**Plasma microRNA array analysis identifies overexpressed miR-19b-3p as a biomarker of bipolar depression distinguishing from unipolar depression**

*Yu Chena, Jiabo Shia, Haiyan Liua, Qiang Wange, Xiangxiang Chena, Hao Tanga, Rui Yana, Qing Lub,c\* , Zhijian Yaoa,d\**

Supplemental data 1. Amplification primer

|  |  |
| --- | --- |
| **Name** | **Sequence** |
| **U6-F** | CTCGCTTCGGCAGCACA |
| **U6-R** | AACGCTTCACGAATTTGCGT |
| **hsa-miR-3921-F** | GCGCGTCTCTGAGTACCATATG |
| **hsa-miR-3921-RT** | GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGACACAAGG |
| **hsa-miR-1180-3p-F** | TTTCCGGCTCGCGTGG  |
| **hsa-miR-1180-3p-RT** | GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGACACACAC |
| **hsa-miR-19b-3p-F** | CGTGTGCAAATCCATGCAA  |
| **hsa-miR-19b-3p-RT** | GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGACTCAGTT |
| **Reverse Primer** | AGTGCAGGGTCCGAGGTATT |

Supplementary data 2.

**Demographic and clinical characteristics of the subjects for miRNA array screening**

|  |  |  |
| --- | --- | --- |
| **variables** | **The subjects for miRNA profiling screening** |  **Significance** |
| **UD(n=7)****Mean (SD)** | **BD(n=7)****Mean (SD)** | **HC(n=6)****Mean (SD)** |  ***p*(two groups)** | ***p*(three groups)** |
| **Age (years)** | 37.57±6.90 | 33.57±8.87 | 37.50±5.99 | 0.365 | 0.535 |
| **Female** | 3 (42.9%) | 3 (42.9%) | 3 (50.0%) | 1.000 | 0.958 |
| **Male** | 4 (57.1%) | 4 (57.1%) | 3 (50.0%) |  |  |
| **Education (years)** | 14.71±2.56 | 14.00±1.92 | 13.00±1.55 | 0.957 | 0.355 |
| **Duration of illness (months)** | 16.57±15.92 | 52.00±58.70 |  | 0.149 |  |
| **Total score of HAM-D24** | 33.29±4.96 | 28.00±6.11 |  | 0.101 |  |
| **Subscore of HAM-D24** |
| Anxiety/somatization | 9.43±2.94 | 5.71±2.75 |  | 0.031\* |  |
| Cognitive disturbance | 4.29±2.22 | 4.29±2.14 |  | 1.000 |  |
| Retardation | 8.86±1.07 | 7.71±1.98 |  | 0.203 |  |
| Hopelessness | 5.57±1.51 | 5.29±1.80 |  | 0.753 |  |
| Sleep disturbance | 3.57±1.40 | 4.00±1.41 |  | 0.579 |  |
| Weight loss | 0.14±0.38 | 0.43±0.79 |  | 0.064 |  |
| Circadian fluctuation | 0.33±0.61 | 0.26±0.51 |  | 0.403 |  |
| **Total score of CTQ** | 47.14±11.19 | 56.00±17.72 |  | 0.285 |  |
| **Subscore of CTQ** |
| Emotional abuse | 8.00±4.76 | 11.86±7.11 |  | 0.256 |  |
| Physical abuse | 5.57±1.13 | 7.71±3.73 |  | 0.171 |  |
| Sexual abuse | 5.57±1.13 | 5.00±0.00 |  | 0.207 |  |
| Emotional neglect | 12.00±5.26 | 14.00±6.58 |  | 0.542 |  |
| Physical neglect | 8.71±4.19 | 10.86±5.52 |  | 0.429 |  |

UD: unipolar depression; BD: bipolar depression; HC: healthy controls; \*p<0.05.

Supplementary data 3

 **Differential expression of miRNAs between healthy groups and patients with unipolar depression and bipolar depression**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| miRNA |  UD (FC) |  BD (FC) |  HC (FC) |  *p* | Style |
| hsa-miR-1180-3p | 1.793  | 2.489  | 1.053  | 0.000  | up |
| hsa-miR-1281 | 5.531  | 5.088  | 4.187  | 0.200  | up |
| hsa-miR-1298-3p | 2.990  | 1.779  | 0.909  | 0.282  | up |
| hsa-miR-297 | 1.948  | 2.342  | 0.911  | 0.042  | up |
| hsa-miR-3148 | 1.407  | 1.640  | 0.748  | 0.041  | up |
| hsa-miR-337-3p | 2.760  | 2.272  | 1.029  | 0.011  | up |
| hsa-miR-3619-5p | 4.004  | 2.562  | 2.207  | 0.667  | up |
| hsa-miR-378h | 4.576  | 3.525  | 2.273  | 0.105  | up |
| hsa-miR-3910 | 2.030  | 1.473  | 0.678  | 0.134  | up |
| hsa-miR-3921 | 5.110  | 4.136  | 2.427  | 0.035  | up |
| hsa-miR-4706 | 4.618  | 3.520  | 2.692  | 0.249  | up |
| hsa-miR-5094 | 1.820  | 1.450  | 0.793  | 0.187  | up |
| hsa-miR-548aa | 1.433  | 1.199  | 0.746  | 0.131  | up |
| hsa-miR-548ap-3p | 1.559  | 1.274  | 0.765  | 0.179  | up |
| hsa-miR-548t-3p | 1.432  | 1.197  | 0.745  | 0.132  | up |
| hsa-miR-570-3p | 1.399  | 0.896  | 0.572  | 0.392  | up |
| hsa-miR-628-5p | 2.377  | 1.641  | 0.927  | 0.205  | up |
| hsa-miR-6511b-5p | 3.972  | 2.936  | 1.976  | 0.129  | up |
| hsa-miR-668-5p | 3.553  | 2.552  | 2.189  | 0.531  | up |
| hsa-miR-6732-5p | 8.281  | 7.494  | 7.145  | 0.427  | up |
| hsa-miR-6750-5p | 3.960  | 3.040  | 2.151  | 0.170  | up |
| hsa-miR-6794-5p | 4.983  | 4.438  | 3.920  | 0.184  | up |
| hsa-miR-6800-3p | 4.125  | 3.584  | 2.642  | 0.146  | up |
| hsa-miR-8075 | 7.500  | 6.679  | 6.158  | 0.363  | up |
| hsa-miR-877-5p | 3.602  | 2.833  | 2.219  | 0.267  | up |
| hsa-miR-106a-5p | 2.561  | 5.773  | 5.713  | 0.844  | down |
| hsa-miR-106b-5p | 1.208  | 2.920  | 4.084  | 0.294  | down |
| hsa-miR-130b-3p | 2.028  | 2.325  | 3.098  | 0.171  | down |
| hsa-miR-140-3p | 2.664  | 4.110  | 5.221  | 0.238  | down |
| hsa-miR-150-5p | 1.320  | 4.119  | 4.007  | 0.784  | down |
| hsa-miR-16-5p | 3.603  | 7.757  | 7.517  | 0.750  | down |
| hsa-miR-181a-5p | 1.643  | 3.574  | 4.639  | 0.343  | down |
| hsa-miR-19b-3p | 3.501  | 4.259  | 6.272  | 0.019  | down |
| hsa-miR-22-3p | 2.953  | 4.030  | 6.345  | 0.051  | down |
| hsa-miR-378a-3p | 1.582  | 2.553  | 3.719  | 0.114  | down |
| hsa-miR-378c | 0.665  | 1.129  | 1.671  | 0.085  | down |
| hsa-miR-3937 | 1.409  | 1.274  | 2.146  | 0.042  | down |
| hsa-miR-423-3p | 0.896  | 2.246  | 2.694  | 0.536  | down |
| hsa-miR-425-5p | 1.646  | 5.059  | 5.358  | 0.931  | down |
| hsa-miR-6813-5p | 1.264  | 1.043  | 1.965  | 0.024  | down |
| hsa-miR-7641 | 0.992  | 1.967  | 3.611  | 0.115  | down |
| hsa-miR-93-5p | 2.653  | 6.362  | 6.494  | 0.954  | down |

UD: unipolar depression; BD: bipolar depression; HC: healthy controls; FC: fold change;style: up: overexpression; style: down: downexpression.

Supplemental data 4.  **The 288 predicted target mRNAs of has-miR-19b-3p:**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| NR3C2BACE1PTENATXN1HIPK3ARID4BMYLIPESR1NCOA3KAT2BSOCS1BCL2L11TGFBR2CUL5TLR2PRKAA1PPP2R5EZMYND11RPS4Y1PRRG4LCLAT1SKILBAMBISLC38A2DEF8RNF167BCL3EVI5LSLC6A8KCNJ2ASNA1MB21D1PTPRBTNFRSF10BZNF800YY1 | MCCJAZF1HNRNPFGNPTABFRS2DYNC1LI2DEPDC1DBN1CFL2GDNFARL8AAGO3ZNF680ZNF107PABPC4LC15orf38-AP3S2CLVS2CCDC80ZNF544ZDHHC7RACGAP1FGFR1OPHOMER1ODF4MBD3MTX3PTCD2ETV3C6orf132DIP2AMTHFD1UBL3KIAA0907TMEM2KITLGFKBP15 | PHLDA3NRBF2MAPK1CAMSAP2ZNF154SLC46A1UBE2D3SESN3SATB1NUP54LZICBEND3PALM2-AKAP2AKAP2USP8RANPPTC7PFN2MRPL17DCCZNF134VPS37BRBM20GRB10DDX3XRRAGDCEP170MALT1HADHBTMEM64SLC12A7PFN1DGKHCLOCKADSSZNF367 | MTMR12MKL2MEF2AMCM3AP-AS1MBD4MAP3K14LOC613266LIN9KLHL3KIF3ACCSER2ATG14INO80HNRNPUHIC1HECW2HDAC4GRSF1GPAMGAKFOXP1FBXO48FBXO10MIGA1DENND6AFAM102AEXOC7EPS15EPN2EIF4E2EHD1DUTDSCR3CITCBX7CBX5 | WNT7BTHBS1TGOLN2STX6SGK1RHOBPPP6R1NACC1MTMR6MAP3K9KLHL11KIF13AIMPDH1P11FBLIM1EOGTELL2DLG5CD164CCNA2CAPRIN2ANKRD50ACTBABHD14BYTHDF1ZFYVE26FOXQ1DICER1ARPP19WDR45BSLC48A1MMGT1BRWD3NICN1PTBP2ZMAT3TRIM37 | TMTC1XIAPWNT10AWDR1VAMP1TRAK2TP53INP1TNPO2TNIP1TNFAIP3TFB1MSTK4SOCS3SNX17SLC9A6SLC25A12SH3KBP1SERBP1SEPHS2SEL1LSEC63SBF2S1PR2RNF216RGL1RAPGEF6RAF1RAB2BPIK3R3PIGSPGM2L1PGK1PCDH10PRKNOTUD7BNAPB | TNFRSF11ATMEM117RPF2NDRG1MFFSTOX2SNX5RLIMSFTPA1MBNL3GIGYF1GFPT1DCUN1D3CREBRFCERCAMCHEK2CASZ1BMP3ARCACSL4ACBD5ZNF138MAVSRBM38TMEM138DAD1WNK3WASLUBE2ATXLNGSOX6RAP1APURGPRICKLE2MPRIPMECP2 | IDNKC2orf42PRR14LSDE2ARPINSPTSSAGSKIPBTBD7BRD9BCL7BB4GALT1AZIN1ATXN7ATPAF1ATG5ATG2BARMC8ARAP2ANGEL2AHDC1PTENP1PKNOX1MTUS1PITX1CSNK2A1DCBLD2EREGPHLDA1PKMB3GALNT2DSELIFITM1TPRG1LZNF423RPAP2ZNF618 |