-- SUPPLEMENTARY INFORMATION--

Responder and nonresponder patients exhibit different peripheral transcriptional signatures during Major Depressive Episode

Raoul Belzeaux[1,2,3]; Aurélie Bergon[2,4,5]; Valérie Jeanjean[1,2]; Béatrice Loriod[4,5]; Christine Formisano-Tréziny[6,7]; Lore Verrier[2]; Anderson Loundou[8,9]; Karine Baumstarck-Barrau[8,9]; Laurent Boyer[9,10]; Valérie Gall[4,5]; Jean Gabert[6,7,11]; Catherine Nguyen[4,5]; Jean-Michel Azorin[2,3], Jean Naudin[2]; El Chérif Ibrahim[1,*].

[1]Aix-Marseille Université, CNRS, CRN2M UMR 7286, [2]Pôle de Psychiatrie Universitaire Solaris, Hôpital Sainte Marguerite, Assistance Publique–Hôpitaux de Marseille, Marseille, France, [3]FondaMental, Fondation de Recherche et de Soins en Santé Mentale, Paris, France, [4]INSERM, TAGC-UMR 1090, [5]Aix-Marseille Université, TAGC-UMR 1090, Parc scientifique de Luminy, Marseille, France, [6]INSERM, UNIS, U-1072, [7]Aix-Marseille Université, UNIS, U-1072, 13015, Marseille, France, [8]Unité d'aide méthodologique, Faculté de Médecine Timone, [9]Department of Public Health, Hôpital La Timone, Assistance Publique–Hôpitaux de Marseille, France, [10]Aix-Marseille Université, Research Unit EA 3279, [11]Laboratoire de Biochimie-Biologie Moléculaire, Hôpital Nord, Assistance Publique–Hôpitaux de Marseille, France

*To whom correspondence should be addressed. E-mail: el-cherif.ibrahim@univ-amu.fr

CONTENTS **Page**

1 SUPPLEMENTARY METHODS

1.1 Design setting and subjects

The study design was a naturalistic, prospective, longitudinal and comparative study with assessments of major depressive episode (MDE) patients and healthy controls at baseline (week 0), 2 and 8 weeks after inclusion. Sixteen patients who met the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision (DSM-IV-TR) criteria for major depressive disorder (MDD) participated in the study.[1] Inclusion criteria were: (i) treated or untreated MDE (ii) 17-item Hamilton Rating Scale for Depression (HDRS) score $\geq$ 20 corresponding to severe or very severe MDE.[2] Patients with bipolar disorder, schizophrenia, personality disorder, substance use disorder, medical problems, abnormal body temperature or laboratory tests (especially blood cell count), and neurological exploration were excluded. Patients were clinically evaluated using an adapted standardized procedure (SCID-I/P)[3]. Socio-demographic information including age, gender, marital status and educational level was collected. The severity of MDE was evaluated with a French version of 17-item HDRS at each evaluation.[4] Presence of recurrent MDD, episode duration, familial history of MDE and other severe psychiatric disorders, suicide attempts history, and tobacco smocking were evaluated.

At the end of the 8-week clinical follow-up, patients were classified as responders and nonresponders based on the consensual definition of clinical response corresponding to a minimal reduction of 50 % of the HDRS score from the initial evaluation.[5] The first nine patients, classified as responders, and their matched controls were organized by pairs within cohort A. The other patient/control pairs formed cohort B.

For the control group, age- and sex-matched subjects were evaluated to exclude any patients with a history of psychiatric disorder using the French version of standardized interview validated for health control subjects (SCID-NP). Moreover, all participants were

carefully interviewed and had clinical examinations to eliminate any psychiatric or medical conditions. Tobacco smoking was also evaluated.

All experiments on human subjects were conducted in accordance with the latest version of the Declaration of Helsinki. The project was approved by the local ethics committee (Comité de Protection des Personnes, CPP Sud Méditerranée II, Marseille, France, study registered under number 09.025) and written informed consent was obtained after a complete description of the study to the subjects.

1.2 Blood mRNA extraction

At each evaluation, 8-10 ml venous blood was collected from fasting patients and matched-controls in EDTA tubes between 7:00 a.m. and 9:00 a.m. and processed within two hours. Peripheral blood mononuclear cells (PBMCs) were isolated from the blood by Ficoll density centrifugation. Total RNAs were extracted from the PBMCs with the mirVana miRNA isolation kit (Ambion, Austin, TX) according to the manufacturer's protocol. RNA concentration was determined using a nanodrop ND-1000 spectrophotometer (NanoDrop Technologies, Wilmington, DE). RNA integrity was assessed on an Agilent 2100 Bioanalyzer (Agilent Technologies, Santa Clara, CA). To ensure a robust analysis for the following procedures, samples with an RNA integrity number (RIN) inferior to 8 were excluded.

1.3 Preparation of samples and micorarray assay

Sample amplification, labeling, and hybridization essentially followed the one-color microarray-based gene expression analysis (low RNA input linear amplification PLUS kit) recommended by Agilent Technologies. In brief, 200 ng of each total RNA sample was reverse transcribed into cDNA using oligo dT-T7 promoter primer. Labeled cRNA was prepared from the cDNA. The reaction was performed in a solution containing dNTP mix, cyanine 3-dCTP, and T7 RNA polymerase, and incubated at 40°C for 2h. It was followed by

RNeasy column purification (QIAGEN, Valencia, CA). Dye incorporation and cRNA yield were checked with the NanoDrop ND-1000 Spectrophotometer. 600 ng of cyanine 3-labeled cRNA (specific activity > 6 pmol Cy3/ug cRNA) was fragmented at 60°C for 30 minutes before hybridization, for 17 hours at 65°C in a rotating Agilent hybridization oven, onto Agilent whole human genome oligo microarrays containing 50 599 different oligonucleotide probes (SurePrint G3 Human GE 8x60K, Agilent Technologies, Santa Clara, CA) and covering 27 958 Entrez Gene RNAs and 7 419 lincRNAs. Microarrays were then washed according to manufacturer's instructions. Slides were scanned immediately after washing on the Agilent DNA microarray scanner (G2505C) using one color scan setting for 8x60K array slides. The scanned images were analyzed with Agilent feature extraction software 10.5.1.1 using default parameters (protocol GE1_107_Sep09 and Grid 028004_D_F_20110325) to obtain background subtracted and spatially detrended processed signal intensities. All data were normalized by quantile normalization using limma R/bioconductor package (v.2.16.4). Only 39 784 oligonucleotide probes with signal intensities detectable (i.e. above background according to the "gIsWellAboveBg" Agilent feature extraction value) in ≥ 70% of samples (from either MDE patients or controls and at either baseline or 8 weeks later) were subsequently analyzed. This filtering step was obtained using the AgiND R package (http://tagc.univ-mrs.fr/tagc/index.php/software/agind, v1.0.5). The microarray data are available from the gene expression omnibus (GEO, http://www.ncbi.nlm.nih.gov/geo/) under the series accession number GSE38206.

1.4 Gene and chromosome band enrichment analyses

Lists of genes with significant changes were uploaded on DAVID (database for annotation, visualization and integrated discovery) for identifying statistically relevant signaling pathways[6] using high classification stringency, P-value (p) < 0.05 and false discovery rate (FDR) ≤ 5%. The sequences for the boundaries of the chromosomal regions where the probes

to detect differential expression are located were obtained from the Ensembl database (Human reference assembly GRCh37, WTSI/EBI). To determine the chromosomal cytoband enrichment in our lists of genes, we used the ToppFun algorithm and restricted the search to $p<0.05$.[7] To take into account multiple testings, the FDR was calculated with the PROC MULTTEST statement as previously described.

1.5 MiRNA quantification

400 ng of total RNA were reverse transcribed using the TaqMan MicroRNA RT kit (Applied Biosystems, Foster City, CA) in combination with the stem-loop Megaplex^{TM} primer pools (A and B v3.0, Applied Biosystems) without preamplification and according to manufacturer's recommendation. For each RT pool, the equivalent of 320 ng of total RNA converted into cDNA was mixed with TaqMan Universal PCR Master Mix II No AmpErase UNG (Applied Biosystems, Foster City, CA). 100 µl of mix (A or B) was loaded into each port of the corresponding 384 wells Human miRNA TaqMan low density array (i.e. A or B) and run for 40 cycles on a ABI PRISM 7900 HT according to manufacturer's protocol with SDS v2.4 software. Raw Ct values were calculated using the RQ Manager software v1.2.1 with manual baseline settings for each miRNA. Only those miRNAs detectable ($Ct < 33$) in PBMCs of $\geq$ 60% the samples (MDE patients or controls) were subsequently analyzed. The raw Ct values were then normalized based on the expression level of a combination of 2 to 5 reference miRNAs, exhibiting a stable level of expression among all samples, and selected with both the genorm^{PLUS} (Biogazelle, Zulte, Belgium)[8] and DataAssist softwares. In order to normalize the target miRNA with reference miRNAs exhibiting a proximal expression level (i.e. difference between the target and the reference miRNAs < 3 Ct), 5 windows of expression levels ($Ct < 21$; $21 < Ct < 24$; $24 < Ct < 27$; $27 < Ct < 30$; $Ct > 30$) were defined in which a specific set of reference miRNAs were selected. Normalized expression levels of each miRNA are also quantified as $2^{-\Delta\Delta Ct}$,[9] with the DataAssist software (Applied Biosystems,

v3.0), relative to the normalized expression level of the same miRNA in a calibrator sample (either the mean of 9 samples from the 9 control subjects when comparing patients to controls, or the week 0 sample of the MDE patient when comparing patient at week 0 to the same patient 8 weeks later).

1.6 Target prediction

For each list of differentially expressed miRNAs, the Ingenuity pathway analysis (IPA) software (Ingenuity systems), which relies on 3 popular algorithms (TargetSan, TarBase and miRecords), was queried to identify targets within lists of differentially expressed genes in our microarray analysis. Only highly predicted and experimentally validated targets were considered for further analysis.

1.7 Real-time RT-PCR for candidate gene validation

1.6 µg of RNA was reverse transcribed with the High Capacity cDNA archive kit (Applied Biosystems, Foster City, CA, USA). 200 ng of the resulting cDNA was combined with a TaqMan® universal PCR Master Mix (Applied Biosystems) and 48 PCR reactions were simultaneously performed on an ABI PRISM 7900HT thermocycler using tLDA technology according to manufacturer recommendations (Applied Biosystems). All PCR reactions were performed in triplicate. For each tested candidate gene, primer sets and probes were selected using the web portal of the manufacturer (Applied Biosystems) to amplify sequences matching as close as possible the transcripts detected by the Agilent probe in our initial microarray screen. In addition, after a search within our microarray data for probes showing minimal variation of signal intensity among the 36 samples tested from both MDE patients and controls, we selected 3 genes, in addition to very highly expressed gene *GAPDH*

(imposed by the manufacturer), to be used as highly (*PAFAH1B1*), moderately (*ALDOC*) and weakly (*SV2A*) expressed reference genes. After verifying with DataAssist that our 4 selected reference genes were stably expressed among all the samples from MDE patients and controls tested by RT-qPCR, we set-up 4 windows of expression intensities to normalize target gene expression (21<Ct<24; 24<Ct<27; 27<Ct<30; Ct>30) using adequate reference genes alone or in combination (Supplementary Table 17). The expression level of each candidate gene was calculated as $2^{-\Delta\Delta Ct}$ with the DataAssist software (Applied Biosystems, v3.0), in which each candidate gene is quantified relative to the expression of a single, or a combination of two reference genes, to calculate a proximal level (i.e. difference between the target and the reference miRNA < 3 Ct) of expression compared to the target gene, and compared to a calibrator sample (the mean of the samples from the control subjects at week 0 when comparing patients to controls).

1.8 Statistical Analysis

1.8.1 Demographic and clinical data

Demographic and clinical variables were compared between patients and matched-controls for cohort A and between responder and nonresponder patients with a Fisher exact test for qualitative variables and a t-test for quantitative variables. All statistical tests were made using the IBM SPSS Statistics v20 software.

1.8.2 Microarray data

To calculate the number of samples required to draw conclusions with enough statistical power for our microarray screen, we determined a minimum sample size (n=9) by using sizepower tool within the R/bioconductor package[10] with the following parameters: FDR = 5 %, number of significant genes (π_0) ≥ 0.5%, power of the study = 90%, expected difference

between groups = 1.5, and standard deviation = 0.5 (Supplementary Figure 1). Accordingly, samples of the first 9 responder MDE patients and matched controls at the inclusion visit and eight weeks later were assessed in the microarray analysis and constituted 4 different groups: "MDE_{0w}" for responder patients at the inclusion, "MDE_{8w}" for responders patients eight weeks later, "C_{0w}" for matched control subjects at the inclusion and "C_{8w}" for matched control subjects eight weeks later.

For each comparison ("MDE_{0w}" versus "C_{0w}", "MDE_{0w}" versus "C_{8w}", "MDE_{8w}" versus "C_{0w}", "MDE_{8w}" versus "C_{8w}", "MDE_{0w}" versus "MDE_{8w}", and "C_{0w}" versus "C_{8w}"), measurements of differential gene expression were obtained using the MultiExperiment Viewer 4 (MeV4, TM4 software suite), and the significant analysis for microarrays program (SAM) was set at FDR threshold of 5%.[11,12] Student's t-tests were also applied to determine P-values. The data were analyzed using either a two-class unpaired (for patients versus controls comparison) or paired (for internal comparisons within patients or within controls) response types.

The gene list that distinguishes "MDE_{0w}" and "$C_{0w,8w}$" was obtained by crossing the lists "MDE_{0w}" versus "C_{0w}" and "MDE_{0w}" versus "C_{8w}". Similarly, the gene list that distinguishes "MDE_{8w}" and "$C_{0w,8w}$" was obtained by crossing the lists "MDE_{8w}" versus "C_{0w}" and "MDE_{8w}" versus "C_{8w}".

1.8.3 MiRNA study

To select differentially expressed miRNAs (at 0 and 8-week visits), non-parametric unpaired Mann-Whitney tests were used to compare the fold change (FC) between patients and matched-controls with a threshold P-value of 0.05. Non-parametric paired Wilcoxon tests were used to compare the FC between the two evaluations within the MDE group with a threshold P-value of 0.05.

1.8.4 Candidate gene validation

For exploratory purposes and to compare microarray data with RT-qPCR data, parametric unpaired t-tests were used to compare the FC between patients and matched-controls at the first evaluation, and 8 weeks later, within either the whole cohort (FC_{all}), the intial sub-cohort A (FC_A), or the subsequent sub- cohort B (FC_B).

Since we conducted a prospective study with three visits and have repeated measures for each subject, a mixed linear model method was used for each candidate mRNA to test the differences between responders and nonresponders patients. As potential confounding factors could introduce bias in the observed results, additional characteristics were taken into account and tested as co-variables in the mixed linear model such as sex, age, and treatments received. To explore differences between responders and nonresponders, we calculated and compared marginal estimated mean of each group.

Finally, to quantitatively explore the predictive value of the best mRNA candidates in the previous analysis, we calculated Spearman's correlations between HDRS evolution (0 to 8- and 2 to 8-week intervals) and FC at inclusion or at 2 weeks, respectively. Moreover, a discriminant function analysis was used with the goal of establishing a predictive score to classify patients in the responder versus nonresponder groups. Sensitivity, specificity, positive/negative predictive value, and the confidence intervals of each selected mRNA candidates, or a combination of the best classifiers, were computed for the combination of selected variables. Receiver-operating characteristic (ROC) curves analysis was used to determine the area under the curve (AUC).

2 SUPPLEMENTARY TABLES

Supplementary Table ST1: Baseline characteristics of the major depression cohort

Pairs	Age of onset	Familial history of MDE	Familial history of other severe psychiatric disorders	Episode duration at the inclusion (month)	Suicide attempts	Smoking	Educational level	Marital status
1	60	Y	Y	12	N	N	Grad.	Married
2	20	Y	Y	16	N	N	Grad.	Married
3	45	Y	N	2	N	N	Undergrad.	Married
4	33	N	Y	4	Y	N	Undergrad.	Divorced
5	37	Y	N	3	N	Y	High School	Divorced
6	57	Y	N	12	Y	N	Undergrad.	Married
7	43	N	Y	4	Y	N	Undergrad.	Married
8	46	Y	N	6	N	N	Grad.	Married
9	18	N	Y	2	N	N	Grad.	Married
10	55	Y	N	11	Y	N	Grad.	Divorced
11	70	Y	N	6	Y	N	Undergrad.	Married
12	37	Y	N	3	N	N	Grad.	Married
13	51	Y	N	3	Y	N	High School	Divorced
14	32	N	Y	1	N	N	Grad.	Married
15	39	Y	N	1	N	N	Undergrad.	Single
16	29	Y	Y	16	Y	Y	Undergrad.	Married

Abbreviations: Grad., graduate studies; N, no; Undergrad., incompleted undergraduate degree; Y, yes.

Supplementary Table ST2: Baseline characteristics of the healthy control cohort

Pairs	Familial history of MDE	Familial history of other severe psychiatric disorders	Smoking	Educational level	Marital status
1	N	N	Y	Grad.	Married
2	N	N	Y	High School	Divorced
3	N	Y	N	Undergrad.	Divorced
4	Y	N	N	Grad.	Married
5	N	N	N	Grad.	Married
6	N	N	N	Grad.	Married
7	N	N	N	Grad.	Married
8	N	N	N	Grad.	Married
9	N	N	Y	Grad.	Married
10	N	N	N	Undergrad.	Married
11	N	Y	N	Grad.	Married
12	N	N	N	Grad.	Married
13	N	N	N	Undergrad.	Married

Abbreviations: Grad., graduate studies; N, no; Undergrad., incompleted undergraduate degree; Y, yes.

Supplementary Table ST3: Demographic and clinical characteristics of study participants

Variable	MDE patients	Control subjects	P-value[1]
Sex (female/male)	7/9	7/6	0.715
Age (years)	55.3 ± 2.7	55.5 ± 2.6	0.940
Smocking (yes/no)	2/14	3/10	0.632
Educational level (graduate studies, yes/no)	7/9	9/4	0.264
Married (yes/no)	11/5	11/2	0.410
Familial history of MDD (yes/no)	**12/4**	**1/12**	**0.000498**
Familial history of severe psychiatric disorder (yes/no)	7/9	2/11	0.130

[1]t-test was used for quantitative variables and a Fisher's exact test for categorical variables

Supplementary Table ST4: Comparison of demographic and clinical characteristics of MDE patients between responders and nonresponders

Variable	Responder patients	Nonresponder patients	P-value[1]
Sex (female/male)	6/4	1/5	0.145
Age (years)	56.2 ± 2.7	53.7 ± 5.9	0.666
Smocking (yes/no)	1/9	1/5	1.000
Educational level (graduate studies, yes/no)	5/5	2/4	0.633
Married (yes/no)	8/2	3/3	0.299
HDRS at the inclusion	27.2 ± 1.6	27.0 ± 2.5	0.945
Episode duration prior to inclusion (months)	6.4 ± 1.6	6.3 ± 2.5	0.981
Recurrent MDD (yes/no)	8/2	4/2	0.604
Personal history of suicide attempts (yes/no)	2/8	3/3	0.299
Familial history of MDD (yes/no)	7/3	5/1	1.000
Familial history of severe psychiatric disorder (yes/no)	5/5	2/4	0.633

[1]t-test was used for quantitative variables and a Fisher's exact test for categorical variables

Supplementary Table ST5: Overexpressed transcripts in MDE subjects at week 0 compared to controls (weeks 0 and 8)

Probe	Accession	Gene description	Gene symbol	Cytoband	Fold change	P-value
A_23_P115885	**NM_004897**	**multiple inositol-polyphosphate phosphatase 1, transcript variant 1**	**MINPP1**	**10q23.2**	**3.80**	**2.92E-8**
A_33_P3249046	NM_001171092	claudin 2, transcript variant 2	CLDN2	Xq22.3	3.08	1.57E-5
A_19_P00809807		**lincRNA:chr10:131973130-131978637_R**		**10q26.3**	**3.05**	**1.95E-5**
A_19_P00812661		**lincRNA:chr8:129503568-129843218_R**		**8q24.21**	**2.80**	**1.20E-7**
A_23_P59261	NM_006670	trophoblast glycoprotein, transcript variant 1	TPBG	6q14.1	2.67	3.05E-4
A_24_P242646	NM_004079	cathepsin S, transcript variant 1	CTSS	1q21.3	2.64	8.82E-4
A_33_P3232945	NM_005242	coagulation factor II (thrombin) receptor-like 1	F2RL1	5q13.3	2.53	2.74E-5
A_19_P00331948		**lincRNA:chr6:34244122-34253868_F**		**6p21.33**	**2.51**	**7.33E-9**
A_24_P333663	NM_002748	mitogen-activated protein kinase 6	MAPK6	15q21.2	2.44	2.82E-5
A_33_P3358824	NM_000302	procollagen-lysine 1, 2-oxoglutarate 5-dioxygenase 1	PLOD1	1p36.22	2.35	6.20E-7
A_24_P226108	NM_019027	RNA binding motif protein 47, transcript variant 2	RBM47	4p14	2.32	8.71E-5
A_24_P276628	**NM_000310**	**palmitoyl-protein thioesterase 1, transcript variant 1**	**PPT1**	**1p34.2**	**2.30**	**1.24E-6**
A_33_P3276713	NM_001010931	hepatocyte growth factor (hepapoietin A; scatter factor), transcript variant 2	HGF	7q21.11	2.28	7.22E-6
A_23_P396777	NM_006315	polycomb group ring finger 3	PCGF3	4p16.3	2.25	8.11E-5
A_23_P36611	NM_181861	apoptotic peptidase activating factor 1, transcript variant 3	APAF1	12q23.1	2.24	1.49E-4
A_33_P3403418	NM_001903	catenin (cadherin-associated protein), alpha 1, 102kDa	CTNNA1	5q31.2	2.22	1.82E-4
A_23_P171054	**NM_005229**	**ELK1, member of ETS oncogene family, transcript variant 2**	**ELK1**	**Xp11.23**	**2.09**	**2.59E-6**
A_24_P605190	NM_005023	protein geranylgeranyltransferase type I, beta subunit	PGGT1B	5q22.3	2.08	1.25E-4
A_23_P66891	NM_012121	CDC42 effector protein (Rho GTPase binding) 4	CDC42EP4	17q25.1	2.07	1.03E-4
A_33_P3337981	NM_014845	FIG4 homolog, SAC1 lipid phosphatase domain containing (S. cerevisiae)	FIG4	6q21	2.06	2.84E-4
A_33_P3224212	**NM_015361**	**R3H domain containing 1**	**R3HDM1**	**2q21.3**	**2.05**	**1.70E-4**
A_33_P3299754	NM_021252	RAB18, member RAS oncogene family	RAB18	10p12.1	2.05	6.88E-5
A_19_P00319055		lincRNA:chr22:31369198-31371363_R		22q12.1	2.04	5.99E-7
A_23_P381203	NM_015202	KIAA0556	KIAA0556	16p12.1	2.03	6.35E-5
A_23_P37988	**NM_152727**	**copine II**	**CPNE2**	**16q13**	**2.00**	**6.01E-6**
A_23_P125082	**NM_002199**	**interferon regulatory factor 2**	**IRF2**	**4q35.1**	**2.00**	**3.67E-6**
A_24_P272761	NM_020946	DENN/MADD domain containing 1A, transcript variant 1	DENND1A	9q33.3	2.00	2.59E-5
A_23_P347048	NM_030791	sphingosine-1-phosphate phosphatase 1	SGPP1	14q23.2	1.99	6.88E-5
A_23_P217564	**NM_004458**	**acyl-CoA synthetase long-chain family member 4, transcript variant 1**	**ACSL4**	**Xq23**	**1.98**	**4.03E-5**
A_32_P18159	NM_181705	Lyrm7 homolog (mouse)	LYRM7	5q23.3	1.95	1.41E-4

A_33_P3279545	NM_005734	homeodomain interacting protein kinase 3, transcript variant 1	HIPK3	11p13	1.95	2.17E-4
A_32_P155506	**NM_152653**	**ubiquitin-conjugating enzyme E2E 2 (UBC4/5 homolog, yeast)**	**UBE2E2**	**3p24.3**	**1.95**	**1.74E-6**
A_24_P312692	**NM_006595**	**apoptosis inhibitor 5, transcript variant 2**	**API5**	**11p12**	**1.94**	**8.01E-9**
A_23_P330836	**ENST00000357412**	**chromosome X open reading frame 24 [Source:HGNC Symbol;Acc:27333]**	**CXORF24**	**Xp11.23**	**1.94**	**5.69E-7**
A_23_P122375	**NM_021943**	**zinc finger, AN1-type domain 3**	**ZFAND3**	**6p21.2**	**1.93**	**6.61E-9**
A_24_P383901	**XR_017601**	**PREDICTED: similar to Actin, cytoplasmic 1**	**LOC391334**	**22q13.2**	**1.91**	**1.13E-8**
A_23_P133438	NM_019018	family with sequence similarity 105, member A	FAM105A	5p15.2	1.89	4.71E-6
A_23_P355455	**NM_014744**	**TBC1 domain family, member 5, transcript variant 2**	**TBC1D5**	**3p24.3**	**1.88**	**6.20E-9**
A_33_P3238993	NM_001135187	ArfGAP with FG repeats 1, transcript variant 1	AGFG1	2q36.3	1.88	2.04E-4
A_33_P3330841	NM_004507	HUS1 checkpoint homolog (S. pombe)	HUS1	7p13-p12	1.87	6.41E-4
A_23_P146379	NM_012416	RAN binding protein 6, transcript variant 1	RANBP6	9p24.1	1.86	1.24E-4
A_24_P14367	NM_002819	polypyrimidine tract binding protein 1, transcript variant 1	PTBP1	19p13.3	1.86	1.19E-6
A_33_P3338956	NM_018184	ADP-ribosylation factor-like 8B	ARL8B	3p26.1	1.84	4.45E-4
A_24_P353794	NM_004481	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 2 (GalNAc-T2)	GALNT2	1q42.13	1.84	1.24E-6
A_24_P267522	NM_152655	zinc finger protein 585A, transcript variant 1	ZNF585A	19q13.12	1.84	4.05E-7
A_24_P174341	NM_058241	cyclin T2 (CCNT2), transcript variant b	CCNT2	2q21.3	1.83	2.27E-5
A_24_P103060	NM_139279	multiple coagulation factor deficiency 2, transcript variant 1	MCFD2	2p21	1.81	7.93E-5
A_23_P105571	NM_020244	choline phosphotransferase 1	CHPT1	12q23.2	1.80	3.84E-6
A_33_P3398533	NM_025138	proline and serine rich 1	PROSER1	13q13.3	1.80	7.55E-6
A_23_P145584	NM_003344	ubiquitin-conjugating enzyme E2H (UBC8 homolog, yeast), transcript variant 1	UBE2H	7q32.2	1.76	1.23E-4
A_33_P3254191	NM_020841	oxysterol binding protein-like 8, transcript variant 1	OSBPL8	12q21.2	1.76	1.51E-5
A_23_P37598	NM_012428	neuroplastin, transcript variant b	NPTN	15q24.1	1.76	1.81E-6
A_24_P374319	NM_021183	RAP2C, member of RAS oncogene family	RAP2C	Xq26.2	1.76	2.25E-4
A_23_P210538	NM_182764	engulfment and cell motility 2, transcript variant 2	ELMO2	20q13.12	1.73	8.49E-7
A_23_P338325	NM_005230	ELK3, ETS-domain protein (SRF accessory protein 2)	ELK3	12q23.1	1.72	3.19E-5
A_24_P141786	**NM_001681**	**ATPase, Ca++ transporting, cardiac muscle, slow twitch 2, transcript variant 2**	**ATP2A2**	**12q24.11**	**1.72**	**4.87E-5**
A_23_P121527	NM_015990	kelch-like 5 (Drosophila), transcript variant 1	KLHL5	4p14	1.71	8.19E-7
A_23_P130352	NM_198991	potassium channel tetramerisation domain containing 1, transcript variant 2	KCTD1	18q11.2	1.71	3.19E-4
A_24_P116805	NM_213662	signal transducer and activator of transcription 3 (acute-phase response factor), transcript variant 3	STAT3	17q21.2	1.70	1.80E-4
A_24_P238744	**NM_001145442**	**POTE ankyrin domain family, member M**	**POTEM**	**14q11.2**	**1.70**	**2.21E-6**
A_24_P6903	**NM_001017992**	**actin, beta-like 2**	**ACTBL2**	**5q11.2**	**1.69**	**2.54E-8**
A_33_P3305974	NM_003825	synaptosomal-associated protein, 23kDa, transcript variant 1	SNAP23	15q15.1	1.69	2.93E-4

A_33_P3376636	NM_001017989	optic atrophy 3 (autosomal recessive, with chorea and spastic paraplegia), nuclear gene encoding mitochondrial protein, transcript variant 1	OPA3	19q13.32	1.69	7.54E-8
A_24_P156049	NM_012319	solute carrier family 39 (zinc transporter), member 6, transcript variant 1	SLC39A6	18q12.2	1.69	1.84E-5
A_23_P75330	NM_004966	heterogeneous nuclear ribonucleoprotein F, transcript variant 3	HNRNPF	10q11.21	1.68	1.52E-6
A_23_P111228	NM_017421	coenzyme Q3 homolog, methyltransferase (S. cerevisiae)	COQ3	6q16.2	1.67	2.17E-5
A_24_P387609	NM_030940	iron-sulfur cluster assembly 1 homolog (S. cerevisiae)	ISCA1	9q21.33	1.67	1.11E-4
A_23_P306507	NM_033360	v-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog, transcript variant a	KRAS	12p12.1	1.67	1.72E-5
A_23_P216894	NM_001006617	mitogen-activated protein kinase associated protein 1, transcript variant 1	MAPKAP1	9q33.3	1.67	4.98E-6
A_23_P110345	NM_012110	cysteine-rich hydrophobic domain 2	CHIC2	4q12	1.67	1.77E-4
A_23_P399501	NM_182470	pyruvate kinase, muscle, transcript variant 2	PKM2	15q23	1.67	2.24E-4
A_23_P29036	NM_005534	interferon gamma receptor 2 (interferon gamma transducer 1)	IFNGR2	21q22.11	1.66	4.10E-4
A_32_P155776	**NR_033885**	**POTE ankyrin domain family, member K, pseudogene**	**POTEKP**	**2q21.1**	**1.66**	**7.79E-7**
A_24_P73669	NM_002094	G1 to S phase transition 1, transcript variant 1	GSPT1	16p13.13	1.65	2.63E-7
A_33_P3403044	**NM_005911**	**methionine adenosyltransferase II, alpha**	**MAT2A**	**2p11.2**	**1.65**	**4.84E-11**
A_33_P3248765	**NM_015999**	**adiponectin receptor 1, transcript variant 1**	**ADIPOR1**	**1q32.1**	**1.65**	**7.80E-8**
A_23_P115366	NM_016308	cytidine monophosphate (UMP-CMP) kinase 1, cytosolic, transcript variant 1	CMPK1	1p33	1.65	1.90E-4
A_24_P942630	NM_001080424	lysine (K)-specific demethylase 6B	KDM6B	17p13.1	1.64	4.55E-5
A_24_P410017	**NM_001083538**	**POTE ankyrin domain family, member E**	**POTEE**	**2q21.1**	**1.64**	**2.61E-9**
A_33_P3232562	NM_005610	retinoblastoma binding protein 4, transcript variant 1	RBBP4	1p35.1	1.64	1.01E-4
A_32_P22338	NM_013374	programmed cell death 6 interacting protein, transcript variant 1	PDCD6IP	3p22.3	1.63	1.76E-5
A_24_P228875	**NM_004840**	**Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6**	**ARHGEF6**	**Xq26.3**	**1.62**	**2.84E-9**
A_33_P3289835	ENST00000531819	oxysterol binding protein-like 9 [Source:HGNC Symbol;Acc:16386]	OSBPL9	1p32.3	1.62	8.32E-8
A_23_P156049	NM_000521	hexosaminidase B (beta polypeptide)	HEXB	5q13.3	1.62	2.20E-4
A_33_P3418516	NM_001949	E2F transcription factor 3	E2F3	6p22.3	1.61	7.01E-6
A_23_P255257	NM_015397	DDB1 and CUL4 associated factor 12	DCAF12	9p13.3	1.61	4.70E-6
A_24_P349039	NM_020754	Rho GTPase activating protein 31	ARHGAP31	3q13.33	1.60	1.17E-4
A_23_P6651	NM_015224	chromosome 3 open reading frame 63, transcript variant 2	C3orf63	3p14.3	1.60	1.22E-6
A_24_P418044	NR_024240	major histocompatibility complex, class I, J (pseudogene)	HLA-J	6p22.1	1.60	2.05E-4
A_24_P312041	NM_006718	pleiomorphic adenoma gene-like 1, transcript variant 2	PLAGL1	6q24.2	1.59	3.42E-4
A_24_P59220	**NM_001099771**	**POTE ankyrin domain family, member F**	**POTEF**	**2q21.1**	**1.59**	**3.64E-8**
A_23_P149892	NM_018590	chondroitin sulfate N-acetylgalactosaminyltransferase 2	CSGALNACT2	10q11.21	1.59	2.97E-5
A_33_P3343155	NM_002072	guanine nucleotide binding protein (G protein), q polypeptide	GNAQ	9q21.2	1.59	1.69E-6
A_23_P16139	NM_006387	calcium homeostasis endoplasmic reticulum protein	CHERP	19p13.11	1.59	1.33E-6
A_23_P41292	NM_001012614	C-terminal binding protein 1, transcript variant 2	CTBP1	4p16.3	1.58	1.36E-7
A_23_P166135	NM_012255	5'-3' exoribonuclease 2	XRN2	20p11.23	1.58	1.78E-8

A_23_P75516	NM_003626	protein tyrosine phosphatase, receptor type, f polypeptide (PTPRF), interacting protein (liprin), alpha 1, transcript variant 2	PPFIA1	11q13.3	1.57	9.25E-5
A_24_P408424	NM_002473	myosin, heavy chain 9, non-muscle	MYH9	22q12.3	1.56	2.80E-5
A_23_P10858	NM_015114	ankyrin repeat and LEM domain containing 2	ANKLE2	12q24.33	1.55	1.38E-6
A_23_P118150	NM_015161	ADP-ribosylation factor-like 6 interacting protein 1	ARL6IP1	16p12.3	1.55	7.12E-6
A_24_P38815	**NM_000391**	**tripeptidyl peptidase I**	**TPP1**	**11p15.4**	**1.55**	**1.26E-6**
A_23_P321201	NM_015213	DENN/MADD domain containing 5A	DENND5A	11p15.4	1.54	1.69E-4
A_23_P250380	NM_015274	mannosidase, alpha, class 2B, member 2	MAN2B2	4p16.1	1.53	6.96E-7
A_23_P109928	NM_014814	proteasome (prosome, macropain) 26S subunit, non-ATPase, 6	PSMD6	3p14.1	1.53	1.65E-6
A_33_P3321230	NM_052831	chromosome 6 open reading frame 192	C6orf192	6q23.2	1.53	1.75E-4
A_24_P58337	NM_002032	ferritin, heavy polypeptide 1	FTH1	11q12.3	1.52	5.03E-5
A_23_P115645	NM_001025076	CUGBP, Elav-like family member 2, transcript variant 1	CELF2	10p14	1.51	1.66E-11
A_23_P110606	NM_014757	mastermind-like 1 (Drosophila)	MAML1	5q35.3	1.51	1.22E-5
A_23_P162228	NM_005594	nascent polypeptide-associated complex alpha subunit, transcript variant 3	NACA	12q13.3	1.50	3.53E-7
A_23_P381449	NM_003110	Sp2 transcription factor	SP2	17q21.32	1.50	7.66E-6
A_23_P98092	NM_000274	ornithine aminotransferase, nuclear gene encoding mitochondrial protein, transcript variant 1	OAT	10q26.13	1.50	3.65E-4

This list contains 111 genes differentially overexpressed in MDE versus control at baseline. Changes were assessed by a SAM analysis set with a FDR of 5% and then challenged with a t-test (FC ≥ 1.50; $p<0.001$). Genes in bold are also significant with a FDR set at 1%.

Supplementary Table ST6: Underexpressed transcripts in MDE subjects at week 0 compared to controls (weeks 0 and 8)

Probe	Accession	Gene description	Gene symbol	Cytoband	Fold change	P-value
A_19_P00316854		**lincRNA:chr18:53750605-53752602_F**		**18q21.2**	**-4,21**	**1.64E-6**
A_32_P46594	NR_026979	hypothetical LOC145837	LOC145837	15q23	-3.39	9.00E-4
A_33_P3241145	BC047414	cDNA clone IMAGE:5273698	BC047414	16p11.2	-3.27	5.05E-5
A_33_P3379606	NM_001029875	regulator of G-protein signaling 7 binding protein	RGS7BP	5q12.3	-3.13	1.01E-5
A_23_P337270	ENST00000383770	NIMA (never in mitosis gene a)-related kinase 10 [Source:HGNC Symbol;Acc:18592]	NEK10	3p24.2	-2.89	3.62E-5
A_33_P3274439	DA109127	BRACE3 Homo sapiens cDNA clone BRACE3025572 5'	DA109127	11q22.3	-2.81	1.31E-5
A_33_P3226542	NR_003271	small nucleolar RNA, C/D box 3B-1	SNORD3B-1	17p11.2	-2.70	2.39E-5
A_24_P260639	**NM_005320**	**histone cluster 1, H1d**	**HIST1H1D**	**6p22.2**	**-2.63**	**1.47E-4**
A_33_P3709317	**NR_002964**	**small nucleolar RNA, H/ACA box 28**	**SNORA28**	**14q32.32**	**-2.58**	**1.64E-9**
A_23_P315836	NM_017451	BAI1-associated protein 2, transcript variant 2	BAIAP2	17q25.3	-2.57	4.52E-5
A_33_P3236392	NM_030916	poliovirus receptor-related 4	PVRL4	1q23.3	-2.52	3.90E-4
A_33_P3227551	ENST00000509069	zinc finger protein 331	ZNF331	19q13.41	-2.49	1.51E-4
A_19_P00319456		**lincRNA:chr19:53151418-53152966_R**		**19q13.33**	**-2.41**	**2.17E-5**
A_19_P00324238		lincRNA:chr3:129602510-129611708_R		3q21.3	-2.41	4.84E-5
A_19_P00800237		**lincRNA:chr19:53149513-53154883_R**		**19q13.41**	**-2.35**	**1.33E-10**
A_19_P00810480		**lincRNA:chr2:102597068-102606493_F**		**2q11.2**	**-2.34**	**9.54E-5**
A_23_P67952	NR_026766	v-myc myelocytomatosis viral related oncogene, neuroblastoma derived (avian) opposite strand	MYCNOS	2p24.1	-2.31	2.32E-4
A_33_P3335366	NM_018717	mastermind-like 3 (Drosophila)	MAML3	4q28	-2.29	3.40E-6
A_19_P00808575		lincRNA:chr14:23018310-23025460_R		14q11.2	-2.26	1.04E-6
A_33_P3578325	NR_000005	small nucleolar RNA, C/D box 15A	SNORD15A	11q13.4	-2.25	6.84E-5
A_23_P415411	**NM_003545**	**histone cluster 1, H4e**	**HIST1H4E**	**6p22.2**	**-2.23**	**1.48E-5**
A_19_P00813557		lincRNA:chr1:118374652-118400852_F		1p13.1	-2.22	3.32E-6
A_24_P232790	NR_024630	chromosome 14 open reading frame 162	C14orf162	14q24.1	-2.18	8.19E-5
A_24_P219378	**NM_020764**	**CASK interacting protein 1**	**CASKIN1**	**16p13.3**	**-2.17**	**6.09E-11**
A_33_P3257678	NM_001005464	histone cluster 2, H3a	HIST2H3A	1q21.2	-2.15	5.60E-5
A_19_P00319448		**lincRNA:chr19:53151411-53151829_R**		**19q13.33**	**-2.14**	**4.46E-6**
A_33_P3377763	NR_027084	hypothetical FLJ36000	FLJ36000	17p11.2	-2.13	1.32E-5

A_24_P217834	**NM_003530**	**histone cluster 1, H3d**	**HIST1H3D**	**6p22.2**	**-2.08**	**3.17E-5**
A_33_P3344229	NM_003538	histone cluster 1, H4a	HIST1H4A	6p22.2	-2.08	1.20E-5
A_33_P3214785	AK094801	cDNA FLJ37482 fis, clone BRAWH2013941	LEPROT	1p31.3	-2.05	9.43E-7
A_33_P3299781	ENST00000380201	DDRGK domain containing 1 [Source:HGNC Symbol;Acc:16110]	DDRGK1	20p13	-2.01	2.15E-4
A_19_P00324774		lincRNA:chr3:13093175-13147525_R		3p25.1	-2.00	2.91E-4
A_19_P00318708		**lincRNA:chr17:70442671-70443408_R**		**17q24.3**	**-1.99**	**1.38E-4**
A_33_P3318946	**NM_021817**	**hyaluronan and proteoglycan link protein 2**	**HAPLN2**	**1q23.1**	**-1.98**	**1.68E-4**
A_23_P30799	NM_021018	histone cluster 1, H3f	HIST1H3F	6p22.2	-1.98	7.85E-4
A_23_P7976	**NM_005321**	**histone cluster 1, H1e**	**HIST1H1E**	**6p22.2**	**-1.94**	**6.27E-5**
A_23_P218784	NM_006386	DEAD (Asp-Glu-Ala-Asp) box polypeptide 17, transcript variant 1	DDX17	22q13.1	-1.94	4.75E-6
A_23_P70448	NM_005325	histone cluster 1, H1a	HIST1H1A	6p22.2	-1.93	1.66E-6
A_33_P3363082	NR_003008	small Cajal body-specific RNA 5	SCARNA5	2q37.1	-1.93	2.20E-6
A_23_P75790	NM_013279	chromosome 11 open reading frame 9, transcript variant 1	C11orf9	11q12.2	-1.90	1.28E-4
A_19_P00329774		lincRNA:chr7:33679675-33695300_F		7p14.3	-1.88	1.26E-4
A_19_P00812282		lincRNA:chr3:154957056-155055681_F		3q25.2	-1.86	1.42E-7
A_33_P3387931	**NM_001012267**	**centromere protein P**	**CENPP**	**9q22.31**	**-1.85**	**2.74E-6**
A_33_P3812815	**NM_000296**	**polycystic kidney disease 1 (autosomal dominant), transcript variant 2**	**PKD1**	**16p13.3**	**-1.84**	**2.64E-5**
A_23_P416774	NM_016929	chloride intracellular channel 5, nuclear gene encoding mitochondrial protein, transcript variant 2	CLIC5	6p21.1	-1.84	1.41E-4
A_23_P391778	**NM_033044**	**microtubule-actin crosslinking factor 1, transcript variant 2**	**MACF1**	**1p34.3**	**-1.83**	**6.07E-6**
A_33_P3382595	**NR_001445**	**RNA, 7SK small nuclear**	**RN7SK**	**6p12.2**	**-1.82**	**1.24E-6**
A_24_P273413	NM_019063	echinoderm microtubule associated protein like 4, transcript variant 1	EML4	2p21	-1.77	3.36E-7
A_19_P00802156		lincRNA:chr6:86386083-86388435_R		6q14.1	-1.77	2.72E-4
A_33_P3304824	ENST00000435624	chromosome 14 open reading frame 63	C14orf63	14q32.2	-1.76	1.87E-4
A_24_P481783	NM_001163692	ubiquitin-associated protein 1-like	UBAP1L	15q22.31	-1.76	3.14E-4
A_19_P00806618		lincRNA:chr5:1130775-1186275_R		5p15.33	-1.76	5.94E-5
A_33_P3399028	NM_006852	tousled-like kinase 2, transcript variant A	TLK2	17q23.2	-1.75	1.42E-5
A_19_P00322542		lincRNA:chr3:129611381-129612189_R		3q21.3	-1.75	5.31E-6
A_32_P66020	NM_032167	sorting nexin 29	SNX29	16p13.13	-1.74	1.77E-5
A_23_P502957	NM_021810	cadherin 26, transcript variant b	CDH26	20q13.33	-1.73	5.18E-4
A_33_P3245922	**NM_006724**	**mitogen-activated protein kinase kinase kinase 4, transcript variant 2**	**MAP3K4**	**6q26**	**-1.73**	**3.53E-6**
A_33_P3209497	NP511207	BAC05833.1 seven transmembrane helix receptor	NP511207	7q34	-1.72	4.65E-4
A_33_P3299865	NM_003541	histone cluster 1, H4k	HIST1H4K	6p22.1	-1.71	2.03E-4
A_19_P00329800		lincRNA:chr1:204525202-204541352_F		1q32.1	-1.69	9.04E-5
A_33_P3401284	NR_003051	RNA component of mitochondrial RNA processing endoribonuclease,	RMRP	9p13.3	-1.68	3.53E-7

		RNase MRP RNA				
A_33_P3254695	ENST00000363217	small nucleolar RNA, H/ACA box 73B	SNORA73B	1p35.3	-1.64	4.69E-6
A_33_P3301620	NM_001184997	ring finger protein 32, transcript variant 2	RNF32	7q36.3	-1.64	1.42E-5
A_33_P3302652	ENST00000415882	chromosome 1 open reading frame 132	C1orf132	1q32.1	-1.64	9.45E-6
A_23_P331943	NM_020823	transmembrane protein 181	TMEM181	6q25.3	-1.63	6.22E-5
A_23_P214821	NM_001955	endothelin 1, transcript variant 1	EDN1	6p24.1	-1.63	1.23E-4
A_23_P105592	NM_000431	mevalonate kinase, transcript variant 1	MVK	12q24.11	-1.62	6.24E-6
A_24_P214598	NM_152542	protein phosphatase, Mg2+/Mn2+ dependent, 1K, nuclear gene encoding mitochondrial protein	PPM1K	4q22.1	-1.62	1.09E-4
A_24_P163113	NM_017548	CDV3 homolog (mouse), transcript variant 2	CDV3	3q22.1	-1.61	2.80E-7
A_33_P3339066	NM_017619	RNA-binding region (RNP1, RRM) containing 3	RNPC3	1p21.1	-1.61	3.39E-4
A_23_P360874	NM_152892	leucine-rich repeats and WD repeat domain containing 1	LRWD1	7q22.1	-1.61	1.00E-5
A_23_P70480	NM_003546	histone cluster 1, H4l	HIST1H4L	6p22.1	-1.60	9.85E-5
A_33_P3309365	NR_002314	solute carrier family 24 (sodium/potassium/calcium exchanger), member 3 pseudogene 1	SLC25A3P1	1p32.3	-1.59	1.18E-4
A_19_P00803182		lincRNA:chr2:37776096-37862046_R		2p22.3	-1.59	3.87E-6
A_33_P3218760	NM_080599	UPF2 regulator of nonsense transcripts homolog (yeast), transcript variant 1,	UPF2	10p14	-1.57	3.18E-5
A_23_P97283	NM_024897	progestin and adipoQ receptor family member VI, transcript variant 1	PAQR6	1q22	-1.57	1.04E-4
A_23_P97021	NM_024852	eukaryotic translation initiation factor 2C, 3, transcript variant 1	EIF2C3	1p34.3	-1.57	2.50E-5
A_33_P3535175	BX095413	NCI_CGAP_Kid3 Homo sapiens cDNA clone IMAGp998P233802	BX095413	20p13	-1.55	2.22E-7
A_23_P372874	NM_001024210	S100 calcium binding protein A13, transcript variant 1	S100A13	1q21.3	-1.54	1.26E-4
A_23_P398275	NR_027001	hypothetical LOC388152	LOC388152	15q25.2	-1.54	7.34E-5
A_32_P106732	NM_020937	Fanconi anemia, complementation group M	FANCM	14q21.2	-1.54	1.44E-6
A_23_P89155	NM_001258	cyclin-dependent kinase 3	CDK3	17q25.1	-1.53	2.21E-4
A_33_P3313595	NM_033487	cyclin-dependent kinase 11B, transcript variant 3	CDK11B	1p36.33	-1.53	9.72E-5
A_23_P59022	NM_033502	transcriptional regulating factor 1	TRERF1	6p21.1	-1.51	4.41E-6

This list contains 84 genes differentially underexpressed in MDE versus control at baseline. Changes were assessed by a SAM analysis set with a FDR of 5% and then challenged with a t-test (FC ≥ 1.50; $p<0.001$). Genes in bold are also significant with a FDR set at 1%.

Supplementary Table ST7: Overexpressed transcripts in MDE treatment responders at week 8 responding compared to controls (weeks 0 and 8)

Probe	Accession	Gene description	Gene symbol	Cytoband	Fold change	P-value
A_24_P461497	XM_002343637	PREDICTED: similar to cytoskeletal beta actin	LOC646048	19p13.2	2.41	5.11E-6
A_23_P407096	NM_152625	zinc finger protein 366	ZNF366	5q13.2	2.36	1.28E-5
A_24_P276628	NM_000310	palmitoyl-protein thioesterase 1, transcript variant 1	PPT1	1p34.2	2.22	1.93E-8
A_33_P3248765	NM_015999	adiponectin receptor 1, transcript variant 1	ADIPOR1	1q32.1	2.15	3.18E-5
A_33_P3403418	NM_001903	catenin (cadherin-associated protein), alpha 1, 102kDa	CTNNA1	5q31.2	2.11	8.88E-5
A_19_P00806748		lincRNA:chr6:139809107-140148457_F		6q24.1	2.10	1.86E-4
A_23_P145035	NM_153042	lysine (K)-specific demethylase 1B	KDM1B	6p22.3	2.05	8.47E-5
A_33_P3382236	NM_018330	KIAA1598, transcript variant 2	KIAA1598	10q25.3	2.05	6.44E-3
A_24_P156049	NM_012319	solute carrier family 39 (zinc transporter), member 6, transcript variant 1	SLC39A6	18q12.2	2.05	6.04E-5
A_23_P500364	NM_001707	B-cell CLL/lymphoma 7B, transcript variant 1	BCL7B	7q11.23	2.00	1.77E-4
A_23_P396777	NM_006315	polycomb group ring finger 3	PCGF3	4p16.3	2.00	1.64E-4
A_23_P122375	NM_021943	zinc finger, AN1-type domain 3	ZFAND3	6p21.2	2.00	2.35E-8
A_23_P379020	NR_002328	gonadotropin-releasing hormone (type 2) receptor 2	GNRHR2	1q21.1	1.98	8.43E-9
A_24_P383901	XR_017601	PREDICTED: similar to Actin, cytoplasmic 1	LOC391334	22q13.2	1.96	1.20E-7
A_24_P312041	NM_006718	pleiomorphic adenoma gene-like 1, transcript variant 2	PLAGL1	6q24.2	1.95	8.33E-10
A_23_P37988	NM_152727	copine II	CPNE2	16q13	1.93	1.20E-5
A_24_P16856	ENST00000381261	A kinase (PRKA) anchor protein 17A [Source:HGNC Symbol;Acc:18783]	AKAP17A	Xp22.33	1.91	3.27E-6
A_33_P3331307	NM_006449	CDC42 effector protein (Rho GTPase binding) 3	CDC42EP3	2p22.2	1.90	1.06E-4
A_23_P105571	NM_020244	choline phosphotransferase 1	CHPT1	12q23.2	1.86	1.74E-6
A_24_P272761	NM_020946	DENN/MADD domain containing 1A, transcript variant 1	DENND1A	9q33.3	1.86	4.72E-5
A_23_P53557	NM_002342	lymphotoxin beta receptor (TNFR superfamily, member 3)	LTBR	12p13.31	1.85	1.14E-5
A_33_P3410093	NM_000895	leukotriene A4 hydrolase	LTA4H	12q23.1	1.80	2.04E-5
A_24_P70888	NM_012401	plexin B2	PLXNB2	22q13.33	1.80	3.76E-5
A_23_P217564	NM_004458	acyl-CoA synthetase long-chain family member 4, transcript variant 1	ACSL4	Xq23	1.76	3.52E-4
A_24_P6903	NM_001017992	actin, beta-like 2	ACTBL2	5q11.2	1.76	5.68E-9
A_23_P156049	NM_000521	hexosaminidase B (beta polypeptide)	HEXB	5q13.3	1.76	6.71E-8
A_23_P149892	NM_018590	chondroitin sulfate N-acetylgalactosaminyltransferase 2	CSGALNACT2	10q11.21	1.73	7.68E-7

A_23_P355455	NM_014744	TBC1 domain family, member 5, transcript variant 2	TBC1D5	3p24.3	1.73	1.28E-4
A_24_P14367	NM_002819	polypyrimidine tract binding protein 1, transcript variant 1	PTBP1	19p13.3	1.72	3.68E-4
A_33_P3406927	NM_031284	ADP-dependent glucokinase, transcript variant 1	ADPGK	15q24.1	1.71	4.82E-6
A_19_P00803502		lincRNA:chr4:8490675-8515950_F		4p16.1	1.70	3.96E-5
A_33_P3223503	NM_023037	furry homolog (Drosophila)	FRY	13q13.1	1.70	6.75E-6
A_23_P75330	NM_004966	heterogeneous nuclear ribonucleoprotein F, transcript variant 3	HNRNPF	10q11.21	1.70	1.78E-5
A_32_P22338	NM_013374	programmed cell death 6 interacting protein, transcript variant 1	PDCD6IP	3p22.3	1.70	4.98E-6
A_24_P141786	NM_001681	ATPase, Ca++ transporting, cardiac muscle, slow twitch 2, transcript variant 2	ATP2A2	12q24.11	1.68	2.03E-4
A_23_P321388	NM_153341	ring finger protein 19B (RNF19B), transcript variant 1, mRNA [NM_153341]	RNF19B	1p35.1	1.68	2.92E-6
A_33_P3343155	NM_002072	guanine nucleotide binding protein (G protein), q polypeptide	GNAQ	9q21.2	1.67	1.87E-6
A_32_P95823	NM_014607	UBX domain protein 4	UBXN4	2q21.3	1.66	2.25E-7
A_23_P83098	NM_000689	aldehyde dehydrogenase 1 family, member A1	ALDH1A1	9q21.13	1.64	3.14E-5
A_33_P3289835	ENST0000053189	oxysterol binding protein-like 9 [Source:HGNC Symbol;Acc:16386]	OSBPL9	1p32.3	1.64	3.38E-9
A_24_P410017	NM_001083538	POTE ankyrin domain family, member E	POTEE	2q21.1	1.64	1.01E-9
A_23_P17855	NM_001039141	TRIO and F-actin binding protein, transcript variant 6	TRIOBP	22q13.1	1.63	3.89E-6
A_24_P387609	NM_030940	iron-sulfur cluster assembly 1 homolog (S. cerevisiae)	ISCA1	9q21.33	1.62	3.79E-6
A_32_P209624	NR_026640	makorin ring finger protein 1 pseudogene	LOC100240726	20q13.11	1.62	9.57E-5
A_32_P155776	NR_033885	POTE ankyrin domain family, member K, pseudogene	POTEKP	2q21.1	1.61	5.05E-8
A_33_P3385870	NM_004354	cyclin G2	CCNG2	4q21.1	1.60	2.12E-6
A_23_P133438	NM_019018	family with sequence similarity 105, member A	FAM105A	5p15.2	1.60	4.66E-5
A_23_P37598	NM_012428	neuroplastin (NPTN), transcript variant b	NPTN	15q24.1	1.59	3.17E-6
A_33_P3321230	NM_052831	chromosome 6 open reading frame 192	C6orf192	6q23.2	1.58	2.05E-5
A_24_P408457	NM_000262	N-acetylgalactosaminidase, alpha	NAGA	22q13.2	1.57	2.56E-5
A_23_P426809	NM_198236	Rho guanine nucleotide exchange factor (GEF) 11, transcript variant 2	ARHGEF11	1q23.1	1.55	4.80E-5
A_24_P391368	NM_013236	ataxin 10, transcript variant 1	ATXN10	22q13.31	1.55	6,73E-5
A_23_P134347	NM_019029	carboxypeptidase, vitellogenic-like, transcript variant 2	CPVL	7p14.3	1.55	9.48E-5
A_23_P206324	NM_031463	hydroxysteroid dehydrogenase like 1, transcript variant 1	HSDL1	16q23.3	1.54	1.55E-4
A_23_P118427	NM_145109	mitogen-activated protein kinase kinase 3, transcript variant B	MAP2K3	17p11.2	1.53	8.85E-5
A_23_P216894	NM_001006617	mitogen-activated protein kinase associated protein 1, transcript variant 1	MAPKAP1	9q33.3	1.51	4.78E-6
A_24_P38815	NM_000391	tripeptidyl peptidase I	TPP1	11p15.4	1.51	6.56E-8
A_24_P228875	NM_004840	Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6	ARHGEF6	Xq26.3	1.50	6.10E-5

This list contains 58 genes differentially overexpressed in MDE at 8-week of follow-up versus control. Changes were assessed by a SAM analysis set with a FDR of 5% and then challenged with a t-test (FC ≥ 1.50; $p<0.001$).

Supplementary Table ST8: Underexpressed transcripts in MDE treatment responders at week 8 compared to controls (weeks 0 and 8)

Probe	Accession	Gene description	Gene symbol	Cytoband	Fold change	P-value
A_23_P501538	NM_153631	homeobox A3, transcript variant 2	HOXA3	7p15.2	-5,10	4.12E-4
A_24_P217834	NM_003530	histone cluster 1, H3d	HIST1H3D	6p22.2	-2.04	2.23E-7
A_33_P3355266	NM_022164	tubulointerstitial nephritis antigen-like 1	TINAGL1	1p35.2	-2.06	7.25E-6
A_33_P3578325	NR_000005	small nucleolar RNA, C/D box 15A	SNORD15A	11q13.4	-2.09	1.14E-6
A_33_P3236392	**NM_030916**	**poliovirus receptor-related 4**	**PVRL4**	**1q23.3**	**-3.13**	**2.48E-7**
A_19_P00808575		lincRNA:chr14:23018310-23025460_R		14q11.2	-2.13	1.33E-6
A_19_P00316854		**lincRNA:chr18:53750605-53752602_F**		**18q21.2**	**-4.19**	**3.03E-5**
A_23_P415411	**NM_003545**	**histone cluster 1, H4e**	**HIST1H4E**	**6p22.2**	**-2.18**	**9.99E-10**
A_24_P219378	**NM_020764**	**CASK interacting protein 1**	**CASKIN1**	**16p13.3**	**-2.22**	**3.75E-9**
A_32_P210202	NM_203394	E2F transcription factor 7	E2F7	12q21.2	-2.25	2.14E-5
A_19_P00805446		lincRNA:chr3:88108419-88178191_R		3p12.1	-3.27	7.00E-5
A_24_P260639	NM_005320	histone cluster 1. H1d	HIST1H1D	6p22.2	-2.26	3.49E-6
A_19_P00810480		**lincRNA:chr2:102597068-102606493_F**		**2q11.2**	**-2.49**	**1.14E-7**
A_33_P3709317	NR_002964	small nucleolar RNA, H/ACA box 28	SNORA28	14q32.32	-2.49	3.68E-6
A_19_P00317666		lincRNA:chr6:86387046-86387917_F		6q14.1	-1.50	2.95E-6
A_23_P391778	NM_033044	microtubule-actin crosslinking factor 1, transcript variant 2	MACF1	1p34.3	-1.50	1.30E-5
A_23_P256933	NM_000986	ribosomal protein L24	RPL24	3q12.3	-1.52	1.86E-5
A_33_P3376379	NM_001139459	consortin, connexin sorting protein, transcript variant 2	CNST	1q44	-1.54	1.21E-4
A_33_P3399028	NM_006852	tousled-like kinase 2, transcript variant A	TLK2	17q23.2	-1.54	9.79E-6
A_33_P3297205	NM_024627	chromosome 22 open reading frame 29	C22orf29	22q11.21	-1.55	5.77E-5
A_33_P3299781	ENST00000380201	DDRGK domain containing 1 [Source:HGNC Symbol;Acc:16110]	DDRGK1	20p13	-1.55	6.66E-5
A_33_P3230090	NM_001128619	leucine zipper protein 6	LUZP6	7q33	-1.55	6.42E-6
A_33_P3218760	NM_080599	UPF2 regulator of nonsense transcripts homolog (yeast), transcript variant 1	UPF2	10p14	-1.55	1.00E-4
A_24_P216253	NM_014902	discs, large (Drosophila) homolog-associated protein 4, transcript variant 1	DLGAP4	20q11.23	-1.56	2.09E-5
A_33_P3408962	XR_110352	PREDICTED: hypothetical protein FLJ33996	FLJ33996	12q13.11-q13.12	-1.56	1.13E-5
A_23_P70480	NM_003546	histone cluster 1, H4l	HIST1H4L	6p22.1	-1.57	7.42E-5
A_24_P199655	NM_138959	vang-like 1 (van gogh, Drosophila), transcript variant 1	VANGL1	1p13.1	-1.57	5.20E-5
A_32_P106732	NM_020937	Fanconi anemia, complementation group M	FANCM	14q21.2	-1.59	1.11E-8

A_33_P3302652	ENST00000415882	chromosome 1 open reading frame 132	C1orf132	1q32.1	-1.60	4.84E-5
A_33_P3299865	NM_003541	histone cluster 1, H4k	HIST1H4K	6p22.1	-1.60	1.95E-6
A_24_P233078	NR_003064	peptide YY, 2 (seminalplasmin)	PYY2	17q11.2	-1.60	1.03E-5
A_23_P98410	NM_000073	CD3g molecule, gamma (CD3-TCR complex)	CD3G	11q23.3	-1.61	4.03E-5
A_33_P3290909	NM_006306	structural maintenance of chromosomes 1A	SMC1A	Xp11.22	-1.62	1.87E-4
A_33_P3254695	ENST00000363217	small nucleolar RNA, H/ACA box 73B	SNORA73B	1p35.3	-1.64	1.73E-7
A_33_P3395274	NM_175907	zinc binding alcohol dehydrogenase domain containing 2	ZADH2	18q22.3	-1.64	2.10E-5
A_19_P00809635		lincRNA:chr21:16633404-16851904_F		21q21.1	-1.65	3.61E-6
A_24_P411186	NM_022893	B-cell CLL/lymphoma 11A (zinc finger protein), transcript variant 1	BCL11A	2p16.1	-1.66	4.30E-5
A_23_P218784	NM_006386	DEAD (Asp-Glu-Ala-Asp) box polypeptide 17, transcript variant 1	DDX17	22q13.1	-1.66	4.77E-6
A_23_P97021	NM_024852	eukaryotic translation initiation factor 2C, 3, transcript variant 1	EIF2C3	1p34.3	-1.66	1.15E-9
A_23_P7976	NM_005321	histone cluster 1, H1e	HIST1H1E	6p22.2	-1.66	4.60E-6
A_19_P00322225		lincRNA:chr6:53493403-53495987_F		6p12.2	-1.71	2.54E-4
A_19_P00329774		lincRNA:chr7:33679675-33695300_F		7p14.3	-1.71	1.88E-4
A_33_P3812815	NM_000296	polycystic kidney disease 1 (autosomal dominant), transcript variant 2	PKD1	16p13.3	-1.71	1.85E-8
A_23_P30799	NM_021018	histone cluster 1, H3f	HIST1H3F	6p22.2	-1.72	7.58E-6
A_23_P99515	NM_032849	chromosome 13 open reading frame 33	C13orf33	13q12.3	-2.74	4.50E-4
A_23_P30805	NM_021968	histone cluster 1, H4j	HIST1H4J	6p22.1	-1.73	3.16E-5
A_33_P3363082	NR_003008	small Cajal body-specific RNA 5	SCARNA5	2q37.1	-1.73	1.68E-8
A_23_P75790	NM_013279	chromosome 11 open reading frame 9, transcript variant 1	C11orf9	11q12.2	-1.74	8.71E-7
A_33_P3241741	NR_002962	small nucleolar RNA, H/ACA box 23	SNORA23	11p15.4	-1.74	2.32E-4
A_33_P3245922	NM_006724	mitogen-activated protein kinase kinase kinase 4, transcript variant 2	MAP3K4	6q26	-1.76	1.05E-4
A_19_P00324238		lincRNA:chr3:129602510-129611708_R		3q21.3	-1.77	1.20E-6
A_19_P00812171		lincRNA:chr3:88177960-88183660_R		3p11.1	-2.78	7.09E-5
A_19_P00808067		lincRNA:chr7:102025498-102034795_R		7q22.1	-1.77	1.29E-4
A_33_P3387931	NM_001012267	centromere protein P	CENPP	9q22.31	-1.78	1.31E-7
A_19_P00329800		lincRNA:chr1:204525202-204541352_F		1q32.1	-1.80	2.78E-7
A_23_P11005	NM_014272	ADAM metallopeptidase with thrombospondin type 1 motif, 7	ADAMTS7	15q25.1	-1.80	1.70E-4
A_23_P214821	NM_001955	endothelin 1, transcript variant 1	EDN1	6p24.1	-1.81	3.15E-6
A_33_P3343828	AK126677	cDNA FLJ44722 fis, clone BRACE3022847	FLJ42627	16p13.3	-1.81	2.78E-4
A_33_P3382595	NR_001445	RNA, 7SK small nuclear	RN7SK	6p12.2	-1.81	6.12E-7
A_19_P00808072		lincRNA:chr14:101538287-101539271_R		14q32.2	-1.82	4.44E-5
A_33_P3402725	NM_018489	ash1 (absent, small, or homeotic)-like (Drosophila)	ASH1L	1q22	-1.84	4.27E-6
A_23_P416774	NM_016929	chloride intracellular channel 5, nuclear gene encoding mitochondrial protein, transcript variant 2	CLIC5	6p21.1	-1.84	3.92E-5

A_33_P3381292	ENST00000404197		ENST00000404197	11q13.2	-1.84	3.54E-5
A_33_P3350202	NM_014484	molybdenum cofactor synthesis 3	MOCS3	20q13.13	-1.85	2.97E-5
A_33_P3295148	AK128169	chromosome 10 open reading frame 102	C10orf102	10q22.1	-1.86	7.69E-5
A_23_P502957	NM_021810	cadherin 26, transcript variant b	CDH26	20q13.33	-1.86	1.36E-4
A_19_P00812282		lincRNA:chr3:154957056-155055681_F		3q25.2	-1.87	2.07E-8
A_19_P00322784		**lincRNA:chr4:43995-46718_R**		**4p16.3**	**-2.90**	**8.42E-5**
A_23_P122443	NM_005319	histone cluster 1, H1c	HIST1H1C	6p22.2	-1.90	2.14E-5
A_19_P00318366		lincRNA:chr3:197338442-197350253_F		3q29	-2.93	3.78E-4
A_23_P70968	NM_006896	homeobox A7	HOXA7	7p15.2	-3.97	4.34E-4
A_33_P3344229	NM_003538	histone cluster 1, H4a	HIST1H4A	6p22.2	-1.97	2.60E-6
A_33_P3335366	NM_018717	mastermind-like 3 (Drosophila)	MAML3	4q28	-1.98	2.19E-4

This list contains 73 genes differentially underexpressed in MDE at baseline versus control. Changes were assessed by a SAM analysis set with a FDR of 5% and then challenged with a t-test (FC ≥ 1.50; $p<0.001$). Genes in bold are also significant with a FDR set at 1%.

Supplementary Table ST9: Overexpressed transcripts in MDE treatment responders (weeks 0 and 8) compared to controls (weeks 0 and 8)

Probe	Accession	Gene description	Gene symbol	Cytoband	Fold change	P-value
A_24_P276628	NM_000310	palmitoyl-protein thioesterase 1, transcript variant 1	PPT1	1p34.2	2.26	1.15E-11
A_23_P396777	NM_006315	polycomb group ring finger 3	PCGF3	4p16.3	2.22	9.09E-8
A_33_P3403418	NM_001903	catenin (cadherin-associated protein), alpha 1, 102kDa	CTNNA1	5q31.2	2.17	7.08E-8
A_24_P156049	NM_012319	solute carrier family 39 (zinc transporter), member 6, transcript variant 1	SLC39A6	18q12.2	2.06	7.58E-8
A_23_P37988	NM_152727	copine II	CPNE2	16q13	1.97	3.36E-9
A_24_P383901	XR_017601	PREDICTED: similar to Actin, cytoplasmic 1	LOC391334	22q13.2	1.92	3.79E-13
A_23_P122375	NM_021943	zinc finger, AN1-type domain 3	ZFAND3	6p21.2	1.91	1.88E-10
A_24_P272761	NM_020946	DENN/MADD domain containing 1A, transcript variant 1	DENND1A	9q33.3	1.89	4.95E-9
A_24_P312041	NM_006718	pleiomorphic adenoma gene-like 1, transcript variant 2	PLAGL1	6q24.2	1.89	3.90E-9
A_24_P14367	NM_002819	polypyrimidine tract binding protein 1, transcript variant 1	PTBP1	19p13.3	1.84	4.42E-7
A_23_P217564	NM_004458	acyl-CoA synthetase long-chain family member 4, transcript variant 1	ACSL4	Xq23	1.82	2.91E-8
A_23_P355455	NM_014744	TBC1 domain family, member 5, transcript variant 2	TBC1D5	3p24.3	1.79	1.42E-9
A_23_P105571	NM_020244	choline phosphotransferase 1	CHPT1	12q23.2	1.78	2.21E-6
A_23_P156049	NM_000521	hexosaminidase B (beta polypeptide)	HEXB	5q13.3	1.73	3.58E-8
A_24_P6903	NM_001017992	actin, beta-like 2	ACTBL2	5q11.2	1.72	4.92E-11
A_33_P3248765	NM_015999	adiponectin receptor 1, transcript variant 1	ADIPOR1	1q32.1	1.71	4.28E-9
A_23_P149892	NM_018590	chondroitin sulfate N-acetylgalactosaminyltransferase 2	CSGALNACT2	10q11.21	1.71	3.38E-10
A_33_P3343155	NM_002072	guanine nucleotide binding protein (G protein), q polypeptide	GNAQ	9q21.2	1.70	1.07E-8
A_23_P75330	NM_004966	heterogeneous nuclear ribonucleoprotein F, transcript variant 3	HNRNPF	10q11.21	1.69	4.42E-10
A_23_P133438	NM_019018	family with sequence similarity 105, member A	FAM105A	5p15.2	1.66	7.28E-10
A_32_P22338	NM_013374	programmed cell death 6 interacting protein, transcript variant 1	PDCD6IP	3p22.3	1.66	7.10E-9
A_24_P387609	NM_030940	iron-sulfur cluster assembly 1 homolog (S. cerevisiae)	ISCA1	9q21.33	1.64	5.97E-6
A_24_P410017	NM_001083538	POTE ankyrin domain family, member E	POTEE	2q21.1	1.64	2.93E-13
A_33_P3289835	ENST00000531819	oxysterol binding protein-like 9 [Source:HGNC Symbol;Acc:16386]	OSBPL9	1p32.3	1.63	5.06E-10
A_32_P155776	NR_033885	POTE ankyrin domain family, member K, pseudogene	POTEKP	2q21.1	1.63	2.14E-13
A_24_P141786	NM_001681	ATPase, Ca++ transporting, cardiac muscle, slow twitch 2, transcript variant 2	ATP2A2	5q11.2	1.62	1.89E-8
A_23_P37598	NM_012428	neuroplastin, transcript variant b	NPTN	15q24.1	1.62	1.06E-10

A_23_P216894	NM_001006617	mitogen-activated protein kinase associated protein 1, transcript variant 1	MAPKAP1	9q33.3	1.61	1.07E-7
A_33_P3321230	NM_052831	chromosome 6 open reading frame 192	C6orf192	6q23.2	1.58	8.53E-8
A_24_P228875	NM_004840	Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6	ARHGEF6	Xq23	1.57	1.89E-9
A_24_P38815	NM_000391	tripeptidyl peptidase I	TPP1	11p15.4	1.54	1.96E-12

This list contains 31 genes differentially overexpressed in MDE at both baseline and at 8-weeks versus control. Changes were assessed by a SAM analysis set with a FDR of 5% and then challenged with a t-test (FC ≥ 1.50; $p<0.001$).

Supplementary Table ST10: Underexpressed transcripts in MDE treatment responders (weeks 0 and 8) compared to controls (weeks 0 and 8)

Probe	Accession	Gene description	Gene symbol	Cytoband	Fold change	P-value
A_19_P00316854		lincRNA:chr18:53750605-53752602_F		18q21.2	-4.20	2.52E-10
A_33_P3236392	NM_030916	poliovirus receptor-related 4	PVRL4	1q23.3	-3.12	1.02E-8
A_33_P3709317	NR_002964	small nucleolar RNA, H/ACA box 28	SNORA28	14q32.32	-2.50	6.89E-11
A_19_P00810480		**lincRNA:chr2:102597068-102606493_F**		**2q11.2**	**-2.43**	**1.05E-10**
A_24_P260639	NM_005320	histone cluster 1, H1d	HIST1H1D	6p22.2	-2.30	1.44E-9
A_24_P219378	**NM_020764**	**CASK interacting protein 1**	**CASKIN1**	**16p13.3**	**-2.20**	**1.52E-13**
A_23_P415411	**NM_003545**	**histone cluster 1, H4e**	**HIST1H4E**	**6p22.2**	**-2.20**	**4.23E-13**
A_33_P3578325	NR_000005	small nucleolar RNA, C/D box 15A	SNORD15A	11q13.4	-2.19	3.89E-9
A_19_P00808575		lincRNA:chr14:23018310-23025460_R		14q11.2	-2.16	5.16E-12
A_33_P3335366	NM_018717	mastermind-like 3 (Drosophila)	MAML3	4q28	-2.08	3.04E-8
A_24_P217834	NM_003530	histone cluster 1, H3d	HIST1H3D	6p22.2	-2.05	3.61E-11
A_33_P3344229	NM_003538	histone cluster 1, H4a	HIST1H4A	6p22.2	-2.05	1.79E-8
A_33_P3363082	NR_003008	small Cajal body-specific RNA 5	SCARNA5	2q37.1	-1.90	2.96E-12
A_23_P75790	NM_013279	chromosome 11 open reading frame 9, transcript variant 1	C11orf9	11q12.2	-1.88	1.52E-8
A_19_P00329774		lincRNA:chr7:33679675-33695300_F		7p14.3	-1.87	3.31E-8
A_19_P00812282		lincRNA:chr3:154957056-155055681_F		3q25.2	-1.86	1.75E-14
A_19_P00324238		lincRNA:chr3:129602510-129611708_R		3q21.3	-1.85	1.17E-8
A_23_P416774	NM_016929	chloride intracellular channel 5, nuclear gene encoding mitochondrial protein, transcript variant 2	CLIC5	6p21.1	-1.84	9.93E-8
A_23_P30799	NM_021018	histone cluster 1, H3f	HIST1H3F	6p22.2	-1.83	6.41E-8
A_33_P3387931	NM_001012267	centromere protein P	CENPP	9q22.31	-1.82	1.40E-12
A_33_P3382595	NR_001445	RNA, 7SK small nuclear	RN7SK	6p12.2	-1.81	2.06E-13
A_23_P502957	NM_021810	cadherin 26, transcript variant b	CDH26	20q13.33	-1.80	3.06E-7
A_23_P391778	NM_033044	microtubule-actin crosslinking factor 1, transcript variant 2	MACF1	1p34.3	-1.80	1.50E-10
A_33_P3812815	NM_000296	polycystic kidney disease 1 (autosomal dominant)	PKD1	16p13.3	-1.75	6.14E-11
A_23_P7976	NM_005321	histone cluster 1, H1e	HIST1H1E	6p22.2	-1.74	3.04E-9
A_33_P3245922	NM_006724	mitogen-activated protein kinase kinase kinase 4, transcript variant 2	MAP3K4	6q26	-1.74	3.01E-9

A_19_P00329800		lincRNA:chr1:204525202-204541352_F		1q32.1	-1.72	4.71E-8
A_33_P3299781	ENST00000380201	DDRGK domain containing 1 [Source:HGNC Symbol;Acc:16110]	DDRGK1	20p13	-1.72	6.66E-8
A_23_P218784	NM_006386	DEAD (Asp-Glu-Ala-Asp) box polypeptide 17, transcript variant 1	DDX17	22q13.1	-1.71	3.18E-9
A_23_P214821	NM_001955	endothelin 1, transcript variant 1	EDN1	6p24.1	-1.65	1.27E-7
A_23_P97021	NM_024852	eukaryotic translation initiation factor 2C, 3, transcript variant 1	EIF2C3	1p34.3	-1.65	9.15E-11
A_33_P3254695	ENST00000363217	small nucleolar RNA, H/ACA box 73B	SNORA73B	1p35.3	-1.64	1.14E-9
A_33_P3302652	ENST00000415882	chromoseome 1 open reading frame 132	C1orf132	1q32.1	-1.62	1.13E-9
A_19_P00802156		lincRNA:chr6:86386083-86388435_R		6q14.1	-1.60	1.01E-6
A_33_P3299865	NM_003541	histone cluster 1, H4k	HIST1H4K	6p22.1	-1.60	9.55E-9
A_33_P3399028	NM_006852	tousled-like kinase 2, transcript variant A	TLK2	17q23.2	-1.60	1.25E-8
A_23_P70480	NM_003546	histone cluster 1, H4l	HIST1H4L	6p22.1	-1.59	6.72E-8
A_32_P106732	NM_020937	Fanconi anemia, complementation group M	FANCM	14q21.2	-1.57	1.01E-10
A_33_P3218760	NM_080599	UPF2 regulator of nonsense transcripts homolog (yeast), transcript variant 1	UPF2	10p14	-1.57	4.56E-9

This list contains 39 genes differentially underexpressed in MDE at baseline and at 8-weeks versus control. Changes were assessed by a SAM analysis set with a FDR of 5% and then challenged with a t-test (FC ≥ 1.50; $p<0.001$). Genes in bold are also significant with a FDR set at 1%.

Supplementary Table ST11: Overexpressed transcripts in control subjects at week 0 compared to week 8

Probe	Accession	Gene description	Gene symbol	Cytoband	Fold change	P-value
A_19_P00317592		lincRNA:chr5:18664830-18665773_F		5p15.1	3.31	3.62E-3
A_33_P3369371	NM_002084	glutathione peroxidase 3 (plasma)	GPX3	5q32	2.55	9.40E-3
A_19_P00323342		lincRNA:chr2:76808692-76823142_R		2q11.2	2.52	4.88E-3
A_33_P3816042	NR_027714	ARP3 actin-related protein 3 homolog B (yeast) pseudogene 2	ACTR3BP2	2p11.1	2.41	1.00E-2
A_33_P3221234	NM_001145349	intracisternal A particle-promoted polypeptide, transcript variant 2	IPP	1p34.1	2.31	2.61E-3
A_19_P00322552		lincRNA:chr12:112757053-112819896_F		12q24.11	2.24	8.29E-4
A_19_P00328893		lincRNA:chr15:41577883-41589833_R		15q14	2.05	2.02E-3
A_24_P282547	NM_006684	complement factor H-related 4	CFHR4	1q31.3	2.05	4.01E-3
A_33_P3246593	NM_001010906	chromosome 8 open reading frame 80	C8orf80	8p21.1	1.94	3.34E-3
A_19_P00324529		lincRNA:chr1:98439262-98699162_R		1p21.3	1.87	2.57E-3
A_33_P3371115	NR_026558	aquaporin 7 pseudogene 3	AQP7P3	9p12	1.87	9.38E-3
A_19_P00324163		lincRNA:chr6:40304947-40323847_F		6q14.1	1.85	6.60E-3
A_19_P00801344	ENST00000400306			4q28.3	1.82	4.13E-4
A_23_P121545	NM_201591	glycoprotein M6A, transcript variant 2	GPM6A	4q34.1	1.77	2.40E-3
A_23_P218002	NM_002728	proteoglycan 2, bone marrow (natural killer cell activator, eosinophil granule major basic protein)	PRG2	11q12.1	1.75	8.39E-3
A_33_P3356371	AK127766	cDNA FLJ45867 fis, clone OCBBF3003745	LOC100133089	10q21.1	1.74	6.80E-3
A_23_P135257	NM_002771	protease serine 3, transcript variant 2	PRSS3	9p13.3	1.73	6.58E-3
A_23_P129014	NM_145231	chromosome 14 open reading frame 143	C14orf143	14q32.11	1.72	3.96E-3
A_23_P431853	ENST00000361453	mitochondrially encoded NADH dehydrogenase 2 [Source:HGNC Symbol;Acc:7456]	MT-ND2	MT	1.70	5.71E-3
A_33_P3369520	A_33_P3369520	membrane-associated guanylate kinase, WW and PDZ domain containing 3, transcript variant 2	MAGI3	1p13.2	1.67	9.52E-3
A_19_P00316590		lincRNA:chr15:38364787-38365169_F		15q14	1.67	6.47E-3
A_33_P3356985	AB529250	Synthetic construct DNA clone: pF1KE0817 Homo sapiens OLFR827 gene for olfactory receptor 827 without stop codon in Flexi system	AB529250	12q13.13	1.67	6.71E-3
A_23_P71649	NM_005592	muscle skeletal receptor tyrosine kinase, transcript variant 1	MUSK	9q31.3	1.65	2.30E-4
A_33_P3335735	NR_024559	hypothetical LOC100128977	LOC100128977	17q21.31	1.65	3.06E-3
A_23_P110288	NM_024751	glutathione S-transferase C-terminal domain containing, transcript variant 2	GSTCD	4p24	1.65	3.77E-3

A_23_P10291	NM_001910	cathepsin E, transcript variant 1	CTSE	1q32.1	1.62	4.12E-3
A_19_P00322966		lincRNA:chrX:62648777-62780763_R		Xp11.1	1.62	9.23E-3
A_33_P3268734	CR748640	CR748640 Soares_NFL_T_GBC_S1 cDNA clone IMAGp971L0898 ; IMAGE:2348699 5'	CR748640	9q34.13	1.58	3.28E-3
A_23_P420196	NM_003745	suppressor of signaling 1	SOCS1	16p13.12	1.57	7.92E-3
A_33_P3219517	NM_000905	neuropeptide Y	NPY	7p15.3	1.57	4.30E-3
A_24_P119545	ENST00000366784		ENST00000366784	1q42.12	1.55	2.39E-3
A_23_P379020	NR_002328	gonadotropin-releasing hormone (type 2) receptor 2	GNRHR2	1q21.1	1.54	2.60E-3
A_33_P3742500	BC132887	hypothetical protein LOC642947	LOC642947	9q21.2	1.53	5.44E-3
A_19_P00320819		lincRNA:chr7:22895704-22896694_F		7p15.3	1.53	2.63E-3
A_19_P00811707		lincRNA:chr8:8480290-8488065_F		8p23.1	1.51	1.92E-3

This list contains 35 genes differentially overexpressed in control subjects at baseline versus 8-weeks. Changes were assessed by a t-test (FC ≥ 1.50; $p<0.001$).

Supplementary Table ST12: Underexpressed transcripts in control subjects at week 0 compared to week 8

Probe	Accession	Gene description	Gene symbol	Cytoband	Fold change	P-value
A_23_P34637	NM_000537	renin	REN	1q32.1	-2.30	8.98E-3
A_23_P90925	NM_173178	interleukin 36 beta, transcript variant 2	IL36B	2q13	-2.17	3.60E-3
A_33_P3353979	NM_181519	synaptotagmin XV, transcript variant b	SYT15	10q11.22	-2.09	9.56E-3
A_24_P250922	NM_000963	prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	PTGS2	1q31.1	-2.02	1.33E-3
A_33_P3240637	AK124325	cDNA FLJ42334 fis, clone TUTER20009	AK124325	4q32.3	-1.93	2.62E-3
A_23_P151870	NM_015554	glucuronic acid epimerase	GLCE	15q23	-1.92	7.76E-3
A_33_P3382236	NM_018330	KIAA1598	KIAA1598	10q25.3	-1.90	3.66E-3
A_23_P116624	NM_004211	solute carrier family 6 (neurotransmitter transporter glycine) member 5	SLC6A5	11p15.1	-1.87	4.71E-3
A_24_P51909	NM_006651	complexin 1	CPLX1	4p16.3	-1.81	2.65E-4
A_23_P155301	NM_145910	NIMA (never in mitosis gene A)-related kinase 11, transcript variant 2	NEK11	3q22.1	-1.74	4.14E-3
A_33_P3251480	NM_021970	MAPK scaffold protein 1, transcript variant 1	MAPKSP1	4q23	-1.69	1.12E-3
A_33_P3232945	NM_005242	coagulation factor II (thrombin) receptor-like 1	F2RL1	5q13.3	-1.67	2.43E-3
A_33_P3281283	NM_005226	sphingosine-1-phosphate receptor 3	S1PR3	9q22.1	-1.66	4.20E-3
A_33_P3281191	NM_002508	nidogen 1	NID1	1q42.2	-1.65	4.16E-3
A_23_P16063	NM_002088	glutamate receptor, ionotropic, kainate 5	GRIK5	19q13.2	-1.59	6.44E-3
A_33_P3394978	NR_027276	hypothetical LOC100128239	LOC100128239	11q25	-1.56	6.63E-3
A_19_P00315746		lincRNA:chr5:92747114-92758113_R		5q14.3	-1.55	1.24E-3
A_23_P148568	NM_017809	nuclear RNA export factor 2, transcript variant 1	NXF2	Xq22.1	-1.54	2.96E-3
A_33_P3363560	NM_001136216	transmembrane protein 51, transcript variant 1	TMEM51	1p36.21	-1.54	6.09E-3
A_23_P67453	NM_000363	troponin I type 3 (cardiac)	TNNI3	19q13.42	-1.52	9.55E-4

This list contains 20 genes differentially underexpressed in control subjects at baseline versus at 8-weeks. Changes were assessed by a t-test (FC ≥ 1.50; $p<0.001$).

Supplementary Table ST13: Gene ontology analysis of dysregulated genes in MDE 0 and 8-weeks (responders) vs controls (FDR ≤ 5%)

Category	ID	Term	Genes	Count	%	P-value
FC ≥ 1.50						
Biological process	GO:0007040	Lysosome organization	*HEXB*, ***PPT1***, ***TPP1***	3	9.7	7.4E-4
Cellular component	GO:0016023	Cytoplasmic membrane-bounded vesicle	*DENND1A, HEXB, MAPKAP1,* ***PPT1****, PDCD6IP,* ***TPP1***	6	19.4	1.7E-3
Biological process	GO:0007033	Vacuole organization	*HEXB,* ***PPT1****,* ***TPP1***	3	9.7	1.9E-3
FC ≤ -1.50						
Cellular component	GO:0000786	Nucleosome	*HIST1H1D,* ***HIST1H1E****, HIST1H3D, HIST1H4A/HIST1H4L/****HIST1H4E****/HIST1H4K*	4	14.8	5.0E-5
Cellular component	GO:0044427	Chromosomal part	*CENPP, HIST1H1D,* ***HIST1H1E****, HIST1H3D, HIST1H4A/HIST1H4L/****HIST1H4E****/HIST1H4K*	5	18.5	8.6E-4
Biological process	GO:0006325	Chromatin organization	*HIST1H1D,* ***HIST1H1E****, HIST1H3D, HIST1H4A/HIST1H4L/****HIST1H4E****/HIST1H4K, TLK2*	5	18.5	1.1E-3

Bold entries refer to candidate transcripts tested for RT-qPCR validation.

Supplementary Table ST14: Analysis of chromosomal cytoband enrichment among dysregulated genes

Cytoband	Genes	Count	Total number in cytoband	P-value	FDR
MDE_{0w} vs C, (FC ≥ 1.50)					
2q21	***CCNT2, POTEE, POTEF, POTEKP, R3HDM1***	**5**	**83**	**1.3E-5**	**0.0010**
12q23	*APAF1, ELK3, CHPT1*	3	103	6.2E-3	0.24
4p14	*KLHL5, RBM47*	2	44	1.1E-2	0.29
4p16	*CTBP1, MAN2B2, PCGF3*	3	158	2.0E-2	0.38
3p24	*TBC1D5, UBE2E2*	2	74	2.9E-2	0.45
MDE_{0w} vs C, (FC ≤ -1.50)					
6p22	***HIST1H1A, HIST1H1D, HIST1H1E, HIST1H3D, HIST1H3F, HIST1H4A, HIST1H4E, HIST1H4K, HIST1H4L***	**9**	**288**	**8.6E-9**	**<0.0001**
6p12	*CLIC5, RN7SK*	2	102	1.9E-2	0.28
16p13	*CASKIN1, PKD1, SNX29*	3	328	3.1E-2	0.30
MDE_{8w} vs C, (FC ≥ 1.50)					
22q13	***ATXN10, LOC391334, NAGA, PLXNB2, TRIOBP***	**5**	**256**	**1.1E-4**	**0.0041**
2q21	***POTEE, POTEKP, UBXN4***	**3**	**83**	**4.9E-4**	**0.0093**
9p21	***ISCA1, ALDH1A1, GNAQ***	**3**	**99**	**8.1E-4**	**0.010**
15q24	*ADPGK, NPTN*	2	98	1.4E-2	0.091
5q13	*HEXB, ZNF366*	2	99	1.4E-2	0.091
12q23	*LTA4H, CHPT1*	2	103	1.6E-2	0.091
9q33	*DENND1A, MAPKAP1*	2	107	1.7E-2	0.091
10q11	*CSGALNACT2, HNRNPF*	2	153	3.2E-2	0.15
MDE_{8w} vs C, (FC ≤ -1.50)					
6p22	***HIST1H1A, HIST1H1C, HIST1H1D, HIST1H1E, HIST1H3D, HIST1H3F, HIST1H4A, HIST1H4E, HIST1H4K, HIST1H4L***	**10**	**288**	**9.0E-11**	**<0.0001**
6p12	*CLIC5, RN7SK*	2	102	1.5E-2	0.16
7p15	*HOXA3, HOXA7*	2	112	1.8E-2	0.16

Bold entries refer to significantly enriched cytobands after considering a FDR set at 1%.

Supplementary Table ST15: Mean Ct of miRNAs and other non-coding RNA expressed in PBMCs of both MDE and control samples

Small RNA	Mean Ct	S.D.
hsa-miR-517b	15.97	1.37
hsa-miR-223	18.01	0.91
hsa-miR-150	**19.06**	**0.53**
hsa-miR-1305	19.09	0.51
U6 snRNA	**19.35**	**0.44**
hsa-miR-519b-3p	19.37	0.72
MammU6	19.45	0.60
hsa-miR-1267	19.52	0.98
hsa-miR-338-5P	19.53	0.90
hsa-miR-142-3p	20.65	1.44
RNU48	**20.80**	**0.46**
RNU48	**20.83**	**0.53**
hsa-miR-100-3p	20.84	1.68
hsa-miR-126	21.09	1.10
hsa-miR-16	21.21	1.00
hsa-miR-376a-5p	21.29	2.11
hsa-miR-106a	21.37	0.89
hsa-miR-19b	21.47	1.22
hsa-miR-17	21.53	0.91
hsa-miR-24	21.55	0.86
hsa-miR-146a	21.91	0.94
hsa-miR-342-3p	21.98	0.71
hsa-miR-484	22.35	0.63
hsa-miR-222	**22.46**	**0.67**
hsa-miR-26a	22.56	1.02
hsa-miR-146b-5p	22.63	1.13
RNU44	23.12	0.66
hsa-miR-720	23.17	0.42
hsa-miR-191	23.17	0.76
hsa-miR-30c	**23.26**	**0.77**
hsa-miR-1274b	23.32	0.51
hsa-miR-20a	23.38	1.12
hsa-miR-26b	23.42	1.19
hsa-miR-29a	23.79	1.15
hsa-miR-21	23.88	1.40
hsa-miR-19a	23.89	1.35
hsa-miR-30b	23.91	0.92
RNU44	23.94	0.81
hsa-miR-186	**24.04**	**0.75**
hsa-miR-29c	24.22	0.80
hsa-miR-374b	24.37	1.06
hsa-let-7g	24.52	1.28

hsa-miR-126-5p	24.64	1.48
hsa-miR-93	24.95	2.93
hsa-miR-140-5p	25.02	1.10
hsa-miR-15b	25.18	0.99
hsa-miR-92a	25.24	0.69
hsa-miR-221	25.56	0.99
hsa-miR-31	25.65	1.10
hsa-miR-106b	25.68	1.29
hsa-miR-374a	25.73	1.34
hsa-miR-let-7e	25.75	1.13
hsa-miR-331-3p	25.81	0.67
hsa-miR-766	25.87	0.80
hsa-miR-320	25.93	0.97
hsa-miR-30a-5p	**26.02**	**0.82**
hsa-miR-155	26.06	0.68
hsa-miR-486-5p	26.08	0.76
hsa-miR-1243	26.13	0.94
hsa-miR-454	26.16	1.04
hsa-miR-618	26.17	2.05
hsa-miR-199a-3p	26.17	1.43
hsa-miR-590-5p	26.23	1.24
hsa-miR-425	26.24	0.84
hsa-miR-151-3p	26.28	1.09
hsa-miR-20b-3p	26.29	2.30
hsa-miR-145	26.32	1.22
hsa-miR-28-3p	**26.32**	**0.60**
hsa-miR-1233	26.34	0.62
hsa-miR-1260	26.37	0.33
hsa-miR-27a	26.50	1.30
hsa-miR-103	26.53	0.99
hsa-miR-345	26.57	0.75
hsa-miR-574-3p	26.59	0.51
hsa-miR-30d	**26.83**	**0.85**
hsa-miR-140-3p	26.89	0.78
hsa-miR-328	26.95	0.62
hsa-miR-93-3p	26.97	0.57
hsa-miR-195	26.98	1.11
hsa-miR-1225-3p	27.08	1.16
hsa-miR-532-5p	27.25	0.91
hsa-miR-340	27.30	1.44
hsa-miR-1274a	**27.35**	**0.43**
hsa-miR-744	27.49	0.87
hsa-miR-652	27.55	1.18
hsa-miR-660	27.60	1.35
hsa-miR-20b	27.70	1.04
hsa-miR-512-3p	27.72	1.57
hsa-miR-625-3p	27.74	0.87

hsa-miR-30e-3p	27.85	1.04
hsa-miR-339-5p	27.87	0.90
hsa-miR-142-5p	27.87	1.47
hsa-miR-596	27.88	0.79
hsa-miR-25	**27.88**	**0.90**
hsa-miR-409-3p	27.91	2.00
hsa-miR-139-5p	27.92	1.06
hsa-let-7d	27.96	1.19
hsa-miR-181a	27.98	1.01
hsa-miR-197	27.99	0.49
hsa-miR-376c	28.00	1.89
hsa-miR-642	28.07	1.22
hsa-miR-130a	28.07	1.25
hsa-miR-28-5p	28.08	1.16
hsa-miR-451	28.12	1.84
rno-miR-7a-1*	28.22	1.31
hsa-miR-301a	28.23	1.25
hsa-miR-339-3p	28.24	0.88
hsa-miR-132	**28.25**	**0.64**
hsa-miR-664	**28.38**	**0.82**
hsa-let-7a	28.42	1.42
hsa-miR-let-7b	28.56	1.51
hsa-miR-532-3p	28.60	0.64
hsa-miR-939	28.65	0.76
hsa-miR-422a	28.79	0.89
hsa-miR-335	28.92	1.31
hsa-miR-185	28.99	1.24
hsa-miR-151-5p	29.00	1.20
hsa-miR-340-3p	29.02	1.19
hsa-miR-148a	29.15	1.32
hsa-miR-149-3p	29.16	0.95
hsa-miR-101	29.16	1.56
hsa-miR-342-5p	29.16	1.24
hsa-miR-125a-5p	29.29	0.94
hsa-miR-152	29.30	1.08
hsa-miR-494	29.30	1.42
hsa-miR-223-5p	29.33	1.26
hsa-miR-192	29.35	1.22
hsa-miR-27b	29.36	1.36
hsa-miR-23a	29.40	1.06
hsa-miR-491-5p	29.42	0.98
hsa-miR-378	29.47	1.08
hsa-miR-193b	29.48	0.96
hsa-miR-22	29.50	2.15
hsa-miR-27a-5p	**29.54**	**0.84**
hsa-miR-106b-3p	29.58	1.12
hsa-miR-15a	29.58	1.40

hsa-miR-200c	29.61	0.83
hsa-miR-425-3p	29.64	0.95
hsa-miR-99b	29.66	0.99
hsa-miR-127-3p	29.72	1.44
hsa-miR-769-5p	**29.75**	**0.88**
hsa-miR-148b	29.81	1.10
hsa-miR-362-5p	29.81	0.87
hsa-miR-323-3p	29.86	1.03
hsa-miR-144-5p	29.97	2.12
hsa-miR-1227	29.98	0.92
hsa-let-7f	29.98	1.26
hsa-miR-1275	30.02	1.52
hsa-miR-29b	30.06	2.43
hsa-miR-143	30.09	2.04
hsa-miR-324-3p	**30.11**	**0.69**
hsa-miR-486-3p	30.15	0.93
hsa-miR-486-3p	30.15	0.93
hsa-miR-130b	30.22	1.26
hsa-miR-95	30.24	0.95
hsa-miR-15b-3p	30.27	2.69
hsa-miR-628-5p	30.31	0.91
hsa-miR-181a-2-3p	30.32	2.04
hsa-miR-671-3p	**30.32**	**0.69**
hsa-miR-324-5p	30.38	1.1
hsa-miR-590-3p	30.40	2.36
hsa-miR-210	30.42	1.12
hsa-miR-495	30.42	2.07
hsa-miR-302c-5p	30.47	1.32
hsa-miR-501-5p	30.62	1.3
hsa-miR-539	30.69	2.44
hsa-miR-22-5p	30.84	1.95
hsa-miR-34a	30.84	2.33
hsa-miR-1201	**30.84**	**0.63**
hsa-miR-9	30.86	1.69
hsa-miR-382	30.87	2.9
hsa-miR-370	30.89	3.08
hsa-miR-224	30.96	2.03
hsa-miR-605	30.99	1.19
hsa-miR-20a-3p	31.00	1.28
hsa-miR-346	31.05	0.81
hsa-miR-500	31.06	1.17
hsa-miR-638	**31.07**	**0.71**
hsa-miR-31-3p	31.08	1.72
hsa-miR-296-5p	31.08	0.86
hsa-miR-194	31.10	1.84
hsa-miR-376a	31.14	1.75
hsa-miR-431	31.14	3.29

hsa-miR-1208	**31.14**	**0.62**
hsa-miR-24-2-5p	31.19	1.41
hsa-miR-18a	31.19	1.79
hsa-miR-320b	31.20	1.43
hsa-miR-133a	31.21	1.71
hsa-miR-571	31.22	0.91
hsa-miR-98	31.24	1.02
hsa-miR-485-3p	31.28	1.48
hsa-miR-625	31.31	1.47
hsa-miR-26b-3p	31.32	0.72
hsa-miR-487a	31.33	1.30
hsa-miR-411	31.35	2.58
hsa-miR-361-5p	31.36	1.85
hsa-miR-1290	31.37	0.95
hsa-miR-331-5p	31.37	1.93
hsa-miR-301b	31.40	1.42
hsa-miR-487b	31.42	2.20
hsa-miR-128	31.43	1.21
hsa-miR-335-3p	31.46	1.10
hsa-miR-100	31.53	1.46
hsa-miR-212	**31.54**	**0.69**
hsa-miR-213	31.55	1.20
hsa-miR-138	31.56	1.12
hsa-miR-219-5p	31.56	2.15
hsa-miR-598	31.57	1.45
hsa-miR-30a-3p	31.61	1.80
hsa-miR-200b	31.64	1.76
hsa-miR-99a	31.66	2.40
hsa-miR-107	31.67	2.13
hsa-miR-381	31.71	1.27
hsa-miR-10a	31.76	1.52
hsa-miR-125b	31.82	1.39
hsa-miR-193a-5p	31.92	1.07
hsa-miR-34b	**31.92**	**0.63**
hsa-miR-330-3p	**31.97**	**0.79**
hsa-miR-636	32.11	0.70
hsa-miR-410	32.11	2.21
hsa-miR-636	32.11	0.70
hsa-miR-432	32.15	2.47
hsa-miR-629	32.19	1.62
hsa-miR-363	32.21	2.01
hsa-miR-758	32.23	1.72
hsa-miR-361-3p	32.24	1.95
hsa-miR-941	32.25	1.83
hsa-miR-433	32.26	3.19
hsa-miR-378	32.30	0.95
hsa-miR-1271	32.30	1.29

hsa-miR-23b	32.31	2.08
hsa-miR-1247	32.35	1.68
hsa-miR-181c	32.37	1.24
hsa-miR-628-3p	32.40	1.44
hsa-miR-148b-5p	32.43	2.06
hsa-miR-659	**32.47**	**0.82**
hsa-miR-942	32.48	1.16
hsa-miR-1254	32.49	2.37
hsa-miR-33a-3p	32.54	3.00
hsa-miR-26a-1-3p	32.57	2.13
hsa-miR-545	32.58	1.80
hsa-miR-579	32.6	2.44
hsa-miR-32	32.68	2.24
hsa-miR-1296	32.73	1.68
hsa-miR-215	32.79	1.39
hsa-miR-656	32.83	1.70
hsa-miR-589	32.86	1.84
hsa-miR-16-1-3p	32.92	2.14
hsa-miR-365	32.97	1.95
hsa-miR-19b-1-5p	32.98	1.86
hsa-miR-191-3p	32.99	1.78

MiRNAs assayed from 384 well TaqMan Human miRNA Array plate A are indicated in black, while those from plate B are in blue. Bold entries refer to reference miRNA used for relative quantification calculations.

Supplementary Table ST16: Dysregulated miRNAs predicted to interact with oppositely dysregulated mRNAs

miRNA ↗	mRNA ↘	Prediction source	miRNA ↘	mRNA ↗	Prediction source
MDE_{0w} vs C					
hsa-miR-107	EIF2C3	miRecords	hsa-miR-636	KLHL5	TargetScan
hsa-miR-107	CDV3, ELMO2, NEK10, UPF2	TargetScan	hsa-miR-1243	ARL8B	TargetScan
hsa-miR-133a	C11orf9, MAML3	TargetScan	hsa-miR-381	AGFG1, APAF1, **CELF2**, DCAF12, KRAS, MYH9, PCGF3, PPFIA1, C12orf23, R3HDM1, RAP2C, UBE2E2, ZFAND3	TargetScan
hsa-miR-148a	MAP3K4	TargetScan	hsa-miR-200c	ELMO2	miRecords
hsa-miR-494	EIF2C3, EML4, UPF2	TargetScan	hsa-miR-200c	AGFG1, APAF1, **CELF2**, DENND5A, E2F3, GALNT2, KRAS, MCFD2, PPFIA1, PTBP1, RAB18, RAP2C, SGPP1	TargetScan
hsa-miR-579	CLIC5	TargetScan			
MDE_{8w} vs C					
hsa-let-7b	SMC1A	miRecords, TargetScan, TarBase	hsa-miR-571	KIAA1598	TargetScan
hsa-let-7b	CASKIN1, DLGAP4, EDN1, EIF2C3	TargetScan	hsa-miR-454	ACSL4	TargetScan
hsa-miR-363	BCL11A, CASKIN1, EIF2C3	TargetScan			
hsa-miR-331-3p	VANGL1	TargetScan			

Supplementary Table ST17: Candidate genes tested by RT-qPCR

Reference gene	Detector	Ct mean
	GAPDH-Hs99999905_m1	19.80
GAPDH/PAFAH1B1	*HIST1H1E*-Hs00271195_s1	21.04
GAPDH/PAFAH1B1	*PPT1*-Hs00165579_m1	22.65
GAPDH/PAFAH1B1	*TPP1*-Hs00166099_m1	23.54
	PAFAH1B1-Hs00181182_m1	24.03
PAFAH1B1/ALDOC	*IRF2*-Hs01082884_m1	24.08
PAFAH1B1/ALDOC	*HIST1H1A*-Hs00271225_s1	24.74
PAFAH1B1/ALDOC	*HIST1H4E*-Hs00374346_s1	25.00
PAFAH1B1/ALDOC	*POTEKP*-Hs02598440_g1	25.08
PAFAH1B1/ALDOC	*CELF2*-Hs00990166_m1	25.43
PAFAH1B1/ALDOC	*SORT1*-Hs00361760_m1	26.07
PAFAH1B1/ALDOC	*ACTBL2*-Hs01101944_s1	26.11
PAFAH1B1/ALDOC	*TNF*-Hs00174128_m1	26.41
	ALDOC-Hs00193059_m1	27.15
ALDOC/SV2A	*IL1B*-Hs00174097_m1	27.38
ALDOC/SV2A	*NRG1*-Hs00247624_m1	29.62
ALDOC/SV2A	*SLC6A4*-Hs00169010_m1	29.70
	SV2A-Hs00372069_m1	30.10
SV2A	*ATP2A2*-Hs00155939_m1	32.64

Supplementary Table ST18: A comparison of mixed linear model for candidate mRNA expression between responders and nonresponders, adjusted with co-variables and tested in combination with age and sex

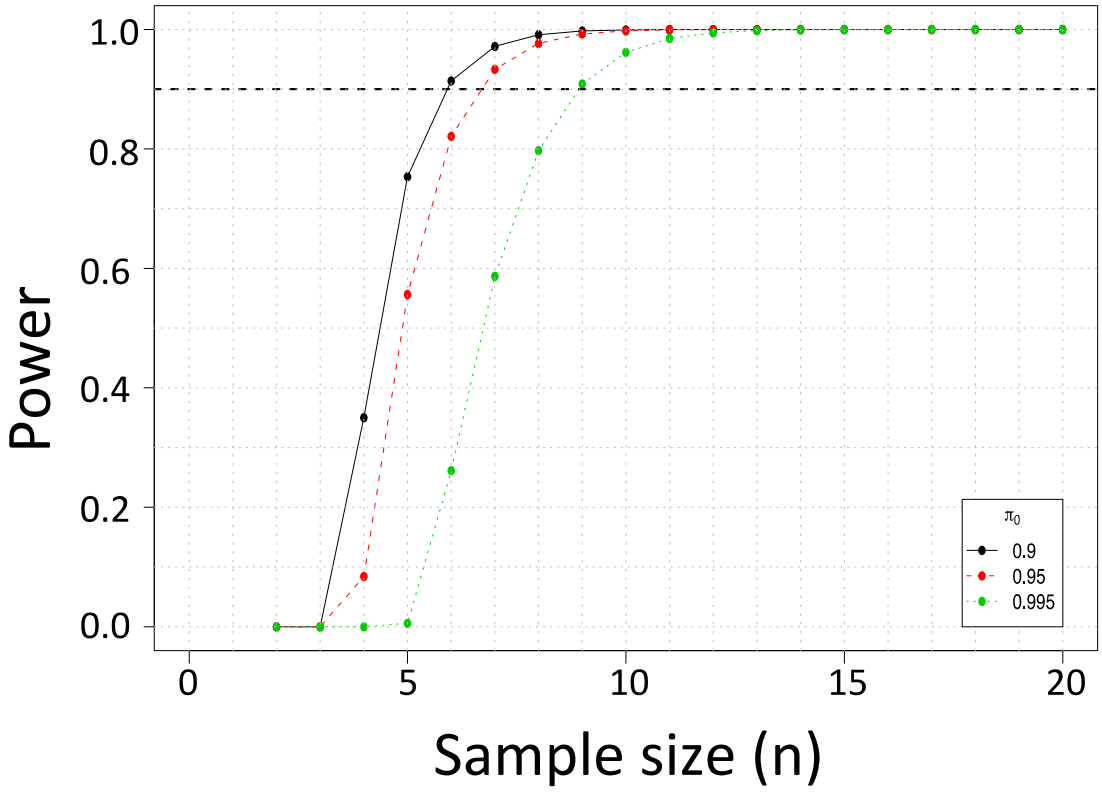
Gene	Age & sex only	Smocking	Treat	Mono	Mirt	SNRI	SSRI	Other antidep	Lithium	AAP	ECT	Rec MDE	Age of onset	Episode duration	Suicide
ACTBL2	**0.025**	**0.028**	**0.026**	**0.004**	**0.011**	**0.011**	0,063	**0.026**	**0.040**	0.082	**0.027**	**0.029**	0.055	**0.004**	**0.032**
ATP2A2	0.904	0.880	0.919	0,905	0.650	0.780	0.872	0.850	0.865	0.977	0.868	0.927	0.525	0.793	0.863
CELF2	0.985	0.941	0.987	0.407	0.108	0.663	0.485	0.900	0.963	0.974	0.997	0.943	0.965	0.886	0.888
HIST1H1A	**0.019**	**0.013**	**0.011**	**0.003**	**0.004**	**0.006**	**0.024**	**0.011**	**0.019**	**0.034**	**0.012**	**0.013**	**0.025**	**0.001**	**0.014**
HIST1H1E	**0.005**	**0.002**	**0.005**	0.310	0.201	0.051	**0.048**	**0.005**	**0.013**	**0.003**	**0.006**	**0.010**	**0.011**	**0.005**	**0.006**
HIST1H4E	**0.010**	**0.012**	**0.011**	**0.003**	**0.004**	**0.008**	**0.018**	**0.010**	**0.017**	**0.038**	**0.012**	**0.011**	**0.030**	**0.002**	**0.013**
IL1B	**0.001**	**0.0003**	**0.001**	**0.005**	**0.042**	**0.002**	**0.003**	**0.0005**	**0.002**	**0.001**	**0.002**	**0.0005**	**0.001**	**0.001**	**0.0003**
IRF2	0.194	0.260	0.190	**0.019**	**0.011**	0.442	0.134	0.150	0.217	0.864	0.292	0.142	0.153	0.191	0.195
NRG1	0.327	0.323	0.231	0.332	0.450	0.580	0.623	0.167	0.652	0.648	0.323	0.355	0.687	0.342	0.414
POTEKP	**0.011**	**0.013**	**0.012**	**0.001**	**0.004**	**0.004**	**0.027**	**0.010**	**0.019**	**0.039**	**0.014**	**0.011**	**0.024**	**0.002**	**0.014**
PPT1	**0.00005**	**0.00009**	**0.00001**	**0.0001**	**0.001**	**0.001**	**0.00006**	**0.00005**	**0.00007**	**0.0005**	**0.00004**	**0.00008**	**0.0002**	**0.00005**	**0.00005**
SORT1	0.775	0.907	0.741	0.780	0.753	0.773	0.744	0.663	0.973	0.960	0.704	0.902	0.830	0.953	0.619
TNF	**0.0005**	**0.001**	**0.0002**	**0.001**	**0.007**	**0.005**	**0,003**	**0.001**	**0.001**	**0.002**	**0.001**	**0.001**	**0.001**	**0,0003**	**0.0002**
TPP1	0.051	0.052	**0.045**	0.177	**0.028**	0.326	**0.027**	0.061	**0.025**	**0.014**	**0.041**	0.077	**0.045**	0.056	0.051

Abbreviations: AAP, atypical antipsychotics; Mirt, mirtazapine; Mono, monotherapy; Other antidep, tricyclic and IMAO antidepressant; Rec, recurrent; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; Treat, treatment

3 SUPPLEMENTARY FIGURES

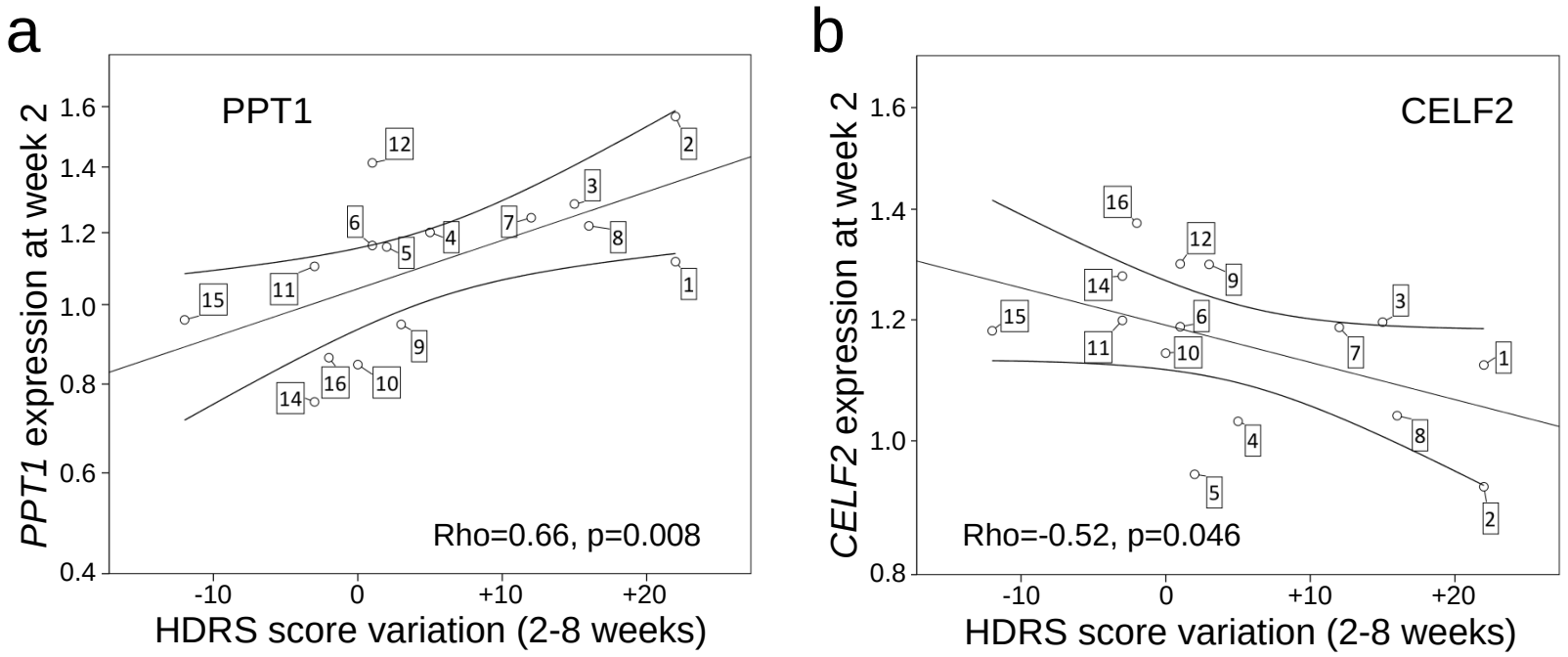
Supplementary Figure S1: Sample size calculation

To evaluate the number of samples required for the microarray screen, a minimum sample size was determined by using sizepower tool within the R package with the following parameters: FDR = 5 %, power of the study = 90%, expected difference between groups = 1.5, and standard deviation = 0.5. Three curves were drawn according to different values for the percentage of significant genes (1-π_0). The dashed line indicate that with a power of 90% and π_0 = 0.095, the minimum sample size is 9.



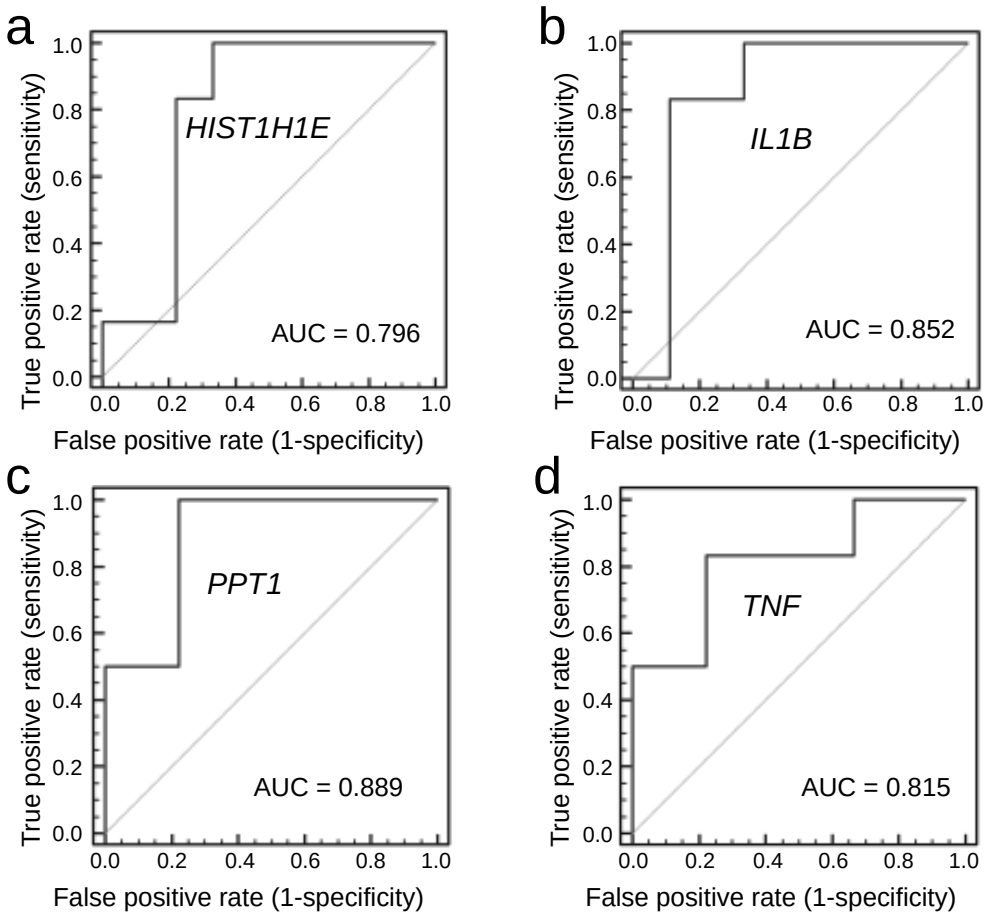
Supplementary Figure S2: Spearman's correlation between HDRS score evolution and mRNA expression level for *PPT1* and *CELF2*

Each circle indicates, for a specified MDE patient (the label attached to the circle refers to the case number in Table 1), the difference of HDRS scores at week 2 and 8 weeks after inclusion as a function of the *PPT1* (**a**) or *CELF2* FC (**b**) for MDE_{2w} sample, calculated with the $2^{-\Delta\Delta Ct}$ method. The calibrator was a mathematical pool of control sample Ct. Normalization was performed using *GAPDH* and *PAFAH1B1* for *PPT1,* and *PAFAH1B1* and *ALDOC* for *CELF2*.



Supplementary Figure S3: ROC curve for prediction of treatment response after 8 weeks considering the individual expression of 4 transcripts

(a) *HIST1H1E*, (**b**) *IL1B*, (**c**) *PPT1*, (**d**) and *TNF*.



4 REFERENCES

1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR)*. American Psychiatric Association: Arlington, VA, 2000.

2. American Psychiatric Association. *Handbook of psychiatric measures*. 2d edn. American Psychiatric Association (APA): Washington, DC, 2008, 864pp.

3. Fist MB, Spitzer RL, Gibbon M, Williams JBW. Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition. (SCID-I/P). New York: New York State Psychiatric Institute; 2002.

4. Guelfi JD. *L'évaluation clinique standardisée en psychiatrie*. Editions médicales Pierre Fabre: Boulogne, 1997.

5. Frank E, Prien RF, Jarrett RB, Keller MB, Kupfer DJ, Lavori PW *et al.* Conceptualization and rationale for consensus definitions of terms in major depressive disorder. Remission, recovery, relapse, and recurrence. *Arch Gen Psychiatry* 1991; **48:** 851-855.

6. Huang da W, Sherman BT, Lempicki RA. Systematic and integrative analysis of large gene lists using DAVID bioinformatics resources. *Nat Protoc* 2009; **4:** 44-57.

7. Chen J, Bardes EE, Aronow BJ, Jegga AG. ToppGene Suite for gene list enrichment analysis and candidate gene prioritization. *Nucleic Acids Res* 2009; **37:** W305-311.

8. Vandesompele J, De Preter K, Pattyn F, Poppe B, Van Roy N, De Paepe A *et al.* Accurate normalization of real-time quantitative RT-PCR data by geometric averaging of multiple internal control genes. *Genome Biol* 2002; **3:** RESEARCH0034.

9. 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:** 402-408.

10. Lee ML, Whitmore GA. Power and sample size for DNA microarray studies. *Stat Med* 2002; **21:** 3543-3570.

11. Tusher VG, Tibshirani R, Chu G. Significance analysis of microarrays applied to the ionizing radiation response. *Proc Natl Acad Sci U S A* 2001; **98:** 5116-5121.

12. Saeed AI, Bhagabati NK, Braisted JC, Liang W, Sharov V, Howe EA *et al.* TM4 microarray software suite. *Methods Enzymol* 2006; **411:** 134-193.