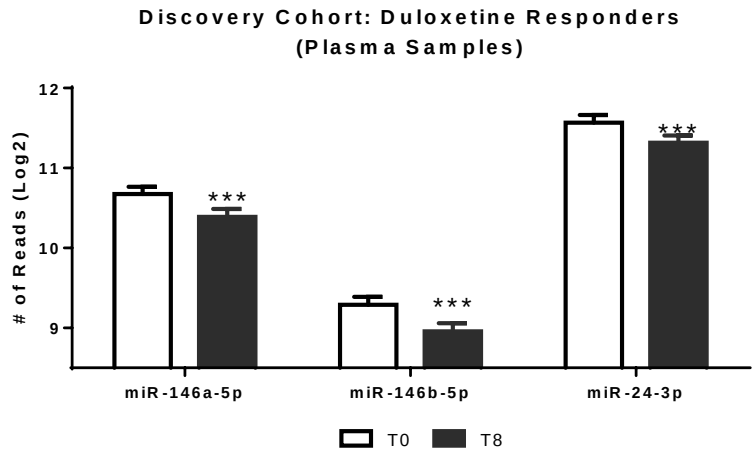
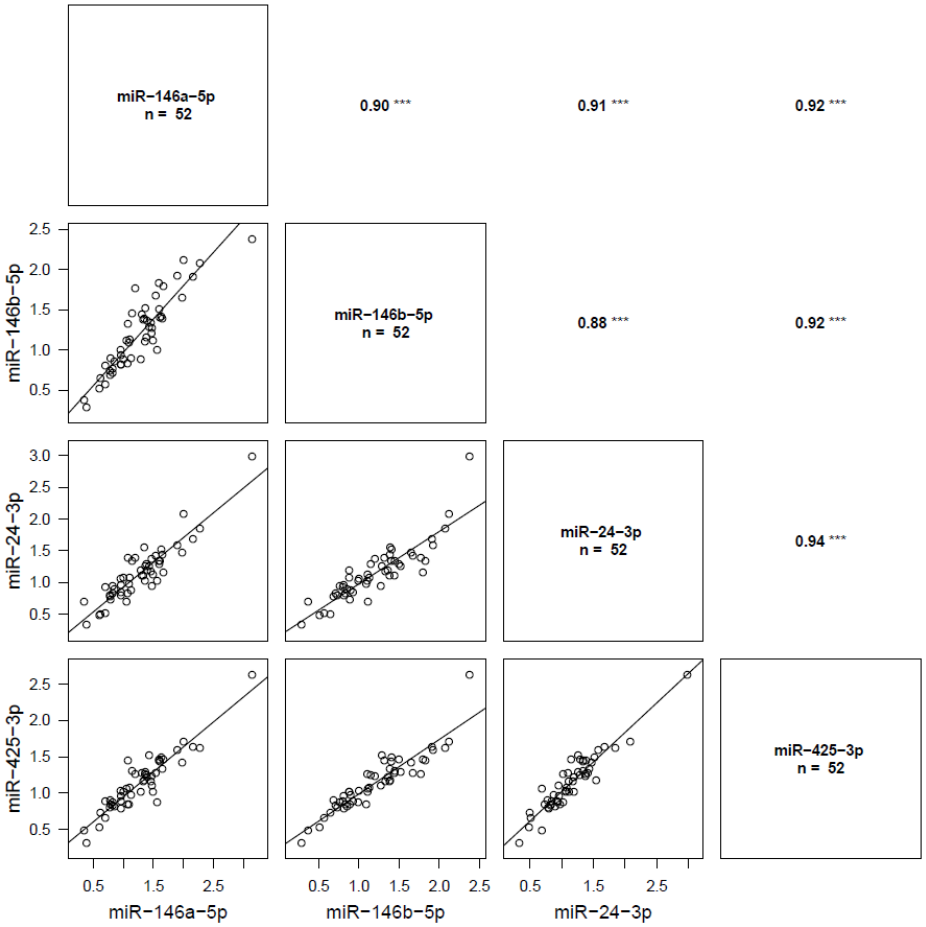
SUPPLEMENTARY FIGURES

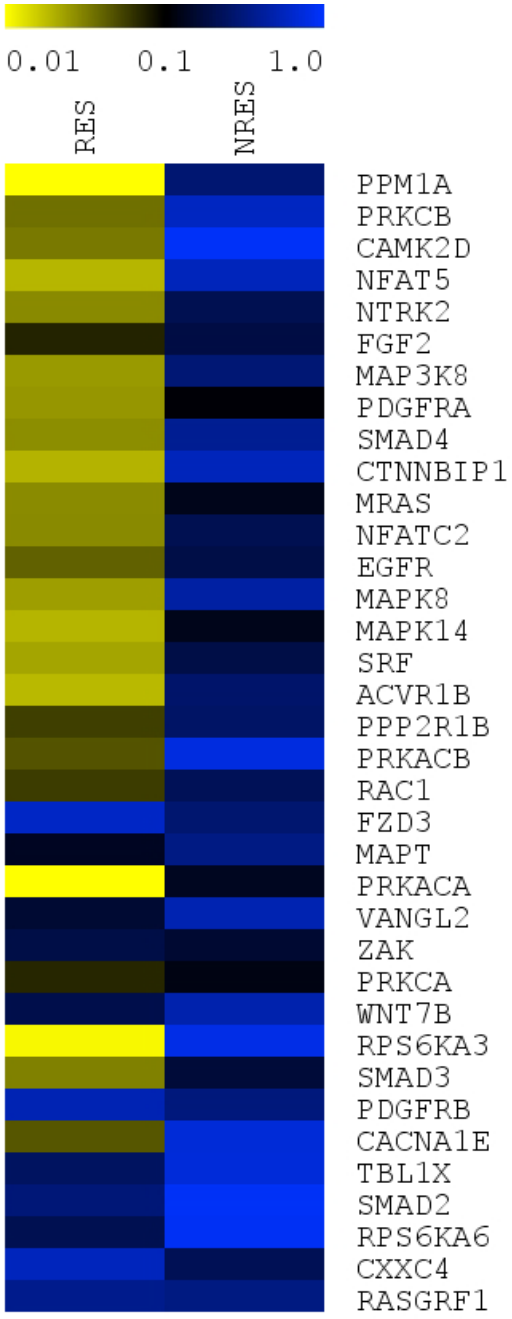
Supplementary Figure. 1. Validation in Plasma: Expression (number of reads/million, Log2) levels of miR-146a-5p, miR-146b-5p, and miR-24-3p after 8 weeks in MDD patients who responded to duloxetine treatment. ***indicates P<0.001. Levels of miRNA in plasma are considerably lower and more variable than in whole blood. We were not able to obtain reliable measures for miR-425-3p in plasma samples.



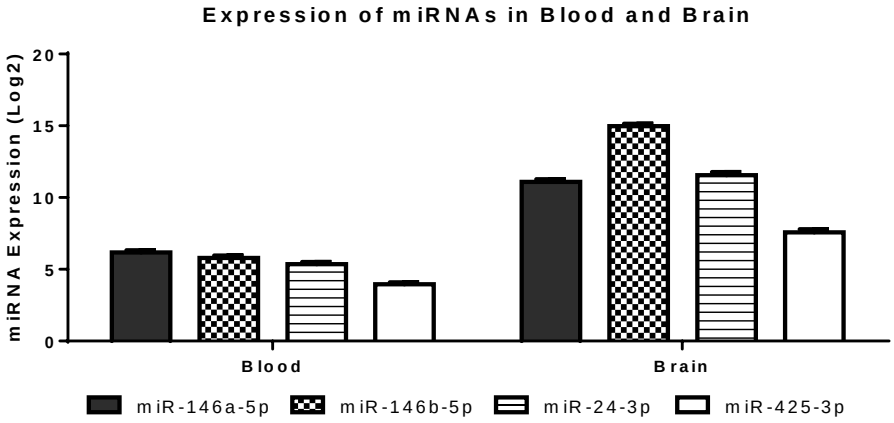
Supplementary Figure. 2. MicroRNA correlations in brain: Scatterplots of Pearson correlations between differentially expressed miRNAs in postmortem brain (vPFC) samples.



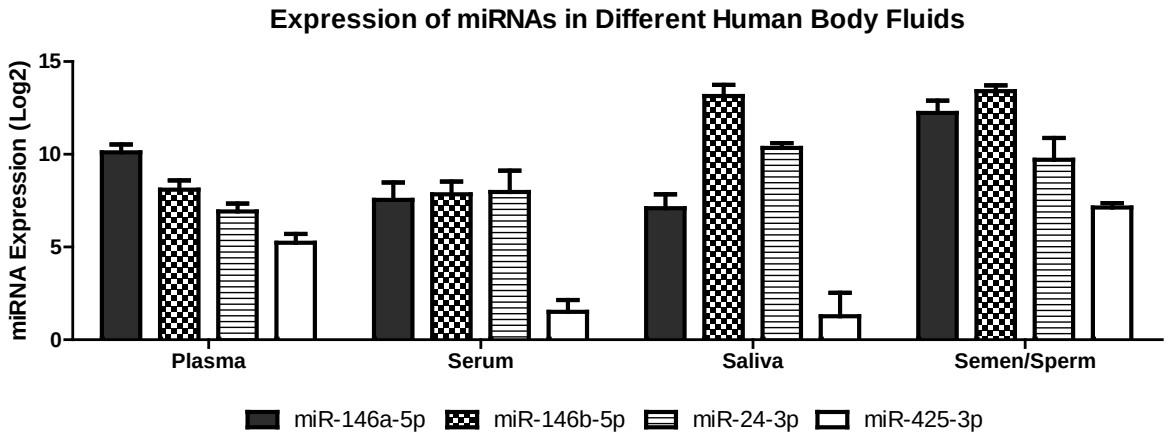
Supplementary Figure. 3. Discovery Cohort – Predicted target genes involved in MAPK and Wnt signaling pathways: Differential expression analysis of MAPK/Wnt genes identified through our computational analysis. Most of the predicted targets were significantly dysregulated after duloxetine treatment (25 out of 36 genes, 69%).



Supplementary Figure. 4. Expression of miR-146a-5p, miR-146b-5p, miR-24-3p and miR-425-3p in human whole-blood and postmortem brain samples: Small RNA sequencing data (number of reads/million, Log2) expression data for miR-146a-5p, miR-146b-5p, miR-24-3p and miR-425-3p in whole-blood and vPFC of postmortem brains.



Supplementary Figure. 5. Expression of miR-146a-5p, miR-146b-5p, miR-24-3p and miR-425-3p in other human biological fluids: Small RNA sequencing data (number of reads/million, Log2) expression data for miR-146a-5p, miR-146b-5p, miR-24-3p and miR-425-3p in human plasma (N=37), serum (N=13), saliva (N=3) and semen/sperm (N=4). miRmine Database: http://guanlab.ccmb.med.umich.edu/mirmine/



SUPPLEMENTARY TABLES

Supplementary Table 1. Duloxetine Treated Samples: Expression of miR-146a-5p, miR-146b-5p, miR-24-3p, and miR-425-3p in responders vs. non-responders from the discovery cohort.

microRNA	Adj P value - Responders	Adj P value – Non-Responders
hsa-miR-425-3p	2.63949E-08	0.205673072
hsa-miR-24-3p	6.81342E-06	0.271682804
hsa-miR-146a-5p	3.74787E-05	0.271682804
hsa-miR-146b-5p	0.001448493	0.722733069

Supplementary Table 2. Placebo Treated Samples: Expression of miR-146a-5p, miR-146b-5p, miR-24-3p, and miR-425-3p in responders vs. non-responders from the discovery cohort.

microRNA	Adj P value - Responders	Adj P value – Non-Responders
hsa-miR-425-3p	0.000141454	0.278461101
hsa-miR-24-3p	0.000325475	0.203927569
hsa-miR-146a-5p	1.86011E-05	0.269224663
hsa-miR-146b-5p	0.003720756	0.59572429

Supplementary Table 3. Technical Validation: MicroRNAs selected for technical validation. In total, 13 out 15 (87%) miRNA targets tested were validated. Small RNA sequencing results were validated with a custom miRNA panel using circulatory miRNA assays by Firefly (BioWorks). Bold font denotes statistical significance.

miRNA	Group	FC	*P* value - RES
miR-24-3p	Target	**0,75**	**1,691E-07**
miR-425-3p	Target	**0,62**	**5,373E-04**
miR-324-5p	Target	0,77	**1,366E-03**
miR-361-3p	Target	0,78	**0,002**
miR-425-5p	Target	0,83	**0,002**
miR-423-3p	Target	1,23	**0,004**
miR-361-5p	Target	0,81	**0,006**
miR-146a-5p	Target	**0,88**	**0,011**
miR-6750-3p	Target	1,41	**0,031**
miR-146b-5p	Target	**0,87**	**0,035**
miR-3173-5p	Target	1,20	**0,036**
miR-3605-3p	Target	1,22	**0,040**
miR-3074-5p	Target	0,69	**0,086**
miR-1180-3p	Target	1,03	0,417
miR-6511a-3p	Target	1,00	0,487
Let-7b-5p	End Control	0,99	0,462
Let-7i-5p	End Control	1,02	0,319
miR-19b-3p	End Control	0,97	0,311

Supplementary Table 4. Correlation between the five differentially expressed miRNAs in duloxetine and placebo responders. Significant *P* values and Pearson coefficients (r).

Pearson's r / (*P* Values)	miR-146a-5p	miR-146b-5p	miR-24-3p	miR-3074-5p	miR-425-3p
miR-146a-5p	1	X	X	X	X
miR-146b-5p	0.70 (6.9E-38)	1	X	X	X
miR-24-3p	0.70 (8.5E-38)	0.39 (3.1E-10)	1	X	X
miR-3074-5p	0.62 (3.2E-27)	0.29 (3.1E-6)	0.97 (1.2E-162)	1	X
miR-425-3p	0.77 (1.6E-50)	0.55 (2.8E-21)	0.73 (6.8E-43)	0.64 (2.1E-30)	1

Supplementary Table 5. Replication Cohort 1. Differential expression of miRNAs after 8 weeks of antidepressant treatment. MiRNAs are ranked according to *P* values and fold change (FC).

miRNA	FC (T0 vs T8)	P value - RES
miR-425-3p	0.81	0.023
miR-24-3p	0.83	0.035
miR-146a-5p	0.82	0.030
miR-146b-5p	0.83	0.041
miR-3074-5p	**0.95**	**0.333**

Supplementary Table 6. Replication Cohort 2. Differential expression of miRNAs after 8 weeks of antidepressant treatment. MiRNAs are ranked according to *P* values and fold change (FC).

miRNA	FC (T0 vs T8)	P value - RES
miR-425-3p	0.99	0.480
miR-24-3p	0.89	0.023
miR-146a-5p	0.80	0.045
miR-146b-5p	0.73	0.030

Supplementary Table 7. Hematology data analysis: Cell count analysis performed in blood samples from MDD patients treated with Duloxetine (Discovery Cohort).

	Responders -Duloxetine			Non-Responders – Duloxetine		
Cell Type	**Baseline**	**After Treatment**	**P-value**	**Baseline**	**After Treatment**	**P-value**
Leukocytes	6.5 ± 1.6	6.4 ± 1.4	**0,76**	6.69 ± 1.9	6.9 ± 2.1	**0,25**
Basophils	0.35 ± 0.19	0.33 ± 0.2	**0,84**	0.36 ± 0.19	0.37 ± 0.2	**0,55**
Eosinophils	2.3 ± 0.16	2.5 ± 0.16	**0,11**	2.9 ± 0.21	2.9 ± 0.22	**0,45**
Lymphocytes	29.2 ± 6.8	29.5 ± 6.8	**0,95**	32.4 ± 9.2	30.1 ± 7.3	**0,41**
Monocytes	6.6 ± 2.3	6.7 ± 2.0	**0,51**	6.5 ± 2.0	6.7 ± 2.2	**0,64**
Neutrophils	61.6 ± 8.6	60.7 ± 8.3	**0,57**	57.9 ± 10.8	58.6 ± 8.4	**0,80**

Supplementary Table 8. Hematology data analysis: Cell count analysis performed in blood samples from MDD patients treated with a placebo control (Discovery Cohort).

	Responders -Placebo			Non-Responders – Placebo		
Cell Type	**Baseline**	**After Treatment**	**P-value**	**Baseline**	**After Treatment**	**P-value**
Leukocytes	6.6 ± 2.1	6.5 ± 1.5	**0,67**	6.8 ± 1.9	6.7 ± 1.9	**0,61**
Basophils	0.44 ± 0.3	0.43 ± 0.2	**0,86**	0.35 ± 0.2	0.41 ± 0.2	**0,24**
Eosinophils	2.3 ± 0.17	2.9 ± 0.2	**0,34**	2.5 ± 0.14	2.5 ± 0.177	**0,57**
Lymphocytes	30.2 ± 8.6	31.0 ± 7.0	**0,62**	31.1 ± 8.2	31.4 ± 6.9	**0,70**
Monocytes	6.8 ± 2.9	7.2 ± 2.9	**0,37**	6.6 ± 2.4	6.1 ± 2.2	**0,28**
Neutrophils	59.1 ± 10.6	57.4 ± 9.4	**0,39**	59.5 ± 9.4	58.7 ± 7.7	**0,95**

Supplementary Table 9. Correlation between miR-146a-5p, miR-146b-5p, miR-24-3p and miR-425-3p in postmortem brains of subjects with MDD and controls. Significant P values and Pearson coefficients (r).

Pearson's r / (*P* Values)	**miR-146a-5p**	**miR-146b-5p**	**miR-24-3p**	**miR-425-3p**
miR-146a-5p	1	X	X	X
miR-146b-5p	0.91 (9.2E-20)	1	X	X
miR-24-3p	0.91 (2.8E-20)	0.88 (7.0E-18)	1	X
miR-425-3p	0.92 (9.9E-22)	0.92 (6.2E-22)	0.94 (2.5E-24)	1

Supplementary Table 10. Discovery Cohort – Predicted target genes involved in MAPK and Wnt signaling pathways: Correlation analysis between the expression of miR-146a-5p, miR-146b-5p, miR-24-3p and miR-425-3p with genes identified through our computational analysis. Most of the predicted targets were significantly correlated with one or more of the miRNAs tested (32 out of 36 genes, 89%).

Gene Symbol	# of Pathways	Signaling Pathway	Correlated with miRNAs
CACNA1E	2	MAPK	**Yes**
MAPT	1	MAPK	**Yes**
NTRK2	1	MAPK	**Yes**
PDGFRB	2	MAPK	**Yes**
PPM1A	1	MAPK	**Yes**
SRF	1	MAPK	**Yes**
PRKACA	3	MAPK, Wnt	**Yes**
PRKCA	3	MAPK, Wnt	**Yes**
PRKCB	3	MAPK, Wnt	**Yes**
RAC1	3	MAPK, Wnt	**Yes**
CTNNBIP1	1	Wnt	**Yes**
NFAT5	1	Wnt	**Yes**
PPP2R1B	1	Wnt	**Yes**
SMAD3	2	Wnt	**Yes**
RPS6KA3	1	MAPK	**Yes**
MAPK8	2	MAPK, Wnt	**Yes**
PRKACB	3	MAPK, Wnt	**Yes**
CAMK2D	2	Wnt	**Yes**
TBL1X	1	Wnt	**Yes**
WNT7B	1	Wnt	**Yes**
ACVR1B	3	MAPK	**Yes**
EGFR	4	MAPK	**Yes**
FGF2	1	MAPK	**Yes**
MAP3K8	1	MAPK	**Yes**
MRAS	1	MAPK	**Yes**
PDGFRA	3	MAPK	**Yes**
ZAK	1	MAPK	**Yes**
NFATC2	2	MAPK, Wnt	**Yes**
FZD3	1	Wnt	**Yes**
SMAD4	2	Wnt	**Yes**
VANGL2	1	Wnt	**Yes**
MAPK14	1	MAPK	**Yes**
RASGRF1	1	MAPK	No
RPS6KA6	2	MAPK	No
CXXC4	1	Wnt	No
SMAD2	1	Wnt	No

Supplementary Table 11. Discovery Cohort – Predicted target genes involved in MAPK and Wnt signaling pathways: Differential expression analysis of MAPK/Wnt genes identified through our computational analysis. Most of the predicted targets were significantly dysregulated after duloxetine treatment (25 out of 36 genes, 69%).

	Responders				Non-Responders			
Gene Name	**T0 Mean**	**T8 Mean**	**FC**	**P value**	**T0 Mean**	**T8 Mean**	**FC**	**P value**
PPM1A	4.55	5.41	1.19	0.004420326	4.62	4.34	0.94	0.49965897
PRKCB	319.72	338.64	1.06	0.060316585	322.24	326.96	1.01	0.7897703
CAMK2D	2.61	2.82	1.08	0.057039768	2.69	2.69	1.00	0.98554325
NFAT5	6.50	7.31	1.12	0.03572427	7.75	7.50	0.97	0.7655441
NTRK2	2.36	2.52	1.07	0.051177796	2.44	2.33	0.95	0.3864045
FGF2	2.61	2.79	1.07	0.08750842	2.82	2.66	0.94	0.3462899
MAP3K8	45.66	49.45	1.08	0.045875274	38.48	43.25	1.12	0.5140519
PDGFRA	2.89	3.12	1.08	0.046876404	2.89	2.63	0.91	0.13049328
SMAD4	94.10	100.68	1.07	0.049906548	83.09	89.14	1.07	0.6193001
CTNNBIP1	8.75	10.30	1.18	0.036455154	12.65	11.97	0.95	0.7602985
MRAS	3.14	3.41	1.09	0.050751105	3.31	3.72	1.13	0.19830658
NFATC2	2.36	2.52	1.07	0.051177796	2.44	2.33	0.95	0.3864045
EGFR	2.61	2.80	1.07	0.06554178	2.17	2.26	1.04	0.3559935
MAPK8	3.12	3.42	1.08	0.044178944	3.28	3.41	1.04	0.6857121
MAPK14	5.04	5.74	1.14	0.03593131	6.52	5.15	0.79	0.19701816
SRF	182.04	191.19	1.05	0.041735854	178.86	185.74	1.04	0.3582986
ACVR1B	38.13	41.21	1.08	0.034682844	38.13	41.15	1.08	0.48104617
PPP2R1B	2.53	2.70	1.07	0.07770063	2.96	2.82	0.95	0.46333113
PRKACB	6.91	7.87	1.06	0.07025041	7.00	7.14	1.02	0.8925169
RAC1	503.27	522.19	1.04	0.07871647	507.27	493.01	0.97	0.41145188
FZD3	4.72	4.66	0.99	0.8001341	4.83	4.48	0.93	0.49779695
MAPT	4.66	4.32	0.93	0.22382466	3.99	4.15	1.04	0.5721705
PRKACA	2.31	2.54	1.10	0.002043212	2.28	2.48	1.09	0.21436845
VANGL2	3.20	3.04	0.95	0.28532743	3.11	3.22	1.03	0.7330913
ZAK	3.16	3.04	0.96	0.3574143	3.47	3.03	0.87	0.2767202
PRKCA	59.32	62.56	1.05	0.08641608	61.85	56.12	0.91	0.16824569
WNT7B	3.29	3.15	0.96	0.37274805	3.10	3.04	0.98	0.7147429
RPS6KA3	2.97	3.28	1.09	0.012417246	3.08	3.11	1.01	0.9133113
SMAD3	72.74	77.46	1.07	0.05446795	80.96	78.07	0.96	0.3105279
PDGFRB	3.55	3.61	1.02	0.7372547	4.35	4.11	0.95	0.53927463
CACNA1E	3.84	4.22	1.10	0.069353946	4.02	4.08	1.02	0.86569136
TBL1X	317.96	309.47	0.97	0.44723037	304.89	307.98	1.01	0.87157595
SMAD2	8.45	8.17	0.97	0.5262408	8.00	7.97	1.00	0.97446495
RPS6KA6	2.69	2.62	0.97	0.39195198	2.64	2.65	1.00	0.9641064
CXXC4	2.60	2.63	1.01	0.76980865	2.69	2.90	1.08	0.4009055
RASGRF1	2.79	2.85	1.02	0.5967571	2.76	2.66	0.96	0.5654304

Supplementary Table 12. Replication cohort – Predicted target genes involved in MAPK and Wnt signaling pathways: Correlation analysis between the expression of miR-146a-5p, miR-146b-5p, miR-24-3p and miR-425-3p with genes identified through our computational analysis. Most of the predicted targets were significantly correlated with one or more of the miRNAs tested (20 out of 28 genes, 71%).

Gene Symbol	# of Pathways	Signaling Pathway	Correlated with miRNAs
PRKCA	3	MAPK, Wnt	**Yes**
PRKCB	3	MAPK, Wnt	**Yes**
RAC1	3	MAPK, Wnt	**Yes**
CTNNBIP1	1	Wnt	**Yes**
NFAT5	1	Wnt	**Yes**
SMAD3	2	Wnt	**Yes**
RPS6KA3	1	MAPK	**Yes**
PRKACB	3	MAPK, Wnt	**Yes**
CAMK2D	2	Wnt	**Yes**
ACVR1B	3	MAPK	**Yes**
EGFR	4	MAPK	**Yes**
MAPK14	1	MAPK	**Yes**
FZD3	1	Wnt	**Yes**
SMAD2	1	Wnt	**Yes**
MAPT	1	MAPK	**Yes**
NTRK2	1	MAPK	**Yes**
PPP2R1B	1	Wnt	**Yes**
ZAK	1	MAPK	**Yes**
CXXC4	1	Wnt	**Yes**
VANGL2	1	Wnt	**Yes**
PDGFRB	2	MAPK	No
SRF	1	MAPK	No
MRAS	1	MAPK	No
PPM1A	1	MAPK	No
PRKACA	3	MAPK, Wnt	No
TBL1X	1	Wnt	No
RASGRF1	1	MAPK	No
NFATC2	2	MAPK, Wnt	No

Supplementary Table 13. Overexpression of miRNAs – Dysregulation of MAPK and Wnt genes: HEK293 cells were transfected for 24 hrs with a miRNA mimic for each of the individual miRNAs (miR-146a-5p, miR-146b-5p, miR-24-3p and miR-425-3p), a mock vehicle control or a miRNA-mimic scramble control. Results were compared to untreated control cells. All of the MAPK/Wnt genes tested were down-regulated by at least one of the miRNA mimics transfected. Bold font denotes statistical significance.

Gene	Untrs Ctrl	Vehicle Ctrl	Mimic Scramble	Mimic (miR-146a-5p)	Mimic (miR-146b-5p)	Mimic (miR-24-3p)	Mimic (miR-425-3p)
NTRK2 (T1)	1	0,9563	0,6539	**0,0308**	**0,0046**	**0,0044**	**0,0008**
MAPK8	1	0,1684	0,1195	**0,0052**	**0,0153**	**0,0305**	**0,0006**
MAPT	1	0,3775	0,2521	**0,0070**	**0,0012**	**0,0764**	**0,0173**
PRKACA	1	0,5554	0,4658	**0,0312**	**0,0183**	**0,0929**	**0,0094**
PDGFRB	1	0,1432	0,6751	**0,0287**	**0,0500**	**0,0530**	**0,0313**
RPS6KA3	1	0,5985	0,3422	**0,0284**	**0,0091**	**0,0137**	0,1300
ZAK	1	0,6916	0,2545	**0,0178**	**0,0122**	**0,0115**	0,1437
PPM1A	1	0,7750	0,2107	**0,0013**	**0,0091**	**0,0004**	0,1782
FGF2	1	0,6269	0,8467	**0,0039**	**0,0162**	**0,0187**	0,2939
PDGFRA	1	0,6373	0,3221	0,3271	**0,0370**	**0,0245**	**0,0347**
MAPK14	1	0,7948	0,5130	**0,0265**	**0,0335**	**0,0447**	0,3475
PRKCA	1	0,2576	0,4252	0,7020	**0,0037**	**0,0036**	**0,0277**
PRKACB	1	0,7682	0,2054	**0,0042**	0,8559	**0,0087**	**0,0403**
SRF	1	0,4667	0,4550	**0,0610**	**0,0111**	**0,0481**	**0,0630**
RAC1	1	0,9366	0,0897	**0,0581**	**0,0005**	**0,0994**	**0,0301**
ACVR1B	1	0,6816	0,3242	**0,0279**	0,1644	**0,0756**	**0,0079**
EGFR	1	0,8678	0,2799	**0,0126**	**0,0395**	**0,0972**	0,1635
MAP3K8	1	0,4425	0,8417	0,2709	**0,0226**	**0,0047**	**0,0733**
RPS6KA6	1	0,3079	0,7932	0,8192	**0,0102**	**0,0025**	**0,0835**
NFATC2	1	0,7783	0,4279	0,9689	**0,0305**	**0,0488**	0,1449
PRKCB	1	0,4853	0,7585	0,7473	0,6636	**0,0344**	**0,0312**
MRAS	1	0,2844	0,2957	**0,0865**	**0,0563**	0,5540	**0,0455**
RASGRF1	1	0,7801	0,1900	0,2000	0,2403	**0,0777**	0,3971
B Actin	1	0,6533	0,2446	0,5980	0,5678	0,3883	0,1525
GAPDH	1	0,5548	0,3238	0,3210	0,1964	0,7436	0,6392

Supplementary Table 14. MAPK and Wnt genes: Most of these genes have been previously associated with MDD or antidepressant activity (*supplementary references*).

#	Gene Symbol	Signaling Pathway	Literature References MDD or AD Treatment	Literature References Other Psychiatric Disorders
1	CACNA1E	MAPK	[1,2]	
2	MAPT	MAPK	[3]	
3	NTRK2	MAPK	[4,5,6]	
4	PDGFRB	MAPK	[7]	
5	PPM1A	MAPK	[8]	
6	SRF	MAPK	[9,1]	
7	PRKACA	MAPK, Wnt	[11]	
8	PRKCA	MAPK, Wnt	[12]	
9	PRKCB	MAPK, Wnt	[13,14]	
10	RAC1	MAPK, Wnt	[15]	
11	CTNNBIP1	Wnt	[16]	
12	NFAT5	Wnt	[17]	
13	PPP2R1B	Wnt	[18]	
14	SMAD3	Wnt	[19,2]	
15	RPS6KA3	MAPK	[21]	
16	MAPK8	MAPK, Wnt	[22]	
17	PRKACB	MAPK, Wnt	[11]	
18	CAMK2D	Wnt	[23]	
19	TBL1X	Wnt		
20	WNT7B	Wnt	[21]	
21	ACVR1B	MAPK	[7]	
22	EGFR	MAPK	[24,25]	
23	FGF2	MAPK	[26,27]	
24	MAP3K8	MAPK		[28]
25	MAPK14	MAPK		[29]
26	MRAS	MAPK		
27	PDGFRA	MAPK	[30,31]	
28	RASGRF1	MAPK	[32,33]	
29	RPS6KA6	MAPK	[34]	
30	ZAK	MAPK		
31	NFATC2	MAPK, Wnt	[35]	
32	CXXC4	Wnt		
33	FZD3	Wnt	[36,37]	
34	SMAD2	Wnt	[19,38]	
35	SMAD4	Wnt	[38,39]	
36	VANGL2	Wnt	[40]	

Supplementary Table 15. Primers: Complete list of primers used for qRT-PCR experiments

Gene	TaqMan Assay ID
miR-146a-5p	#000468
miR-146b-5p	#001097
miR-24-3p	#000402
miR-425-3p	#002302
ACVR1B	Hs00244715_m1
EGFR	Hs01076090_m1
FGF2	Hs00266645_m1
MAP3K8	Hs00178297_m1
MAPK14	Hs01051152_m1
MAPK8	Hs01548508_m1
MAPT	Hs00902194_m1
MRAS	Hs00171926_m1
NFATC2	Hs00905451_m1
NTRK2 (T1)	Hs01093110_m1
PDGFRA	Hs00998026_m1
PDGFRB	Hs01019589_m1
PPM1A	Hs01056778_g1
PRKACA	Hs00427274_m1
PRKACB	Hs01086757_m1
PRKCA	Hs00925193_m1
PRKCB	Hs00176998_m1
RAC1	Hs01902432_s1
RASGRF1	Hs00182314_m1
RPS6KA3	Hs00177936_m1
RPS6KA6	Hs00179523_m1

SUPPLEMENTARY REFERENCES

1. Lavebratt, C., Aberg, E., Sjoholm, L. K. & Forsell, Y. Variations in FKBP5 and BDNF genes are suggestively associated with depression in a Swedish population-based cohort. Journal of affective disorders 125, 249-255, doi:10.1016/j.jad.2010.02.113 (2010).
2. Drago, A. et al. AKAP13, CACNA1, GRIK4 and GRIA1 genetic variations may be associated with haloperidol efficacy during acute treatment. European neuropsychopharmacology : the journal of the European College of Neuropsychopharmacology 23, 887-894, doi:10.1016/j.euroneuro.2012.08.013 (2013).
3. Romano, A. et al. Depressive-like behavior is paired to monoaminergic alteration in a murine model of Alzheimer's disease. Int J Neuropsychopharmacol 18, doi:10.1093/ijnp/pyu020 (2015).
4. Maussion, G. et al. Regulation of a truncated form of tropomyosin-related kinase B (TrkB) by Hsa-miR-185* in frontal cortex of suicide completers. PLoS One 7, e39301, doi:10.1371/journal.pone.0039301 (2012).
5. Wang, J. W., Dranovsky, A. & Hen, R. The when and where of BDNF and the antidepressant response. Biol Psychiatry 63, 640-641, doi:10.1016/j.biopsych.2008.01.008 (2008).
6. Ernst, C., Chen, E. S. & Turecki, G. Histone methylation and decreased expression of TrkB.T1 in orbital frontal cortex of suicide completers. Mol Psychiatry 14, 830-832, doi:10.1038/mp.2009.35 (2009).
7. Kruk, J. S. et al. Fluoxetine-induced transactivation of the platelet-derived growth factor type beta receptor reveals a novel heterologous desensitization process. Molecular and cellular neurosciences 65, 45-51, doi:10.1016/j.mcn.2015.02.013 (2015).
8 .Malki, K. et al. Convergent animal and human evidence suggests a role of PPM1A gene in response to antidepressants. Biol Psychiatry 69, 360-365, doi:10.1016/j.biopsych.2010.08.011 (2011).
9. Xu, F. et al. Differential co-expression and regulation analyses reveal different mechanisms underlying major depressive disorder and subsyndromal symptomatic depression. BMC bioinformatics 16, 112, doi:10.1186/s12859-015-0543-y (2015).
10. Nestler, E. J. Role of the Brain's Reward Circuitry in Depression: Transcriptional Mechanisms. International review of neurobiology 124, 151-170, doi:10.1016/bs.irn.2015.07.003 (2015).
11. Shelton, R. C., Hal Manier, D. & Lewis, D. A. Protein kinases A and C in post-mortem prefrontal cortex from persons with major depression and normal controls. Int J Neuropsychopharmacol 12, 1223-1232, doi:10.1017/S1461145709000285 (2009).
12. Carroll, L. S. et al. Evidence for rare and common genetic risk variants for schizophrenia at protein kinase C, alpha. Mol Psychiatry 15, 1101-1111, doi:10.1038/mp.2009.96 (2010).
13. Costas, J. et al. Association study of 44 candidate genes with depressive and anxiety symptoms in post-partum women. J Psychiatr Res 44, 717-724, doi:10.1016/j.jpsychires.2009.12.012 (2010).
14. Sakaida, M. et al. Electroconvulsive seizure-induced changes in gene expression in the mouse hypothalamic paraventricular nucleus. J Psychopharmacol 27, 1058-1069, doi:10.1177/0269881113497612 (2013).
15. Golden, S. A. et al. Epigenetic regulation of RAC1 induces synaptic remodeling in stress disorders and depression. Nature medicine 19, 337-344, doi:10.1038/nm.3090 (2013).
16. Wei, Y. B., Backlund, L., Wegener, G., Mathe, A. A. & Lavebratt, C. Telomerase dysregulation in the hippocampus of a rat model of depression: normalization by lithium. Int J Neuropsychopharmacol 18, pyv002, doi:10.1093/ijnp/pyv002 (2015).
17. Ploski, J. E., Newton, S. S. & Duman, R. S. Electroconvulsive seizure-induced gene expression profile of the hippocampus dentate gyrus granule cell layer. Journal of neurochemistry 99, 1122-1132, doi:10.1111/j.1471-4159.2006.04156.x (2006).
18. Kim, S. & Webster, M. J. Integrative genome-wide association analysis of cytoarchitectural abnormalities in the prefrontal cortex of psychiatric disorders. Mol Psychiatry 16, 452-461, doi:10.1038/mp.2010.23 (2011).
19. Park, S. H. et al. Melittin inhibits TGF-beta-induced pro-fibrotic gene expression through the suppression of the TGFbetaRII-Smad, ERK1/2 and JNK-mediated signaling pathway. The American journal of Chinese medicine 42, 1139-1152, doi:10.1142/S0192415X14500712 (2014).
20. Ganea, K. et al. Convergent animal and human evidence suggests the activin/inhibin pathway to be involved in antidepressant response. Translational psychiatry 2, e177, doi:10.1038/tp.2012.104 (2012).
21. Bergstrom, A., Jayatissa, M. N., Thykjaer, T. & Wiborg, O. Molecular pathways associated with stress resilience and drug resistance in the chronic mild stress rat model of depression: a gene expression study. Journal of molecular neuroscience : MN 33, 201-215 (2007).
22. Malki, K. et al. Antidepressant-dependent mRNA changes in mouse associated with hippocampal neurogenesis in a mouse model of depression. Pharmacogenetics and genomics 22, 765-776, doi:10.1097/FPC.0b013e328356fa90 (2012).

23. Drago, A., Cocchi, E., Crisafulli, C. & Serretti, A. A molecular pathway analysis of the glutamatergic-monoaminergic interplay serves to investigate the number of depressive records during citalopram treatment. J Neural Transm (Vienna) 122, 465-475, doi:10.1007/s00702-014-1267-2 (2015).
24. Tian, W. et al. A study of the functional significance of epidermal growth factor in major depressive disorder. Psychiatric genetics 22, 161-167, doi:10.1097/YPG.0b013e3283539550 (2012).
25. Yamamori, H. et al. Assessment of a multi-assay biological diagnostic test for mood disorders in a Japanese population. Neuroscience letters 612, 167-171, doi:10.1016/j.neulet.2015.12.019 (2016).
26. Birey, F. et al. Genetic and Stress-Induced Loss of NG2 Glia Triggers Emergence of Depressive-like Behaviors through Reduced Secretion of FGF2. Neuron 88, 941-956, doi:10.1016/j.neuron.2015.10.046 (2015).
27. Borroto-Escuela, D. O., Tarakanov, A. O. & Fuxe, K. FGFR1-5-HT1A Heteroreceptor Complexes: Implications for Understanding and Treating Major Depression. Trends in neurosciences 39, 5-15, doi:10.1016/j.tins.2015.11.003 (2016).
28. Schwarz, R. et al. A preliminary study on methylphenidate-regulated gene expression in lymphoblastoid cells of ADHD patients. The world journal of biological psychiatry : the official journal of the World Federation of Societies of Biological Psychiatry 16, 180-189, doi:10.3109/15622975.2014.948064 (2015).
29. Onwuameze, O. E. et al. MAPK14 and CNR1 gene variant interactions: effects on brain volume deficits in schizophrenia patients with marijuana misuse. Psychological medicine 43, 619-631, doi:10.1017/S0033291712001559 (2013).
30. Elsayed, M. et al. Antidepressant effects of fibroblast growth factor-2 in behavioral and cellular models of depression. Biol Psychiatry 72, 258-265, doi:10.1016/j.biopsych.2012.03.003 (2012).
31. Sathyanesan, M. et al. A molecular characterization of the choroid plexus and stress-induced gene regulation. Translational psychiatry 2, e139, doi:10.1038/tp.2012.64 (2012).
32. Fabbri, C. & Serretti, A. Genetics of long-term treatment outcome in bipolar disorder. Progress in neuro-psychopharmacology & biological psychiatry 65, 17-24, doi:10.1016/j.pnpbp.2015.08.008 (2016).
33. Darcy, M. J., Trouche, S., Jin, S. X. & Feig, L. A. Age-dependent role for Ras-GRF1 in the late stages of adult neurogenesis in the dentate gyrus. Hippocampus 24, 315-325, doi:10.1002/hipo.22225 (2014).
34. Smagin, D. A. et al. Dysfunction in Ribosomal Gene Expression in the Hypothalamus and Hippocampus following Chronic Social Defeat Stress in Male Mice as Revealed by RNA-Seq. Neural plasticity 2016, 3289187, doi:10.1155/2016/3289187 (2016).
35. Inkster, B. et al. Pathway-based approaches to imaging genetics association studies: Wnt signaling, GSK3beta substrates and major depression. NeuroImage 53, 908-917, doi:10.1016/j.neuroimage.2010.02.065 (2010).
36. Hashimoto, R. et al. Association study of the frizzled-3 (FZD3) gene with schizophrenia and mood disorders. J Neural Transm (Vienna) 112, 303-307, doi:10.1007/s00702-004-0264-2 (2005).
37. Keri, S., Szabo, C. & Kelemen, O. Blood biomarkers of depression track clinical changes during cognitive-behavioral therapy. Journal of affective disorders 164, 118-122, doi:10.1016/j.jad.2014.04.030 (2014).
38. Dow, A. L., Russell, D. S. & Duman, R. S. Regulation of activin mRNA and Smad2 phosphorylation by antidepressant treatment in the rat brain: effects in behavioral models. The Journal of neuroscience : the official journal of the Society for Neuroscience 25, 4908-4916, doi:10.1523/JNEUROSCI.5155-04.2005 (2005).
39. Suda, S., Segi-Nishida, E., Newton, S. S. & Duman, R. S. A postpartum model in rat: behavioral and gene expression changes induced by ovarian steroid deprivation. Biol Psychiatry 64, 311-319, doi:10.1016/j.biopsych.2008.03.029 (2008).
40. Okerlund, N. D. & Cheyette, B. N. Synaptic Wnt signaling-a contributor to major psychiatric disorders? Journal of neurodevelopmental disorders 3, 162-174, doi:10.1007/s11689-011-9083-6 (2011).