

tiRNA-Gly-GCC-001 in major depressive disorder: Promising diagnostic and therapeutic biomarker

Hiahua Tian¹, Shugui Gao¹, Miaomiao Xu¹, Mei Yang¹, Mengyuan Shen¹, Jimeng Liu¹, Guang Xue¹, Dingding Zhuang¹, Zhenyu Hu¹, and chuang wang¹

¹Ningbo University

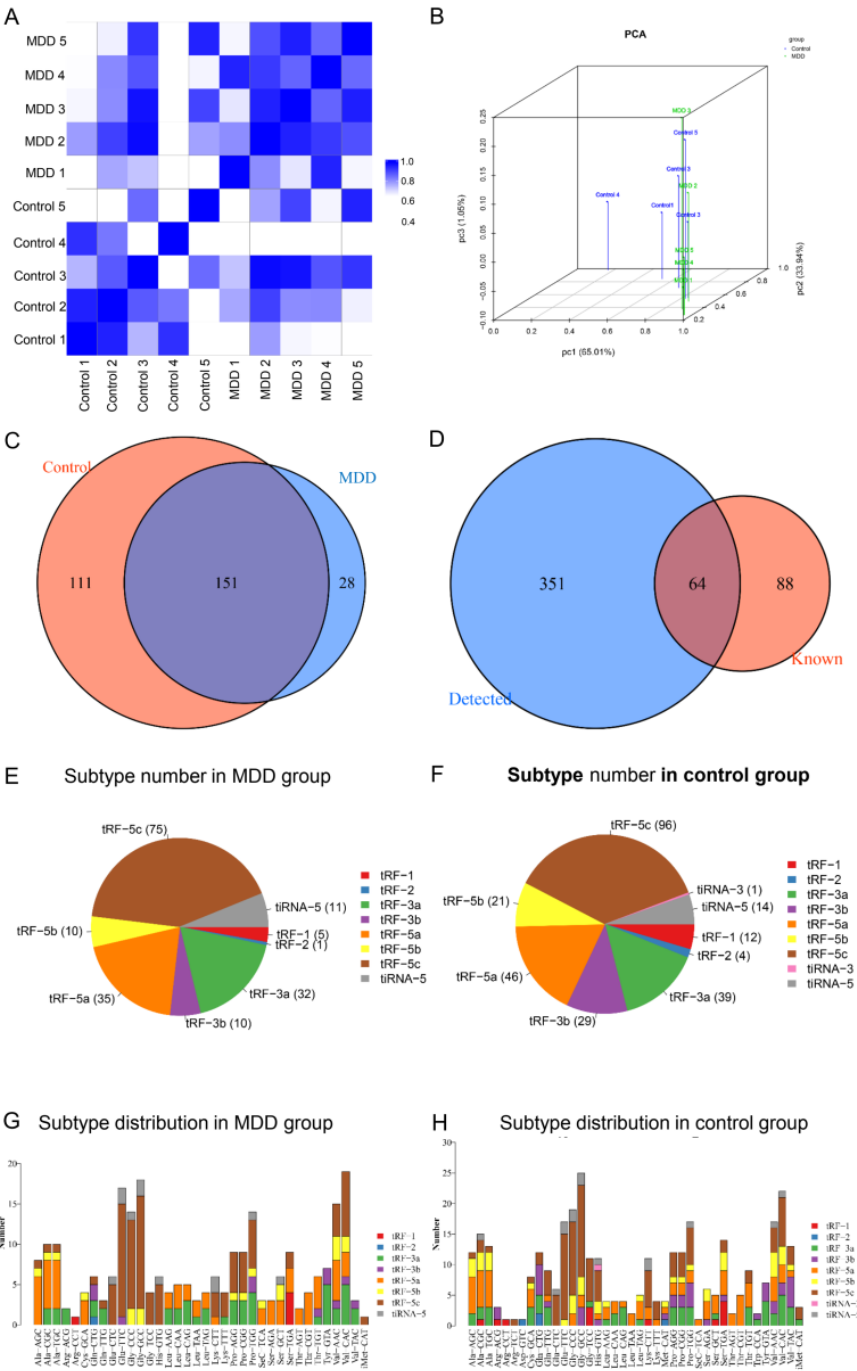
June 8, 2023

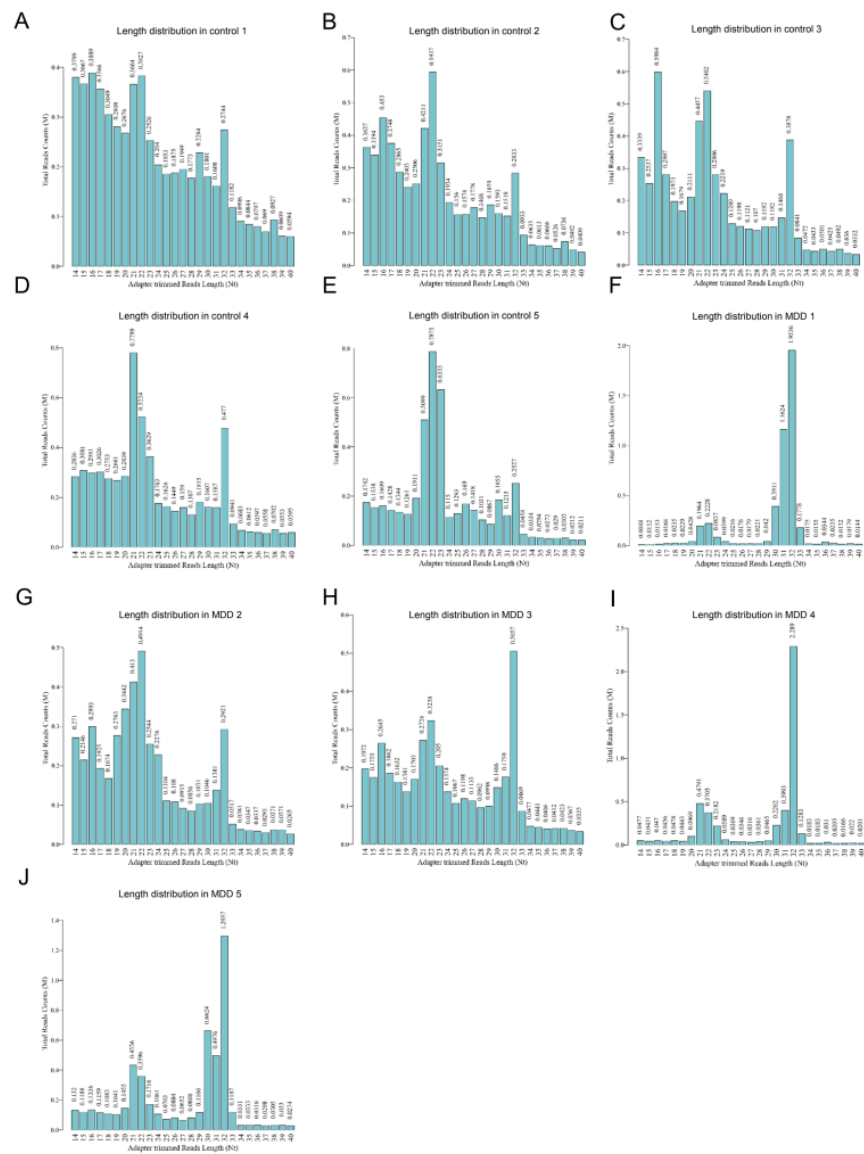
Abstract

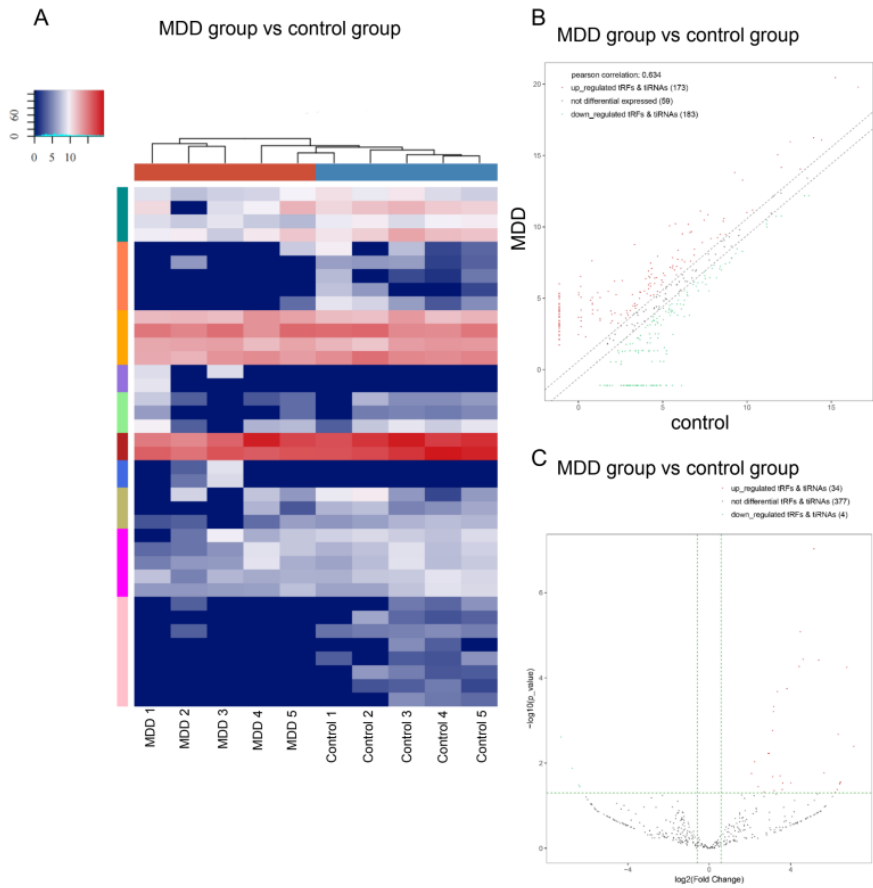
Background and Purpose: In major depressive disorder (MDD), exploration of biomarkers will be helpful in diagnosing the disorder as well as in choosing a treatment, and predicting the treatment response. Currently, tRNA-derived small ribonucleic acids (tsRNAs) have been established as promising non-invasive biomarker candidates that may enable a more reliable diagnosis or monitoring of various diseases. Herein, we aimed to explore tsRNA expression together with functional activities in MDD development. **Experimental Approach:** Serum samples were obtained from patients with MDD and healthy controls, and small RNA sequencing (RNA-Seq) was used to profile tsRNA expression. Dysregulated tsRNAs in MDD were validated by quantitative real-time polymerase chain reaction (qRT-PCR). The diagnostic utility of specific tsRNAs and the expression of these tsRNAs after antidepressant treatment was analyzed. **Key Results:** In total, 38 tsRNAs were significantly differentially expressed in MDD samples relative to healthy individuals (34 upregulated and 4 downregulated). qRT-PCR was used to validate the expression of six tsRNAs that were upregulated in MDD (tiRNA-1:20-chrM. Ser-GCT, tiRNA-1:33-Gly-GCC-1, tRF-1:22-chrM.Ser-GCT, tRF-1:31-Ala-AGC-4-M6, tRF-1:31-Pro-TGG-2, and tRF-1:32-chrM. Gln-TTG). Interestingly, serum tiRNA-Gly-GCC-001 levels exhibited an area under the ROC curve of 0.844. Moreover, tiRNA-Gly-GCC-001 is predicted to suppress brain-derived neurotrophic factor (BDNF) expression. Furthermore, significant tiRNA-Gly-GCC-001 downregulation was evident following an eight-week treatment course and served as a promising baseline predictor of patient response to antidepressant therapy. **Conclusion and Implications:** Our current work firstly found that tiRNA-Gly-GCC-001 is a promising MDD biomarker candidate that can predict patient responses to antidepressant therapy.

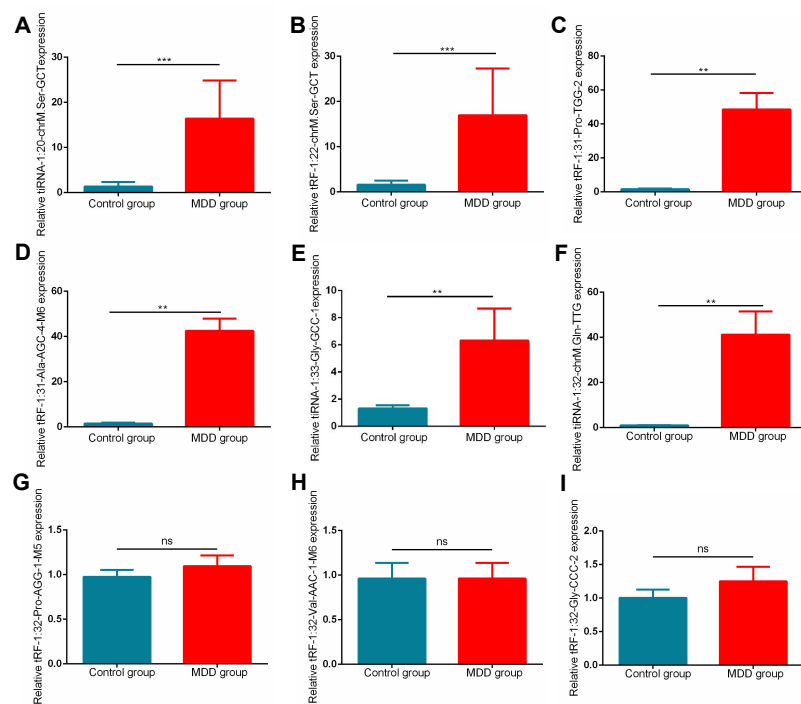
Hosted file

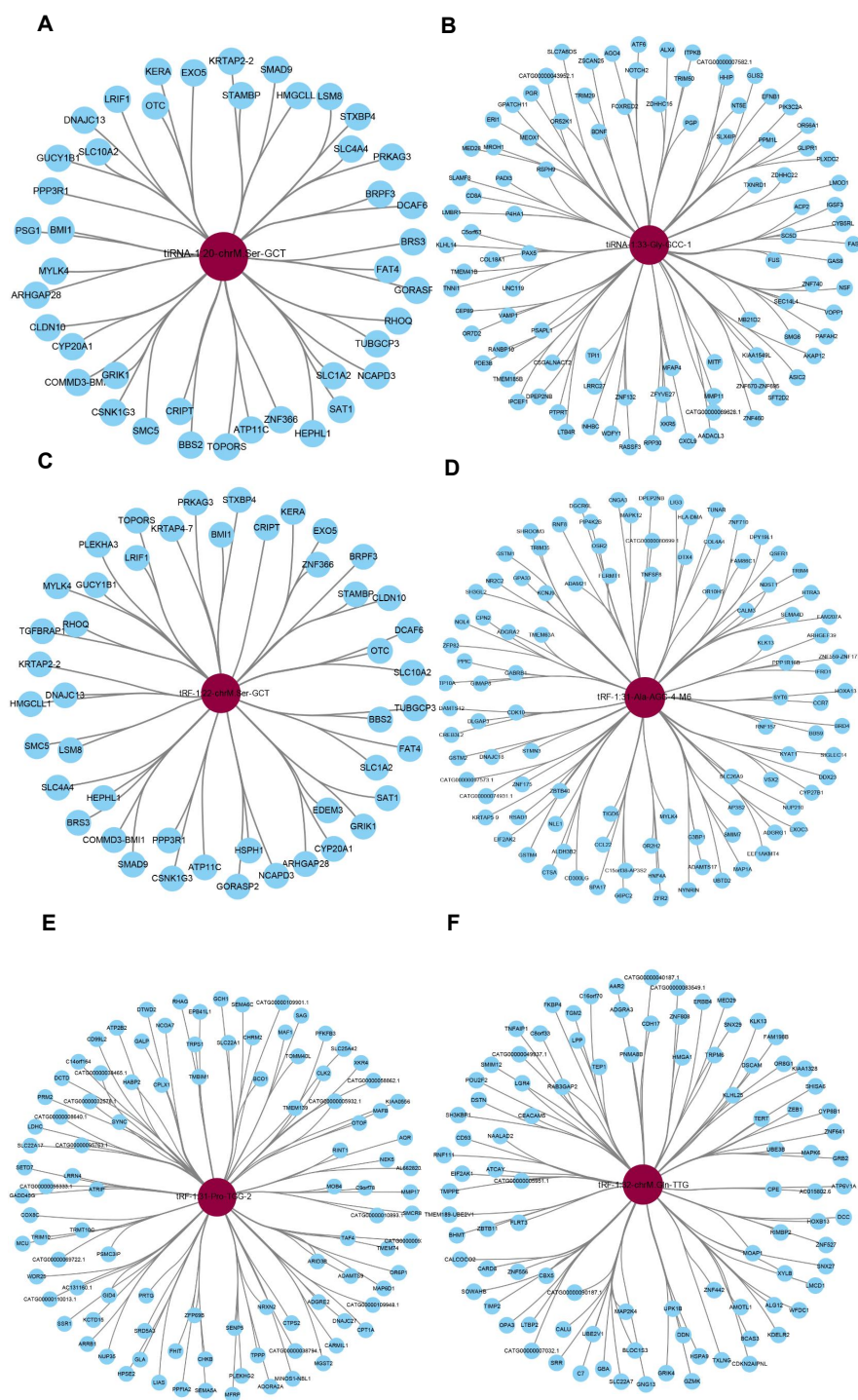
0.MS0607.docx available at <https://authorea.com/users/627089/articles/648167-tirna-gly-gcc-001-in-major-depressive-disorder-promising-diagnostic-and-therapeutic-biomarker>

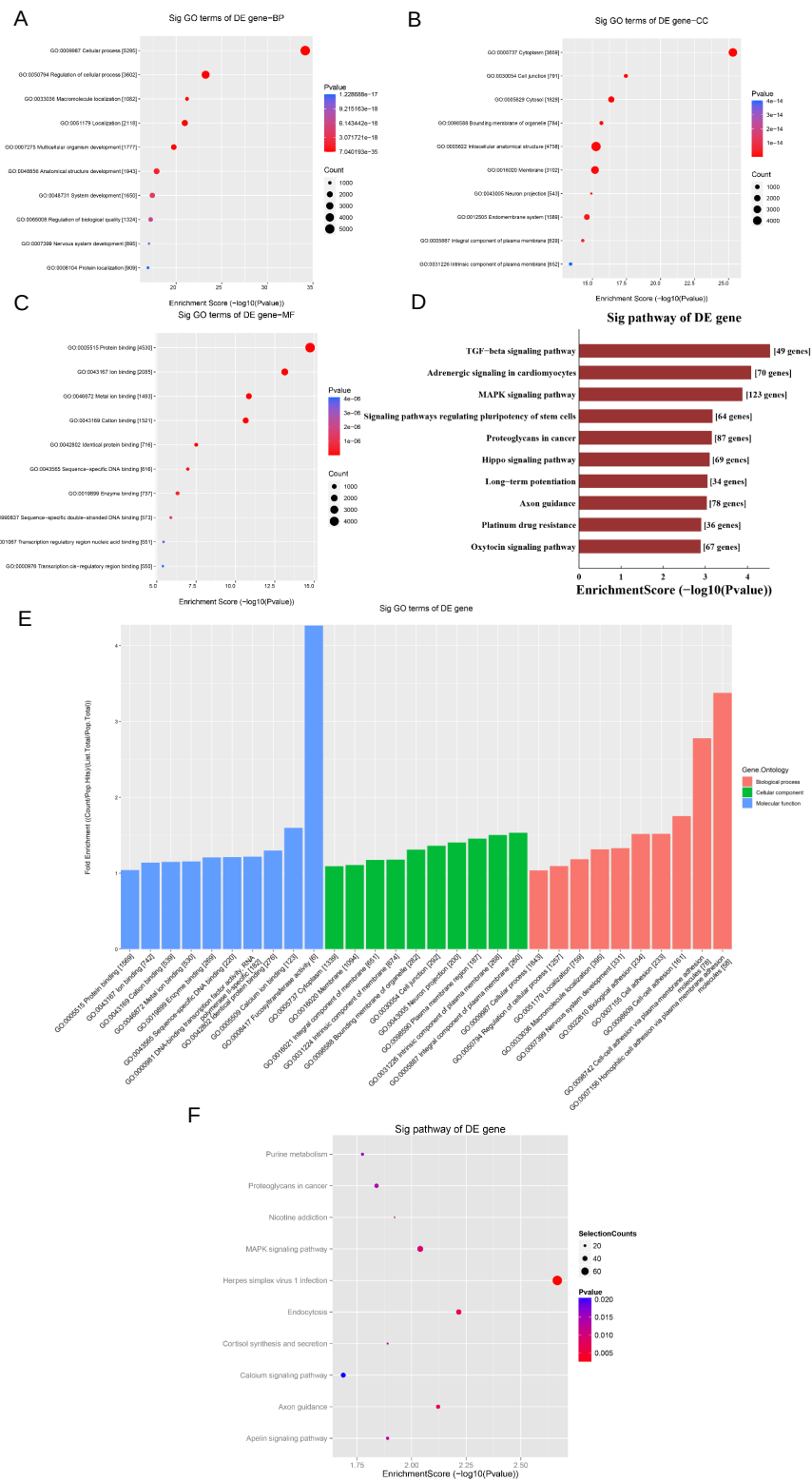


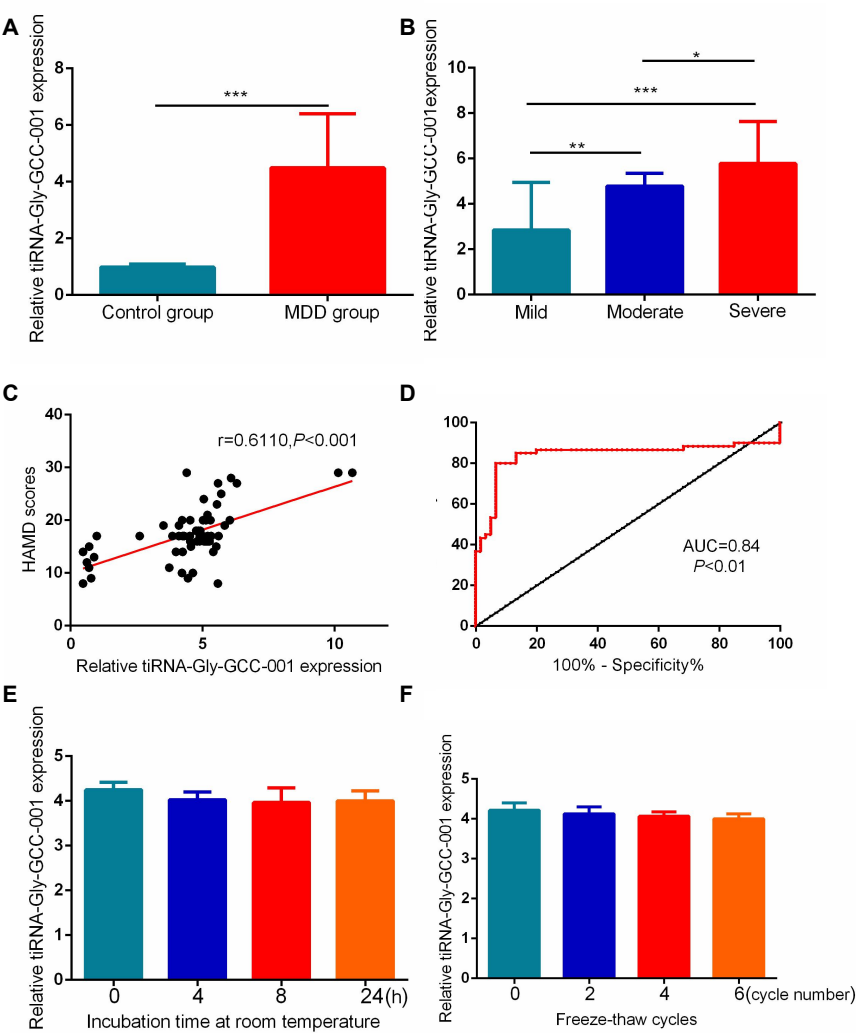


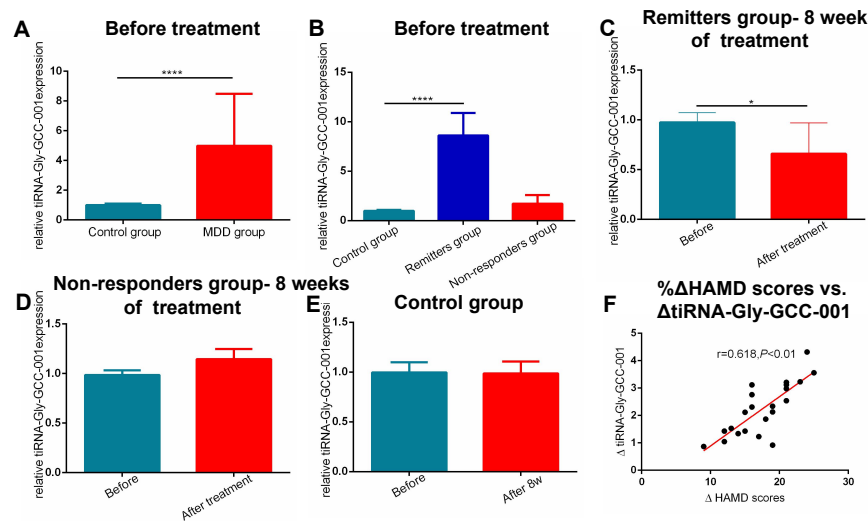












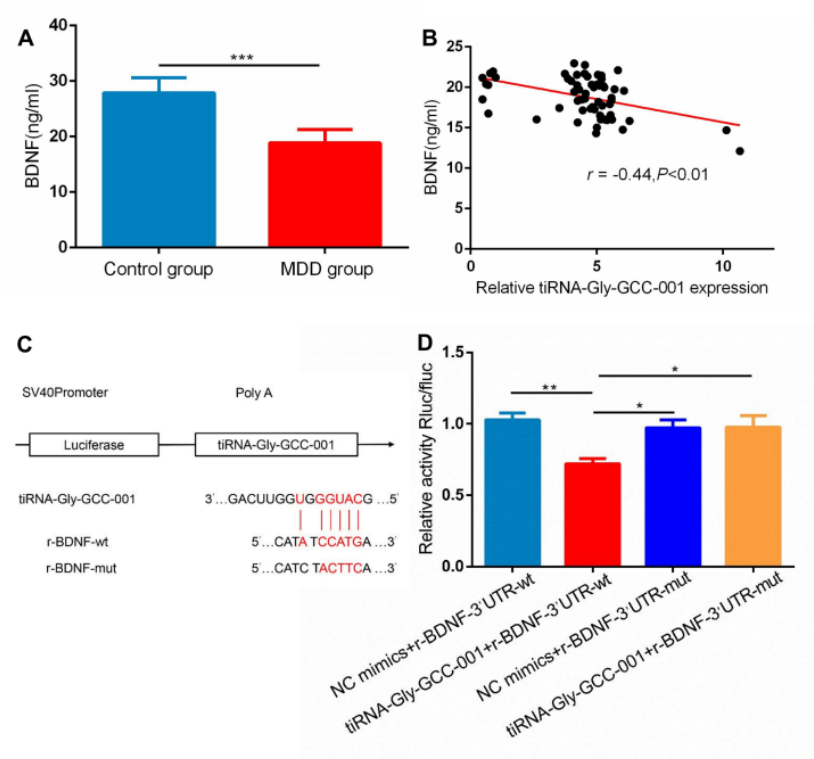


Table 1. Statistics of clinical information of testing group specimens.

	MDD(N=90)	HC(N=90)	<i>t</i> or χ^2 value	<i>P</i> value
Sex(male/female)	36/54	44/46	1.440	0.230
Age	32.34±12.34	33.43±12.98	0.577	0.564
BMI (kg/m ²)	23.12±3.14	22.87±3.34	0.517	0.606
Smoking	18/72	20/70	0.133	0.715
history(smoker/nonsmoker)				
Education level(≥high school/< high school)	43/47	49/41	0.800	0.371
Job	42/48	51/39	1.802	0.180
category(intellectual/manual)				
Diet(vegetarian/non-vegetarian)	3/87	5/85	0.523	0.470
Patients				
With familial history	22			
Without familial history	68			
Idea of suicide	18/72	0/90		<0.0001
Urban	54	62	1.552	0.213
Rural	36	28		
HAMD score	13.76±4.34	5.87±1.69	16.07	<0.0001

Data are shown as the absolute numbers or mean ± standard deviation. Education was categorized into elementary, middle, high school, and college. MDD, major depressive disorder; HC, healthy controls; HAMD, Hamilton Depression Scale. *P*<0.05 indicates statistical significance.

Table 2 Top 10 upregulated and downregulated tsRNAs in patients with MDD

tsRNA-ID	Sequence	Type	Length, bp	Regulation	Fold change
trf-1:31-Gly-CCC-2	GC GCCGCTGGTGTAGTGGTATCATGCAAGAT	trf-5c	31	up	139.378
trf-1:22-chrM.Ser-GCT	GAGAAAGCTCAAGAAGTCTGCT	trf-5b	22	up	110.072
trf-1:32-Phe-TGG-2	GGCTCCTTGGTCTAGGGGTATGATTCTCGGT	trf-5c	31	up	88.264
trf-1:32-chrM.Gln-TTG	TAGATGGGGTGTAGTGGTGGCAGGAGAAAT	trf-5c	32	up	88.230
tiRNA-1:33-Gly-GCC-1	GCATGGGTGTTCACTGGTAGAATTCTCGCCTG	tiRNA-5	33	up	87.158
trf-1:28-Lys-TTT-3-M2	GCCCGATAGCTCAGTCGGTAGAGCATC	trf-5c	28	up	86.145
trf-1:30-Phe-TGG-2	GGCTCCTTGGTCTAGGGGTATGATTCTCGG	trf-5c	30	up	81.628
trf-1:31-Ala-AGC-4-M6	GGGGATGTAGCTCAGTGGTAGAGCGCATGCT	trf-5c	31	up	78.921
tiRNA-1:20-chrM.Ser-GCT	GAGAAAGCTCAAGAAGTCTGCT	tiRNA-5	20	up	73.973
trf-69:86-Leu-TAA-1	ACCCCACTCCTGGTACCA	trf-3a	18	up	73.681
trf-1:24-Gly-GCC-1	GCATGGGTGGTTCAGTGGTAGAAT	trf-5b	24	up	50.501
trf-1:19-Ala-CGC-2	AGGCGATCACGTAGATTTT	trf-1	19	down	0.007
trf-1:23-His-GTG-1	GCCGTGATCGATAGTGGTTAGT	trf-5b	23	down	0.010
trf-1:15-Gly-TCC-1	TGCGGTACCACTTTT	trf-1	15	down	0.012
trf-1:17-Ser-GCT-4-2	ATGTGGTGGCTTACTTT	trf-1	17	down	0.012

bp = base pair, MDD = major depressive disorder, tiRNA = tRNA halve, trf = tRNA-related fragment, tsRNAs = transfer RNA-derived small RNAs.