

METHODS

RNA extraction and miRNA microarray analysis

Total RNA, including miRNA from patients' esophageal biopsy samples, was isolated with the miRNeasy Mini Kit, according to the manufacturer's instructions (Qiagen). RNA quality was assessed by using the Agilent 2100 Bioanalyzer (Agilent Technologies), and only samples with an RNA integrity number of greater than 8 were used. MiRNA expression was profiled by using TaqMan Human MicroRNA Array version 2.0, which includes probes for 667 human miRNAs in the miRBase microRNA Registry (release 10.0), according to the manufacturer's protocols (Applied Biosystems).^{E1} Data analyses were carried out with GeneSpring software (Agilent Technologies). Expression data were normalized to the average of 2 endogenous control probes, U6 and RNU44, and then filtered on cycle threshold values of less than 30 and at least a 2-fold change between healthy control subjects and patients with EoE to identify miRNAs differentially regulated between healthy control subjects and patients with EoE. Statistical significance was determined at a *P* value of less than .05 with a Benjamini-Hochberg false discovery rate correction. The list of differentially expressed miRNAs was clustered by using hierarchical clustering, and a heat map was generated. Similar analyses were carried out comparing healthy control subjects with patients with chronic esophagitis and patients who did not receive glucocorticoid treatment with patients who received glucocorticoid treatment to identify differentially expressed miRNAs between the groups. The microarray data have been deposited into the Array Express database (www.ebi.ac.uk/arrayexpress; accession no. E-MEXP-3298) in compliance with minimum information about microarray experiment (MIAME) standards.

Quantitative RT-PCR for miRNA

MiRNA expression levels were measured quantitatively by using TaqMan MicroRNA Assays (Applied Biosystems), according to the manufacturer's protocol. The expression levels were normalized to the U6 endogenous control. Relative expression was calculated by using the comparative cycle threshold method, as previously described.^{E2}

Correlation of miR-21 and miR-223 with major EoE signature genes

Esophageal mRNA from patients with EoE was reverse transcribed to cDNA by using a High Capacity cDNA Reverse Transcription Kit (Applied Biosystems), according to the manufacturer's protocol. The TaqMan reagents for amplification of EoE signature genes^{E3-E5} were obtained from Applied Biosystems. The EoE signature genes are listed in Table E2. TaqMan real-time PCR amplification was performed with an Applied Biosystems 7900HT Real-Time PCR System. The amplification protocol consisted of a hot start of 95°C for 10 minutes, followed by 40 cycles of 15 seconds at 95°C and 1 minute at 60°C. The expression correlation study between miR-21 and miR-223 and 48 EoE genes was performed in GraphPad Prism software (GraphPad Software, Inc, La Jolla, Calif). Negative logs of *P* values from Pearson correlation analysis were plotted to demonstrate correlation significance with EoE genes. To control for the increased risk of false-positive results caused by the number of statistical tests performed, we applied a Bonferroni correction based on the number of gene expression profiles compared. Because the average pairwise correlation between gene expression profiles was 0.54, we applied principal components analysis to determine the effective number of independent comparisons, as previously described.^{E6} By using this approach, a *P* value of .002 was required to achieve a family-wise error rate of 0.05.

Analysis of miR-21 and miR-223 coregulated genes by using RNA-Seq and gene expression microarray

RNA-Seq data were obtained from esophageal RNA samples from 11 patients with EoE by the Genomic Sequencing Core Laboratory at Cincinnati Children's Hospital Medical Center. The RNA-Seq was aligned to the GrCh37 build of the human genome by using the Ensembl annotations as a guide for TopHat.^{E7} The resulting files were then analyzed with Cufflinks to test for differential expression and differential regulation.^{E8} The region 3' of miR-21 is identified as the best representation of pri-miR-21 (labeled as exon 3 in Fig E3, A). The region 3' of miR-223 is identified as the best representation of pri-miR-223 (labeled as exon 2 in Fig E3, B).^{E9} The pri-miR-21 region was found to be significantly enriched in patients with EoE compared with that seen in healthy control subjects. The expression pattern of the pri-miR-21 was then correlated with the other gene expression patterns present from the RNA-Seq expression profiles. MiR-223 was analyzed in a similar fashion. We also analyzed gene expression microarray experiments from patients with EoE.^{E3,E5} MiR-21 and miR-223 were correlated by using the Affymetrix Human U133 probes (Affymetrix, Santa Clara, Calif) that best corresponded to the miRNA. A correlated gene is one the expression of which follows similar or inverse trends with the miRNA in question. These probes were correlated with microarray expression data, and 470 probes correlated well with at least 1 of the miRNA probes. The genes that showed the highest correlations and the top differentially regulated genes in the previously published EoE transcriptome were used as a training set alongside genes that are related to T_{H1}/T_{H2} differentiation and eosinophilia and that are target genes of miR-21 and miR-223.^{E10} The genes that showed patterns related to miR-21 or miR-223 were then analyzed to determine significant pathways and annotations related to T_{H1}/T_{H2} differentiation and eosinophil development and function. The genes were then clustered based on the strength of the annotations that are associated with them. The results are rendered as a Cytoscape map.

REFERENCES

- Griffiths-Jones S, Saini HK, van Dongen S, Enright AJ. miRBase: tools for microRNA genomics. *Nucleic Acids Res* 2008;36:D154-8.
- Livak KJ, Schmittgen TD. Analysis of relative gene expression data using real-time quantitative PCR and the 2(-Delta Delta C(T)) Method. *Methods* 2001;25:402-8.
- Blanchard C, Wang N, Stringer KF, Mishra A, Fulkerson PC, Abonia JP, et al. Eotaxin-3 and a uniquely conserved gene-expression profile in eosinophilic esophagitis. *J Clin Invest* 2006;116:536-47.
- Blanchard C, Mingler MK, Vicario M, Abonia JP, Wu YY, Lu TX, et al. IL-13 involvement in eosinophilic esophagitis: transcriptome analysis and reversibility with glucocorticoids. *J Allergy Clin Immunol* 2007;120:1292-300.
- Abonia JP, Blanchard C, Butz BB, Rainey HF, Collins MH, Stringer K, et al. Involvement of mast cells in eosinophilic esophagitis. *J Allergy Clin Immunol* 2010;126:140-9.
- Cheverud JM. A simple correction for multiple comparisons in interval mapping genome scans. *Heredity* 2001;87:52-8.
- Trapnell C, Pachter L, Salzberg SL. TopHat: discovering splice junctions with RNA-Seq. *Bioinformatics* 2009;25:1105-11.
- Trapnell C, Williams BA, Pertea G, Mortazavi A, Kwan G, van Baren MJ, et al. Transcript assembly and quantification by RNA-Seq reveals unannotated transcripts and isoform switching during cell differentiation. *Nat Biotechnol* 2010;28:511-5.
- Saini HK, Enright AJ, Griffiths-Jones S. Annotation of mammalian primary microRNAs. *BMC Genomics* 2008;9:564.
- Chen J, Bardes EE, Aronow BJ, Jegga AG. ToppGene Suite for gene list enrichment analysis and candidate gene prioritization. *Nucleic Acids Res* 2009;37:W305-11.

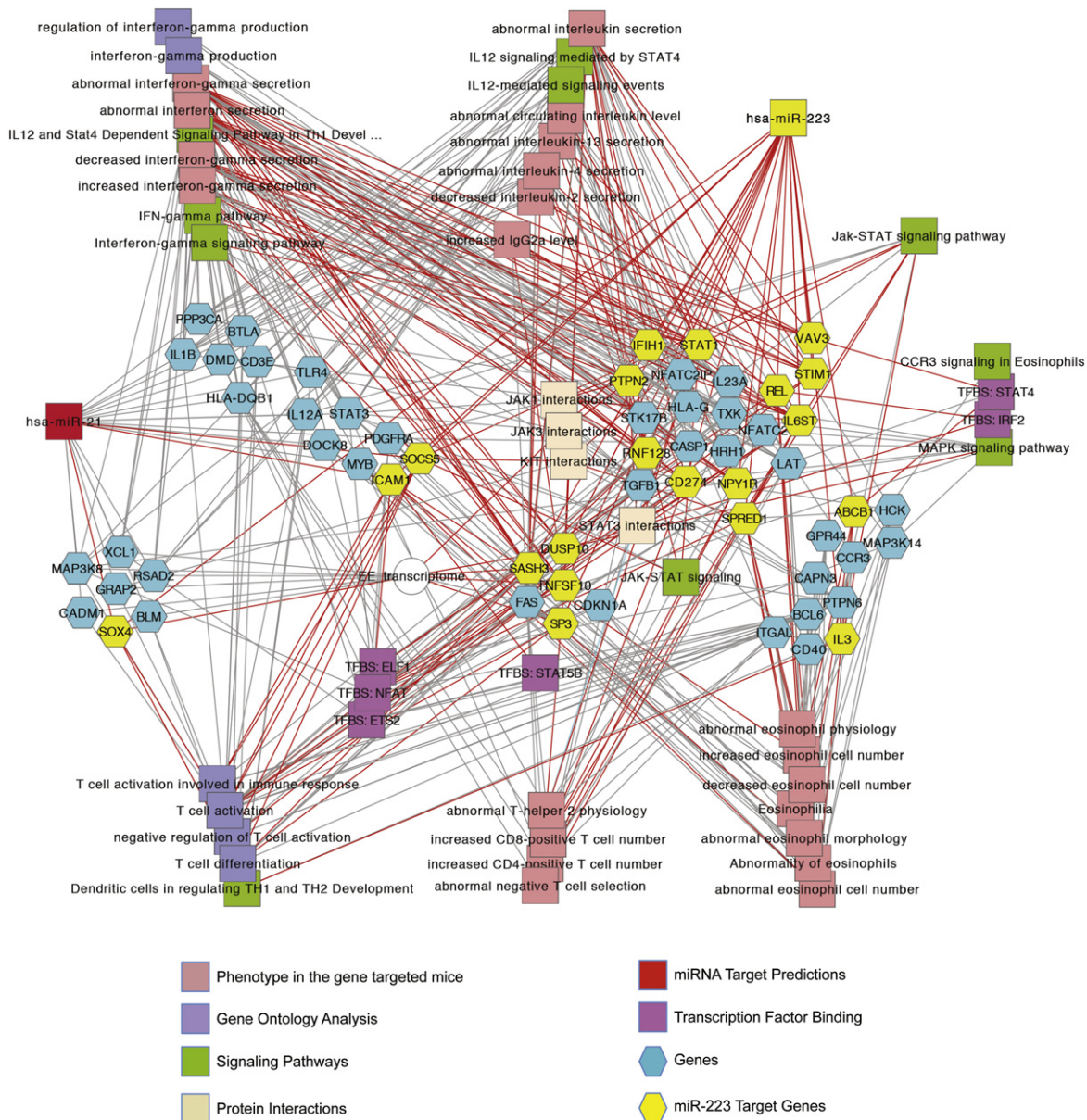


FIG E1. Gene enrichment analysis of miR-21 and miR-223 coregulated genes in patients with EoE. The miR-223 targets that are significantly correlated with miR-223 expression or in the EoE transcriptome are highlighted as yellow hexagons, and their respective feature and function relationships are shown connected through red edges. The features that are highly significant for other genes in the cluster are connected by gray edges. TFBS, Transcription factor binding sites.

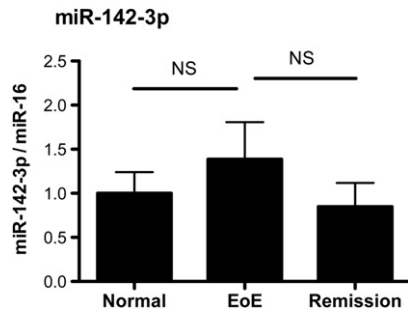


FIG E2. MiR-142-3p expression levels in patients' plasma samples. Expression of miR-142-3p was determined in plasma samples from patients with active EoE and patients with EoE remission compared with healthy control subjects. The relative expression levels were normalized to miR-16 (n = 13-14 plasma samples per group). Data are presented as mean \pm SEM. NS, Not significant ($P > .05$).

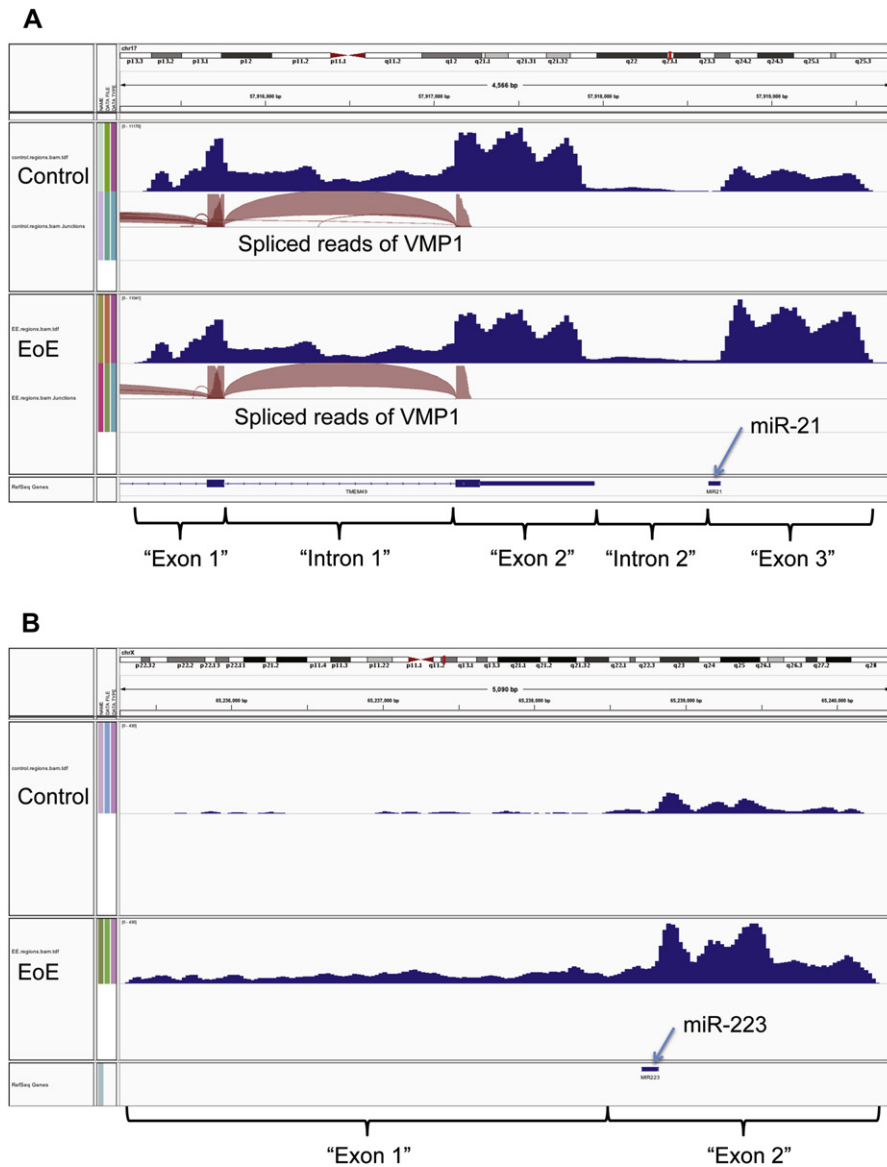


FIG E3. Regions identified as pri-miR-21 and pri-miR-223 in the RNA-Seq analysis. **A**, Identification of the pri-miR-21 region in the RNA-Seq analysis. The *blue regions* are normalized coverage tracks for the mRNA-seq. The *brown tracks* are spliced reads that are present in exons of *VMP1*. The lack of spliced reads present between the regions outside of the exons of *VMP1* leads to the assumption that it is a portion of pri-miR-21. The regions annotated as “exon” or “intron” are not necessarily true exons and introns of a gene but regions that showed significant expression patterns similar to those of a gene’s exons and introns. They were annotated as this to facilitate the identification of the region to use for the correlation analysis. **B**, Identification of the pri-miR-223 region in the RNA-Seq analysis. The *blue regions* are normalized coverage tracks for the mRNA-seq. There are no reads spanning junctions because there are no splicing events present in this region. The regions annotated as “exon” are not necessarily true exons of a gene but regions that showed significant expression patterns similar to those of a gene’s exons. They were annotated as this to facilitate the identification of the region to use for the correlation analysis.

TABLE E1. Patients' clinical characteristics

	Healthy control subjects	Patients with EoE	Patients with chronic esophagitis	Patients with EoE who responded to steroids	Patients with EoE who did not respond to steroids
No. of patients	23	31	9	20	8
Male sex, no. (%)	11 (48)	23 (74)	7 (78)	16 (80)	6 (75)
Age (y)					
Mean	9.26	9.29	9.06	8.32	10.96
Range	1.43-19.01	1.89-32.26	4.50-16.12	3.75-19.43	4.30-18.41
Medications					
PPI, no. (%)*	6 (26)	23 (74)	2 (22)	16 (80)	7 (88)
Steroids, no. (%)	0	0	0	20 (100)	8 (100)

PPI, Proton-pump inhibitor.

*Percentages listed reflect the total number of patients studied who had received at least 8 weeks of proton-pump inhibitor therapy before a diagnostic endoscopy.

TABLE E2. List of EoE signature genes used for correlation analysis

Entrez gene ID	Gene name	Description
55	<i>ACPP</i>	Acid phosphatase, prostate
72	<i>ACTG2</i>	Actin, gamma 2, smooth muscle, enteric
246	<i>ALOX15</i>	Arachidonate 15-lipoxygenase
383	<i>ARG1</i>	Arginase, liver
10344	<i>CCL26</i>	Chemokine (C-C motif) ligand 26
1232	<i>CCR3</i>	Chemokine (C-C motif) receptor 3
131450	<i>CD200R1</i>	CD200 receptor 1
978	<i>CDA</i>	Cytidine deaminase
60437	<i>CDH26</i>	Cadherin-like 26
3426	<i>CFI</i>	Complement factor I
10370	<i>CITED2</i>	Cbp/p300-interacting transactivator, with Glu/Asp-rich carboxy-terminal domain, 2
1178	<i>CLC</i>	Charcot-Leyden crystal protein
9071	<i>CLDN10</i>	Claudin 10
1215	<i>CMA1</i>	Chymase 1, mast cell
1296	<i>COL8A2</i>	Collagen, type VIII, alpha 2
1359	<i>CPA3</i>	Carboxypeptidase A3 (mast cell)
10321	<i>CRISP3</i>	Cysteine-rich secretory protein 3
8727	<i>CTNNA1</i>	Catenin (cadherin-associated protein), alpha-like 1
1828	<i>DSG1</i>	Desmoglein 1
2009	<i>EML1</i>	Echinoderm microtubule-associated protein-like 1
2312	<i>FLG</i>	Filaggrin
9245	<i>GCNT3</i>	Glucosaminyl (N-acetyl) transferase 3, mucin type
134266	<i>GRPEL2</i>	GrpE-like 2, mitochondrial (E. coli)
27306	<i>HPGDS</i>	hematopoietic prostaglandin D synthase
3269	<i>HRH1</i>	Histamine receptor H1
3512	<i>IGJ</i>	Immunoglobulin J polypeptide, linker protein for immunoglobulin alpha and mu polypeptides
3596	<i>IL13</i>	Interleukin 13
3565	<i>IL4</i>	Interleukin 4
3567	<i>IL5</i>	Interleukin 5 (colony-stimulating factor, eosinophil)
3568	<i>IL5RA</i>	Interleukin 5 receptor, alpha
3576	<i>IL8</i>	Interleukin 8
3759	<i>KCNJ2</i>	Potassium inwardly-rectifying channel, subfamily J, member 2
25984	<i>KRT23</i>	Keratin 23 (histone deacetylase inducible)
4321	<i>MMP12</i>	Matrix metalloproteinase 12 (macrophage elastase)
4585	<i>MUC4</i>	Mucin 4, cell surface associated
4747	<i>NEFL</i>	Neurofilament, light polypeptide 68kDa
5367	<i>PMCH</i>	Pro-melanin-concentrating hormone
10631	<i>POSTN</i>	Periostin, osteoblast-specific factor
64092	<i>SAMSN1</i>	SAM domain, SH3 domain and nuclear localization signals 1
9120	<i>SLC16A6</i>	Solute carrier family 16, member 6 (monocarboxylic acid transporter 7)
5172	<i>SLC26A4</i>	Solute carrier family 26, member 4
84651	<i>SPINK7</i>	Serine peptidase inhibitor, Kazal type 7 (putative)
7130	<i>TNFAIP6</i>	Tumor necrosis factor, alpha-induced protein 6
7177	<i>TPSAB1</i>	Tryptase alpha/beta 1
85480	<i>TSLP</i>	Thymic stromal lymphopoietin
23554	<i>TSPAN12</i>	Tetraspanin 12
11045	<i>UPK1A</i>	Uroplakin 1A
7348	<i>UPK1B</i>	Uroplakin 1B

TABLE E3. Log₂ fold change of all miRNAs expressed at greater than background levels

Gene symbol	Healthy control subjects	Patients with chronic esophagitis	Patients with EoE	Fluticasone responders
<i>U6</i>	0.005	0.010	0.070	-0.065
<i>RNU24</i>	0.052	-0.203	0.040	0.170
<i>RNU43</i>	-3.572	-3.124	-0.249	0.020
<i>RNU44</i>	-0.005	-0.010	-0.070	0.065
<i>RNU48</i>	-0.023	-0.031	0.249	0.093
<i>RNU6B</i>	0.055	-0.319	-0.050	-0.039
<i>hsa-let-7a</i>	-0.046	0.026	-0.019	0.007
<i>hsa-let-7b</i>	0.254	0.140	-0.057	-0.230
<i>hsa-let-7c</i>	0.114	-0.092	-0.973	-0.099
<i>hsa-let-7d</i>	0.065	0.033	0.001	0.152
<i>hsa-let-7e</i>	-0.074	-0.141	-0.390	-0.103
<i>hsa-let-7f-2*</i>	-0.033	-0.259	-0.153	-0.109
<i>hsa-let-7f</i>	-0.138	0.146	-0.250	0.151
<i>hsa-let-7g</i>	-0.005	0.261	0.089	0.553
<i>hsa-miR-1</i>	-0.960	-1.173	-2.695	-2.563
<i>hsa-miR-100</i>	-0.027	-0.144	-0.602	0.333
<i>hsa-miR-101</i>	-0.029	-0.117	-0.060	0.353
<i>hsa-miR-103</i>	-0.099	-0.178	-0.184	0.254
<i>hsa-miR-106a</i>	-0.155	0.034	-0.055	0.189
<i>hsa-miR-106b*</i>	-0.749	0.676	2.046	1.049
<i>hsa-miR-106b</i>	-0.111	0.210	0.234	0.628
<i>hsa-miR-107</i>	0.089	0.190	-0.677	0.192
<i>hsa-miR-10a</i>	0.129	-0.352	-0.076	-0.210
<i>hsa-miR-10b*</i>	-0.172	-0.278	-0.183	-0.199
<i>hsa-miR-10b</i>	-0.258	-0.063	-0.083	-0.029
<i>hsa-miR-125a-5p</i>	-0.009	-0.428	0.016	-0.469
<i>hsa-miR-125b</i>	0.170	0.216	-0.067	0.505
<i>hsa-miR-126*</i>	0.146	-0.294	-0.240	0.041
<i>hsa-miR-126</i>	0.160	-0.108	-0.200	-0.188
<i>hsa-miR-127</i>	0.067	-0.726	-0.248	-0.936
<i>hsa-miR-128a</i>	0.019	0.266	0.185	0.369
<i>hsa-miR-130a</i>	0.215	0.323	0.328	1.002
<i>hsa-miR-130b</i>	-0.012	0.359	0.509	0.753
<i>hsa-miR-132</i>	0.062	0.321	1.858	-0.013
<i>hsa-miR-133a</i>	-0.694	-0.988	-2.194	-2.236
<i>hsa-miR-135a*</i>	0.163	-0.495	-0.379	-0.780
<i>hsa-miR-135a</i>	0.278	0.607	-0.381	0.505
<i>hsa-miR-135b*</i>	0.004	0.024	0.465	0.436
<i>hsa-miR-135b</i>	0.076	0.271	-0.243	0.551
<i>hsa-miR-138-1*</i>	0.154	-0.393	0.257	-0.244
<i>hsa-miR-138</i>	-0.241	-0.183	0.684	-0.348
<i>hsa-miR-139-5p</i>	0.184	-0.092	-0.415	0.067
<i>hsa-miR-140-3p</i>	0.101	-0.250	0.203	-0.106
<i>hsa-miR-140</i>	0.199	-0.206	0.521	-0.281
<i>hsa-miR-141</i>	-0.061	0.091	-0.203	0.712
<i>hsa-miR-142-3p</i>	0.184	0.521	2.219	0.489
<i>hsa-miR-142-5p</i>	-0.087	0.206	1.854	0.411
<i>hsa-miR-143</i>	0.420	-0.177	-0.180	-0.706
<i>hsa-miR-144*</i>	-0.112	-0.996	-1.429	0.021
<i>hsa-miR-145*</i>	0.377	-0.590	-0.711	-0.982
<i>hsa-miR-145</i>	0.184	-0.904	-1.032	-1.493
<i>hsa-miR-146a</i>	0.150	0.114	1.635	-0.280
<i>hsa-miR-146b</i>	0.042	0.249	2.153	-0.046
<i>hsa-miR-148a</i>	-0.059	0.132	-0.365	0.372
<i>hsa-miR-148b*</i>	0.072	-0.064	0.174	0.140
<i>hsa-miR-148b</i>	0.024	0.067	-0.033	0.292
<i>hsa-miR-149</i>	0.021	0.007	-0.366	-0.230
<i>hsa-miR-150</i>	-0.143	-0.156	0.692	0.155

(Continued)

TABLE E3. (Continued)

Gene symbol	Healthy control subjects	Patients with chronic esophagitis	Patients with EoE	Fluticasone responders
<i>hsa-miR-151-3p</i>	0.008	-0.311	0.335	0.238
<i>hsa-miR-152</i>	0.046	-0.006	0.413	0.000
<i>hsa-miR-155</i>	-4.901	-2.608	-4.867	0.547
<i>hsa-miR-15a*</i>	-0.096	-0.469	-0.102	-0.108
<i>hsa-miR-15a</i>	-0.157	-0.097	0.677	-5.024
<i>hsa-miR-15b*</i>	-4.120	-2.228	-6.134	0.968
<i>hsa-miR-15b</i>	-0.055	0.034	0.048	0.675
<i>hsa-miR-16-1*</i>	-0.301	-0.355	0.559	-0.062
<i>hsa-miR-16</i>	-0.074	-0.228	-0.223	-0.182
<i>hsa-miR-17*</i>	-0.185	-0.392	-0.473	0.006
<i>hsa-miR-17</i>	-0.121	0.022	-0.037	0.257
<i>hsa-miR-181a-2*</i>	0.021	-0.356	-0.905	0.052
<i>hsa-miR-181a</i>	0.262	0.375	0.407	0.511
<i>hsa-miR-182</i>	0.125	0.342	-0.595	-0.155
<i>hsa-miR-183*</i>	-0.243	-0.314	-1.218	0.182
<i>hsa-miR-183</i>	-0.077	0.052	-0.637	0.135
<i>hsa-miR-185</i>	0.071	0.091	0.930	0.226
<i>hsa-miR-186</i>	-0.203	-0.496	-0.586	-0.520
<i>hsa-miR-188-5p</i>	0.198	-0.605	0.261	-0.333
<i>hsa-miR-18a</i>	0.067	0.444	0.787	0.426
<i>hsa-miR-18b</i>	-3.585	-1.188	-3.780	0.876
<i>hsa-miR-190</i>	-0.061	0.336	-0.107	0.804
<i>hsa-miR-191</i>	0.049	-0.127	0.013	-0.034
<i>hsa-miR-192</i>	0.535	2.019	0.286	1.957
<i>hsa-miR-193a-3p</i>	-0.119	-0.791	-1.513	-0.406
<i>hsa-miR-193a-5p</i>	-0.050	-0.603	-1.261	-0.243
<i>hsa-miR-193b*</i>	-1.347	-1.035	-7.696	0.082
<i>hsa-miR-193b</i>	0.048	-0.346	-1.910	-0.190
<i>hsa-miR-194</i>	0.487	2.388	0.125	1.506
<i>hsa-miR-195</i>	0.157	-0.176	-0.034	-0.107
<i>hsa-miR-197</i>	0.001	-0.021	0.137	0.306
<i>hsa-miR-199a-3p</i>	0.160	-0.182	0.327	-0.202
<i>hsa-miR-19a</i>	-0.010	0.123	0.288	0.119
<i>hsa-miR-19b-1*</i>	0.027	0.074	0.379	0.169
<i>hsa-miR-19b</i>	0.005	0.022	0.071	0.222
<i>hsa-miR-200a*</i>	0.056	-0.064	0.066	0.210
<i>hsa-miR-200a</i>	0.036	0.220	0.003	0.476
<i>hsa-miR-200b*</i>	-0.105	-0.157	-0.270	0.400
<i>hsa-miR-200b</i>	-0.063	0.036	-0.409	0.247
<i>hsa-miR-200c</i>	0.017	0.233	-0.240	0.126
<i>hsa-miR-203</i>	-0.059	-0.324	-1.843	0.099
<i>hsa-miR-204</i>	-0.035	1.078	-1.204	0.139
<i>hsa-miR-205</i>	-0.159	-0.037	-0.283	-0.227
<i>hsa-miR-20a*</i>	0.020	-0.282	-0.181	0.088
<i>hsa-miR-20a</i>	-0.001	0.140	0.047	0.325
<i>hsa-miR-20b</i>	0.028	-0.086	0.094	0.022
<i>hsa-miR-21*</i>	0.019	0.506	2.639	0.227
<i>hsa-miR-21</i>	-0.058	0.840	2.332	0.596
<i>hsa-miR-210</i>	0.038	-0.240	-1.570	0.200
<i>hsa-miR-211</i>	-0.099	-0.728	-2.985	-0.028
<i>hsa-miR-212</i>	0.005	0.377	1.914	0.290
<i>hsa-miR-214</i>	0.158	-0.554	0.644	-0.686
<i>hsa-miR-215</i>	-0.516	1.547	-3.082	1.916
<i>hsa-miR-218</i>	0.090	-0.234	-0.494	0.193
<i>hsa-miR-22*</i>	-0.186	-0.621	-0.697	-0.010
<i>hsa-miR-22</i>	-1.148	1.084	0.308	1.058
<i>hsa-miR-221</i>	-0.144	-0.172	0.286	-0.085
<i>hsa-miR-222*</i>	-0.076	-0.093	1.057	-0.063
<i>hsa-miR-222</i>	0.071	0.118	0.425	-0.019
<i>hsa-miR-223*</i>	0.249	-0.076	3.303	0.183

(Continued)

TABLE E3. (Continued)

Gene symbol	Healthy control subjects	Patients with chronic esophagitis	Patients with EoE	Fluticasone responders
<i>hsa-miR-223</i>	0.042	0.125	3.348	0.223
<i>hsa-miR-224</i>	-0.024	-0.066	-0.455	0.259
<i>hsa-miR-23b</i>	0.040	0.084	-0.265	-0.169
<i>hsa-miR-24</i>	-0.067	-0.062	-0.317	0.165
<i>hsa-miR-25</i>	-0.084	0.041	0.303	0.342
<i>hsa-miR-26a-1*</i>	0.074	-0.096	0.081	0.184
<i>hsa-miR-26a-2*</i>	0.025	-0.433	1.020	0.434
<i>hsa-miR-26a</i>	0.004	0.017	-0.132	0.336
<i>hsa-miR-26b*</i>	0.082	-0.131	0.375	0.114
<i>hsa-miR-26b</i>	-0.024	0.024	-0.115	0.367
<i>hsa-miR-27a*</i>	-0.027	-0.220	0.338	0.153
<i>hsa-miR-27a</i>	-0.081	0.151	0.376	0.414
<i>hsa-miR-27b*</i>	-0.079	-0.130	0.756	0.027
<i>hsa-miR-27b</i>	-0.074	0.227	0.330	0.514
<i>hsa-miR-28-3p</i>	-0.114	-0.221	-0.164	0.146
<i>hsa-miR-28</i>	-0.120	-0.187	0.245	0.067
<i>hsa-miR-296</i>	-0.114	0.207	-0.397	0.756
<i>hsa-miR-29a*</i>	-0.054	-0.524	0.511	-0.266
<i>hsa-miR-29a</i>	0.292	0.414	1.205	0.441
<i>hsa-miR-29b</i>	0.120	0.391	1.290	0.761
<i>hsa-miR-29c*</i>	0.119	-0.226	0.207	-0.057
<i>hsa-miR-29c</i>	-0.166	0.085	-0.067	0.671
<i>hsa-miR-301</i>	0.028	0.035	0.241	0.084
<i>hsa-miR-301b</i>	-0.105	0.141	0.492	0.312
<i>hsa-miR-30a-3p</i>	0.300	-0.599	-0.900	-0.349
<i>hsa-miR-30a-5p</i>	0.254	-0.368	-0.345	0.221
<i>hsa-miR-30b</i>	-0.129	-0.103	-0.399	0.371
<i>hsa-miR-30c</i>	-0.005	-0.013	-0.364	0.220
<i>hsa-miR-30d*</i>	0.011	-0.322	-0.010	0.255
<i>hsa-miR-30d</i>	0.283	-0.406	-0.138	0.155
<i>hsa-miR-30e-3p</i>	0.139	-0.532	-0.413	-0.190
<i>hsa-miR-30e</i>	0.120	-0.367	-0.194	0.070
<i>hsa-miR-31</i>	-0.183	0.077	-0.961	-0.117
<i>hsa-miR-32</i>	0.017	0.297	-0.142	0.299
<i>hsa-miR-320</i>	-0.119	-0.229	-0.331	-0.101
<i>hsa-miR-324-3p</i>	0.024	0.003	-0.348	0.121
<i>hsa-miR-324-5p</i>	-0.038	0.256	0.109	0.583
<i>hsa-miR-328</i>	0.270	-0.074	-0.150	-0.043
<i>hsa-miR-331</i>	0.094	0.230	-0.152	0.418
<i>hsa-miR-335*</i>	-0.246	-0.405	-0.215	0.413
<i>hsa-miR-335</i>	-0.098	-0.256	0.065	0.143
<i>hsa-miR-339-3p</i>	-0.094	-0.140	-0.094	0.037
<i>hsa-miR-339-5p</i>	-0.070	0.592	1.144	1.286
<i>hsa-miR-33a*</i>	-0.059	-0.031	-0.097	0.062
<i>hsa-miR-340*</i>	-0.080	-0.299	0.439	0.018
<i>hsa-miR-340</i>	-0.068	0.209	0.793	0.139
<i>hsa-miR-342-3p</i>	-0.021	0.043	0.754	-0.007
<i>hsa-miR-345</i>	-0.110	0.214	0.626	0.297
<i>hsa-miR-34a*</i>	-0.044	-0.492	0.141	-0.140
<i>hsa-miR-34a</i>	-0.090	-0.132	0.000	0.295
<i>hsa-miR-34c</i>	0.746	-0.396	3.306	0.526
<i>hsa-miR-361</i>	0.020	0.362	0.272	0.389
<i>hsa-miR-362-3p</i>	0.064	0.079	0.143	0.310
<i>hsa-miR-362</i>	0.006	0.136	0.016	0.076
<i>hsa-miR-365</i>	-0.044	-0.564	-1.684	-0.107
<i>hsa-miR-374</i>	-0.017	-0.035	-0.177	0.154
<i>hsa-miR-374-5p</i>	0.025	0.145	-0.151	0.427
<i>hsa-miR-375</i>	-0.032	-0.363	-4.953	0.073
<i>hsa-miR-376c</i>	0.455	-0.335	0.399	-0.088
<i>hsa-miR-378</i>	-0.115	-0.311	-0.219	0.220

(Continued)

TABLE E3. (Continued)

Gene symbol	Healthy control subjects	Patients with chronic esophagitis	Patients with EoE	Fluticasone responders
<i>hsa-miR-378</i>	0.011	-0.378	0.025	0.124
<i>hsa-miR-380-5p</i>	-0.109	-0.638	0.067	-0.462
<i>hsa-miR-411</i>	0.028	-0.413	-0.433	-0.746
<i>hsa-miR-422a</i>	-0.006	0.030	0.210	-0.079
<i>hsa-miR-423-5p</i>	-0.065	-0.254	0.194	0.221
<i>hsa-miR-425*</i>	-0.008	0.205	0.871	0.278
<i>hsa-miR-425-5p</i>	0.021	0.367	0.419	0.443
<i>hsa-miR-429</i>	0.041	0.266	-0.125	0.463
<i>hsa-miR-451</i>	-0.179	-0.586	-1.137	0.210
<i>hsa-miR-452</i>	0.070	0.051	-0.338	0.248
<i>hsa-miR-454</i>	-0.074	0.055	0.436	-0.100
<i>hsa-miR-455-3p</i>	-0.105	0.274	0.742	0.478
<i>hsa-miR-455</i>	0.084	0.246	0.605	0.535
<i>hsa-miR-483-5p</i>	0.751	0.744	0.759	-0.391
<i>hsa-miR-484</i>	0.031	-0.202	0.070	0.001
<i>hsa-miR-491</i>	0.013	-0.162	-0.168	0.141
<i>hsa-miR-494</i>	0.945	1.112	0.886	0.306
<i>hsa-miR-495</i>	-0.057	-0.345	-0.226	-0.848
<i>hsa-miR-497</i>	0.094	-0.847	-0.727	-0.440
<i>hsa-miR-500</i>	-0.709	-0.105	-2.617	0.970
<i>hsa-miR-500</i>	-0.060	0.109	0.228	0.370
<i>hsa-miR-501</i>	0.023	3.372	1.185	5.325
<i>hsa-miR-502-3p</i>	-0.003	-0.068	0.068	0.294
<i>hsa-miR-502</i>	-0.050	0.414	0.395	0.874
<i>hsa-miR-505*</i>	0.090	-0.424	0.469	-0.065
<i>hsa-miR-532-3p</i>	-0.012	-0.071	-0.142	0.239
<i>hsa-miR-532</i>	0.036	-0.263	-0.024	-0.019
<i>hsa-miR-545</i>	0.024	1.117	0.560	1.007
<i>hsa-miR-565</i>	0.039	-0.143	0.907	0.143
<i>hsa-miR-574-3p</i>	0.051	-0.452	-0.657	-0.234
<i>hsa-miR-576-3p</i>	-0.150	-0.269	-0.008	0.064
<i>hsa-miR-579</i>	-0.015	0.073	-0.291	0.445
<i>hsa-miR-590-5p</i>	0.009	-0.127	0.056	0.016
<i>hsa-miR-592</i>	-0.135	0.816	1.663	0.054
<i>hsa-miR-597</i>	0.244	0.582	0.668	0.774
<i>hsa-miR-598</i>	0.003	0.037	-0.302	0.285
<i>hsa-miR-625*</i>	0.129	-0.100	0.664	0.168
<i>hsa-miR-625</i>	0.034	0.236	0.839	0.516
<i>hsa-miR-628-5p</i>	0.041	0.079	0.863	-0.103
<i>hsa-miR-629</i>	-0.013	-0.114	-0.200	0.226
<i>hsa-miR-629</i>	-0.068	-0.584	-0.378	0.187
<i>hsa-miR-642</i>	-0.041	0.403	1.165	1.110
<i>hsa-miR-650</i>	0.166	-3.439	9.602	1.714
<i>hsa-miR-652</i>	0.206	0.504	0.366	0.622
<i>hsa-miR-660</i>	-0.046	0.002	0.038	0.433
<i>hsa-miR-661</i>	0.329	-0.214	0.820	-0.477
<i>hsa-miR-671-3p</i>	0.012	0.069	0.522	0.062
<i>hsa-miR-675</i>	0.150	-0.208	-4.643	7.873
<i>hsa-miR-7-1*</i>	-0.259	-0.202	0.257	0.229
<i>hsa-miR-7</i>	0.158	0.399	1.221	0.640
<i>hsa-miR-708</i>	0.079	-0.180	-0.563	0.407
<i>hsa-miR-744*</i>	-0.005	-0.212	-0.678	0.095
<i>hsa-miR-744</i>	0.055	0.034	-0.335	0.107
<i>hsa-miR-760</i>	0.194	-0.633	-0.054	-0.896
<i>hsa-miR-766</i>	-2.682	-0.455	1.014	0.580
<i>hsa-miR-768-3p</i>	-0.005	-0.081	0.770	0.167
<i>hsa-miR-769-5p</i>	-0.064	-0.285	0.263	0.196
<i>hsa-miR-801</i>	0.084	-0.460	3.908	-0.568
<i>hsa-miR-877</i>	0.233	-0.078	0.571	-0.423
<i>hsa-miR-885-5p</i>	-0.184	0.003	-0.027	0.781

(Continued)

TABLE E3. (Continued)

Gene symbol	Healthy control subjects	Patients with chronic esophagitis	Patients with EoE	Fluticasone responders
<i>hsa-miR-886-3p</i>	-0.032	-0.099	1.583	-0.316
<i>hsa-miR-886-5p</i>	0.094	0.177	1.528	-0.277
<i>hsa-miR-9</i>	-0.123	0.018	-0.222	0.145
<i>hsa-miR-923</i>	0.853	0.445	-0.866	-0.802
<i>hsa-miR-92a-1*</i>	-0.333	0.151	1.129	0.872
<i>hsa-miR-92a</i>	-0.052	0.107	0.198	0.491
<i>hsa-miR-93*</i>	-0.051	0.006	0.242	0.308
<i>hsa-miR-93</i>	-0.008	0.004	0.385	-0.081
<i>hsa-miR-942</i>	-0.347	0.008	0.164	0.530
<i>hsa-miR-944</i>	0.007	-0.182	-0.081	0.130
<i>hsa-miR-95</i>	-0.051	0.229	0.301	0.565
<i>hsa-miR-96</i>	-0.063	-0.129	-0.525	0.195
<i>hsa-miR-99a*</i>	0.158	-0.326	-0.600	0.285
<i>hsa-miR-99a</i>	-0.052	-0.113	-0.619	0.274
<i>hsa-miR-99b*</i>	-0.088	0.298	0.204	1.290
<i>hsa-miR-99b</i>	0.043	-0.055	0.131	-0.018

Asterisks (*) after the name of the miRNA indicate the minor form of the miRNA derived from the passenger strand.