GATA5</i>	ENSG00000130700	-2.16	1.00E-02
<i>COL16A1</i>	ENSG00000084636	-2.17	2.16E-03
<i>ASPA</i>	ENSG00000108381	-2.17	2.15E-03
<i>PAPSS1</i>	ENSG00000138801	-2.18	2.94E-07
<i>RTN1</i>	ENSG00000139970	-2.18	1.00E-02
<i>PRX</i>	ENSG00000105227	-2.18	3.00E-02
<i>SULT1B1</i>	ENSG00000173597	-2.19	2.70E-03
<i>EIF4EBP3</i>	ENSG00000243056	-2.19	1.00E-02
<i>GFRA1</i>	ENSG00000151892	-2.19	2.07E-03
<i>TSPOAP1</i>	ENSG00000005379	-2.19	4.05E-04
<i>PGR</i>	ENSG00000082175	-2.20	3.00E-02
<i>FAM20C</i>	ENSG00000177706	-2.21	4.03E-03
<i>SLC7A2</i>	ENSG00000003989	-2.21	1.00E-02
<i>COL27A1</i>	ENSG00000196739	-2.21	7.60E-05
<i>DUSP19</i>	ENSG00000162999	-2.22	2.71E-03
<i>SUCNR1</i>	ENSG00000198829	-2.22	4.00E-02
<i>MACROD1</i>	ENSG00000133315	-2.22	7.52E-04
<i>PER1</i>	ENSG00000179094	-2.22	4.00E-02
<i>PER3</i>	ENSG00000049246	-2.23	5.04E-04
<i>NUPR1</i>	ENSG00000176046	-2.23	2.00E-02
<i>ANGPT1</i>	ENSG00000154188	-2.24	7.55E-04
<i>KLRK1</i>	ENSG00000213809	-2.24	3.00E-02
<i>RIMBP2</i>	ENSG00000060709	-2.24	3.00E-02
<i>SYP</i>	ENSG00000102003	-2.24	1.00E-02
<i>ACVR1C</i>	ENSG00000123612	-2.25	7.32E-05
<i>GPR158</i>	ENSG00000151025	-2.25	2.00E-02

<i>PEG10</i>	ENSG00000242265	-2.26	1.00E-02
<i>ADGRG5</i>	ENSG00000159618	-2.26	4.06E-03
<i>ZNF835</i>	ENSG00000127903	-2.26	4.00E-02
<i>HHIP-AS1</i>	ENSG00000248890	-2.27	4.00E-02
<i>ZIK1</i>	ENSG00000171649	-2.28	1.24E-05
<i>ADAMTS5</i>	ENSG00000154736	-2.28	3.71E-04
<i>SCML2</i>	ENSG00000102098	-2.29	3.00E-02
<i>AUTS2</i>	ENSG00000158321	-2.30	2.00E-02
<i>CFAP46</i>	ENSG00000171811	-2.30	1.60E-03
<i>KLRC1</i>	ENSG00000134545	-2.30	3.00E-02
<i>BHLHE41</i>	ENSG00000123095	-2.30	3.00E-02
<i>SCAMP5</i>	ENSG00000198794	-2.30	3.31E-04
<i>PDZD4</i>	ENSG00000067840	-2.30	5.00E-02
<i>PRLR</i>	ENSG00000113494	-2.31	5.22E-07
<i>ST3GAL1</i>	ENSG00000008513	-2.31	1.00E-02
<i>BRSK2</i>	ENSG00000174672	-2.32	1.00E-02
<i>GRIA4</i>	ENSG00000152578	-2.32	4.00E-02
<i>BAIAP3</i>	ENSG00000007516	-2.33	1.00E-02
<i>ZFPM1</i>	ENSG00000179588	-2.33	1.33E-03
<i>GHR</i>	ENSG00000112964	-2.34	2.00E-02
<i>ZNF579</i>	ENSG00000218891	-2.34	2.00E-02
<i>CELSR1</i>	ENSG00000075275	-2.34	9.76E-06
<i>TMEM35A</i>	ENSG00000126950	-2.34	5.00E-02
<i>PTGFR</i>	ENSG00000122420	-2.35	6.83E-03
<i>STK32B</i>	ENSG00000152953	-2.35	4.97E-03
<i>NEURL1</i>	ENSG00000107954	-2.35	4.76E-04
<i>SYT8</i>	ENSG00000149043	-2.35	3.00E-02
<i>AC084859.1</i>	ENSG00000254670	-2.35	4.89E-03
<i>SYT1</i>	ENSG00000067715	-2.36	3.00E-02
<i>SPATC1L</i>	ENSG00000160284	-2.36	2.00E-02
<i>QPCT</i>	ENSG00000115828	-2.37	7.28E-03
<i>TMEM171</i>	ENSG00000157111	-2.37	2.15E-05
<i>KCNQ3</i>	ENSG00000184156	-2.37	4.00E-02
<i>SEZ6L2</i>	ENSG00000174938	-2.37	1.19E-03
<i>CSTA</i>	ENSG00000121552	-2.38	4.32E-03
<i>CCL5</i>	ENSG00000271503	-2.38	7.45E-03
<i>AC093227.1</i>	ENSG00000267152	-2.38	4.00E-02
<i>CD8A</i>	ENSG00000153563	-2.39	6.18E-04
<i>ENPP6</i>	ENSG00000164303	-2.40	4.00E-03
<i>DACT2</i>	ENSG00000164488	-2.40	4.00E-02
<i>TUSC3</i>	ENSG00000104723	-2.40	1.06E-06
<i>LINC00982</i>	ENSG00000177133	-2.41	2.83E-03
<i>DPT</i>	ENSG00000143196	-2.41	2.00E-02
<i>ZMIZ1-AS1</i>	ENSG00000224596	-2.41	4.00E-02

<i>OAF</i>	ENSG00000184232	-2.41	9.82E-05
<i>RUNDC3A</i>	ENSG00000108309	-2.41	2.00E-02
<i>HIF3A</i>	ENSG00000124440	-2.41	4.00E-02
<i>CLGN</i>	ENSG00000153132	-2.42	3.00E-02
<i>PNPLA7</i>	ENSG00000130653	-2.42	9.98E-05
<i>FP565324.1</i>	ENSG00000283199	-2.42	2.00E-02
<i>ZNF667</i>	ENSG00000198046	-2.42	1.00E-02
<i>TMPRSS6</i>	ENSG00000187045	-2.42	1.00E-02
<i>TEF</i>	ENSG00000167074	-2.42	1.74E-03
<i>IL7R</i>	ENSG00000168685	-2.43	1.09E-03
<i>THEMIS</i>	ENSG00000172673	-2.43	2.72E-03
<i>PRKAG2-AS1</i>	ENSG00000239911	-2.43	3.00E-02
<i>RIMS2</i>	ENSG00000176406	-2.43	4.00E-02
<i>MT1X</i>	ENSG00000187193	-2.43	1.00E-02
<i>OTUD1</i>	ENSG00000165312	-2.44	9.97E-05
<i>AL365181.2</i>	ENSG00000272068	-2.45	4.00E-02
<i>PDE6B</i>	ENSG00000133256	-2.45	8.44E-03
<i>RASSF10</i>	ENSG00000189431	-2.45	3.35E-05
<i>GUCY2C</i>	ENSG00000070019	-2.45	1.00E-02
<i>CCDC169</i>	ENSG00000242715	-2.45	1.00E-02
<i>ZNF667-AS1</i>	ENSG00000166770	-2.45	4.41E-03
<i>AATBC</i>	ENSG00000215458	-2.45	3.00E-02
<i>STXBP5L</i>	ENSG00000145087	-2.46	1.09E-03
<i>AC139491.2</i>	ENSG00000248596	-2.46	2.45E-03
<i>ZNF257</i>	ENSG00000197134	-2.46	1.05E-03
<i>ZNF135</i>	ENSG00000176293	-2.46	1.74E-03
<i>NR1H4</i>	ENSG00000012504	-2.47	3.00E-02
<i>NR1I2</i>	ENSG00000144852	-2.48	3.97E-03
<i>RGS6</i>	ENSG00000182732	-2.48	5.00E-02
<i>KCNE2</i>	ENSG00000159197	-2.48	5.00E-02
<i>CELF3</i>	ENSG00000159409	-2.49	2.00E-02
<i>TRIM73</i>	ENSG00000178809	-2.49	2.00E-02
<i>PNMA2</i>	ENSG00000240694	-2.49	3.39E-03
<i>NKX6-3</i>	ENSG00000165066	-2.49	2.00E-02
<i>ADIRF-AS1</i>	ENSG00000272734	-2.49	1.00E-02
<i>MSI1</i>	ENSG00000135097	-2.49	2.00E-02
<i>SDK2</i>	ENSG00000069188	-2.49	3.77E-03
<i>SAMD13</i>	ENSG00000203943	-2.50	3.56E-05
<i>PFN2</i>	ENSG00000070087	-2.50	1.37E-08
<i>ADAMTSL2</i>	ENSG00000197859	-2.50	7.92E-03
<i>LINC00638</i>	ENSG00000258701	-2.50	4.00E-02
<i>PIWIL2</i>	ENSG00000197181	-2.51	6.07E-05
<i>OLFM1</i>	ENSG00000130558	-2.51	4.33E-04
<i>INA</i>	ENSG00000148798	-2.51	5.00E-02

<i>KCNJ6</i>	ENSG00000157542	-2.51	4.00E-02
<i>MYCL</i>	ENSG00000116990	-2.52	3.59E-05
<i>LHFPL4</i>	ENSG00000156959	-2.52	4.00E-02
<i>ARHGAP20</i>	ENSG00000137727	-2.52	9.32E-05
<i>HTR7</i>	ENSG00000148680	-2.53	2.00E-02
<i>SERPINA4</i>	ENSG00000100665	-2.53	6.77E-03
<i>AC097468.1</i>	ENSG00000224090	-2.54	2.00E-02
<i>AC010998.3</i>	ENSG00000278484	-2.54	5.00E-02
<i>OGN</i>	ENSG00000106809	-2.55	8.09E-03
<i>RAB26</i>	ENSG00000167964	-2.55	3.54E-04
<i>LIMS3</i>	ENSG00000256977	-2.56	3.00E-02
<i>NPM2</i>	ENSG00000158806	-2.56	2.00E-02
<i>ENHO</i>	ENSG00000168913	-2.56	4.95E-03
<i>FAM181B</i>	ENSG00000182103	-2.56	3.00E-02
<i>SCN8A</i>	ENSG00000196876	-2.58	9.79E-05
<i>MEGF6</i>	ENSG00000162591	-2.59	2.40E-04
<i>ISL1</i>	ENSG00000016082	-2.59	7.72E-05
<i>RGN</i>	ENSG00000130988	-2.59	2.00E-02
<i>CACNA2D1</i>	ENSG00000153956	-2.60	9.26E-10
<i>RAP1GAP</i>	ENSG00000076864	-2.61	6.00E-03
<i>KIF1A</i>	ENSG00000130294	-2.61	6.10E-03
<i>CPE</i>	ENSG00000109472	-2.61	7.72E-05
<i>COLEC12</i>	ENSG00000158270	-2.61	3.56E-05
<i>CD8B</i>	ENSG00000172116	-2.62	8.66E-03
<i>FGF14</i>	ENSG00000102466	-2.62	2.67E-03
<i>TPH1</i>	ENSG00000129167	-2.63	3.93E-03
<i>ZSCAN4</i>	ENSG00000180532	-2.63	2.00E-02
<i>CXorf57</i>	ENSG00000147231	-2.63	3.95E-06
<i>PCSK1</i>	ENSG00000175426	-2.64	5.05E-04
<i>VEGFB</i>	ENSG00000173511	-2.64	3.58E-04
<i>SSPN</i>	ENSG00000123096	-2.64	7.62E-06
<i>AMIGO2</i>	ENSG00000139211	-2.65	4.04E-03
<i>ZNF610</i>	ENSG00000167554	-2.65	4.21E-04
<i>DPP6</i>	ENSG00000130226	-2.66	2.00E-02
<i>ASAH2</i>	ENSG00000188611	-2.66	2.41E-03
<i>MFAP5</i>	ENSG00000197614	-2.66	2.38E-03
<i>ABCA8</i>	ENSG00000141338	-2.66	2.21E-03
<i>SVOP</i>	ENSG00000166111	-2.67	2.00E-02
<i>PMP2</i>	ENSG00000147588	-2.69	3.00E-02
<i>GNLY</i>	ENSG00000115523	-2.70	2.00E-02
<i>CLSTN2</i>	ENSG00000158258	-2.70	1.31E-04
<i>CDO1</i>	ENSG00000129596	-2.70	2.00E-02
<i>RPS6KA6</i>	ENSG00000072133	-2.70	1.13E-06
<i>TPCN2</i>	ENSG00000162341	-2.71	1.00E-02

<i>PPM1E</i>	ENSG00000175175	-2.72	5.00E-02
<i>CA11</i>	ENSG00000063180	-2.72	2.85E-03
<i>VWA5B2</i>	ENSG00000145198	-2.73	9.44E-03
<i>LHFPL3</i>	ENSG00000187416	-2.73	5.00E-02
<i>FXYD1</i>	ENSG00000266964	-2.74	5.00E-02
<i>NKX3-2</i>	ENSG00000109705	-2.75	4.00E-02
<i>NPY1R</i>	ENSG00000164128	-2.75	2.81E-03
<i>GRIP2</i>	ENSG00000144596	-2.76	2.81E-05
<i>AC011503.2</i>	ENSG00000269397	-2.76	6.45E-03
<i>RYR1</i>	ENSG00000196218	-2.76	2.35E-03
<i>C22orf42</i>	ENSG00000205856	-2.76	4.00E-02
<i>UST</i>	ENSG00000111962	-2.77	9.38E-05
<i>GATM</i>	ENSG00000171766	-2.77	5.05E-11
<i>UBE2QL1</i>	ENSG00000215218	-2.78	2.00E-02
<i>NOL4</i>	ENSG00000101746	-2.78	2.00E-02
<i>CXXC4</i>	ENSG00000168772	-2.79	6.98E-04
<i>ROBO3</i>	ENSG00000154134	-2.79	7.68E-03
<i>SLC1A7</i>	ENSG00000162383	-2.80	2.00E-02
<i>VANGL2</i>	ENSG00000162738	-2.80	8.32E-04
<i>CASR</i>	ENSG00000036828	-2.80	2.00E-02
<i>RFX6</i>	ENSG00000185002	-2.80	1.00E-02
<i>LINC00958</i>	ENSG00000251381	-2.80	3.92E-03
<i>MAPK8IP2</i>	ENSG00000008735	-2.80	1.00E-02
<i>NYAP1</i>	ENSG00000166924	-2.81	2.00E-02
<i>CHRM4</i>	ENSG00000180720	-2.81	5.00E-02
<i>ZNF185</i>	ENSG00000147394	-2.81	1.40E-06
<i>MGAM</i>	ENSG00000257335	-2.82	2.00E-03
<i>CHGA</i>	ENSG00000100604	-2.82	2.58E-04
<i>KNDC1</i>	ENSG00000171798	-2.83	2.00E-02
<i>CD3G</i>	ENSG00000160654	-2.84	3.38E-06
<i>ASCL1</i>	ENSG00000139352	-2.85	5.02E-03
<i>LRAT</i>	ENSG00000121207	-2.86	1.00E-02
<i>GSTA2</i>	ENSG00000244067	-2.86	2.00E-02
<i>EPHB6</i>	ENSG00000106123	-2.86	3.26E-03
<i>PCDH9</i>	ENSG00000184226	-2.86	9.25E-03
<i>GCK</i>	ENSG00000106633	-2.87	4.00E-02
<i>NACAD</i>	ENSG00000136274	-2.87	3.02E-03
<i>SCGB2A1</i>	ENSG00000124939	-2.87	4.07E-05
<i>DBP</i>	ENSG00000105516	-2.87	4.66E-05
<i>MPP2</i>	ENSG00000108852	-2.88	3.12E-04
<i>GNG4</i>	ENSG00000168243	-2.89	3.69E-03
<i>AGAP11</i>	ENSG00000271880	-2.89	2.00E-02
<i>MAST1</i>	ENSG00000105613	-2.89	4.00E-02
<i>PHLDA3</i>	ENSG00000174307	-2.90	1.05E-03

<i>FAM19A4</i>	ENSG00000163377	-2.91	4.00E-02
<i>IYD</i>	ENSG00000009765	-2.91	4.08E-06
<i>CPNE6</i>	ENSG00000100884	-2.91	3.00E-02
<i>UGT2B7</i>	ENSG00000171234	-2.92	2.00E-02
<i>CA4</i>	ENSG00000167434	-2.92	2.00E-02
<i>PLCH2</i>	ENSG00000149527	-2.93	9.10E-04
<i>RGS4</i>	ENSG00000117152	-2.93	1.29E-04
<i>DRAIC</i>	ENSG00000245750	-2.93	1.00E-02
<i>KIF5C</i>	ENSG00000168280	-2.94	6.35E-05
<i>KCNJ3</i>	ENSG00000162989	-2.94	3.27E-03
<i>DPP10</i>	ENSG00000175497	-2.95	7.75E-03
<i>PCSK2</i>	ENSG00000125851	-2.95	4.42E-03
<i>EEF1A2</i>	ENSG00000101210	-2.95	4.00E-03
<i>PNMA6A</i>	ENSG00000235961	-2.95	3.00E-02
<i>GUCA2B</i>	ENSG00000044012	-2.96	2.00E-02
<i>KCNMB2</i>	ENSG00000197584	-2.96	9.98E-05
<i>RMST</i>	ENSG00000255794	-2.96	1.00E-08
<i>KL</i>	ENSG00000133116	-2.96	1.63E-04
<i>NDNF</i>	ENSG00000173376	-2.97	4.70E-04
<i>REEP2</i>	ENSG00000132563	-2.97	9.00E-03
<i>PAX6</i>	ENSG00000007372	-2.97	3.00E-02
<i>DUSP26</i>	ENSG00000133878	-2.98	1.07E-03
<i>NELL2</i>	ENSG00000184613	-2.98	1.00E-02
<i>AJAP1</i>	ENSG00000196581	-2.99	3.35E-03
<i>CNTN1</i>	ENSG00000018236	-2.99	5.00E-02
<i>SLC39A5</i>	ENSG00000139540	-2.99	3.00E-02
<i>LTBP4</i>	ENSG00000090006	-2.99	2.13E-08
<i>SNAP91</i>	ENSG00000065609	-3.00	1.00E-02
<i>DCX</i>	ENSG00000077279	-3.00	6.77E-03
<i>TRPV6</i>	ENSG00000165125	-3.01	2.07E-03
<i>DSCAML1</i>	ENSG00000177103	-3.01	3.53E-03
<i>HMGCLL1</i>	ENSG00000146151	-3.02	2.62E-03
<i>UNC5B-AS1</i>	ENSG00000237512	-3.02	3.85E-03
<i>KLRC4-KLRK1</i>	ENSG00000255819	-3.02	1.00E-02
<i>KLK11</i>	ENSG00000167757	-3.02	2.71E-03
<i>CHGB</i>	ENSG00000089199	-3.02	4.00E-02
<i>F10</i>	ENSG00000126218	-3.03	2.46E-04
<i>GSG1L</i>	ENSG00000169181	-3.03	3.00E-02
<i>FOXJ1</i>	ENSG00000129654	-3.03	2.62E-03
<i>TTR</i>	ENSG00000118271	-3.03	1.00E-02
<i>TFPI2</i>	ENSG00000105825	-3.05	3.00E-02
<i>SYN2</i>	ENSG00000157152	-3.06	4.00E-02
<i>LRRC3B</i>	ENSG00000179796	-3.06	5.00E-02
<i>ADGRB1</i>	ENSG00000181790	-3.06	2.04E-03

<i>APOH</i>	ENSG00000091583	-3.06	3.00E-02
<i>FNDC1</i>	ENSG00000164694	-3.07	3.00E-02
<i>AC008808.2</i>	ENSG00000250360	-3.10	3.00E-02
<i>IGFBP3</i>	ENSG00000146674	-3.11	1.33E-10
<i>PID1</i>	ENSG00000153823	-3.12	4.28E-08
<i>EDARADD</i>	ENSG00000186197	-3.14	9.31E-06
<i>SLC2A12</i>	ENSG00000146411	-3.14	2.00E-02
<i>CADM3</i>	ENSG00000162706	-3.15	1.83E-03
<i>SYT14</i>	ENSG00000143469	-3.16	4.00E-03
<i>AC130371.2</i>	ENSG00000274370	-3.16	1.00E-02
<i>SLC26A9</i>	ENSG00000174502	-3.19	1.27E-05
<i>LINC01189</i>	ENSG00000232827	-3.20	5.00E-02
<i>TMEM151A</i>	ENSG00000179292	-3.20	2.00E-02
<i>MYOZ3</i>	ENSG00000164591	-3.22	2.24E-03
<i>AC005520.2</i>	ENSG00000259065	-3.22	2.00E-02
<i>CPS1</i>	ENSG00000021826	-3.23	3.00E-02
<i>PROX1-AS1</i>	ENSG00000230461	-3.24	5.00E-02
<i>AC090092.1</i>	ENSG00000255418	-3.24	2.00E-02
<i>RIIAD1</i>	ENSG00000178796	-3.25	5.00E-02
<i>SSTR2</i>	ENSG00000180616	-3.27	4.87E-04
<i>AC092652.2</i>	ENSG00000257277	-3.28	4.00E-02
<i>AC021016.3</i>	ENSG00000273361	-3.28	9.18E-04
<i>LGI1</i>	ENSG00000108231	-3.28	3.00E-02
<i>TMEM229A</i>	ENSG00000234224	-3.30	6.14E-03
<i>ATP13A5</i>	ENSG00000187527	-3.32	8.47E-03
<i>AC129507.2</i>	ENSG00000262294	-3.32	3.00E-02
<i>ACSM6</i>	ENSG00000173124	-3.33	2.00E-02
<i>KCNK3</i>	ENSG00000171303	-3.34	3.04E-04
<i>PTH1R</i>	ENSG00000160801	-3.34	1.00E-02
<i>AC093627.7</i>	ENSG00000261795	-3.34	4.00E-02
<i>VSTM2L</i>	ENSG00000132821	-3.34	8.16E-04
<i>GALNT13</i>	ENSG00000144278	-3.35	3.29E-03
<i>AQP10</i>	ENSG00000143595	-3.37	4.00E-02
<i>MFSD4A</i>	ENSG00000174514	-3.37	2.01E-03
<i>BMPR1B</i>	ENSG00000138696	-3.37	4.00E-02
<i>LMX1B</i>	ENSG00000136944	-3.37	4.00E-02
<i>NKX2-2</i>	ENSG00000125820	-3.37	9.36E-03
<i>PCDH19</i>	ENSG00000165194	-3.37	1.59E-04
<i>MAPK4</i>	ENSG00000141639	-3.39	6.49E-03
<i>RBP4</i>	ENSG00000138207	-3.41	3.38E-03
<i>CELF5</i>	ENSG00000161082	-3.43	8.40E-03
<i>BEX1</i>	ENSG00000133169	-3.43	3.27E-04
<i>AL606970.1</i>	ENSG00000224417	-3.44	4.00E-02
<i>PIRT</i>	ENSG00000233670	-3.44	1.80E-04

<i>DHRS2</i>	ENSG00000100867	-3.45	6.79E-03
<i>CYS1</i>	ENSG00000205795	-3.46	3.31E-04
<i>SCG3</i>	ENSG00000104112	-3.46	2.80E-05
<i>CLIC6</i>	ENSG00000159212	-3.46	6.16E-03
<i>GPR119</i>	ENSG00000147262	-3.47	5.00E-02
<i>PTGER3</i>	ENSG00000050628	-3.48	5.00E-02
<i>SFRP5</i>	ENSG00000120057	-3.49	2.75E-03
<i>SLC7A9</i>	ENSG00000021488	-3.49	4.00E-02
<i>AK5</i>	ENSG00000154027	-3.51	6.85E-06
<i>CSMD3</i>	ENSG00000164796	-3.51	2.62E-03
<i>NECAB2</i>	ENSG00000103154	-3.51	2.88E-03
<i>AL161658.1</i>	ENSG00000280229	-3.51	2.00E-02
<i>HLF</i>	ENSG00000108924	-3.53	1.21E-05
<i>SPOCK3</i>	ENSG00000196104	-3.55	5.00E-02
<i>SEMA3D</i>	ENSG00000153993	-3.55	8.99E-06
<i>ADAMTS13</i>	ENSG00000160323	-3.57	1.56E-07
<i>ELAVL4</i>	ENSG00000162374	-3.58	4.61E-04
<i>ERO1B</i>	ENSG00000086619	-3.58	1.16E-10
<i>MIR7-3HG</i>	ENSG00000176840	-3.58	6.77E-03
<i>AATK</i>	ENSG00000181409	-3.59	2.71E-05
<i>SIGLEC11</i>	ENSG00000161640	-3.59	5.00E-02
<i>FAM163A</i>	ENSG00000143340	-3.60	2.00E-02
<i>SLC6A4</i>	ENSG00000108576	-3.60	4.01E-04
<i>GRIA2</i>	ENSG00000120251	-3.61	2.10E-04
<i>NRIP3</i>	ENSG00000175352	-3.61	1.00E-02
<i>AC023794.5</i>	ENSG00000260470	-3.61	2.07E-03
<i>LINC02446</i>	ENSG00000256039	-3.64	4.00E-03
<i>MYO18B</i>	ENSG00000133454	-3.64	3.00E-02
<i>NUDT10</i>	ENSG00000122824	-3.64	4.00E-02
<i>DIRAS3</i>	ENSG00000162595	-3.66	9.86E-04
<i>AC093642.2</i>	ENSG00000280119	-3.66	3.23E-03
<i>FGF9</i>	ENSG00000102678	-3.66	3.49E-05
<i>ARX</i>	ENSG00000004848	-3.66	3.79E-04
<i>GRIA1</i>	ENSG00000155511	-3.67	7.04E-03
<i>CPLX2</i>	ENSG00000145920	-3.67	1.66E-04
<i>SYT7</i>	ENSG00000011347	-3.68	2.28E-05
<i>INSM1</i>	ENSG00000173404	-3.68	5.69E-04
<i>PCSK1N</i>	ENSG00000102109	-3.68	4.71E-04
<i>MARCH4</i>	ENSG00000144583	-3.69	2.44E-03
<i>SNAP25</i>	ENSG00000132639	-3.69	4.84E-05
<i>KCTD16</i>	ENSG00000183775	-3.70	3.00E-02
<i>SCG5</i>	ENSG00000166922	-3.70	3.64E-04
<i>CES1</i>	ENSG00000198848	-3.70	1.75E-04
<i>CFAP65</i>	ENSG00000181378	-3.72	1.73E-03

<i>RNF157-AS1</i>	ENSG00000267128	-3.73	2.00E-02
<i>PLCXD3</i>	ENSG00000182836	-3.74	3.80E-06
<i>VSTM2A-OT1</i>	ENSG00000224223	-3.74	5.98E-03
<i>IL33</i>	ENSG00000137033	-3.75	7.45E-13
<i>AC006030.1</i>	ENSG00000264324	-3.77	4.00E-02
<i>AC105277.1</i>	ENSG00000232453	-3.79	4.78E-05
<i>TMEM27</i>	ENSG00000147003	-3.80	9.81E-06
<i>TMEM190</i>	ENSG00000160472	-3.81	4.00E-02
<i>PRPH</i>	ENSG00000135406	-3.82	8.57E-04
<i>NDST4</i>	ENSG00000138653	-3.83	2.07E-05
<i>AC116407.1</i>	ENSG00000214708	-3.83	3.00E-02
<i>WSCD2</i>	ENSG00000075035	-3.88	1.18E-06
<i>ALDOB</i>	ENSG00000136872	-3.89	9.87E-03
<i>FGF20</i>	ENSG00000078579	-3.90	2.00E-02
<i>CX3CR1</i>	ENSG00000168329	-3.92	8.16E-04
<i>RALYL</i>	ENSG00000184672	-3.94	9.09E-03
<i>TDRD1</i>	ENSG00000095627	-3.95	7.68E-03
<i>APLP1</i>	ENSG00000105290	-3.95	6.71E-03
<i>GREM2</i>	ENSG00000180875	-3.96	7.75E-05
<i>RGS7</i>	ENSG00000182901	-3.96	1.31E-04
<i>SLC6A19</i>	ENSG00000174358	-3.96	1.09E-03
<i>FFAR1</i>	ENSG00000126266	-3.96	3.53E-03
<i>DIO3OS</i>	ENSG00000258498	-3.97	1.00E-02
<i>SYT4</i>	ENSG00000132872	-3.99	2.32E-05
<i>AC123912.1</i>	ENSG00000268081	-3.99	3.00E-02
<i>AL032819.2</i>	ENSG00000279930	-4.01	1.00E-02
<i>PRSS35</i>	ENSG00000146250	-4.05	3.89E-03
<i>MYOZ1</i>	ENSG00000177791	-4.07	4.00E-02
<i>PRLHR</i>	ENSG00000119973	-4.07	1.53E-03
<i>CLEC9A</i>	ENSG00000197992	-4.09	1.00E-02
<i>CARTPT</i>	ENSG00000164326	-4.11	1.04E-03
<i>PCDHB1</i>	ENSG00000171815	-4.15	9.78E-03
<i>CADM2</i>	ENSG00000175161	-4.16	2.30E-03
<i>NSG2</i>	ENSG00000170091	-4.20	1.16E-04
<i>FLG2</i>	ENSG00000143520	-4.23	9.32E-06
<i>KRT40</i>	ENSG00000204889	-4.29	2.41E-03
<i>MRO</i>	ENSG00000134042	-4.29	1.72E-08
<i>TAGLN3</i>	ENSG00000144834	-4.35	4.61E-04
<i>DIRAS2</i>	ENSG00000165023	-4.38	6.30E-05
<i>AL032819.3</i>	ENSG00000284395	-4.42	8.52E-03
<i>C8orf48</i>	ENSG00000164743	-4.43	2.10E-06
<i>C1orf127</i>	ENSG00000175262	-4.44	2.32E-04
<i>CALY</i>	ENSG00000130643	-4.45	7.00E-05
<i>NKX6-1</i>	ENSG00000163623	-4.47	1.46E-03

<i>FAM159B</i>	ENSG00000145642	-4.47	3.16E-03
<i>NRAP</i>	ENSG00000197893	-4.48	8.07E-05
<i>PTPRN</i>	ENSG00000054356	-4.49	5.16E-07
<i>PCDHB8</i>	ENSG00000120322	-4.49	2.00E-02
<i>SLC34A2</i>	ENSG00000157765	-4.51	6.42E-04
<i>SLC26A7</i>	ENSG00000147606	-4.53	7.63E-08
<i>SCGN</i>	ENSG00000079689	-4.54	1.61E-06
<i>VTN</i>	ENSG00000109072	-4.55	3.60E-05
<i>SRPX</i>	ENSG00000101955	-4.56	1.85E-08
<i>HCN1</i>	ENSG00000164588	-4.57	6.55E-03
<i>TMEM132B</i>	ENSG00000139364	-4.59	1.02E-07
<i>PIFO</i>	ENSG00000173947	-4.65	2.00E-02
<i>LINC01933</i>	ENSG00000254226	-4.66	9.05E-04
<i>C2orf40</i>	ENSG00000119147	-4.67	1.38E-03
<i>AC008736.1</i>	ENSG00000267475	-4.67	3.00E-02
<i>CDH2</i>	ENSG00000170558	-4.72	3.00E-02
<i>TMEM196</i>	ENSG00000173452	-4.74	1.88E-04
<i>AC091551.1</i>	ENSG00000267699	-4.78	3.85E-03
<i>VSTM2A</i>	ENSG00000170419	-4.79	3.21E-08
<i>TMEM132C</i>	ENSG00000181234	-4.80	2.58E-04
<i>NEUROG3</i>	ENSG00000122859	-4.81	2.00E-02
<i>AC069228.1</i>	ENSG00000258162	-4.81	2.00E-02
<i>FABP3</i>	ENSG00000121769	-4.86	3.91E-03
<i>KCNK16</i>	ENSG00000095981	-4.94	5.41E-05
<i>MT1G</i>	ENSG00000125144	-4.94	2.94E-03
<i>AC020656.1</i>	ENSG00000257764	-5.00	2.00E-02
<i>GABRG2</i>	ENSG00000113327	-5.03	1.66E-04
<i>PCP4L1</i>	ENSG00000248485	-5.07	1.00E-02
<i>AC104985.1</i>	ENSG00000267746	-5.09	4.00E-02
<i>UCN3</i>	ENSG00000178473	-5.14	6.72E-05
<i>OLFM3</i>	ENSG00000118733	-5.16	2.00E-02
<i>NEUROD1</i>	ENSG00000162992	-5.17	6.09E-06
<i>OTOP3</i>	ENSG00000182938	-5.18	8.38E-04
<i>SLC17A8</i>	ENSG00000179520	-5.25	3.76E-03
<i>AGMO</i>	ENSG00000187546	-5.32	5.20E-03
<i>MUC15</i>	ENSG00000169550	-5.33	1.00E-02
<i>LRFN2</i>	ENSG00000156564	-5.40	2.00E-02
<i>RIPPLY2</i>	ENSG00000203877	-5.40	1.00E-02
<i>CARNS1</i>	ENSG00000172508	-5.41	3.21E-07
<i>C10orf67</i>	ENSG00000179133	-5.42	1.00E-02
<i>LINC01902</i>	ENSG00000283503	-5.45	3.36E-03
<i>RIMS4</i>	ENSG00000101098	-5.46	2.94E-03
<i>LINC01594</i>	ENSG00000225328	-5.51	4.73E-03
<i>HTR1F</i>	ENSG00000179097	-5.51	3.16E-03

<i>TF</i>	ENSG00000091513	-5.52	7.92E-03
<i>NTRK3</i>	ENSG00000140538	-5.53	3.63E-06
<i>MT1H</i>	ENSG00000205358	-5.55	3.00E-02
<i>KLHL1</i>	ENSG00000150361	-5.57	3.41E-05
<i>GS1-594A7.3</i>	ENSG00000225833	-5.62	2.00E-02
<i>SLITRK5</i>	ENSG00000165300	-5.67	4.76E-08
<i>KLHDC8A</i>	ENSG00000162873	-5.72	2.30E-03
<i>OTC</i>	ENSG00000036473	-5.76	1.35E-04
<i>TACR3</i>	ENSG00000169836	-5.79	1.00E-02
<i>TRIM63</i>	ENSG00000158022	-5.80	3.00E-02
<i>CYP3A4</i>	ENSG00000160868	-5.80	5.00E-02
<i>SH3GL2</i>	ENSG00000107295	-5.82	3.02E-04
<i>TM4SF4</i>	ENSG00000169903	-5.87	2.64E-07
<i>RMST_9</i>	ENSG00000276398	-5.87	1.29E-04
<i>AL137793.1</i>	ENSG00000236975	-5.92	3.00E-02
<i>MEP1B</i>	ENSG00000141434	-5.92	2.00E-02
<i>AC008268.1</i>	ENSG00000235584	-5.93	2.00E-02
<i>IGFALS</i>	ENSG00000099769	-5.95	7.00E-05
<i>NMUR2</i>	ENSG00000132911	-6.08	5.13E-06
<i>GABRA1</i>	ENSG00000022355	-6.27	2.31E-06
<i>LY6H</i>	ENSG00000176956	-6.33	7.93E-09
<i>DEFB1</i>	ENSG00000164825	-6.41	1.72E-06
<i>FRMPD4</i>	ENSG00000169933	-6.42	3.00E-02
<i>NPW</i>	ENSG00000183971	-6.50	1.33E-05
<i>AP003071.5</i>	ENSG00000284713	-6.57	1.32E-03
<i>SST</i>	ENSG00000157005	-6.60	2.67E-07
<i>LINC01370</i>	ENSG00000237767	-6.66	3.90E-03
<i>ELFN1-AS1</i>	ENSG00000236081	-6.79	4.00E-02
<i>TAC1</i>	ENSG00000006128	-6.81	5.00E-05
<i>HOXC5</i>	ENSG00000172789	-6.99	7.78E-03
<i>ATP4A</i>	ENSG00000105675	-7.16	2.00E-02
<i>SLITRK3</i>	ENSG00000121871	-7.54	5.00E-02
<i>RBP2</i>	ENSG00000114113	-7.56	3.00E-02
<i>ZNF492</i>	ENSG00000229676	-7.59	5.06E-06
<i>C5orf17</i>	ENSG00000248874	-7.68	3.18E-03
<i>CHST9</i>	ENSG00000154080	-7.68	2.11E-06
<i>MTTP</i>	ENSG00000138823	-7.78	9.65E-04
<i>AC005944.1</i>	ENSG00000267469	-7.88	3.00E-02
<i>GLDN</i>	ENSG00000186417	-7.93	1.53E-09
<i>LCT</i>	ENSG00000115850	-8.04	2.65E-03
<i>AF131216.3</i>	ENSG00000255020	-8.07	5.00E-02
<i>APOB</i>	ENSG00000084674	-8.31	2.00E-02
<i>F11</i>	ENSG00000088926	-8.59	2.00E-02
<i>NTS</i>	ENSG00000133636	-8.59	1.34E-03

<i>MDGA2</i>	ENSG00000139915	-8.77	1.18E-06
<i>MRPL23-AS1</i>	ENSG00000226416	-9.09	5.67E-03
<i>IGHD</i>	ENSG00000211898	-9.11	1.54E-04
<i>AC093772.1</i>	ENSG00000248491	-9.19	3.28E-03
<i>APOC3</i>	ENSG00000110245	-9.21	3.00E-02
<i>MS4A10</i>	ENSG00000172689	-9.28	5.00E-02
<i>MATR3_2</i>	ENSG00000015479	-9.49	4.00E-02
<i>FSTL5</i>	ENSG00000168843	-9.56	2.00E-02
<i>BMP3</i>	ENSG00000152785	-9.80	9.83E-09
<i>MUM1L1</i>	ENSG00000157502	-10.37	2.22E-12
<i>TMPRSS15</i>	ENSG00000154646	-10.46	4.00E-02
<i>SLC5A7</i>	ENSG00000115665	-10.47	5.86E-11
<i>AC126544.2</i>	ENSG00000280022	-10.63	4.48E-03
<i>NPY</i>	ENSG00000122585	-10.91	7.85E-05
<i>ALPI</i>	ENSG00000163295	-11.12	2.00E-02
<i>FGG</i>	ENSG00000171557	-11.13	2.00E-02
<i>NECAB1</i>	ENSG00000123119	-11.35	1.00E-15
<i>CNTFR</i>	ENSG00000122756	-11.57	2.59E-07
<i>CYP4F22</i>	ENSG00000171954	-11.66	1.17E-06
<i>DDIT4-AS1</i>	ENSG00000269926	-11.82	2.00E-02
<i>SULT1E1</i>	ENSG00000109193	-12.06	1.17E-03
<i>ALB</i>	ENSG00000163631	-12.25	1.59E-04
<i>GSTA3</i>	ENSG00000174156	-12.57	4.17E-04
<i>AL512638.2</i>	ENSG00000228035	-13.39	5.00E-02
<i>APOA4</i>	ENSG00000110244	-13.53	3.00E-02
<i>COL2A1</i>	ENSG00000139219	-13.59	4.66E-05
<i>S100G</i>	ENSG00000169906	-13.74	1.00E-02
<i>APOA1</i>	ENSG00000118137	-14.50	5.20E-04
<i>CYP1A1</i>	ENSG00000140465	-14.54	2.45E-03
<i>SULT2A1</i>	ENSG00000105398	-15.58	1.10E-05
<i>UGT2A3</i>	ENSG00000135220	-24.63	1.00E-15
<i>MCHR2</i>	ENSG00000152034	-30.37	8.32E-04
<i>TBC1D3K</i>	ENSG00000273513	-31.73	5.00E-02
<i>AC073174.1</i>	ENSG00000227121	-34.74	3.00E-02
<i>TBC1D3G</i>	ENSG00000260287	-40.92	3.00E-02
<i>AC087190.4</i>	ENSG00000263244	-45.72	3.00E-02
<i>AC009133.6</i>	ENSG00000280893	-47.30	1.00E-02
<i>PGA5</i>	ENSG00000256713	-51.71	7.66E-05
<i>SFT2D3</i>	ENSG00000173349	-54.98	1.00E-02
<i>CHIA</i>	ENSG00000134216	-389.59	7.55E-11

Consortium of Eosinophilic Gastrointestinal Disease Researchers (CEGIR) questionnaires

- Registry for Eosinophilic Gastrointestinal Diseases (REGID) Provider Questionnaire
- CEGIR Outcomes Measures in Eosinophilic Gastrointestinal disorders Across the ages (OMEGA) Patient Intake Questionnaire

Office Use Only

Visit Date: / /
 Month Day Year

Visit Type: ☐ Initial Visit ☐ Follow-Up Clinic ☐ Follow-Up Endoscopy ☐ Chart Review Only

Eosinophilic Gastrointestinal Disorder (EGID) Diagnosis

If the patient has been given an EGID diagnosis, please answer the questions below.

Diagnosis	Diagnosed?	Age diagnosed	Treatment (choose all that apply)
Eosinophilic Esophagitis (EoE) Patient treated for 8 or more weeks with a proton pump inhibitor (any dose) before diagnosed with EoE? ≥ 15 ☐ Yes ☐ No ☐ Not sure If Yes, indicate the name of PPI and the dosage. Name: _____ Dosage: _____ Patient treated for 8 or more weeks with <u>high dose</u> * proton pump inhibitor before diagnosed with EoE? ☐ Yes ☐ No ☐ Not sure * 20-40 mg daily in adults (depends on patient and chosen PPI) and 1 mg/kg twice daily (for maximal dosing use in children) Normal pH or impedance probe test before diagnosed with EoE? ☐ Yes ☐ No ☐ Not sure	☐ Yes ☐ No ☐ Not sure	 ☐ Months ☐ Years	☐ Swallowed Topical Steroids ☐ Oral Systemic Steroids ☐ Elimination Diet ☐ Empiric Elimination Diet ☐ Elemental Diet ☐ Other _____
Eosinophilic Gastritis	☐ Yes ☐ No ☐ Not sure	 ☐ Months ☐ Years	☐ Swallowed Topical Steroids ☐ Oral Systemic Steroids ☐ Elimination Diet ☐ Empiric Elimination Diet ☐ Elemental Diet ☐ Other _____
Eosinophilic Colitis	☐ Yes ☐ No ☐ Not sure	 ☐ Months ☐ Years	☐ Swallowed Topical Steroids ☐ Oral Systemic Steroids ☐ 5-ASA ☐ Elimination Diet ☐ Empiric Elimination Diet ☐ Elemental Diet ☐ Other _____

EoE diagnosis by a physician:

Age at Diagnosis: years months

Age at First Endoscopy: years months

Age at First Symptoms: years months

Please indicate which therapy(ies) has been used to treat the patient's EGID. Also indicate which therapy(ies) has been effective based on symptoms and / or pathology.

☐ None. No therapy has been used to treat the patient's EGID.

 If None, please skip to the next section.

	Used			Effective for Sx			Effective for Path		
	Yes	No	Not sure	Yes	No	Not sure	Yes	No	Not sure
Swallowed topical steroids (i.e. fluticasone, budesonide)	☐	☐	☐	☐	☐	☐	☐	☐	☐
Oral systemic steroids (i.e. Prednisone®)	☐	☐	☐	☐	☐	☐	☐	☐	☐
Elimination Diet (removing food(s) the patient is allergic to)	☐	☐	☐	☐	☐	☐	☐	☐	☐
Empiric Elimination Diet (avoiding food(s) that the doctor has recommended to avoid)	☐	☐	☐	☐	☐	☐	☐	☐	☐
Elemental Diet (taking elemental formula and up to one food)	☐	☐	☐	☐	☐	☐	☐	☐	☐
Swallowed topical steroids AND Diet elimination	☐	☐	☐	☐	☐	☐	☐	☐	☐
Esophageal Dilation	☐	☐	☐	☐	☐	☐	☐	☐	☐
Anti-IL5	☐	☐	☐	☐	☐	☐	☐	☐	☐
Anti-IL13	☐	☐	☐	☐	☐	☐	☐	☐	☐
Leukotriene Modifier (e.g. Monteleukast)	☐	☐	☐	☐	☐	☐	☐	☐	☐
5-ASA	☐	☐	☐	☐	☐	☐	☐	☐	☐
Other:	☐	☐	☐	☐	☐	☐	☐	☐	☐

Physician Global Assessment

If you consider the patient's most recent clinical status, how active is the EoE?

☐ Quiescent ☐ Mild ☐ Moderate ☐ Severe

If you consider the patient's histologic status, how active is the EoE?

☐ Quiescent ☐ Mild ☐ Moderate ☐ Severe

If you consider the patient's overall status, how active is the EoE?

☐ Quiescent ☐ Mild ☐ Moderate ☐ Severe

Please rate the patient's change in height on the growth chart since their last visit.

☐ No change ☐ Up ☐ Down

Please rate the patient's change in weight on the growth chart since their last visit.

☐ No change ☐ Up ☐ Down

Height: . cm

Weight: . Kg

Surgical History

Has the patient had food impactions that required urgent endoscopic removal?

☐ Yes ☐ No ☐ Not sure

If Yes, how many times?

If Yes, please specify the date for the last three (3) times this occurred.

/ /
 / /
 / /

Has the patient had dilation (stretching) of the esophagus?

☐ Yes ☐ No ☐ Not sure

If Yes, how many times?

If Yes, please specify the date for the last three (3) times this occurred.

/ /
 / /
 / /

Has the patient had an esophageal perforation?

☐ Yes ☐ No ☐ Not sure

If Yes, how many times?

If Yes, please specify the date for the last three (3) times this occurred.

/ /
 / /
 / /

Current Therapy(ies)

Which therapy(ies) is currently being used to treat the patient's EGID? (choose all that apply)

- ☐ Swallowed topical steroids (i.e. fluticasone, budesonide)
- ☐ Oral systemic steroids (i.e. Prednisone®)
- ☐ Proton pump inhibitor (i.e. esomeprazole, lansoprazole, pantoprazole, omeprazole)
- ☐ Elimination Diet (removing food(s) the patient is allergic to)
- ☐ Empiric Elimination Diet (avoiding food(s) that the doctor has recommended to avoid)
- ☐ Elemental Diet (taking elemental formula and up to one food)
- ☐ Esophageal Dilation
- ☐ Anti-IL5
- ☐ Anti-IL13
- ☐ Leukotriene Modifier (e.g. Montelukast)
- ☐ 5-ASA
- ☐ Other

If Other, please specify: _____

Have any of the following EGID diagnoses changed since the last visit / endoscopy? (choose all that apply)

- ☐ No. None of the following EGID diagnoses has changed since the last visit / endoscopy.
- ☐ Eosinophilic Esophagitis (EoE) ☐ Eosinophilic Gastritis
- ☐ Eosinophilic Enteritis ☐ Eosinophilic Colitis
- ☐ Other

If Other, please specify: _____

At this visit, which therapy(ies) is recommended for the patient for the EGID? (choose all that apply)

- ☐ Swallowed topical steroids (i.e. fluticasone, budesonide)
- ☐ Oral systemic steroids (i.e. Prednisone®)
- ☐ Proton pump inhibitor (i.e. esomeprazole, lansoprazole, pantoprazole, omeprazole)
- ☐ Elimination Diet (removing food(s) the patient is allergic to)
- ☐ Empiric Elimination Diet (avoiding food(s) that the doctor has recommended to avoid)
- ☐ Elemental Diet (taking elemental formula and up to one food)
- ☐ Esophageal Dilation
- ☐ Anti-IL5
- ☐ Anti-IL13
- ☐ Leukotriene Modifier (e.g. Monteleukast)
- ☐ 5-ASA
- ☐ Other

If Other, please specify: _____

At this visit, are any medications or supplements recommended / modified for the patient for the EGID?

☐ Yes ☐ No

If Yes, list all medications or supplements recommended / modified for the patient for the EGID.

Medication Name	Approximate Start Date (mm/dd/yyyy)	Dose	Frequency (1, 2, 3x / day)	Route (Oral, Inhaled, G Tube)	Indication
For example: Flovent	05/01/2010	110 mcg	2 puffs twice a day	Oral (by mouth)	Eosinophilic Esophagitis

What is the patient's current diet for the EGID? (choose all that apply)

- | | | |
|--|---|--|
| ☐ No Restrictions: Patient eats whatever s/he wants | ☐ Elimination Diet: Patient avoids food (s) s/he is allergic to by allergy testing results | ☐ Empiric Elimination Diet: Patient avoids food(s) that the doctor has recommended to avoid |
| ☐ Elemental Formula (up to one food) | ☐ Elemental Formula and Food | ☐ Elemental Formula and Food Trial |
| ☐ Non-elemental Formula | ☐ Non-elemental Formula and Food | ☐ TPN |
| ☐ Food Trial | ☐ Other | |

If Other, please specify:

Only

Office Use

Visit Date: / /
Month Day Year

Visit Type: ☐ Initial Visit ☐ Annual Follow Up

RDCRN Participant ID:

Person Completing this Form

What is your relationship to the patient?

☐ Self ☐ Parent ☐ Legal Guardian ☐ Other

If Other, please specify: _____

Note that throughout this document, references to "patient" stand for the research participant. "Patient" refers to you if you are the research participant or your child / ward if s/he is the research participant and you are completing the form because s/he is under 18 years of age or otherwise unable to complete the form.

Is the patient a product of a multiple birth (e.g. twin, triplet)?

☐ Yes, Identical ☐ Yes, Not Identical ☐ No

OMEGA
Patient Intake Questionnaire
2

Initials:

Local

Subject ID:

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Patient History

Please complete the following to inform us of the patient's past medical history.

☐ No Change since last visit

Past Medical History (diagnosed by a physician)			
ALLERGY / IMMUNOLOGY	Yes	No	Not sure
1. Allergic conjunctivitis (itchy, watery eyes) or Allergic rhinitis (seasonal stuffy, runny nose or hayfever) Triggers (Check all that apply): ☐ Grass ☐ Mold ☐ Trees ☐ Weeds ☐ Cockroach ☐ Dust mites ☐ Cat ☐ Dog			
2. Angioedema (swelling of skin)			
3. Asthma (breathing problem requiring the use of an inhaler / nebulizer at least once a year) Please check any that apply for the previous 12 months: ☐ Emergency Department visit ☐ Steroid course ☐ Daily asthma medication ☐ daytime Albuterol use more than 2x a week ☐ nighttime Albuterol use more than 2x a month Triggers (Check all that apply): ☐ Upper Respiratory Infection ☐ Weather Changes ☐ Pollen			
4. Autoimmune disease (Lupus, Diabetes Type I, Hashimoto's Thyroiditis, etc.)			
5. Drug anaphylaxis (severe, sudden reaction to drug)			
6. Eczema (chronic dry, itchy skin rash)			
7. Environmental allergies (such as dust, pollen, grass, cats)			
8. Food allergy (immediate rash, trouble breathing or feeling unwell after eating food; not limited to the esophagus)			
9. Hypereosinophilic syndrome (excessive blood eosinophils $\geq$ 6 months)			
10. Immunodeficiency (known immune problem causing recurrent infections)			
11. Latex allergy (emergent or prolonged reaction to latex such as rash, hives, or trouble breathing)			
12. Oral allergy syndrome (burning, tingling sensation, or rash around mouth following eating food)			
13. Sinusitis (infection of sinus with headache or pressure)			
14. Urticaria (hives)			
15. Vocal cord dysfunction			
GASTROINTESTINAL	Yes	No	Not sure
16. Achalasia (disease of the esophageal muscle)			
17. Barrett's esophagus (disease with an abnormal change in the cells of the esophagus that is pre-cancerous)			
18. Celiac disease (disease that damages the small intestine because of an immune reaction to gluten)			
19. Esophageal cancer			
20. Esophageal dilation (dilate or stretch the esophagus)			
21. Esophageal perforation (hole / tear in the esophagus either spontaneous or procedure related)			
22. Esophageal stricture (narrowing / tightening of the esophagus on endoscopy or x-ray)			



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23. Failure to thrive (poor growth in childhood, smaller than the 5th percentile on doctor's growth chart)			
25. Food getting stuck in chest or throat (impaction) - self-cleared (not requiring a doctor)			
26. Food getting stuck in chest or throat (impaction) - treated / removed by a physician			
27. GERD (heartburn / reflux)			
28. Inflammatory bowel disease (Crohns disease / Ulcerative colitis) (bowel disease <u>with</u> inflammation)			
29. Irritable Bowel Syndrome (bowel disorder characterized by abdominal pain and changes in bowel habits but <u>no</u> inflammation)			

Past Medical History (diagnosed by a physician) - Continued			
MISCELLANEOUS	Yes	No	Not sure
30. Anxiety			
31. Arthritis / Joint pain			
32. Autism			
33. Behavioral disorders (ADHD, OCD)			
34. Connective Tissue Disease (Marfan's syndrome, Ehlers-Danlos, Joint hypermobility)			
35. Depression			
36. Developmental delay			
37. Mitochondrial disorder			
38. Prematurity (less than 37 weeks)			

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Surgical History

Please specify whether the patient has had any of the the following surgical procedures (Not including endoscopies).

☐ None. The patient hasn't had any surgical procedures (except endoscopies). ☐ No Change since last visit

 If None, please go to the next question.

Surgical History	Yes	No	Not sure
1. Adenoidectomy			
2. Sinus surgery			
3. Tonsillectomy			
4. Fundoplication (i.e. Nissen)			
5. Gastrostomy tube			
6. Tracheoesophageal fistula (TEF) repair			
7. Tracheostomy			
8. Appendectomy			
9. Bronchoscopy			
10. Hernia Repair			
11. Ear tubes			
12. Other: _____			

Foods

Is the patient currently avoiding / not eating certain food(s)?

- ☐ The patient has no restrictions and eats whatever s/he wants.
☐ The patient is currently not eating any food(s) (elemental diet or TPN only).
☐ The patient is currently taking an elemental diet and some food(s).
☐ The patient is currently avoiding certain food(s).

 If the patient is not currently avoiding certain food(s), please go to the next question.

Please specify which food(s) the patient is currently avoiding / not eating. (choose all that apply)

- | | | | | |
|--------------------------------|------------------------------------|---------------------------------------|-------------------------------------|----------------------------------|
| ☐ Corn | ☐ Fish | ☐ Apple | ☐ Beef | ☐ Chicken |
| ☐ Egg | ☐ Shellfish | ☐ Avocado | ☐ Broccoli | ☐ Pea |
| ☐ Milk | | ☐ Banana | ☐ Cantaloupe | ☐ Pork |
| ☐ Soy | ☐ Peanut | ☐ Barley | ☐ Carrot | ☐ Rice |
| ☐ Wheat | ☐ Tree nuts | ☐ Bean, String | ☐ Celery | ☐ Turkey |
| ☐ Other | | | | |

If Other, please specify: _____

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Food Related Problems

Please complete the following to inform us of the patient's food allergy reactions.

☐

None. The patient does not have any known food allergy reactions.

☐

No change since last visit

	Never tried	Rash	Difficulty breathing	Vomiting	Difficulty swallowing	Diarrhea	Abdominal pain	Low Blood Pressure	If Other, specify.	RAST (IU/mL)	Skin prick (w/f mm)	Patch (0-4)
Example		x					x	x	Muscle pain.	1.54	10 / 20	2
Milk											/	
Soy											/	
Egg											/	
Wheat											/	
Peanut											/	
Corn											/	
Shellfish											/	
Other fish											/	
Beef											/	
Tree nuts*											/	
Oat											/	
Barley											/	
Potato											/	
Peas											/	
Chicken											/	
Turkey											/	
Pork											/	
Rice											/	
Other:											/	
Other:											/	

* Tree nuts (Almond, walnut, hazelnut, brazil nut, pecans)



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Environmental Allergies

Please complete the following to inform us of the patient's environmental allergy reactions.

☐ None. The patient does not have any known environmental allergy reactions. ☐ No change since last visit

Example	1.54	10 / 20
Tree		/
Grass		/
Ragweed		/
Cat		/
Dog		/
Dust mite		/
Weeds		/
Mold		/
Cockroach		/
Mice		/

Environmental History

What locale does the patient live in?

☐ City ☐ Suburbs ☐ Country ☐ Not sure ☐ Other

If Other, please specify: _____

What type of structure does the patient live in?

☐ House ☐ Apartment ☐ Not sure ☐ Other

If Other, please specify: _____

Indicate where the is mold in the patient's home. (choose all that apply)

☐ Basement ☐ Bathroom ☐ Windows ☐ None ☐ Not sure ☐ Other

If Other, please specify: _____

Please indicate which pets are currently living in the patient's home. (choose all that apply)

☐ Cats ☐ Dogs ☐ None ☐ Not sure ☐ Other

If Other, please specify: _____

What pests have been in the patient's home. (choose all that apply)

☐ Cockroaches ☐ Mice ☐ Rats ☐ None ☐ Not Sure ☐ Other

If Other, please specify: _____



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Does the patient have dust-proof allergy covers for the mattress and/or pillow? ☐ Yes ☐ No ☐ Not sure

Does the patient have a prolonged history of smoking? ☐ Yes ☐ No ☐ Not sure

Has the patient had prolonged exposure to smoke (family member, etc.)? ☐ Yes ☐ No ☐ Not sure

Family History

Was the patient adopted? ☐ Yes ☐ No

Please indicate whether the patient was delivered by vaginal delivery or C-section.

☐ Vaginal

☐ C-section

☐ Not sure

What was the age of the patient's mother at the time of birth? Years: ☐ Not sure

What was the age of the patient's father at the time of birth? Years: ☐ Not sure

What was the patient's birth weight?

Pounds: Ounces: ☐ Not sure

What was the patient's birth length?

Inches: ☐ Not sure ☐

Was the patient born more than 3 weeks before his/her due date? Yes ☐ No ☐ Not sure

At what week of gestation was he/she born? ☐ 37 or more weeks ☐ 32-36 weeks

☐ Less than 32 weeks ☐ Don't know

Did the patient take any antibiotics when he/she was a baby, less than one year of age? ☐ Yes ☐ No ☐ Not sure

If Yes, what happened? _____

Were there any emergency room visits during the first 3 months of life? ☐ Yes ☐ No ☐ Not sure

If Yes, what happened? _____

Did the patient spend any time in the neonatal intensive care unit (NICU) after he/she was born? ☐ Yes ☐ No ☐ Not Sure

Were there any hospitalizations in the first year of life? ☐ Yes ☐ No ☐ Not sure

If Yes, what happened? _____

Did the mother smoke at any time during the pregnancy the patient? ☐ Yes ☐ No ☐ Not sure

When the patient was born was he/she fed any breastmilk? ☐ Yes ☐ No ☐ Not sure

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⚠ If Yes and information is not available regarding the biological family history of the patient, please check unknown / unavailable history.

Please complete the following to inform us of the patient's family history (BIOLOGICAL relatives only).

Biological Relatives	Mother	Father	Maternal Grandma	Maternal Grandpa	Paternal Grandma	Paternal Grandpa	Patient's Sibling 1	Patient's Sibling 2	Patient's Sibling 3	Patient's Sibling 4	Patient's Child 1	Patient's Child 2	Patient's Child 3	Patient's Child 4
Not applicable/ history unavailable														
Date of Birth (mm/dd/yyyy) example: 02/24/ 1974	____/____/____	____/____/____					____/____/____	____/____/____	____/____/____	____/____/____	____/____/____	____/____/____	____/____/____	____/____/____
Sex							☐ M ☐ F	☐ M ☐ F	☐ M ☐ F	☐ M ☐ F	☐ M ☐ F	☐ M ☐ F	☐ M ☐ F	☐ M ☐ F

ALLERGY / IMMUNOLOGY

Allergic rhinitis (hayfever)														
Angioedema (tissue swelling disorder)														
Asthma														
Eczema / Atopic dermatitis														
Food allergy														
Hypereosinophilic syndrome														
Immunodeficiency														
Oral Allergy Syndrome														
Urticaria (recurrent hives)														

GASTROINTESTINAL

Achalasia														
Barrett's esophagus														
Celiac disease														
Eosinophilic Esophagitis (EoE)														
Eosinophilic GI disorder (other than EoE)														
Esophageal cancer														
Esophageal dilation or stricture														
Food impaction (getting stuck in throat)														
Gastroesophageal reflux disease (GERD)														
Inflammatory Bowel Disease (IBD)														
Reflux surgery														
Stomach or duodenal ulcer														



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Biological Relatives	Mother	Father	Maternal Grandma	Maternal Grandpa	Paternal Grandma	Paternal Grandpa	Patient's Sibling 1	Patient's Sibling 2	Patient's Sibling 3	Patient's Sibling 4	Patient's Child 1	Patient's Child 2	Patient's Child 3	Patient's Child 4
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MISCELLANEOUS

Arthritis / Joint pain														
Diabetes														
Connective Tissue Disorder														
Other:														
Unknown / Unavailable history														

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Questionnaire Reviewed By