

Blood Transcriptome Profiling in Myasthenia Gravis Patients to Assess Disease Activity: A Pilot RNA-seq Study

Kee Hong Park¹, Junghee Jung², Jung-Hee Lee³ and Yoon-Ho Hong^{4*}

¹Department of Neurology, Gyeongsang National University Hospital, Jinju 52727,

²Department of Bioinformatics, Macrogen Inc., Seoul 08511, ³Department of Biomedical Science, Hallym University, Chuncheon 24252, ⁴Department of Neurology, Seoul Metropolitan Government Seoul National University Boramae Medical Center, Seoul 07061, Korea

Myasthenia gravis (MG) is an antibody-mediated autoimmune disease characterized by exertional weakness. There is no biomarker to reflect disease activity and guide treatment decision. Here, we reported a pilot blood transcriptome study using RNA sequencing (RNA-seq) that identified differences of 5 samples in active status and 5 in remission from 8 different patients and 2 patients provided samples for both active and remission phase. We found a total of 28 differentially expressed genes (DEGs) possibly related to disease activity (23 up-regulated and 5 down-regulated). The DEGs were enriched for the cell motion and cell migration processes in which included were ICAM1, CCL3, S100P and GAB2. The apoptosis and cell death pathway was also significantly enriched, which includes NFKBIA, ZC3H12A, TNFAIP3, and PPP1R15A. Our result suggests that transcript abundance profiles of the genes involved in cell trafficking and apoptosis may be a molecular signature of the disease activity in MG patients.

Key words: Transcriptome, RNA sequencing, myasthenia gravis, cell migration, apoptosis

INTRODUCTION

Myasthenia gravis (MG) is an antibody-mediated autoimmune disease characterized by exertional skeletal muscle weakness, caused by auto-antibodies to components of muscle membrane at neuromuscular junction (NMJ) [1]. Acetylcholine receptor (AChR) antibodies are detected in about 85% of MG patients, and antibodies to muscle-specific tyrosine kinase (MuSK) are positive

in approximately half of the generalized seronegative MG patients [2]. The list of pathogenic auto-antibodies in MG has been recently expanded with discovery of antibodies to low-density lipoprotein receptor-related protein 4 (LRP4) and agrin in some of the double-seronegative MG patients [3]. These highly specific auto-antibodies in MG have a crucial role for the diagnosis of disease, and MuSK antibody in particular seem to be useful in predicting adverse effects to acetylcholinesterase inhibitors and refractoriness to conventional immunosuppressive treatment [4]. Although the levels of these auto-antibodies tend to decrease with immunosuppressive treatment, they are highly variable between patients, and do not correlate with disease severity [5]. There is an unmet clinical need to develop biomarkers that can reflect disease activity and/or severity, and to guide treatment decisions.

Received January 6, 2016, Revised February 5, 2016,
Accepted February 5, 2016

* To whom correspondence should be addressed.
TEL: 82-2-840-2474, FAX: 82-2-831-2826
e-mail: nrhong@gmail.com

Gene expression profiling on a genome-wide scale has been increasingly used to investigate pathogenesis, and also to develop potential biomarkers in various human diseases. Advances of high-throughput techniques such as DNA microarrays and recently RNA sequencing (RNA-seq) allow us to analyze gene expression in an unbiased and comprehensive way [6]. In MG, distinct gene expression signatures were found in the thymus of AChR antibody positive patients using microarrays, which include dysregulation of chemokines such as CCL21, CXCL13, CXCL10 and CXCR3 [7-9]. Interferon type I overexpression together with dysregulated expression of dsRNA signaling molecules was found in thymoma-associated MG patients [10]. Of note, previous gene expression studies mostly have used thymic tissues which are not readily accessible. Furthermore, it is not feasible to sample repeatedly in order to monitor disease activity and response to treatment. Since the status of human immune system may be best monitored by the changes of the composition and transcript abundance of circulating immune cells, blood transcriptome could be a good alternative target of investigation. Indeed, recent studies in autoimmune disease such as systemic lupus erythematosus, multiple sclerosis, and psoriasis have demonstrated perturbation of blood transcriptome, and identified molecular signatures to predict clinical relapse and response to treatment [11-13]. Here, we report the results of blood whole transcriptome study using RNA-seq in 8 patients with MG who were in either remission or active

disease states. We found 28 genes that are differentially expressed (DEGs) according to disease activity. Functional analysis suggested that genes expression profiles related to immune cell trafficking and apoptosis might be a molecular signature of the disease activity in MG.

MATERIALS AND METHODS

Patients

This study was approved by the Institutional Review Board of the Seoul Metropolitan Government Boramae Medical Center (IRB no. 16-2013-116). Written informed consent was obtained from the participants who were diagnosed as having MG and on the status of either active or remission. The active group consisted of 5 patients with *de novo* or refractory MG (moderate to severe symptoms despite long-term immunosuppressive treatment). Disease severity was graded according to the Myasthenia Gravis Foundation of America (MGFA) Clinical Classification [14]. Remission was defined by the MGFA post-intervention status, and included complete stable remission (CSR), pharmacologic remission (PR), and minimal manifestation (MM) (Table 1). Two patients provided samples at different time points, one during active disease status and the other in remission state. There were not statistically differences of mean age ($p=0.69$), disease duration ($p=0.31$), and AChR antibody titer ($p=0.69$) between 2 groups.

Table 1. Demographics of study population

| Group | Patient number | Sex | Age | Disease duration (month) | MG type | AChR Ab titer | Thymus | MGFA classification | Treatment at sample date |
|-----------------|----------------|-----|-----|--------------------------|-------------|---------------|---------|---------------------|---|
| Active group | 1* | M | 71 | 2 | Generalized | 6.4 | NL | IIa | Before treatment |
| | 2† | M | 53 | 1 | Generalized | <0.01 | NL | IIIa | Before treatment |
| | 3 | F | 54 | 156 | Generalized | 3.12 | NL | IIIa | Pd 20 mg qod Pyridostigmine 60 mg qid |
| | 4 | M | 76 | 3 | Ocular | 5.69 | NL | I | Before treatment |
| | 5 | F | 62 | 4 | Ocular | 4.47 | Thymoma | I | Before treatment |
| Remission group | 6* | M | 71 | 4 | Generalized | 6.4 | NL | MM | Pd 60 mg qod Pyridostigmine 60 mg tid |
| | 7† | M | 54 | 3 | Generalized | <0.01 | NL | PR | Pd 45 mg qd Tacrolimus 2 mg qd Pyridostigmine 60 mg tid |
| | 8 | F | 53 | 93 | Ocular | 4.08 | NL | MM | Pd 20 mg qod Azathioprine 50 mg qd Pyridostigmine 60 mg tid |
| | 9 | M | 73 | 36 | Generalized | 4.66 | NL | PR | Pd 10 mg qd Pyridostigmine 60 mg tid Tacrolimus 2 mg qd |
| | 10 | F | 77 | 16 | Generalized | 8.72 | NL | PR | Tacrolimus 2 mg qd |

*Patient 1 and 6 are same patients.

†Patient 2 and 7 are same patients.

Abbreviations: MG: myasthenia gravis; AChR Ab: acetylcholine receptor antibody; MGFA: Myasthenia Gravis Foundation of America; M: male; F: female; NL: normal; Pd: prednisolone; MM: minimal manifestation; PR: pharmacologic remission.

PBMC isolation and RNA purification

For isolation of peripheral blood mononuclear cells (PBMC), the Lymphoprep™ was used according to the manufacturer's protocol (Axis-shield, Oslo, Norway). Medium was placed in the tube, and then blood sample diluted with saline with 1:1 was added. After centrifugation for 20 minutes at 600×g, sedimented PBMCs were harvested. RNA purification was performed with the RNeasy Mini kit with the isolated PBMC sample (Qiagen, Seoul, Korea). The cell pellet was mixed with RLT buffer and 70% ethanol. The lysate was then loaded onto the RNeasy Mini spin column to facilitate the binding of RNA to the column and for the removal of contaminants. DNase was added to remove residual DNA efficiently.

RNA-Seq

The mRNA-Seq sample was obtained using Illumina TruSeq™ RNA Sample Preparation Kit (Illumina, Inc., San Diego, CA, USA). In brief, purifying the poly-A containing mRNA molecules with poly-T oligo-attached magnetic beads was the first step, followed by thermal mRNA fragmentation. The RNA fragments were then transcribed into first strand cDNA using reverse transcriptase and random primers. The cDNA was synthesized to second strand cDNA using DNA Polymerase I and RNase H. After the end repair process, single 'A' bases were added to the fragments and adapters were then ligated, preparing cDNA for hybridization onto a flow cell. Finally, the products were purified and enriched with PCR to create the cDNA library (Macrogen, Seoul, Korea).

Aligning RNA-Seq reads and abundance estimation

Fragmented cDNAs were aligned using TopHat v.2.0.11 [15] and subsequently aligned with sequences obtained from the human genome (UCSC version hg19) using the Bowtie 2.1.0 algorithm [16]. Abundance of aligned reads were estimated by Cufflinks v.2.1.1 [17], which accepted aligned reads and assembled the alignments into a simple and clear set of transcripts. Next, RNA-seq fragment counts were measured by the unit of fragments per kilobase of exon per million fragments mapped (FPKM) [18]. DESeq, another tool for DEG analysis, was used to compare the results with Cuffdiff analysis. Cuffdiff determines differential expression using t-test from FPKM values and is based on beta negative binomial model [19], while DESeq uses exact test based on negative binomial model [20]. We compared the results from Cuffdiff and DESeq analyses, and took the intersection of them for downstream pathway analysis.

Statistical analysis

For DEG analysis, the values of log₂ (FPKM+1) were calculated,

and these were normalized by quantile normalization. p-values were obtained by t-test between the active and remission groups, and fold changes were calculated with the mean log₂ (FPKM+1) values, gene by gene. All data analysis of DEG was conducted using R 2.14.1 (www.r-project.org). To segregate the samples according to the disease activity, a multi-dimensional scaling (MDS) analysis was done.

Pathway analysis using DAVID and IPA

For functional enrichment analysis using gene ontology (GO), the Database for Annotation, Visualization and Integrated Discovery (DAVID v.6.7) was used. The list of commonly detected genes both in Cuffdiff and DESeq analysis was uploaded via the web interface (<http://david.abcc.ncifcrf.gov>), and the background was designated as *Homo sapiens* [21]. Functional annotation clusters were selected using the cutoff threshold enrichment score 1.3 which is equivalent to a non-log scale score of 0.05. Gene interaction was visualized by Gene Multiple Association Network Integration Algorithm (GeneMANIA) (<http://www.genemania.org/>). Another functional analysis was performed with the Ingenuity Pathway Analysis (IPA) software (licensed use of Ingenuity Systems, www.qiagen.com/ingenuity).

RESULTS

Differentially expressed genes (DEG)

In total, there were 48,385 transcripts, and we excluded any transcripts with an FPKM value of '0', leaving 10,640 transcripts to be analyzed. MDS analysis showed that our MG samples could be differentiated according to the disease activity along the first plot dimension (Fig. 1).

The level of expression of 98 genes was significantly different between the two groups (fold change≥2, p-value<0.05) with 63 genes up-regulated and 35 genes down-regulated in the remission group (Supplementary Table 1, Fig. 2). The number of DEGs derived with DESeq analysis was greater with 165 up-regulated and 127 down-regulated in the remission group (Supplementary Table 2). Twenty-eight genes were common in the results of both Cuffdiff and DESeq analyses (23 up-regulated and 5 down-regulated genes, Table 2, Fig. 3). When only the two paired samples were analyzed separately, we found 18 up-regulated genes (fold change≥2, p-value<0.05), with no down-regulated genes (Supplementary Table 3). All the up-regulated genes from the paired sample analysis except for TPGS1 were contained in the list of DEGs analyzed with the whole study samples.

Pathway analysis using DAVID and IPA

DAVID analysis with up-regulated genes revealed two enriched GO functional annotation clusters (Table 3). The first cluster consisted of biological functions of cell motion and cell migration. The second cluster consisted of apoptosis and cell death. Number of down-regulated genes was not sufficient to analyze. Gene interaction of up-regulated genes was shown in Fig. 4.

According to the downstream effect analysis performed by

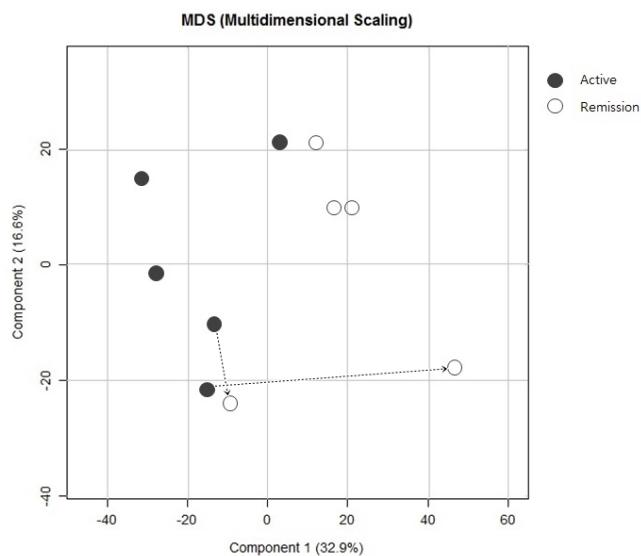


Fig. 1. Multidimensional Scaling plot of gene expression profiles. The first plot dimension roughly corresponds to the disease activity. Paired samples are linked by dotted arrows.

using IPA, top 5 functions affected were hematologic system development and function, immune cell trafficking, cellular movement, inflammatory response and cell-to-cell signaling and interaction pathways. Most of the genes related to these categories were down-regulated in active group.

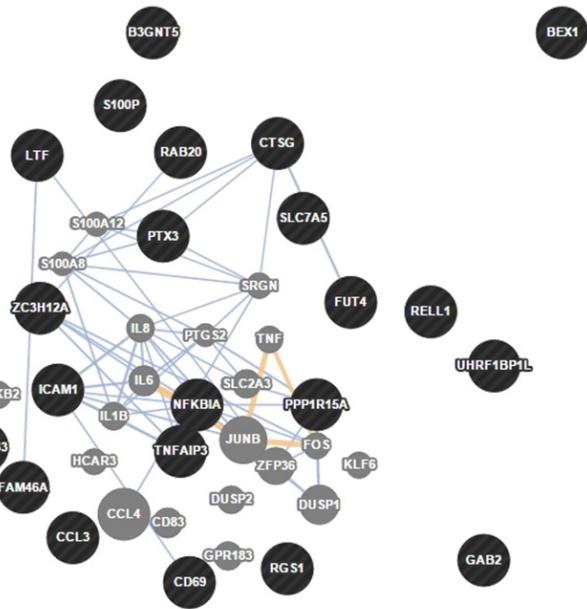


Fig. 3. Venn diagram of DEGs from DESeq and Cuffdiff. (A) Up-regulated genes in the remission group. (B) Down-regulated genes in the remission group.

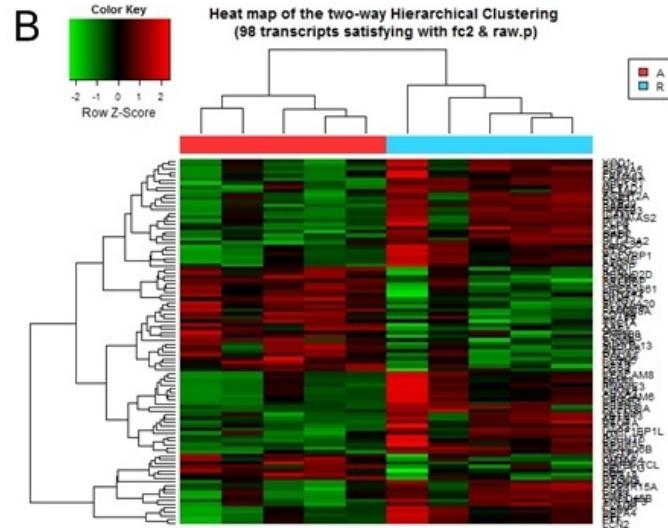
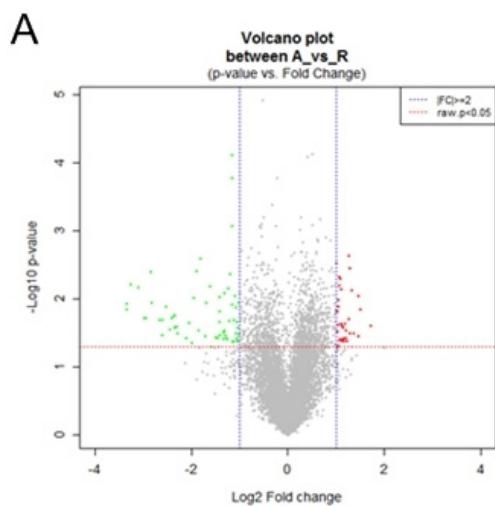


Fig. 2. Differentially expressed genes by Cuffdiff. (A) Volcano plot illustrating the differential expression levels of genes of the active and remission group. Genes that are significantly up- and down-regulated in the active compared to remission group are shown in red and green dots, respectively. (B) Heat map of the hierarchical clustering based on 98 differentially expressed genes (fold change ≥ 2 , $p\text{-value} < 0.05$).

Table 2. List of differentially expressed genes (from both Cuffdiff and DESeq analyses)

| Gene symbol | Description | Cuffdiff | | DESeq | |
|-----------------------|---|-----------------------------------|---------|---|----------|
| | | Fold change (Remission vs Active) | p-value | Log 2 Fold change (Remission vs Active) | p-value |
| Up-regulated | | | | | |
| LTF | Lactotransferrin | 10.17 | 0.014 | 1.11 | 0.004 |
| CTSG | Cathepsin G | 7.18 | 0.004 | 1.88 | 5.67E-06 |
| PFKFB3 | 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3 | 5.75 | 0.013 | 1.97 | 1.13E-06 |
| S100P | S100 calcium binding protein P | 4.15 | 0.023 | 1.50 | 2.85E-04 |
| RAB20 | RAB20, member RAS oncogene family | 3.74 | 0.004 | 1.76 | 7.42E-08 |
| TNFAIP3 | Tumor necrosis factor, alpha-induced protein 3 | 3.60 | 0.029 | 1.27 | 0.002 |
| CCL3 | Chemokine (C-C motif) ligand 3 | 3.22 | 0.011 | 1.35 | 2.66E-05 |
| UHRF1BP1L | UHRF1 binding protein 1-like | 3.07 | 0.006 | 1.28 | 0.002 |
| RGS1 | Regulator of G-protein signaling 1 | 3.00 | 0.050 | 1.13 | 0.003 |
| CD69 | CD69 molecule | 2.68 | 0.034 | 1.21 | 4.45E-04 |
| ICAM1 | Intercellular adhesion molecule 1 | 2.67 | 0.009 | 1.24 | 1.22E-04 |
| NFKBIA | Nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha | 2.67 | 0.015 | 1.24 | 3.27E-04 |
| SLC7A5 | Solute carrier family 7 (amino acid transporter light chain, L system), member 5 | 2.66 | 0.021 | 1.12 | 0.001 |
| ZC3H12A | Zinc finger CCCH-type containing 12A | 2.51 | 0.039 | 1.08 | 9.12E-04 |
| PTX3 | Pentraxin 3, long | 2.46 | 0.034 | 1.36 | 4.08E-04 |
| PPP1R15A | Protein phosphatase 1, regulatory subunit 15A | 2.32 | 0.021 | 1.22 | 6.47E-05 |
| GAB2 | GRB2-associated binding protein 2 | 2.30 | 0.004 | 1.07 | 0.002 |
| RELL1 | RELT-like 1 | 2.22 | 0.012 | 1.25 | 2.71E-05 |
| BEX1 | Brain expressed, X-linked 1 | 2.19 | 0.041 | 1.43 | 4.96E-04 |
| FUT4 | Fucosyltransferase 4 (alpha (1,3) fucosyltransferase, myeloid-specific) | 2.12 | 0.013 | 1.09 | 2.61E-04 |
| FAM46A | Family with sequence similarity 46, member A | 2.07 | 0.038 | 1.09 | 3.12E-04 |
| B3GNT5 | UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 5 | 2.06 | 0.041 | 1.11 | 0.001 |
| HIF1A-AS2 | HIF1A antisense RNA 2 | 2.03 | 0.0333 | 1.08 | 4.88E-04 |
| Down-regulated | | | | | |
| S100B | S100 calcium binding protein B | -3.32 | 0.024 | -1.37 | 3.68E-04 |
| LINC00861 | Long intergenic non-protein coding RNA 861 | -2.85 | 0.014 | -1.10 | 0.002 |
| OAS1 | 2'-5'-oligoadenylate synthetase 1, 40/46kDa | -2.76 | 0.009 | -1.31 | 4.07E-04 |
| SLC25A20 | Solute carrier family 25 (carnitine/acylcarnitinetranslocase), member 20 | -2.39 | 0.002 | -1.23 | 1.76E-06 |
| MAP3K7CL | MAP3K7 C-terminal like | -2.17 | 0.024 | -1.10 | 1.27E-04 |

DISCUSSION

In the present study, whole transcriptome RNA sequencing was performed in 10 PBMC samples obtained from eight MG patients to investigate systemic changes of gene expression possibly relevant to disease activity. Because there is no general consensus regarding the best method for the differential expression analysis of RNA-seq data, two different analysis tools (Cuffdiff and DESeq) were used separately with the intersection of the results being taken for downstream pathway analysis. The results demonstrated that among 10,640 transcripts only 28 genes were differentially expressed with 23 being up-regulated and 5 down-regulated in

remission compared to active status of the disease. Interestingly, major functional themes of the differentially expressed genes include differentiation, trafficking and apoptosis of immune cells, inflammatory response and cell-to-cell signaling.

S100B (S100 calcium-binding protein B), which was the most down-regulated gene in the remission group, is a ligand of the receptor for advanced glycation end products (RAGE). In the experimental autoimmune myasthenia gravis (EAMG) model, S100B levels were significantly higher [22]. Mean value of S100B of MG was higher than the normal controls, but it was not statistically significant [23]. CTTN (cortactin) was another down-regulated gene in the remission group, which is needed for the

Table 3. Functional annotation cluster analysis using DAVID

| Term | p-value | Genes |
|---|----------|------------------------------------|
| Annotation Cluster 1 (Enrichment Score: 1.4384248684673653) | | |
| Cell motion (GO*:0006928) | 1.71E-02 | ICAM1, CCL3, S100P, GAB2 |
| Cell migration (GO:0016477) | 4.12E-02 | ICAM1, S100P, GAB2 |
| Annotation Cluster 2 (Enrichment Score: 1.3933537552043205) | | |
| Apoptosis (GO:0006915) | 3.19E-02 | NFKBIA, ZC3H12A, TNFAIP3, PPP1R15A |
| Cell death (GO:0008219) | 4.99E-02 | NFKBIA, ZC3H12A, TNFAIP3, PPP1R15A |

*Gene Ontology.

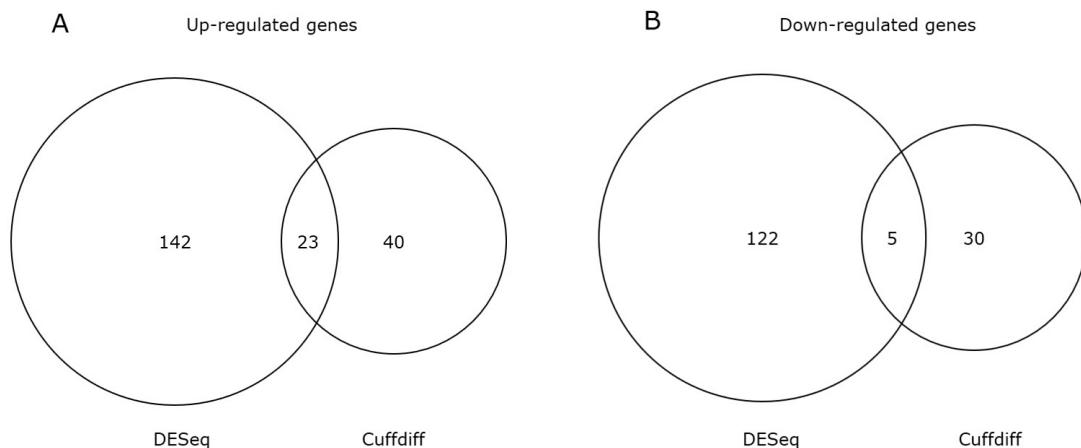


Fig. 4. Gene interactions of up-regulated genes from GeneMANIA. Blue line indicates co-localization of the genes and predicted functional relationships between genes are indicated in orange. Circles filled with black signify the commonly detected genes by Cuffdiff and DESeq. Circles filled with gray indicate their interaction and added by GeneMania.

formation of the AChR cluster and antibody against cortactin was reported in MG patients [24]. ABL1 (Abelson murine leukemia viral oncogene homolog 1) is up-regulated in the remission group, which is critical mediator of postsynaptic assembly at the NMJ via providing a specific tyrosine kinase activity downstream of the MuSK receptor that is required for agrin-induced AChR clustering [25].

One of the significant functional annotation cluster in DAVID analysis was the apoptosis and programmed cell death. Immunosuppressive agents are the mainstay of treatment for MG and their mechanisms are related with these pathways. Corticosteroids induce T lymphocyte apoptosis, and other agents such as azathioprine also inhibit cell proliferation [26]. All of the remission group patients received prednisolone and three patients also received tacrolimus, another T cell apoptosis inducer [27]. CXCL13 and CCL21 were overexpressed in hyperplastic thymus [8, 28] and CXCR5 was overexpressed on T cells of MG patients [29]. Most of the genes associated with chemotaxis, however, were down-regulated in the active group of the present study. This discrepancy needs to be confirmed in

further studies, but might be explained by the followings. First, the previous studies had compared between MG patients and healthy controls. Second, difference of the target samples (thymus or neuromuscular junction in the previous studies) might account for the discrepancy. In a previous study of rheumatoid arthritis, chemokine receptor profile of PBMCs was increased with treatment, which the authors explained as systemic compensation for the changes in the inflamed tissue [30].

There are several limitations to be acknowledged in this pilot study. Sample size was too small to make a robust conclusion. Immunosuppressive treatment varied among patients, which might affect the results. Despite these limitations, to our knowledge, this is the first study investigating the systemic changes of blood whole transcriptome according to the disease activity in MG patients. Genes that are involved in the biological process of immune cell trafficking and apoptosis might be promising candidates for biomarkers, and warrant further studies.

ACKNOWLEDGEMENTS

This study was supported by grant no 16-2013-116 from the SK Telecom Research Fund.

REFERENCES

1. Berrih-Aknin S, Le Panse R (2014) Myasthenia gravis: a comprehensive review of immune dysregulation and etiological mechanisms. *J Autoimmun* 52:90-100.
2. McConville J, Farrugia ME, Beeson D, Kishore U, Metcalfe R, Newsom-Davis J, Vincent A (2004) Detection and characterization of MuSK antibodies in seronegative myasthenia gravis. *Ann Neurol* 55:580-584.
3. Berrih-Aknin S, Frenkian-Cuvelier M, Eymard B (2014) Diagnostic and clinical classification of autoimmune myasthenia gravis. *J Autoimmun* 48-49:143-148.
4. Evoli A, Tonali PA, Padua L, Monaco ML, Scuderi F, Batocchi AP, Marino M, Bartoccioni E (2003) Clinical correlates with anti-MuSK antibodies in generalized seronegative myasthenia gravis. *Brain* 126:2304-2311.
5. Heldal AT, Eide GE, Romi F, Owe JF, Gilhus NE (2014) Repeated acetylcholine receptor antibody-concentrations and association to clinical myasthenia gravis development. *PLoS One* 9:e114060.
6. Chaussabel D, Pascual V, Banchereau J (2010) Assessing the human immune system through blood transcriptomics. *BMC Biol* 8:84.
7. Le Panse R, Cizeron-Clairac G, Bismuth J, Berrih-Aknin S (2006) Microarrays reveal distinct gene signatures in the thymus of seropositive and seronegative myasthenia gravis patients and the role of CC chemokine ligand 21 in thymic hyperplasia. *J Immunol* 177:7868-7879.
8. Meraouna A, Cizeron-Clairac G, Panse RL, Bismuth J, Truffault F, Tallaksen C, Berrih-Aknin S (2006) The chemokine CXCL13 is a key molecule in autoimmune myasthenia gravis. *Blood* 108:432-440.
9. Feferman T, Aricha R, Menon R, Souroujon MC, Berrih-Aknin S, Fuchs S (2007) DNA microarray in search of new drug targets for myasthenia gravis. *Ann N Y Acad Sci* 1107: 111-117.
10. Cufi P, Soussan P, Truffault F, Fetouchi R, Robinet M, Fadel E, Berrih-Aknin S, Le Panse R (2014) Thymoma-associated myasthenia gravis: on the search for a pathogen signature. *J Autoimmun* 52:29-35.
11. Bauer JW, Petri M, Batliwalla FM, Koeuth T, Wilson J, Slattery C, Panoskaltsis-Mortari A, Gregersen PK, Behrens TW,
- Baechler EC (2009) Interferon-regulated chemokines as biomarkers of systemic lupus erythematosus disease activity: a validation study. *Arthritis Rheum* 60:3098-3107.
12. Hecker M, Goertsches RH, Fatum C, Koczan D, Thiesen HJ, Guthke R, Zettl UK (2012) Network analysis of transcriptional regulation in response to intramuscular interferon- β -1a multiple sclerosis treatment. *Pharmacogenomics J* 12:134-146.
13. Jabbari A, Suárez-Fariñas M, Fuentes-Duculan J, Gonzalez J, Cueto I, Franks AG Jr, Krueger JG (2014) Dominant Th1 and minimal Th17 skewing in discoid lupus revealed by transcriptomic comparison with psoriasis. *J Invest Dermatol* 134:87-95.
14. Jaretzki A 3rd, Barohn RJ, Ernstoff RM, Kaminski HJ, Keesey JC, Penn AS, Sanders DB; Task Force of the Medical Scientific Advisory Board of the Myasthenia Gravis Foundation of America (2000) Myasthenia gravis: recommendations for clinical research standards. *Neurology* 55:16-23.
15. Trapnell C, Pachter L, Salzberg SL (2009) TopHat: discovering splice junctions with RNA-Seq. *Bioinformatics* 25:1105-1111.
16. Langmead B, Trapnell C, Pop M, Salzberg SL (2009) Ultrafast and memory-efficient alignment of short DNA sequences to the human genome. *Genome Biol* 10:R25.
17. Trapnell C, Williams BA, Pertea G, Mortazavi A, Kwan G, van Baren MJ, Salzberg SL, Wold BJ, Pachter L (2010) Transcript assembly and quantification by RNA-Seq reveals unannotated transcripts and isoform switching during cell differentiation. *Nat Biotechnol* 28:511-515.
18. Twine NA, Janitz K, Wilkins MR, Janitz M (2011) Whole transcriptome sequencing reveals gene expression and splicing differences in brain regions affected by Alzheimer's disease. *PLoS One* 6:e16266.
19. Seyednasrollah F, Laiho A, Elo LL (2015) Comparison of software packages for detecting differential expression in RNA-seq studies. *Brief Bioinform* 16:59-70.
20. Anders S, Huber W (2010) Differential expression analysis for sequence count data. *Genome Biol* 11:R106.
21. Huang W, Sherman BT, Lempicki RA (2009) Systematic and integrative analysis of large gene lists using DAVID bioinformatics resources. *Nat Protoc* 4:44-57.
22. Mu L, Zhang Y, Sun B, Wang J, Xie X, Li N, Zhang J, Kong Q, Liu Y, Han Z, Wang G, Fu Z, Yu B, Li G, Li H (2011) Activation of the receptor for advanced glycation end products (RAGE) exacerbates experimental autoimmune myasthenia gravis symptoms. *Clin Immunol* 141:36-48.
23. Moser B, Bekos C, Zimprich F, Nickl S, Klepetko W, Ankersmit J (2012) The receptor for advanced glycation endproducts

- and its ligands in patients with myasthenia gravis. *Biochem Biophys Res Commun* 420:96-101.
24. Gallardo E, Martínez-Hernández E, Titulaer MJ, Huijbers MG, Martínez MA, Ramos A, Querol L, Díaz-Manera J, Rojas-García R, Hayworth CR, Verschueren JJ, Balice-Gordon R, Dalmau J, Illa I (2014) Cortactin autoantibodies in myasthenia gravis. *Autoimmun Rev* 13:1003-1007.
25. Finn AJ, Feng G, Pendegast AM (2003) Postsynaptic requirement for Abl kinases in assembly of the neuromuscular junction. *Nat Neurosci* 6:717-723.
26. Sanders DB, Evoli A (2010) Immunosuppressive therapies in myasthenia gravis. *Autoimmunity* 43:428-435.
27. Ponseti JM, Gamez J, Azem J, López-Cano M, Vilallonga R, Armengol M (2008) Tacrolimus for myasthenia gravis: a clinical study of 212 patients. *Ann N Y Acad Sci* 1132:254-263.
28. Berrih-Aknin S, Ruhlmann N, Bismuth J, Cizeron-Clairac G, Zelman E, Shachar I, Darteville P, de Rosbo NK, Le Panse R (2009) CCL21 overexpressed on lymphatic vessels drives thymic hyperplasia in myasthenia. *Ann Neurol* 66:521-531.
29. Saito R, Onodera H, Tago H, Suzuki Y, Shimizu M, Matsumura Y, Kondo T, Itoyama Y (2005) Altered expression of chemokine receptor CXCR5 on T cells of myasthenia gravis patients. *J Neuroimmunol* 170:172-178.
30. Nissinen R, Leirisalo-Repo M, Peltomaa R, Palosuo T, Vaarala O (2004) Cytokine and chemokine receptor profile of peripheral blood mononuclear cells during treatment with infliximab in patients with active rheumatoid arthritis. *Ann Rheum Dis* 63:681-687.

Supplementary Table 2. List of differentially expressed genes derived with DESeq.

| transcript_id | baseMean | log2Fold | d | lfcSE | stat | pvalue | padj | gene | desc |
|---------------|--------------|----------|----------|----------|----------|-----------------|--------------|---|------|
| NM_004566 | 106.4128822 | -1.96534 | 0.403793 | -4.86719 | 1.13E-06 | 0.002696 | PFKFB3 | 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3 | |
| NM_001911 | 482.2042461 | -1.87928 | 0.414083 | -4.5384 | 5.67E-06 | 0.004164 | CTSG | cathespin G | |
| NM_005320 | 8.019862852 | -1.85483 | 0.416428 | -4.45415 | 8.42E-06 | NA | HIST1H1D | histone cluster 1, H1d | |
| NM_017817 | 742.2525507 | -1.7605 | 0.327187 | -5.38071 | 7.42E-08 | 0.000707 | RAB20 | RAB20, member RAS oncogene family | |
| NM_001001791 | 19.8514253 | -1.7101 | 0.403871 | -4.23427 | 2.29E-05 | 0.009496 | C10orf55 | chromosome 10 open reading frame 55 | |
| NM_003740 | 40.07565866 | -1.70168 | 0.39052 | -4.35748 | 1.32E-05 | 0.006962 | KCNKS | potassium channel, subfamily K, member 5 | |
| NM_147195 | 43.89890441 | -1.67303 | 0.390048 | -4.2893 | 1.79E-05 | 0.00813 | ANKRD18 | ankyrin repeat domain 18A | |
| NM_022474 | 7.62699984 | -1.57326 | 0.358053 | -4.39393 | 1.11E-05 | NA | MPP5 | membrane protein, palmitoylated 5 (MAGUK p55 subfamily member 5) | |
| NM_005024 | 132.7823891 | -1.54065 | 0.408513 | -3.77135 | 0.000162 | 0.0251 | SERPINB1C | serpin peptidase inhibitor, clade B (ovalbumin), member 10 | |
| NM_005321 | 26.78624205 | -1.53878 | 0.415633 | -3.70227 | 0.000214 | 0.026402 | HIST1H1E | histone cluster 1, H1e | |
| NM_020370 | 72.74797083 | -1.53505 | 0.30296 | -5.06683 | 4.04E-07 | 0.001926 | GPR84 | G protein-coupled receptor 84 | |
| NM_001134368 | 22.46869363 | -1.51111 | 0.358268 | -4.21782 | 2.47E-05 | 0.00979 | SLC6A6 | solute carrier family 6 (neurotransmitter transporter), member 6 | |
| NM_014466 | 2.394883806 | -1.51091 | 0.415105 | -3.63982 | 0.000273 | NA | TEKT2 | tektin 2 (testicular) | |
| NM_005980 | 310.9356187 | -1.50007 | 0.412274 | -3.63853 | 0.000274 | 0.029679 | S100P | S100 calcium binding protein P | |
| NM_153221 | 3.239196324 | -1.49869 | 0.413039 | -3.62845 | 0.000285 | NA | CILP2 | cartilage intermediate layer protein 2 | |
| NM_013363 | 25.30923826 | -1.47942 | 0.417366 | -3.54465 | 0.000393 | 0.032136 | PCOLCE2 | procollagen C-endopeptidase enhancer 2 | |
| NM_002616 | 7853.795956 | -1.4378 | 0.401205 | -3.58369 | 0.000339 | 0.030813 | PER1 | period circadian clock 1 | |
| NM_001282807 | 8.512139048 | -1.43332 | 0.41132 | -3.48468 | 0.000493 | NA | 07-Mar | membrane-associated ring finger (C3HC4) 7, E3 ubiquitin protein ligase | |
| NM_001011703 | 18.35433977 | -1.43247 | 0.408677 | -3.50514 | 0.000456 | 0.033639 | MVB12B | multivesicular body subunit 12B | |
| NM_018476 | 34.66536757 | -1.4283 | 0.410088 | -3.4829 | 0.000496 | 0.035791 | BEX1 | brain expressed, X-linked 1 | |
| NM_001292033 | 5.036698539 | -1.42116 | 0.399341 | -3.55877 | 0.000373 | NA | CFAP97 | UPF0501 protein KIAA1430 isoform 2 | |
| NM_002228 | 7281.278474 | -1.3964 | 0.413289 | -3.37875 | 0.000728 | 0.041471 | JUN | jun proto-oncogene | |
| NM_001290260 | 24.05936552 | -1.38891 | 0.386955 | -3.5913 | 0.000329 | 0.030813 | PHF3 | PHD finger protein 3 isoform 3 | |
| NR_106808 | 5.774093792 | -1.38732 | 0.40679 | -3.4104 | 0.000649 | NA | MIR6750 | microRNA mir-6750 | |
| NM_001290185 | 13.6450927 | -1.37857 | 0.349321 | -3.94641 | 7.93E-05 | NA | VPS11 | vacuolar protein sorting-associated protein 11 homolog isoform 2 | |
| NM_001206878 | 10.64187264 | -1.36782 | 0.384104 | -3.56105 | 0.000369 | NA | CTDSP1 | CTD (carboxy-terminal domain, RNA polymerase II, polypeptide A) small phosphatase 1 | |
| NM_001131055 | 64.21331629 | -1.36319 | 0.365945 | -3.72513 | 0.000195 | 0.026302 | HRH2 | histamine receptor H2 | |
| NM_002852 | 239.744687 | -1.36303 | 0.385621 | -3.53464 | 0.000408 | 0.032136 | PTX3 | pentraxin 3, long | |
| NM_032108 | 35.37553208 | -1.35925 | 0.382548 | -3.55316 | 0.000381 | 0.031803 | SEMA6B | sema domain, transmembrane domain (TM), and cytoplasmic domain, (semaphorin) 6B | |
| NM_003545 | 2.868264925 | -1.3555 | 0.415571 | -3.26176 | 0.001107 | NA | HIST1H4E | histone cluster 1, H4e | |
| NM_001253800 | 4.229112908 | -1.35494 | 0.416478 | -3.25333 | 0.001141 | NA | ZNF331 | zinc finger protein 331 | |
| NM_181711 | 78.76981035 | -1.35449 | 0.410485 | -3.29973 | 0.000968 | 0.049099 | GRASP | GRP1 (general receptor for phosphoinositides 1)-associated scaffold protein | |
| NM_000138 | 38.00793021 | -1.35085 | 0.339568 | -3.97813 | 6.95E-05 | 0.015752 | FBN1 | fibrillin 1 | |
| NM_007207 | 226.7056419 | -1.34775 | 0.32934 | -4.09228 | 4.27E-05 | 0.013147 | DUSP10 | dual specificity phosphatase 10 | |
| NM_002983 | 515.1672497 | -1.34735 | 0.320724 | -4.20096 | 2.66E-05 | 0.009913 | CCL3 | chemokine (C-C motif) ligand 3 | |
| NM_003039 | 139.0650578 | -1.34321 | 0.390983 | -3.43456 | 0.000592 | 0.037814 | SLC25A15 | solute carrier family 2 (facilitated glucose/fructose transporter), member 5 | |
| NM_006793 | 1.98245195 | -1.33456 | 0.417066 | -3.19988 | 0.001375 | NA | PRDX3 | peroxiredoxin 3 | |
| NM_005143 | 17.26593167 | -1.32117 | 0.416414 | -3.17273 | 0.00151 | 0.056498 | HP | haptoglobin | |
| NM_006732 | 21.48572016 | -1.32097 | 0.415403 | -3.17998 | 0.001473 | 0.056498 | FOSB | FBJ murine osteosarcoma viral oncogene homolog B | |
| NM_001002036 | 21.75168051 | -1.31873 | 0.403379 | -3.26921 | 0.001078 | 0.051193 | ASTL | astacin-like metallo-endopeptidase (M12 family) | |
| NM_004878 | 48.61784569 | -1.30642 | 0.401351 | -3.25507 | 0.001134 | 0.052202 | PTGES | prostaglandin E synthase | |
| NM_001286710 | 27.55870543 | -1.30152 | 0.354962 | -3.66664 | 0.000246 | 0.028547 | ACSL1 | acyl-CoA synthetase long-chain family member 1 | |
| NM_182757 | 2174.620218 | -1.29907 | 0.346526 | -3.74883 | 0.000178 | 0.025912 | RNF144B | ring finger protein 144B | |
| NM_001006947 | 4.38197631 | -1.28091 | 0.413622 | -3.0968 | 0.001956 | NA | UHRF1BP1 | UHRF1 binding protein 1-like | |
| NM_001270508 | 5.691677072 | -1.26841 | 0.416771 | -3.04343 | 0.002339 | NA | TNFAIP3 | tumor necrosis factor, alpha-induced protein 3 | |
| NM_181358 | 7.083344259 | -1.26748 | 0.367452 | -3.44938 | 0.000562 | NA | HIPK3 | homeodomain interacting protein kinase 1 | |
| NM_198189 | 6.044914873 | -1.26181 | 0.392976 | -3.21091 | 0.001323 | NA | COPS8 | COP9 signalosome subunit 8 | |
| NM_001085400 | 401.0977643 | -1.25192 | 0.298295 | -4.19691 | 2.71E-05 | 0.009913 | RELL1 | RELL1-like 1 | |
| NM_000201 | 2227.962317 | -1.24487 | 0.323952 | -3.84276 | 0.000122 | 0.023649 | ICAM1 | intercellular adhesion molecule 1 | |
| NM_020529 | 10474.76871 | -1.24235 | 0.345777 | -3.59293 | 0.000327 | 0.030813 | NFKBIA | nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha | |
| NM_006500 | 31.68777995 | -1.24136 | 0.406302 | -3.05527 | 0.002249 | 0.0651 | MCAM | melanoma cell adhesion molecule | |
| NM_001267043 | 22.94298034 | -1.24107 | 0.384624 | -3.2267 | 0.001252 | 0.053529 | AEBP2 | AE binding protein 2 | |
| NM_152460 | 2.652811029 | -1.22535 | 0.415907 | -2.94621 | 0.003217 | NA | C17orf77 | chromosome 17 open reading frame 77 | |
| NM_014330 | 6535.705451 | -1.22316 | 0.306182 | -3.99486 | 6.47E-05 | 0.015716 | PPP1R15A | protein phosphatase 1, regulatory subunit 15A | |
| NR_106807 | 2.370428865 | -1.21791 | 0.411698 | -2.95826 | 0.003094 | NA | MIR6749 | microRNA mir-6749 | |
| NM_182966 | 12.34695957 | -1.21091 | 0.410941 | -2.94231 | 0.003258 | NA | NEDD9 | neural precursor cell expressed, developmentally down-regulated 9 | |
| NM_001136503 | 19.68514971 | -1.21088 | 0.390821 | -3.09314 | 0.001981 | 0.061819 | C19orf77 | chromosome 19 open reading frame 77 | |
| NM_001025616 | 117.5683576 | -1.20678 | 0.380832 | -3.16879 | 0.001531 | 0.056733 | ARHGAP24 | Rho GTPase activating protein 24 | |
| NM_0017181 | 3672.717561 | -1.20622 | 0.343459 | -3.51198 | 0.000445 | 0.033335 | CD69 | CD69 molecule | |
| NR_106943 | 6.10640019 | -1.20413 | 0.411565 | -2.92572 | 0.003437 | NA | MIR6883 | microRNA mir-6883 | |
| NM_003126 | 14.3465216 | -1.20328 | 0.407319 | -2.95416 | 0.003135 | NA | SPTA1 | spectrin, alpha, erythrocytic 1 (elliptocytosis 2) | |
| NM_000682 | 5.662471381 | -1.20106 | 0.415701 | -2.89053 | 0.003846 | NA | ADRA2B | adrenoceptor alpha 2B | |
| NM_001198803 | 5.928999032 | -1.19935 | 0.417381 | -2.87351 | 0.004059 | NA | EIF4G3 | eukaryotic translation initiation factor 4 gamma, 3 | |
| NM_001198 | 46.73375945 | -1.19727 | 0.335301 | -3.57075 | 0.000356 | 0.031803 | PRDM1 | PR domain containing 1, with ZNF domain | |
| NM_001257293 | 11.78082223 | -1.19541 | 0.36557 | -3.27 | 0.001075 | NA | HNRNPH1 | heterogeneous nuclear ribonucleoprotein H1 (H) | |
| NM_001136044 | 1.388105484 | -1.19409 | 0.393749 | -3.02623 | 0.002424 | NA | TMUB1 | transmembrane and ubiquitin-like domain containing 1 | |
| NM_003076 | 6.327128678 | -1.19287 | 0.368592 | -3.23629 | 0.001211 | NA | SNORD8 | small nucleolar RNA, C/D box 98 | |
| NM_001079519 | 4.244553956 | -1.18993 | 0.415381 | -2.86467 | 0.004174 | NA | FAM177A1 | family with sequence similarity 177, member A1 | |
| NM_005178 | 2510.279723 | -1.18928 | 0.352637 | -3.37253 | 0.000745 | 0.041732 | BCL3 | B-cell CLL/lymphoma 3 | |
| NM_152515 | 28.04895034 | -1.18839 | 0.402524 | -2.95234 | 0.003154 | 0.075184 | CKAP2L | cytoskeleton associated protein 2-like | |
| NM_030928 | 88.52657659 | -1.18385 | 0.300886 | -3.93454 | 8.34E-05 | 0.017916 | CDT1 | chromatin licensing and DNA replication factor 1 | |
| NM_001139495 | 14.09653238 | -1.18208 | 0.337593 | -3.50149 | 0.000463 | NA | ADAR | adenosine deaminase, RNA-specific | |
| NM_004420 | 63.9708748 | -1.18054 | 0.396934 | -2.97415 | 0.002938 | 0.072846 | DUSP8 | dual specificity phosphatase 8 | |
| NM_020651 | 3675.44692 | -1.17976 | 0.371696 | -3.17357 | 0.001506 | 0.056498 | PEL1 | pellino E3 ubiquitin protein ligase 1 | |
| NM_001013646 | 20.70890475 | -1.17812 | 0.311966 | -3.77643 | 0.000159 | 0.0251 | FAM209B | family with sequence similarity 209, member B | |
| NM_000039 | 4.183029825 | -1.17602 | 0.412967 | -2.91658 | 0.003539 | NA | APOA1 | apolipoprotein A-I | |
| NM_001256127 | 3.593855261 | -1.17486 | 0.413619 | -2.84044 | 0.004055 | NA | NSUN4 | NOPI2/Sun domain family, member 4 | |
| NR_073506 | 7.816146656 | -1.1738 | 0.41503 | -2.82824 | 0.00468 | NA | TMEM39A | transmembrane protein 39A | |
| NM_001252079 | 695.3341939 | -1.17129 | 0.365784 | -3.20213 | 0.001364 | 0.055293 | USP15 | ubiquitin specific peptidase 15 | |
| NM_174942 | 21.1889822 | -1.16594 | 0.32541 | -3.5833 | 0.00034 | 0.030813 | GAS2L3 | growth arrest specific 2 like 3 | |
| NM_001114395 | 95.70621012 | -1.16514 | 0.353939 | -3.29192 | 0.000995 | 0.049373 | CNTLN | centilein, centrosomal protein | |
| NM_001077494 | 2.053683944 | -1.16319 | 0.412967 | -2.81666 | 0.004853 | NA | NFKB2 | nuclear factor of kappa light polypeptide gene enhancer in B-cells 2 (p49/p100) | |
| NR_024157 | 81.844377299 | -1.16232 | 0.286411 | -4.05824 | 4.94E-05 | 0.014272 | DGR11 | DiGeorge syndrome critical region gene 11 (non-protein coding) | |
| NM_005746 | 8894.744534 | -1.15867 | 0.371456 | -3.11926 | 0.001813 | 0.060383 | NAMPT | nicotinamide phosphoribosyltransferase | |
| NM_001228836 | 10.87823618 | -1.15818 | 0.404534 | -2.863 | 0.004197 | NA | VRK2 | vaccinia related kinase 2 | |
| NR_120622 | 6.343318213 | -1.15702 | 0.414605 | -2.79067 | 0.00526 | NA | LOC101927472 | | |
| NM_000584 | 15.10440351 | -1.15332 | 0.410887 | -2.80691 | 0.005002 | 0.093052 | IL8 | interleukin 8 | |
| NM_000607 | 143.625295 | -1.15102 | 0.417245 | -2.75862 | 0.005805 | 0.098935 | ORM1 | orosomucoid 1 | |
| NM_001127651 | 2.56616121 | -1.14617 | 0.417382 | -2.74609 | 0.006031 | NA | NCF2 | neutrophil cytosolic factor 2 | |
| NM_133484 | 7.378510681 | -1.14598 | 0.417376 | -2.74568 | 0.006039 | NA | TANK | TRAF family member-associated NFKB activator | |
| NM_002416 | 37.100206 | | | | | | | | |

| | | | | | | | |
|--------------|--------------|------------------|----------|-----------|--------------------|---|--|
| NM_003486 | 1041.504427 | -1.11814 | 0.347803 | -3.21486 | 0.001305 | 0.054046 SLC7A5 | solute carrier family 7 (amino acid transporter light chain, L system), member 5 |
| NM_001270455 | 287.0809337 | -1.11727 | 0.318302 | -3.51008 | 0.000448 | 0.033355 WWP2 | WW domain containing E3 ubiquitin protein ligase 2 |
| NM_178324 | 14.08126592 | -1.11576 | 0.352629 | -3.16411 | 0.001556 NA | SPTLC1 | serine palmitoyltransferase, long chain base subunit 1 |
| NM_004209 | 57.39815766 | -1.11374 | 0.32442 | -3.43302 | 0.000597 | 0.037814 SYNRG3 | synaptogyrin 3 |
| NM_022304 | 16.70742018 | -1.11163 | 0.38355 | -2.89825 | 0.003752 | 0.081604 HRH2 | histamine receptor H2 |
| NM_032047 | 387.6377667 | -1.11061 | 0.342833 | -3.23952 | 0.001197 | 0.053292 B3GNT5 | UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 5 |
| NM_203394 | 16.50173099 | -1.10999 | 0.399022 | -2.78177 | 0.005406 | 0.059538 E2F7 | E2F transcription factor 7 |
| NR_047116 | 172.1329293 | -1.10918 | 0.296881 | -3.73611 | 0.000187 | 0.026302 HIF1A-AS1 | HIF1A antisense RNA 1 |
| NM_001199149 | 1.721741382 | -1.10892 | 0.384473 | -2.88426 | 0.003923 NA | LTF | lactotransferrin |
| NM_001039481 | 9.878539798 | -1.10993 | 0.4015 | -2.73931 | 0.006157 NA | ETNK1 | ethanolamine kinase 1 |
| NR_125739 | 2507.677273 | -1.09713 | 0.309902 | -3.54025 | 0.0004 | 0.032136 CEBPB-AS1 | |
| NM_003577 | 10.36613091 | -1.09521 | 0.402878 | -2.71847 | 0.006558 NA | UTF1 | undifferentiated embryonic cell transcription factor 1 |
| NM_024292 | 2.62669175 | -1.09082 | 0.416047 | -2.62187 | 0.008745 NA | UBL5 | ubiquitin-like 5 |
| NM_017633 | 1581.933509 | -1.09015 | 0.302371 | -3.60536 | 0.000312 | 0.030813 FAM46A | family with sequence similarity 46, member A |
| NM_002033 | 1518.407363 | -1.08928 | 0.298296 | -3.65168 | 0.000261 | 0.029 FUT4 | fucosyltransferase 4 (alpha 1,3 fucosyltransferase, myeloid-specific) |
| NR_104265 | 1.863215939 | -1.08867 | 0.410853 | -2.64979 | 0.008054 NA | GMPR2 | guanosine monophosphate reductase 2 |
| NR_110552 | 176.367707 | -1.08828 | 0.315606 | -3.44822 | 0.000564 | 0.037587 LOC102724153 | |
| NM_018410 | 1.376310662 | -1.08702 | 0.403293 | -2.69535 | 0.007031 NA | HJURP | Holliday junction recognition protein |
| NM_006186 | 10.8072059 | -1.08673 | 0.409973 | -2.65074 | 0.008032 | 0.116262 NR4A2 | nuclear receptor subfamily 4, group A, member 2 |
| NM_001127401 | 29.06487038 | -1.08476 | 0.323619 | -3.35197 | 0.000802 | 0.044358 YPEL5 | yippee-like 5 (Drosophila) |
| NM_001278713 | 7.974999032 | -1.08425 | 0.378031 | -2.86816 | 0.004129 NA | ZNF705E | zinc finger protein 705E |
| NM_001276325 | 2.149234616 | -1.08407 | 0.415491 | -2.60913 | 0.000977 NA | SETMAR | SET domain and mariner transposase fusion gene |
| NM_001805 | 140.1020146 | -1.08234 | 0.41308 | -2.62017 | 0.008789 | 0.121145 CEBPB | CCAAT/enhancer binding protein (C/EBP), epsilon |
| NM_025079 | 1447.638241 | -1.08144 | 0.326088 | -3.3164 | 0.000912 | 0.048253 ZCH12A | zinc finger CCCH-type containing 12A |
| NM_144590 | 75.84091495 | -1.08089 | 0.311154 | -3.47381 | 0.000513 | 0.035968 ANKRD22 | ankyrin repeat domain 22 |
| NM_003965 | 7.517963911 | -1.07959 | 0.411811 | -2.62157 | 0.008752 NA | CCL2 | chemokine (C-C motif) receptor-like 2 |
| NR_045406 | 1218.858876 | -1.07728 | 0.308903 | -3.48742 | 0.000488 | 0.035461 HIF1A-AS2 | HIF1A antisense RNA 2 |
| NM_031419 | 148.2709274 | -1.0759 | 0.34226 | -3.14353 | 0.001669 | 0.059381 NFKBIZ | nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, zeta |
| NM_001172431 | 3.362591837 | -1.07491 | 0.409673 | -2.62382 | 0.008695 NA | AMPD3 | adenosine monophosphate deaminase 3 |
| NM_001098503 | 20.10570975 | -1.07139 | 0.360614 | -2.97102 | 0.002968 | 0.073242 PTPRJ | protein tyrosine phosphatase, receptor type, J |
| NM_080491 | 14.41042198 | -1.07064 | 0.344839 | -3.10476 | 0.001904 NA | GAB2 | GRB2-associated binding protein 2 |
| NM_022134 | 5.398583337 | -1.06851 | 0.416089 | -2.56798 | 0.010229 NA | GAL3ST2 | galactose-3-O-sulfotransferase 2 |
| NM_001137550 | 9.514398469 | -1.06803 | 0.357289 | -2.98926 | 0.002797 NA | LRRKIP1 | leucine rich repeat (in FLII) interacting protein 1 |
| NM_001270399 | 24.9843155 | -1.06449 | 0.286434 | -3.71636 | 0.000202 | 0.026302 TUBA1A | tubulin, alpha 1a |
| NM_172207 | 3.534819495 | -1.06393 | 0.416923 | -2.55187 | 0.010715 NA | CAMKK1 | calmodulin-dependent protein kinase kinase 1, alpha |
| NM_001010935 | 0.992588669 | -1.06198 | 0.386116 | -2.75041 | 0.005952 NA | RAP1A | RAP1A, member of RAS oncogene family |
| NM_001211 | 40.59736437 | -1.06168 | 0.374933 | -2.83166 | 0.004631 | 0.090569 BUB1B | BUB1 mitotic checkpoint serine/threonine kinase B |
| NM_182931 | 15.07303616 | -1.05576 | 0.370673 | -2.84821 | 0.004397 | 0.088023 KMT2E | lysine (K)-specific methyltransferase 2E |
| NM_033018 | 14.52682041 | -1.05452 | 0.321876 | -3.27618 | 0.001052 | 0.050876 CDK16 | cyclin-dependent kinase 16 |
| NM_001289824 | 19.13869146 | -1.05416 | 0.367763 | -2.86642 | 0.004151 | 0.085774 FURIN | furin preproprotein |
| NM_001135589 | 45.96961515 | -1.05131 | 0.29549 | -3.55785 | 0.000374 | 0.031803 GDAP2 | ganglioside induced differentiation associated protein 2 |
| NM_000576 | 647.0094402 | -1.04649 | 0.373504 | -2.80182 | 0.005081 | 0.093619 IL1B | interleukin 1, beta |
| NM_001170820 | 73.37703019 | -1.04041 | 0.36073 | -2.88418 | 0.003294 | 0.083622 IFTM10 | interferon induced transmembrane protein 10 |
| NM_021202 | 418.6206562 | -1.03903 | 0.355255 | -2.92474 | 0.003447 | 0.078183 TP53INP2 | tumor protein p53 inducible nuclear protein 2 |
| NM_001286398 | 70.83796785 | -1.03616 | 0.328671 | -3.15258 | 0.001618 | 0.059014 RNF217 | ring finger protein 217 |
| NM_017628 | 419.5108427 | -1.03503 | 0.333033 | -3.10789 | 0.001884 | 0.061002 TET2 | tet methylcytosine dioxygenase 2 |
| NM_004417 | 16676.84945 | -1.03485 | 0.285782 | -3.62111 | 0.000293 | 0.030813 DUSP1 | dual specificity phosphatase 1 |
| NR_040073 | 2.941613556 | -1.03372 | 0.40231 | -2.56947 | 0.010185 NA | MIR181A1 | MIR181A1 host gene (non-protein coding) |
| NM_005962 | 24.65190137 | -1.03236 | 0.319602 | -3.23015 | 0.001237 | 0.053529 MXII | MAX interactor 1, dimerization protein |
| NM_001199011 | 1.763212443 | -1.03189 | 0.407168 | -2.5343 | 0.011267 NA | DCTN5 | dynactin 5 (p25) |
| NR_02924 | 12.11987734 | -1.03044 | 0.397452 | -2.5926 | 0.009525 NA | TBC1D3P1 | TBC1D3P1-DHX40P1 readthrough transcribed pseudogene |
| NM_201999 | 111.4948779 | -1.02622 | 0.301878 | -3.39944 | 0.000675 | 0.040233 ELF2 | E74-like factor 2 (ets domain transcription factor) |
| NR_003225 | 109.2951034 | -1.02356 | 0.326326 | -3.13662 | 0.001709 | 0.059411 LGALS3 | lectin, galactoside-binding, soluble, 3 |
| NM_005888 | 121.5666068 | -1.02343 | 0.325595 | -3.14326 | 0.001671 | 0.059381 SLC25A3 | solute carrier family 25 (mitochondrial carrier; phosphate carrier), member 3 |
| NM_002099 | 3.849060615 | -1.01902 | 0.406861 | -2.50459 | 0.012259 NA | GYP4 | glycophorin A (MNS blood group) |
| NM_002641 | 25.61951676 | -1.01739 | 0.287276 | -3.5415 | 0.000398 | 0.032136 PIGA | phosphatidylinositol glycan anchor biosynthesis, class A |
| NR_110328 | 24.27332551 | -1.01706 | 0.329816 | -3.08372 | 0.002044 | 0.061819 MFSD1 | major facilitator superfamily domain containing 1 |
| NM_000572 | 12.37056247 | -1.01679 | 0.359062 | -2.83178 | 0.004629 NA | IL10 | interleukin 10 |
| NM_001290190 | 15.36283568 | -1.01539 | 0.396173 | -2.56301 | 0.010377 | 0.13099 MYADM | myeloid-associated differentiation marker |
| NM_001271856 | 17.90008357 | -1.01261 | 0.414025 | -2.44577 | 0.014454 | 0.146619 GRASP | GRP1 (general receptor for phosphoinositides 1)-associated scaffold protein |
| NM_001254 | 47.84514349 | -1.01147 | 0.350386 | -2.88672 | 0.003893 | 0.083512 CDC6 | cell division cycle 6 |
| NR_037601 | 190.3977045 | -1.00923 | 0.312612 | -3.22837 | 0.001245 | 0.053529 LOC100507217 | uncharacterized LOC100507217 |
| NM_001290325 | 4.8446198 | -1.00876 | 0.392979 | -2.56697 | 0.010259 NA | USP38 | ubiquitin carboxyl-terminal hydrolase 38 isoform 2 |
| NM_001130072 | 2.129000493 | -1.00791 | 0.417382 | -2.41485 | 0.015742 NA | EPN1 | epsin 1 |
| NM_170776 | 434.4064892 | -1.00764 | 0.400364 | -2.51682 | 0.011842 | 0.137371 GPR97 | G protein-coupled receptor 97 |
| NM_015878 | 19.59230546 | -1.00637 | 0.314544 | -3.19497 | 0.001377 | 0.055524 AZIN1 | antizyme inhibitor 1 |
| NM_001001479 | 86.9111829 | -1.00455 | 0.256776 | -3.91216 | 9.15E-05 | 0.018538 SLC35E4 | solute carrier family 35, member E4 |
| NR_038278 | 7.713387842 | -1.005042 | 0.415537 | -2.418657 | 0.015578 NA | LINC00665 | long intergenic non-protein coding RNA 665 |
| NM_001077710 | 35.526575159 | -1.006623 | 0.392679 | -2.563474 | 0.010363 | 0.13099 FAM110C | family with sequence similarity 110, member C |
| NM_001282658 | 2.765851595 | -1.006769 | 0.417288 | -2.41265 | 0.015837 NA | CCDC3 | coiled-coil domain containing 3 |
| NM_152751 | 1.044782128 | -1.007514 | 0.426142 | -2.08564 | 0.008256 NA | BEND7 | BEN domain containing 7 |
| NR_047013 | 7.903063656 | -1.007853 | 0.393685 | -2.560052 | 0.010466 NA | LINC00400 | |
| NR_104136 | 5.420818192 | -1.008674 | 0.400985 | -2.515491 | 0.011887 NA | MANEA-A: MANEA antisense RNA 1 (head to head) | |
| NM_001242885 | 72.45741212 | -1.013342 | 0.343173 | -2.95286 | 0.003148 | 0.075184 AC137932 | uncharacterized LOC100287036 |
| NR_049763 | 3.019052648 | -1.014191 | 0.416434 | -2.435417 | 0.014875 NA | CNOT1 | CCR4-NOT transcription complex, subunit 1 |
| NM_080657 | 241.95712152 | -1.014368 | 0.294978 | -3.438787 | 0.000584 | 0.037814 RSAD2 | radical S-adenosyl methionine domain containing 2 |
| NR_120662 | 20.88551505 | -1.014501 | 0.269399 | -3.7658 | 0.000166 | 0.0251 LOC102723703 | |
| NR_023917 | 11.4482714 | -1.015156 | 0.344152 | -2.949727 | 0.003181 NA | PTENP1 | phosphatase and tensin homolog pseudogene 1 |
| NM_198150 | 118.5013019 | -1.018205 | 0.232588 | -4.37728 | 1.20E-05 | 0.006962 ARSK | arylsulfatase family, member K |
| NR_120495 | 4.516000072 | -1.022687 | 0.402632 | -2.540001 | 0.011085 NA | ATE1-AS1 | |
| NM_001159522 | 9.093818635 | -1.022854 | 0.416266 | -2.457212 | 0.014002 NA | ZNF277 | zinc finger protein 727 |
| NM_001284527 | 4.071320807 | -1.028501 | 0.400696 | -2.566787 | 0.010265 NA | ZSCAN32 | zinc finger and SCAN domain containing 32 |
| NR_038343 | 141.7893244 | -1.030838 | 0.367022 | -2.808655 | 0.004975 | 0.092913 MAGI2-AS | MAGI2 antisense RNA 3 |
| NM_006988 | 144.4652624 | -1.031543 | 0.397598 | -2.594435 | 0.009475 | 0.125524 ADAMTS1 | ADAM metallopeptidase with thrombospondin type 1 motif, 1 |
| NM_001007544 | 59.9369092 | -1.032704 | 0.311845 | -3.311599 | 0.000928 | 0.048548 C1orf186 | chromosome 1 open reading frame 186 |
| NM_0331160 | 54.06308769 | -1.030382 | 0.3421 | -3.019822 | 0.002529 | 0.06848 ZNF658 | zinc finger protein 658 |
| NM_021624 | 3.903537936 | -1.033485 | 0.416217 | -2.483041 | 0.013027 NA | HRH4 | histamine receptor H4 |
| NM_003637 | 51.30957824 | -1.034328 | 0.224412 | -4.615226 | 3.93E-06 | 0.004164 ITGA10 | integrin, alpha 10 |
| NM_001127713 | 1.98 | | | | | | |

| | | | | | | | | |
|--------------|--------------|------------------|----------|----------|-----------------|-----------------|-----------------|--|
| NM_001282560 | 2.557014387 | 1.050574 | 0.415193 | 2.530328 | 0.011396 | NA | EYA3 | eyes absent homolog 3 (Drosophila) |
| NM_0010183 | 9.486493342 | 1.054456 | 0.337805 | 3.121491 | 0.01799 | NA | PDE5A | phosphodiesterase 5A, cGMP-specific |
| NR_103511 | 4.744271316 | 1.054745 | 0.417192 | 2.528201 | 0.011465 | NA | ARL6 | ADP-ribosylation factor-like 6 |
| NR_033248 | 31.74505417 | 1.056194 | 0.254497 | 4.150119 | 3.32E-05 | 0.011304 | GCSHP3 | glycine cleavage system protein H (aminomethyl carrier) pseudogene 3 |
| NR_036490 | 2.904643233 | 1.056863 | 0.406912 | 2.597279 | 0.009397 | NA | LOC284641 | uncharacterized LOC284648 |
| NR_038826 | 374.0796649 | 1.057157 | 0.341616 | 3.094576 | 0.001971 | 0.061819 | LINCO0989 | long intergenic non-protein coding RNA 989 |
| NM_001122646 | 2.62147362 | 1.057292 | 0.416107 | 2.540913 | 0.011056 | NA | FAM178B | family with sequence similarity 178, member B |
| NM_000341 | 93.02752649 | 1.058399 | 0.313716 | 3.373747 | 0.000742 | 0.041732 | SLC3A1 | solute carrier family 3 (amino acid transporter heavy chain), member 1 |
| NM_001010893 | 1.621789521 | 1.061178 | 0.381732 | 2.779903 | 0.005438 | NA | SLC10A5 | solute carrier family 10, member 5 |
| NM_018980 | 15.39881527 | 1.061643 | 0.327358 | 3.243065 | 0.001183 | 0.053129 | TAS2R5 | taste receptor, type 2, member 5 |
| NM_001163989 | 12.52342273 | 1.062227 | 0.323527 | 3.283274 | 0.001026 | NA | RAB37 | RAB37, member RAS oncogene family |
| NM_024645 | 1.594186028 | 1.062454 | 0.382159 | 2.780134 | 0.005434 | NA | ZMAT4 | zinc finger, matrin-type 4 |
| NM_001297738 | 13.69103451 | 1.062601 | 0.417179 | 2.547113 | 0.010862 | NA | TBCA | tubulin-specific chaperone A isoform 1 |
| NR_024584 | 7.123516214 | 1.063921 | 0.406511 | 2.617201 | 0.008865 | NA | LINCO0623 | |
| NM_001135592 | 2.392793006 | 1.064115 | 0.417263 | 2.550227 | 0.010765 | NA | RP527A | ribosomal protein S27a |
| NM_001288961 | 18.1835885 | 1.064219 | 0.381433 | 2.790057 | 0.00527 | 0.094436 | LOC400863 | uncharacterized LOC400863 |
| NM_001290264 | 10.71300389 | 1.064292 | 0.401169 | 2.652977 | 0.007979 | NA | SLC35E2B | solute carrier family 35 member E2B |
| NM_004158 | 3.509279512 | 1.064367 | 0.415518 | 2.561545 | 0.010421 | NA | PSPN | persephin |
| NM_003175 | 115.9410156 | 1.064954 | 0.31072 | 3.427371 | 0.000609 | 0.037814 | XCL2 | chemokine (C motif) ligand 2 |
| NM_001039707 | 6.877644079 | 1.066037 | 0.386576 | 2.757637 | 0.005822 | NA | SDCCAG3 | serologically defined colon cancer antigen 3 |
| NR_110032 | 22.90181151 | 1.06761 | 0.307344 | 3.473662 | 0.000513 | 0.035968 | LOC101927045 | |
| NM_000745 | 4.10737762 | 1.071377 | 0.415229 | 2.580209 | 0.009874 | NA | CHRNAS5 | cholinergic receptor, nicotinic, alpha 5 (neuronal) |
| NM_153281 | 1.675161594 | 1.075585 | 0.418055 | 2.597685 | 0.009385 | NA | HYAL1 | hyaluronoglucosaminidase 1 |
| NM_001024675 | 35.29024639 | 1.075978 | 0.34902 | 3.08286 | 0.00205 | 0.061819 | ACTL10 | actin-like 10 |
| NR_73084 | 5.259348631 | 1.078614 | 0.417379 | 2.584256 | 0.009759 | NA | CRIP2 | cysteine-rich protein 2 |
| NM_026675 | 2.890516673 | 1.079379 | 0.407796 | 2.646857 | 0.008124 | NA | CRYM-AS1 | CRYM antisense RNA 1 |
| NM_000067 | 15.03929137 | 1.080138 | 0.303009 | 3.564707 | 0.000364 | 0.031803 | CA2 | carbonic anhydrase II |
| NR_047493 | 8.666952147 | 1.080324 | 0.408811 | 2.642597 | 0.008227 | NA | LINCO0563 | long intergenic non-protein coding RNA 563 |
| NM_108075 | 7.797582176 | 1.086824 | 0.41309 | 2.630905 | 0.008514 | NA | ITPR1-AS1 | ITPR1 antisense RNA 1 (head to head) |
| NM_109827 | 22.39563251 | 1.089125 | 0.269646 | 4.034605 | 5.47E-05 | 0.014885 | CCDC7 | coiled-coil domain containing 7 |
| NM_006208 | 5.400452038 | 1.094381 | 0.407405 | 2.685925 | 0.007233 | NA | ENPP1 | ectonucleotide pyrophosphatase/phosphodiesterase 1 |
| NM_002048 | 19.27264693 | 1.0948 | 0.391949 | 2.793217 | 0.005219 | 0.094436 | GAS1 | growth arrest-specific 1 |
| NR_038446 | 1945.732244 | 1.097002 | 0.33454 | 3.103783 | 0.001911 | 0.061275 | LINCO0861 | long intergenic non-protein coding RNA 861 |
| NM_001286624 | 83.93005874 | 1.100552 | 0.287224 | 3.831692 | 0.000127 | 0.024171 | MAP3K7CL | MAP3K7 C-terminal like |
| NM_153370 | 13.3139873 | 1.108028 | 0.367892 | 3.011827 | 0.002597 | NA | PI16 | peptidase inhibitor 16 |
| NM_001018070 | 7.422734375 | 1.1089125 | 0.269646 | 4.034605 | 5.47E-05 | 0.014885 | CCDC7 | coiled-coil domain containing 7 |
| NM_001301060 | 2.363083082 | 1.113568 | 0.415222 | 2.68186 | 0.007321 | NA | MORN1 | MORN repeat-containing protein 1 isoform 2 |
| NR_104137 | 2.948624981 | 1.116162 | 0.416451 | 2.680175 | 0.007358 | NA | ARMC2-AS | ARMC2 antisense RNA 1 |
| NR_045118 | 21.27231828 | 1.118456 | 0.326124 | 3.429571 | 0.000605 | 0.037814 | KCNIP2-AS | KCNIP2 antisense RNA 1 |
| NM_001099269 | 6.077085276 | 1.119329 | 0.390469 | 2.866625 | 0.004149 | NA | ZNF506 | zinc finger protein 506 |
| NM_021734 | 1.815951144 | 1.125071 | 0.413554 | 2.720496 | 0.006518 | NA | SLC25A19 | solute carrier family 25 (mitochondrial thiamine pyrophosphate carrier), member 19 |
| NR_047510 | 12.93719035 | 1.127957 | 0.38588 | 2.923073 | 0.003466 | NA | N6AMT1 | N-6 adenine-specific DNA methyltransferase 1 (putative) |
| NM_001003690 | 2.292491288 | 1.134997 | 0.416904 | 2.722442 | 0.00648 | NA | MAD2L1BF | MAD2L1 binding protein |
| NM_001172780 | 6.190517816 | 1.139093 | 0.378877 | 3.006497 | 0.002643 | NA | LRRC34 | leucine rich repeat containing 34 |
| NM_015717 | 5.781051208 | 1.139658 | 0.38558 | 2.9557 | 0.00312 | NA | CD207 | CD207 molecule, langerin |
| NR_033850 | 32.686721212 | 1.146723 | 0.280243 | 4.01892 | 4.28E-05 | 0.013147 | WDR11-AS | WDR11 antisense RNA 1 |
| NM_000706 | 24.71965783 | 1.148389 | 0.37654 | 3.049851 | 0.00229 | 0.065687 | AVPR1A | arginine vasopressin receptor 1A |
| NM_006820 | 703.286532 | 1.149267 | 0.306428 | 3.750534 | 0.000176 | 0.025912 | IFI44L | interferon-induced protein 44-like |
| NM_001142797 | 4.036149433 | 1.150933 | 0.416155 | 2.765638 | 0.005681 | NA | CXCR3 | chemokine (C-X-C motif) receptor 3 |
| NM_001290009 | 149.4909843 | 1.15213 | 0.359167 | 3.207785 | 0.001338 | 0.054917 | BIN2 | bridging integrator 2 isoform 4 |
| NM_005961 | 13.66760643 | 1.154017 | 0.321178 | 3.593081 | 0.000327 | NA | MUC6 | mucin 6, oligomeric mucus/gel-forming |
| NM_152399 | 9.531181992 | 1.158381 | 0.363351 | 3.188046 | 0.001432 | NA | TMEM155 | transmembrane protein 155 |
| NM_001962 | 41.54840333 | 1.160486 | 0.380945 | 3.046335 | 0.002316 | 0.065864 | EFNNS1 | ephrin-A5 |
| NM_022046 | 5.680322937 | 1.16291 | 0.390165 | 2.980562 | 0.002877 | NA | KLK14 | kallikrein-related peptidase 14 |
| NM_001007189 | 106.6848392 | 1.163189 | 0.387558 | 3.001329 | 0.002688 | 0.070061 | IGIP | IgA-inducing protein |
| NR_125926 | 2.420662873 | 1.163632 | 0.416392 | 2.794556 | 0.005197 | NA | LOC101929468 | |
| NM_007053 | 100.624859 | 1.170159 | 0.325704 | 3.592704 | 0.000327 | 0.030813 | CD160 | CD160 molecule |
| NM_0003382 | 18.36802772 | 1.171764 | 0.338908 | 3.457473 | 0.000545 | 0.036994 | VIPR2 | vasoactive intestinal peptide receptor 2 |
| NR_108073 | 2.566295173 | 1.177333 | 0.415392 | 2.834271 | 0.004593 | NA | LOC101927354 | |
| NM_033437 | 1.874626367 | 1.179407 | 0.41582 | 2.836343 | 0.004563 | NA | PDE5A | phosphodiesterase 5A, cGMP-specific |
| NR_027257 | 2.046441745 | 1.187336 | 0.414498 | 2.86452 | 0.004176 | NA | FLJ26850 | FLJ26850 protein |
| NR_125406 | 14.09152964 | 1.192205 | 0.388486 | 3.068848 | 0.002149 | NA | LOC102724297 | |
| NM_001005851 | 352.0750816 | 1.192681 | 0.326727 | 3.650394 | 0.000262 | 0.029 | ZNF780B | zinc finger protein 780B |
| NM_001001995 | 19.46901173 | 1.211192 | 0.340754 | 3.554443 | 0.000379 | 0.031803 | GPM6B | glycoprotein M6B |
| NR_027146 | 10.7240057 | 1.219433 | 0.411718 | 2.96182 | 0.003058 | NA | LINCO0469 | long intergenic non-protein coding RNA 469 |
| NM_000387 | 737.2045794 | 1.225546 | 0.256428 | 4.779308 | 1.76E-06 | 0.003351 | SLC25A20 | solute carrier family 25 (carnitine/acylcarnitine translocase), member 20 |
| NM_0020702 | 19.36214065 | 1.231354 | 0.383047 | 3.215114 | 0.001304 | 0.054046 | KIAA1161 | KIAA1161 |
| NM_024565 | 92.45877092 | 1.243946 | 0.303399 | 4.10003 | 4.13E-05 | 0.013147 | CCNL1 | cyclin J-like |
| NM_001013653 | 3.161644436 | 1.255394 | 0.41727 | 3.008591 | 0.002625 | NA | LRRC26 | leucine rich repeat containing 26 |
| NM_001258016 | 1.742412885 | 1.255696 | 0.410848 | 3.056352 | 0.00224 | NA | FDXR | ferredoxin reductase |
| NR_108104 | 5.569594916 | 1.256203 | 0.414986 | 3.027094 | 0.002469 | NA | RP11-166C | uncharacterized LOC101929736 |
| NM_001282941 | 6.259583374 | 1.28086 | 0.400561 | 3.197662 | 0.001385 | NA | RTKN2 | rhotekin 2 |
| NM_018012 | 10.66725655 | 1.287699 | 0.389462 | 3.30635 | 0.000945 | NA | KIF2B | kinesin family member 26B |
| NR_027440 | 2.465317931 | 1.294851 | 0.417304 | 3.102893 | 0.001916 | NA | LOC10027 | uncharacterized LOC100272217 |
| NR_027412 | 9.49727963 | 1.295238 | 0.384378 | 3.369697 | 0.000753 | NA | LINCO0910 | long intergenic non-protein coding RNA 910 |
| NM_001111319 | 17.272262308 | 1.309912 | 0.412636 | 3.174945 | 0.001501 | 0.056498 | CLDN22 | claudin 22 |
| NM_0016816 | 16.07151359 | 1.313354 | 0.371476 | 3.535504 | 0.000407 | 0.032136 | OAS1 | 2'-5'-oligoadenylate synthetase 1, 40/46kDa |
| NR_027442 | 8.150786567 | 1.323258 | 0.366509 | 3.610401 | 0.000306 | NA | LOC100281 | UDP-GlcNAc:betaGal beta 1,3-N-acetylglucosaminyltransferase 5 pseudogene |
| NR_046683 | 5.454195803 | 1.351123 | 0.413883 | 3.264862 | 0.001095 | NA | ST3GAL6+ST3GAL6 | antisense RNA 1 |
| NM_002234 | 2.192658128 | 1.365868 | 0.417259 | 3.27343 | 0.001063 | NA | KCNAS | potassium voltage-gated channel, shaker-related subfamily, member 5 |
| NM_006727 | 32.81311009 | 1.368975 | 0.384304 | 3.562219 | 0.000368 | 0.031803 | S100B | s100 calcium binding protein B |
| NM_001297562 | 9.776594793 | 1.401804 | 0.394095 | 3.557052 | 0.000375 | NA | TNFSF4 | tumor necrosis factor ligand superfamily member 4 isoform 2 |
| NM_001002919 | 9.777359029 | 1.406335 | 0.35617 | 3.948497 | 7.86E-05 | NA | FAM150B | family with sequence similarity 150, member B |
| NM_015719 | 121.5817146 | 1.420213 | 0.402039 | 3.532525 | 0.000412 | 0.032136 | COL5A3 | collagen, type V, alpha 3 |
| NM_001177676 | 18.2560785 | 1.472378 | 0.366445 | 4.018005 | 5.87E-05 | 0.015109 | GPR68 | G protein-coupled receptor 68 |
| NM_003783 | 10.33798 | | | | | | | |

Supplementary Table 3. List of up-regulated genes in the remission group of the paired samples.

| Gene symbol | Raw p value | R/A fc ^a | Description |
|-------------|-------------|---------------------|---|
| DEFA4 | 5.02E-06 | 3.67 | Defensin, alpha 4, corticostatin |
| PRTN3 | 1.54E-02 | 3.57 | Proteinase 3 |
| AZU1 | 2.20E-02 | 3.56 | Azurocidin 1 |
| ELANE | 9.67E-03 | 3.55 | Elastase, neutrophil expressed |
| LTF | 1.66E-02 | 3.44 | Lactotransferrin |
| CAMP | 3.24E-02 | 3.38 | Cathelicidin antimicrobial peptide |
| CTSG | 2.63E-02 | 3.29 | Cathepsin G |
| OLFM4 | 1.07E-02 | 3.20 | Olfactomedin 4 |
| CEACAM8 | 1.94E-02 | 3.18 | Carcinoembryonic antigen-related cell adhesion molecule 8 |
| LCN2 | 9.30E-03 | 3.18 | Lipocalin 2 |
| CEACAM6 | 3.12E-02 | 3.00 | Carcinoembryonic antigen-related cell adhesion molecule 6 (non-specific cross reacting antigen) |
| RNASE3 | 5.04E-03 | 3.00 | Ribonuclease, RNase A family, 3 |
| PGLYRP1 | 1.77E-02 | 2.98 | Peptidoglycan recognition protein 1 |
| TPGS1 | 3.63E-02 | 2.84 | Tubulin polyglutamylase complex subunit 1 |
| S100P | 3.45E-02 | 2.73 | S100 calcium binding protein P |
| SLPI | 3.69E-02 | 2.56 | Secretory leukocyte peptidase inhibitor |
| NDUFS1 | 2.88E-02 | 2.34 | NADH dehydrogenase (ubiquinone) Fe-S protein 1, 75kDa (NADH-coenzyme Q reductase) |
| PRPF38A | 2.16E-02 | 2.04 | Pre-mRNA processing factor 38A |

^aFold change ratio of expression level in the remission group to the active group