Supplemental tables and figures for the manuscript:

Characterization of upregulated adhesion GPCRs in Acute Myeloid Leukemia

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Table S1. The frequencies of patients with upregulated and downregulated aGPCR genes in TCGA-AML dataset

Genes	Number of patients with gene upregulation	Number of patients with gene downregulation
ADGRB1	23	0
CELSR2	19	0
ADGRD1	16	0
ADGRE1	21	0
ADGRE2	28	25
ADGRE5	22	10
ADGRG1	20	0
ADGRG3	23	0
ADGRA1	4	0
ADGRA2	27	0
ADGRA3	22	27
ADGRB2	15	0
ADGRB3	9	0
CELSR1	20	0
CELSR3	15	0
ADGRD2	13	0
ADGRE3	14	0
ADGRE4P	12	0
ADGRF1	5	0
ADGRF2	1	0
ADGRF3	20	18
ADGRF4	3	0
ADGRF5	15	0
ADGRG2	20	11
ADGRG4	15	0
ADGRG5	25	32
ADGRG6	7	0
ADGRG7	2	0
ADGRL1	16	0
ADGRL2	15	0
ADGRL3	13	0
ADGRL4	14	0
ADGRV1	6	0

Table S2a. Expression of *BAI1(ADGRB1)* (Z-score≥1) according to the top mutations present in AML (N=173 patients)

Genes	Z-score(<1) (n=150)		Z-score(≥1） (n=23)		p value
FLT3(n, %)	40	26.7%	9	39.1%	0.223
TP53(n, %)	5	3.3%	9	39.1%	<0.001
WT1(n, %)	10	6.7%	0	0.0%	0.362
IDH1(n, %)	14	9.3%	2	8.7%	>0.999
IDH2(n, %)	17	11.3%	0	0.0%	0.133
CEBPA(n, %)	12	8.0%	1	4.3%	>0.999
RUNX1(n, %)	15	10.0%	0	0.0%	0.225
NRAS(n, %)	10	6.7%	2	8.7%	0.663
TET2(n, %)	11	7.3%	4	17.4%	0.119
NPM1(n, %)	40	26.7%	8	34.8%	0.456
DNMT3A(n, %)	34	22.7%	8	34.8%	0.204

Table S2b. Expression of *CELSR2(ADGRC1)* (Z-score≥1) according to the top mutations present in AML (N=173 patients)

Genes	Z-score(<1) (n=152)		Z-score(≥1） (n=21)		p value
FLT3(n, %)	45	29.6%	4	19.0%	0.440
TP53(n, %)	13	8.6%	1	4.8%	>0.999
WT1(n, %)	9	5.9%	1	4.8%	>0.999
IDH1(n, %)	16	10.5%	0	0.0%	0.224
IDH2(n, %)	15	9.9%	2	9.5%	>0.999
CEBPA(n, %)	13	8.6%	0	0.0%	0.372
RUNX1(n, %)	13	8.6%	2	9.5%	>0.999
NRAS(n, %)	12	7.9%	0	0.0%	0.365
TET2(n, %)	14	9.2%	1	4.8%	0.698
NPM1(n, %)	42	27.6%	6	28.6%	>0.999
DNMT3A(n, %)	37	24.3%	5	23.8%	>0.999

Table S2c. Expression of *GPR133 (ADGRD1)* (Z-score≥1) according to the top mutations present in AML (N=173 patients)

Genes	Z-score(<1) (n=156)		Z-score(≥1） (n=17)		p value
FLT3(n, %)	46	29.5%	3	17.6%	0.402
TP53(n, %)	10	6.4%	4	23.5%	0.035
WT1(n, %)	10	6.4%	0	0.0%	0.601
IDH1(n, %)	16	10.3%	0	0.0%	0.373
IDH2(n, %)	14	9.0%	3	17.6%	0.224
CEBPA(n, %)	11	7.1%	2	11.8%	0.620
RUNX1(n, %)	13	8.3%	2	11.8%	0.645
NRAS(n, %)	9	5.8%	3	17.6%	0.099
TET2(n, %)	15	9.6%	0	0.0%	0.367
NPM1(n, %)	46	29.5%	2	11.8%	0.158
DNMT3A(n, %)	38	24.4%	4	23.5%	>0.999

Table 2d. Expression of *CD97 (ADGRE5)* (Z-score≥1) according to the top mutations present in AML (N=173 patients)

Genes	Z-score(<1) (n=147)		Z-score(≥1） (n=26)		p value
FLT3(n, %)	38	25.9%	11	42.3%	0.101
TP53(n, %)	13	8.8%	1	3.8%	0.697
WT1(n, %)	10	6.8%	0	0.0%	0.362
IDH1(n, %)	15	10.2%	1	3.8%	0.472
IDH2(n, %)	14	9.5%	3	11.5%	0.724
CEBPA(n, %)	12	8.2%	1	3.8%	0.694
RUNX1(n, %)	15	10.2%	0	0.0%	0.131
NRAS(n, %)	10	6.8%	2	7.7%	>0.999
TET2(n, %)	15	10.2%	0	0.0%	0.131
NPM1(n, %)	34	23.1%	14	53.8%	0.003
DNMT3A(n, %)	33	22.4%	9	34.6%	0.215

Table 2e. Expression of *EMR1(ADGRE1)* (Z-score≥1) according to the top mutations present in AML(N=173 patients)

Genes	Z-score(<1)		Z-score(≥1）		p value
	(n=151)		(n=22)		
FLT3(n, %)	41	27.2%	8	36.4%	0.448
TP53(n, %)	14	9.3%	0	0.0%	0.221
WT1(n, %)	10	6.6%	0	0.0%	0.365
IDH1(n, %)	14	9.3%	2	9.1%	>0.999
IDH2(n, %)	12	7.9%	5	22.7%	0.046
CEBPA(n, %)	13	8.6%	0	0.0%	0.378
RUNX1(n, %)	14	9.3%	1	4.5%	0.696
NRAS(n, %)	11	7.3%	1	4.5%	>0.999
TET2(n, %)	14	9.3%	1	4.5%	0.696
NPM1(n, %)	34	22.5%	14	63.6%	<0.001
DNMT3A(n, %)	34	22.5%	8	36.4%	0.184

Table 2f. Expression of *EMR2(ADGRE2)* (Z-score≥1) according to the top mutations present in AML(N=173 patients)

Genes	Z-score(<1)		Z-score(≥1）		p value
	(n=142)		(n=31)		
FLT3(n, %)	40	28.2%	9	29.0%	>0.999
TP53(n, %)	12	8.5%	2	6.5%	>0.999
WT1(n, %)	9	6.3%	1	3.2%	0.693
IDH1(n, %)	13	9.2%	3	9.7%	>0.999
IDH2(n, %)	11	7.7%	6	19.4%	0.087
CEBPA(n, %)	12	8.5%	1	3.2%	0.468
RUNX1(n, %)	12	8.5%	3	9.7%	0.734
NRAS(n, %)	10	7.0%	2	6.5%	>0.999
TET2(n, %)	14	9.9%	1	3.2%	0.313
NPM1(n, %)	35	24.6%	13	41.9%	0.075
DNMT3A(n, %)	31	21.8%	11	35.5%	0.113

Table 2g. Expression of *GPR56 (ADGRG1)* (Z-score≥1) according to the top mutations present in AML (N=173 patients)

Genes	Z-score(<1) (n=147)		Z-score(≥1） (n=26)		p value
FLT3(n, %)	39	26.5%	10	38.5%	0.075
TP53(n, %)	10	6.8%	4	15.4%	0.083
WT1(n, %)	9	6.1%	1	3.8%	1
IDH1(n, %)	15	10.2%	1	3.8%	0.697
IDH2(n, %)	16	10.9%	1	3.8%	0.7
CEBPA(n, %)	12	8.2%	1	3.8%	1
RUNX1(n, %)	13	8.8%	2	7.7%	1
NRAS(n, %)	11	7.5%	1	3.8%	1
TET2(n, %)	12	8.2%	3	11.5%	0.411
NPM1(n, %)	39	26.5%	9	34.6%	0.2
DNMT3A(n, %)	35	23.8%	7	26.9%	0.426

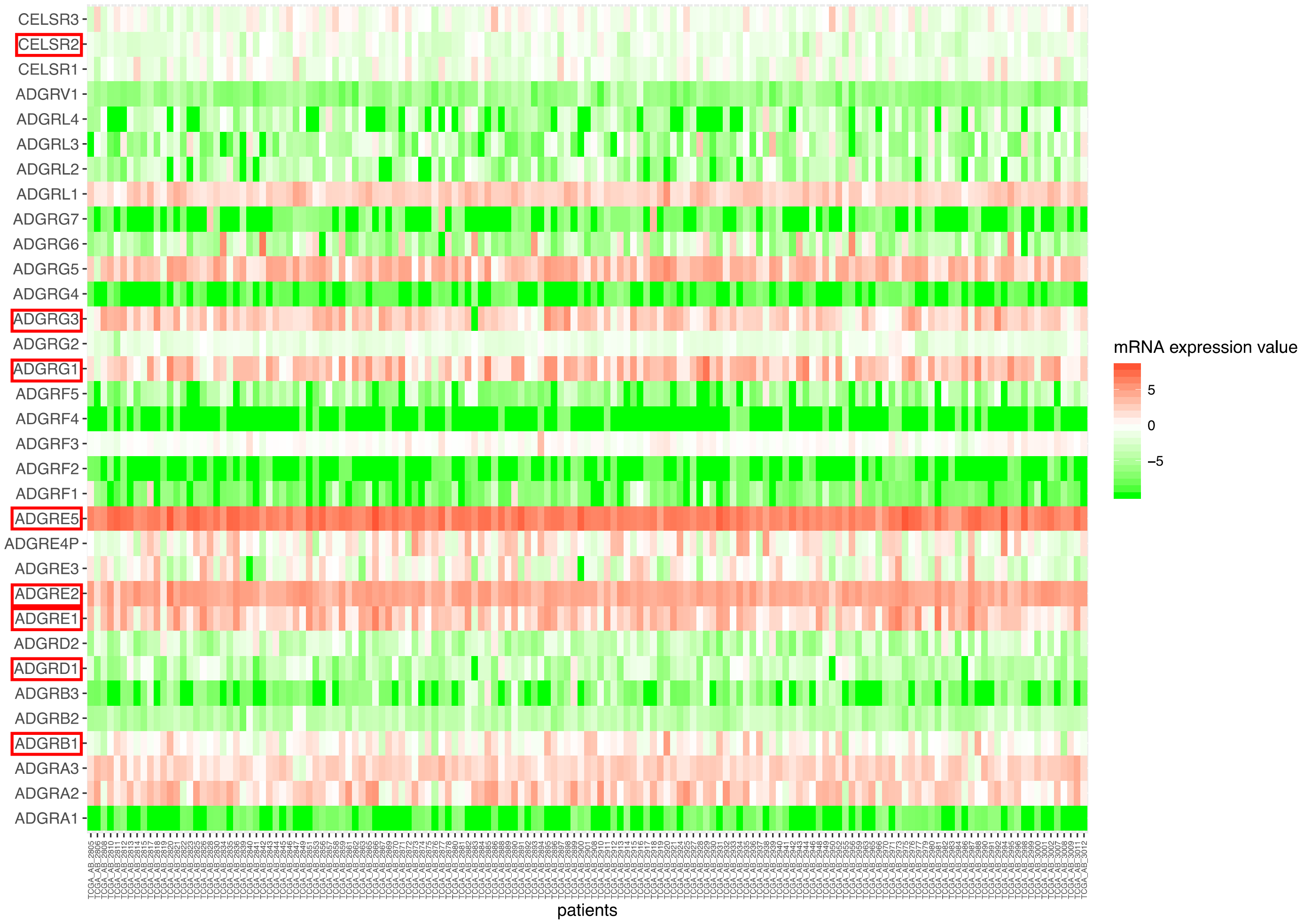
Table 2h. Expression of *GPR97 (ADGRG3)* (Z-score≥1) according to the top mutations present in AML (N=173 patients)

Genes	Z-score(<1) (n=150)		Z-score(≥1） (n=23)		p value
FLT3(n, %)	38	25.3%	11	47.8%	0.044
TP53(n, %)	11	7.3%	3	13.0%	0.404
WT1(n, %)	8	5.3%	2	8.7%	0.624
IDH1(n, %)	13	8.7%	3	13.0%	0.451
IDH2(n, %)	15	10.0%	2	8.7%	1
CEBPA(n, %)	12	8.0%	1	4.3%	1
RUNX1(n, %)	14	9.3%	1	4.3%	0.696
NRAS(n, %)	10	6.7%	2	8.7%	0.663
TET2(n, %)	15	10.0%	0	0.0%	0.225
NPM1(n, %)	37	24.7%	11	47.8%	0.026
DNMT3A(n, %)	34	22.7%	8	34.8%	0.204

Table S3. Ingenuity pathway analysis of differentially expressed adhesion GPCR genes.

Ingenuity Canonical Pathways	-log(p-value)	Ratio	z-score
EIF2 Signaling	**1.48E+01**	**3.48E-01**	**-2.828**
Regulation of eIF4 and p70S6K Signaling	8.96E+00	3.25E-01	0.209
Hereditary Breast Cancer Signaling	8.91E+00	3.33E-01	NaN
Salvage Pathways of Pyrimidine Ribonucleotides	6.88E+00	3.51E-01	1.372
mTOR Signaling	6.69E+00	2.75E-01	0
Role of BRCA1 in DNA Damage Response	6.31E+00	3.62E-01	-1.5
FcŒ≥ Receptor-mediated Phagocytosis in Macrophages and Monocytes	**6.30E+00**	**3.44E-01**	**3.182**
Huntington's Disease Signaling	6.18E+00	2.56E-01	0.392
IL-8 Signaling	**5.87E+00**	**2.66E-01**	**3.286**
ATM Signaling	5.73E+00	3.27E-01	-1.177
Telomerase Signaling	5.67E+00	3.08E-01	0.577
Pyridoxal 5'-phosphate Salvage Pathway	5.50E+00	3.69E-01	2.041
Integrin Signaling	**5.48E+00**	**2.56E-01**	**3.501**
Apoptosis Signaling	5.46E+00	3.23E-01	1.095
PI3K/AKT Signaling	5.26E+00	2.90E-01	-0.164
Chronic Myeloid Leukemia Signaling	5.25E+00	3.04E-01	NaN
Cell Cycle: G1/S Checkpoint Regulation	5.23E+00	3.58E-01	-0.277
B Cell Receptor Signaling	**5.07E+00**	**2.58E-01**	**2.828**
NGF Signaling	**4.94E+00**	**2.88E-01**	**3.212**
DNA Double-Strand Break Repair by Homologous Recombination	4.69E+00	6.43E-01	NaN
Acute Myeloid Leukemia Signaling	4.69E+00	3.03E-01	1.732
p70S6K Signaling	4.69E+00	2.75E-01	1.333
Cell Cycle: G2/M DNA Damage Checkpoint Regulation	4.69E+00	3.80E-01	2
Molecular Mechanisms of Cancer	4.68E+00	2.16E-01	NaN
Cyclins and Cell Cycle Regulation	**4.63E+00**	**3.21E-01**	**-2.324**

a.


CELSR3
CELSR2
CELSR1
ADGRV1
ADGRL4
ADGRL3
ADGRL2
ADGRL1
ADGRG7
ADGRG6
ADGRG5
ADGRG4
ADGRG3
ADGRG2
ADGRG1
ADGRF5
ADGRF4
ADGRF3
ADGRF2
ADGRF1
ADGRE5
ADGRE4P
ADGRE3
ADGRE2
ADGRE1
ADGRD2
ADGRD1
ADGRB3
ADGRB2
ADGRB1
ADGRA3
ADGRA2
ADGRA1
patients
mRNA expression value
5
0
−5

b.

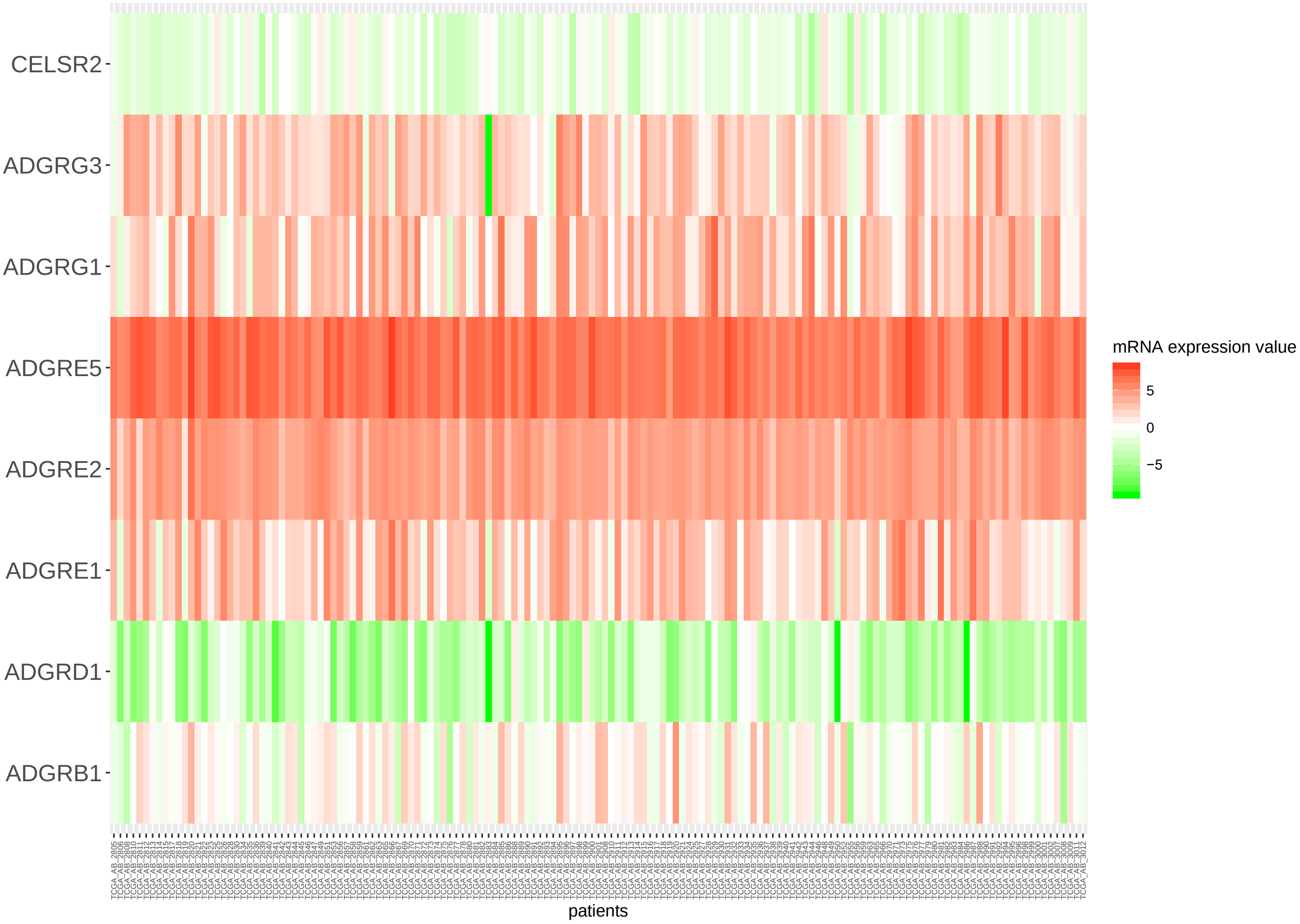
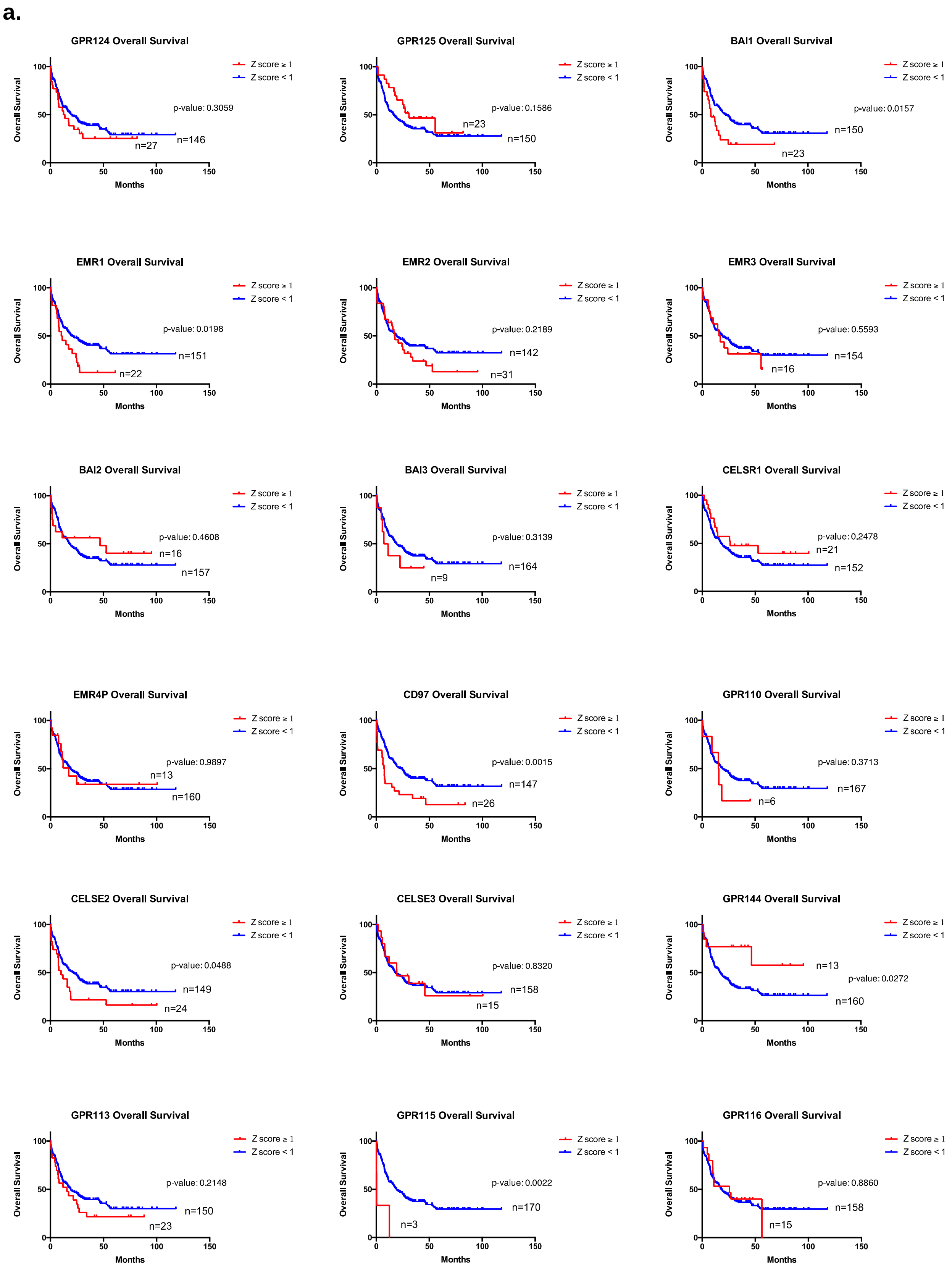
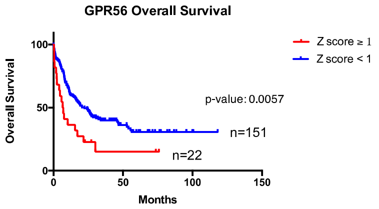
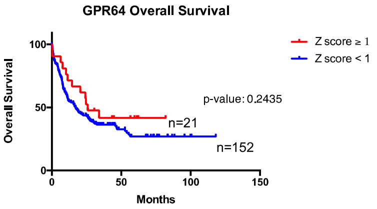
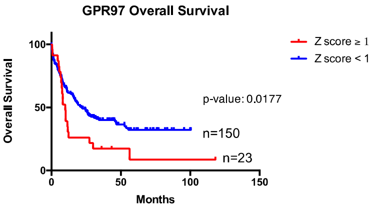


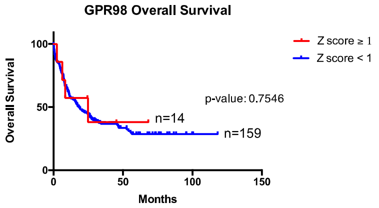
Figure S1. Heatmaps of the adhesion GPCR genes. a. Heatmap of the expression of the 33 aGPCR genes (obtained from TCGA-AML). The red rectangles indicate the eight aGPCRs found to be associated with worse clinical outcome. **b.** Heatmap of the eight aGPCR genes only (red represent high RNA expression, green represent low RNA expression).

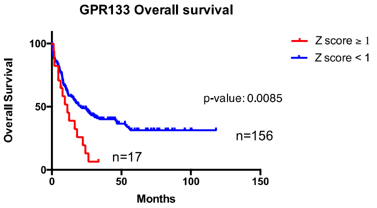

a.
GPR124 Overall Survival
p-value: 0.3059
n=27
n=146
GPR125 Overall Survival
p-value: 0.1586
n=23
n=150
BAI1 Overall Survival
p-value: 0.0157
n=150
n=23
EMR1 Overall Survival
p-value: 0.0198
n=151
n=22
EMR2 Overall Survival
p-value: 0.2189
n=142
n=31
EMR3 Overall Survival
p-value: 0.5593
n=154
n=16
BAI2 Overall Survival
p-value: 0.4608
n=16
n=157
BAI3 Overall Survival
p-value: 0.3139
n=164
n=9
CELSR1 Overall Survival
p-value: 0.2478
n=21
n=152
EMR4P Overall Survival
p-value: 0.9897
n=13
n=160
CD97 Overall Survival
p-value: 0.0015
n=147
n=26
GPR110 Overall Survival
p-value: 0.3713
n=167
n=6
CELSE2 Overall Survival
p-value: 0.0488
n=149
n=24
CELSE3 Overall Survival
p-value: 0.8320
n=158
n=15
GPR144 Overall Survival
n=13
p-value: 0.0272
n=160
GPR113 Overall Survival
p-value: 0.2148
n=150
n=23
GPR115 Overall Survival
p-value: 0.0022
n=170
n=3
GPR116 Overall Survival
p-value: 0.8860
n=158
n=15
Z score ≥ 1
Z score < 1
Overall Survival
Months
0
50
100
150

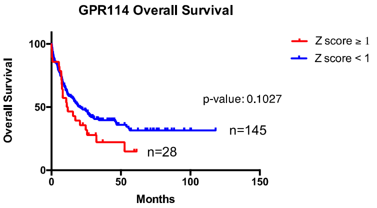

GPR56 Overall Survival

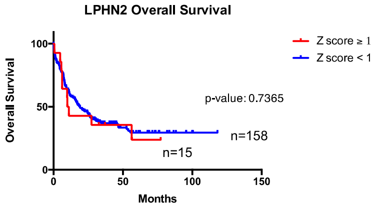

GPR64 Overall Survival

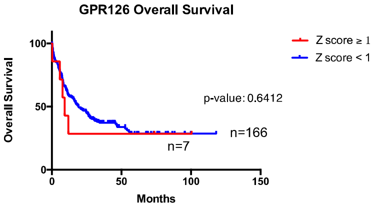

GPR97 Overall Survival

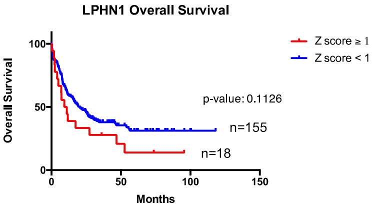

GPR98 Overall Survival

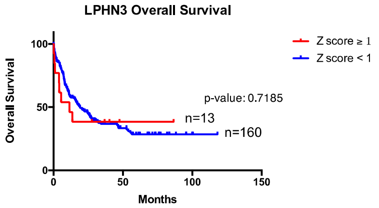

GPR133 Overall survival

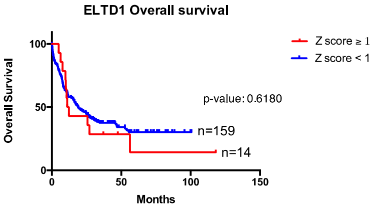

GPR114 Overall Survival


LPHN2 Overall Survival

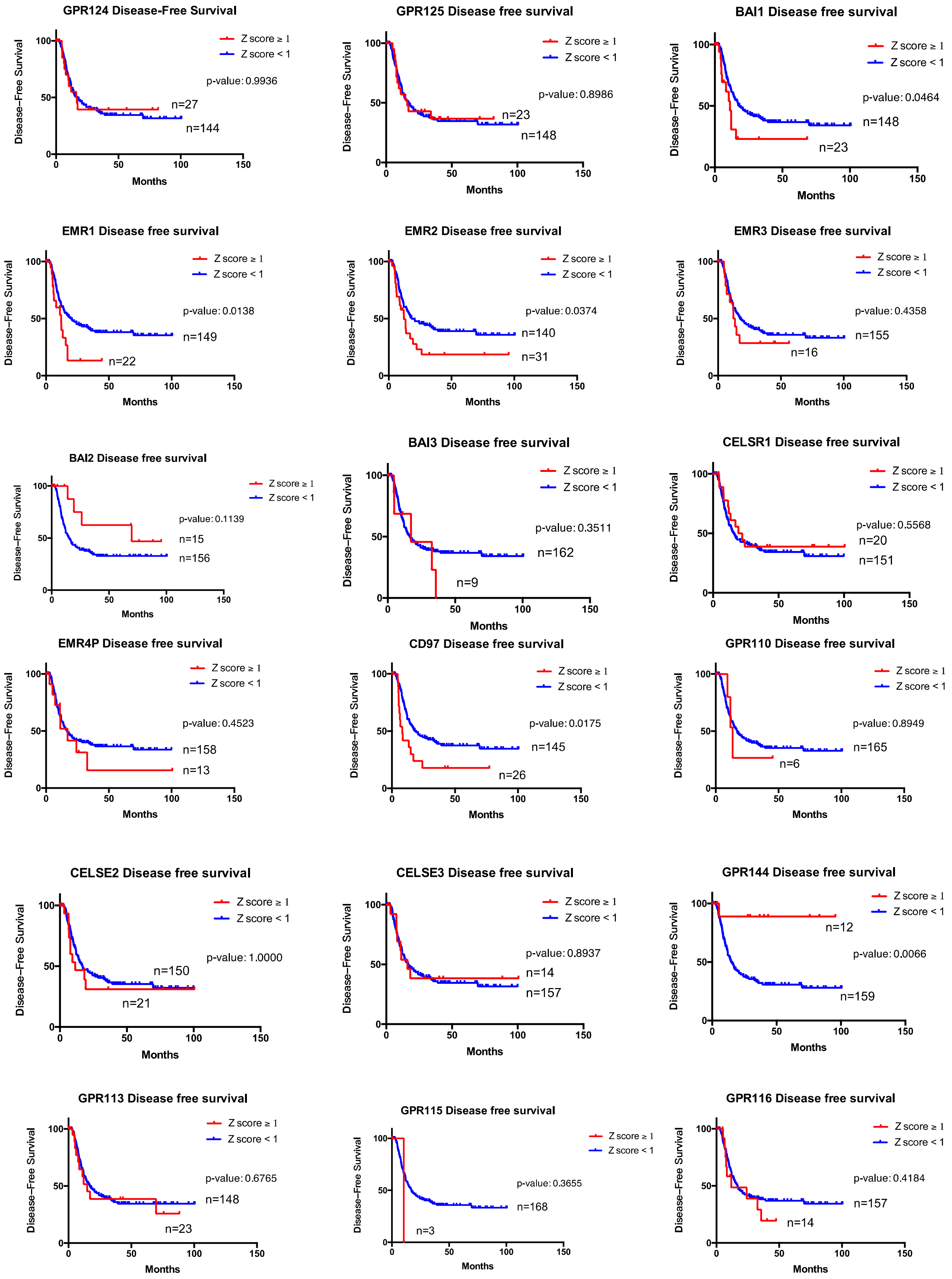

GPR126 Overall Survival


LPHN1 Overall Survival


LPHN3 Overall Survival


ELTD1 Overall survival

b.


GPR124 Disease-Free Survival
Disease-Free Survival
Months
Z score ≥ 1
Z score < 1
p-value: 0.9936
n=27
n=144
GPR125 Disease free survival
p-value: 0.8986
n=23
n=148
BAI1 Disease free survival
p-value: 0.0464
n=148
n=23
EMR1 Disease free survival
p-value: 0.0138
n=149
n=22
EMR2 Disease free survival
p-value: 0.0374
n=140
n=31
EMR3 Disease free survival
p-value: 0.4358
n=155
n=16
BAI2 Disease free survival
p-value: 0.1139
n=15
n=156
BAI3 Disease free survival
p-value: 0.3511
n=162
n=9
CELSR1 Disease free survival
p-value: 0.5568
n=20
n=151
EMR4P Disease free survival
p-value: 0.4523
n=158
n=13
CD97 Disease free survival
p-value: 0.0175
n=145
n=26
GPR110 Disease free survival
p-value: 0.8949
n=165
n=6
CELSE2 Disease free survival
p-value: 1.0000
n=150
n=21
CELSE3 Disease free survival
p-value: 0.8937
n=14
n=157
GPR144 Disease free survival
n=12
p-value: 0.0066
n=159
GPR113 Disease free survival
p-value: 0.6765
n=148
n=23
GPR115 Disease free survival
p-value: 0.3655
n=168
n=3
GPR116 Disease free survival
p-value: 0.4184
n=157
n=14
0
50
100
150

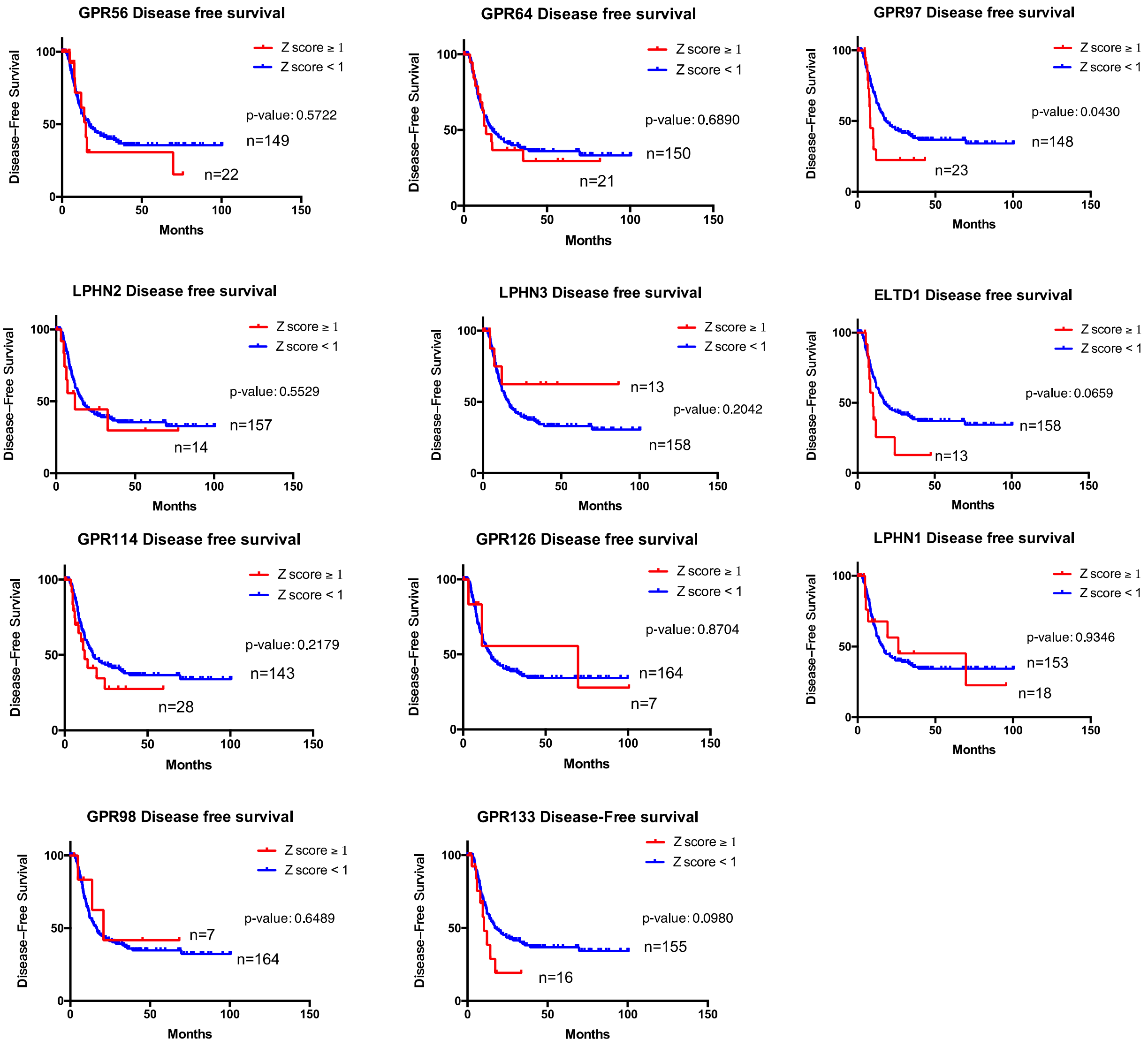
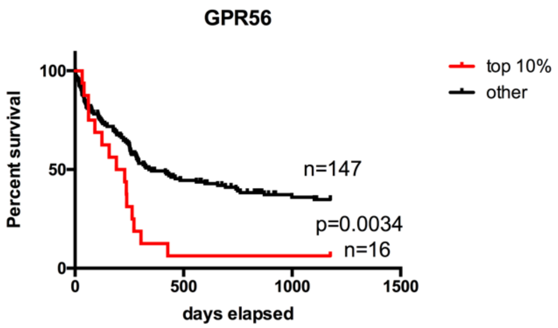
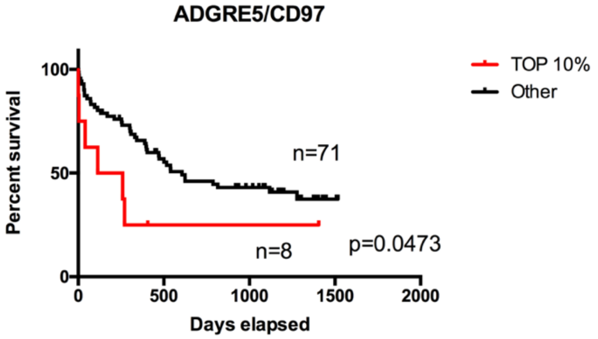


Figure S2. Survival analysis of AML patients associated with 29 adhesion GPCRs mRNA expression. a. Overall survival analysis of AML patients associated with 29 individual aGPCRs. **b.** Disease-free survival analysis of AML patients associated with 29 individual aGPCRs a.



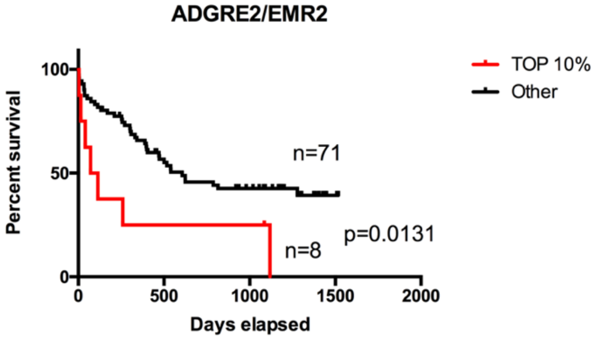
GPR56

b.



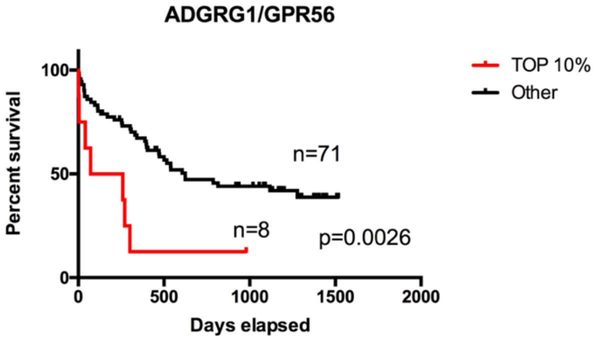
ADGRE5/CD97

c.



ADGRE2/EMR2

d.



ADGRG1/GPR56

e.

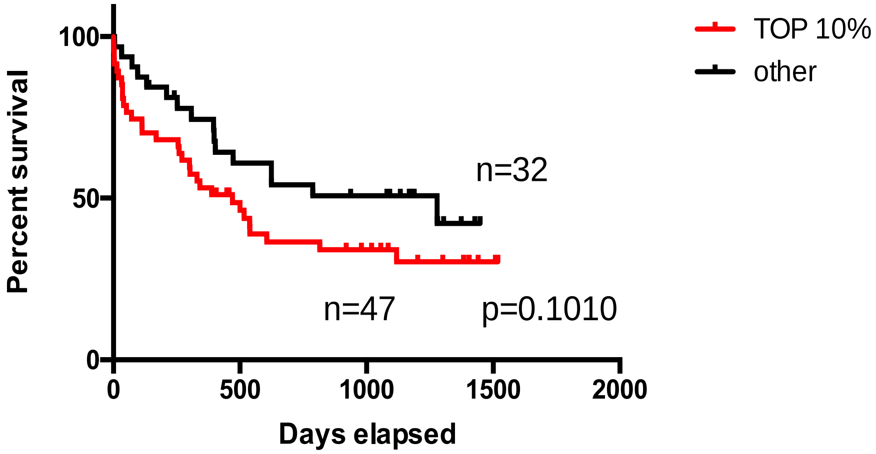
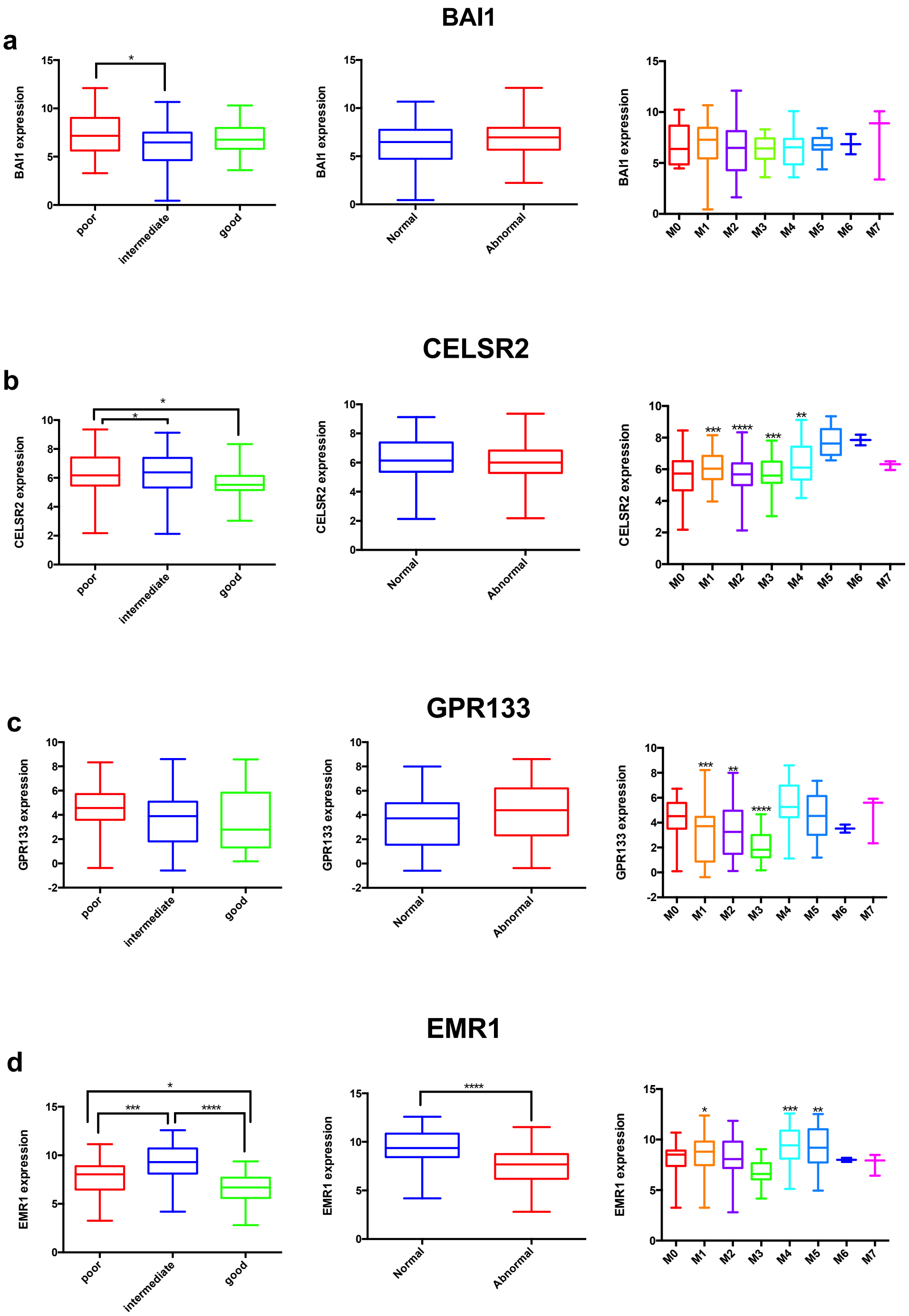


Figure S3. Survival analysis of AML associated with eight adhesion GPCRs mRNA expression in Metzeler Leukemia 1 and 2 datasets. a. Overall survival analysis of AML patients in Metzeler leukemia 1 dataset, associated with *ADGRG1(GPR56*). **b,c,d.** Overall survival analysis of AML patients in Metzeler leukemia 2 dataset, associated with *ADGRG1*(*GPR56*), *ADGRE2*(*EMR2*), *ADGRE5*(*CD97*). **e**. Overall survival of 79 AML patients from the Metzeler2 dataset dichotomized into 8-aGPCRs high (patients with at least one of the eight aGPCRs among the top 10% mRNA expression level) and low group (the remainder patients, or those with none of the eight genes among the top 10% mRNA expression level). The 8 genes are: *ADGRB1* (*BAI1), ADGRC2 (CELSE2), ADGRE1 (EMR1), ADGRE2 (EMR2), ADGRE5 (CD97), ADGRG1 (GPR56), ADGRG3 (GPR97), ADGRG5 (GPR133*).


BAI1
a
BAI1 expression
15
10
5
0
*
poor
intermediate
good
Normal
Abnormal
M0
M1
M2
M3
M4
M5
M6
M7
CELSR2
b
CELSR2 expression
10
8
6
4
2
0
*
*
***
****
***
**
GPR133
c
GPR133 expression
-2
***
**
****
EMR1
d
EMR1 expression
*
***
****
****
*
***
**

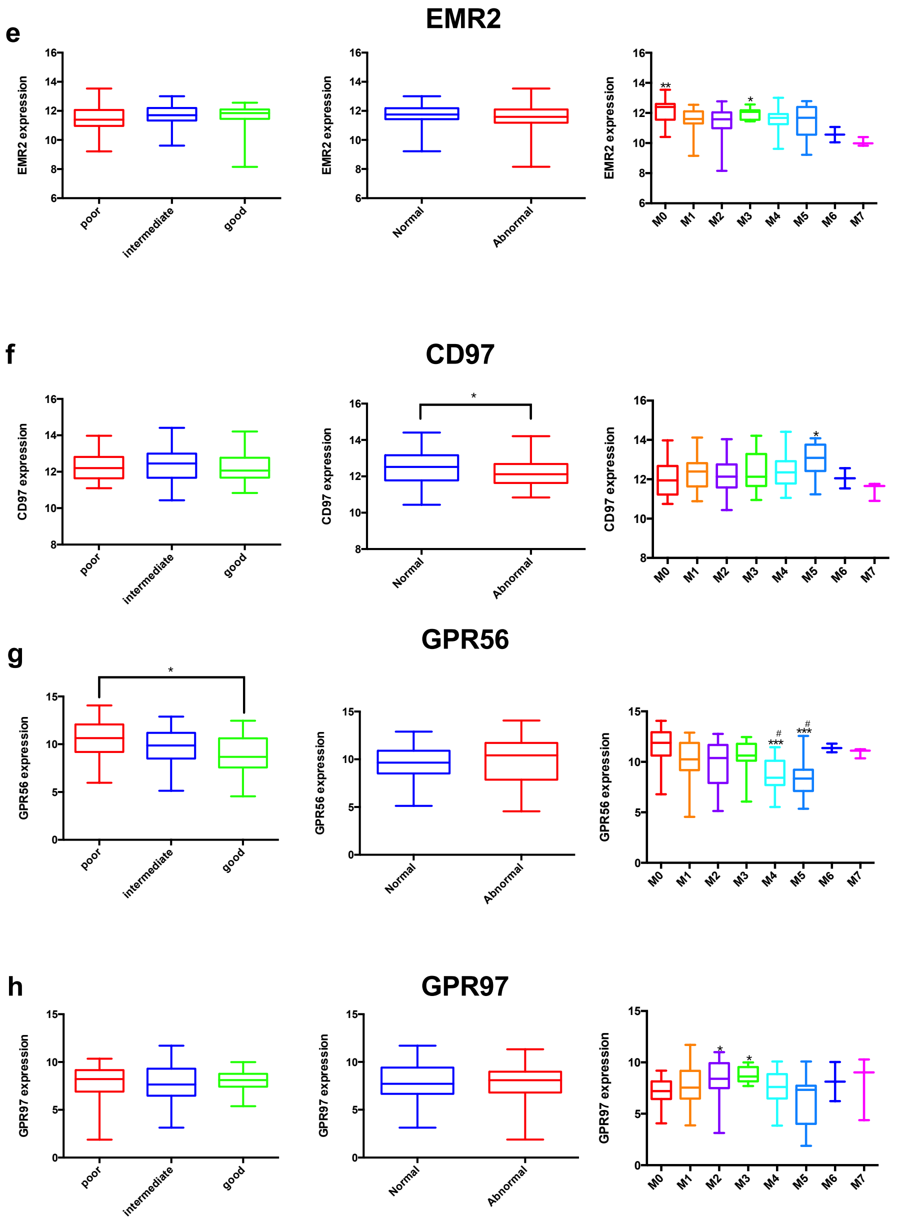


Figure S4. Eight adhesion GPCRs mRNA expression in patients with AML according to molecular risk status, cytogenetic and FAB classifications. log2 mRNA expression for all the eight genes were categorized by Molecular risk status, cytogenetic and FAB classifications (from left to right): *$p < 0.05$; **$p<0.01$; ***$p < 0.001$. **a.** *BAI*; **b.** *CELSR2*; **c.** *GPR133*; **d.** *EMR1*; **e.** *EMR2*; **f.** *CD97*; **g.** *GPR56*; **h.** *GPR97*.

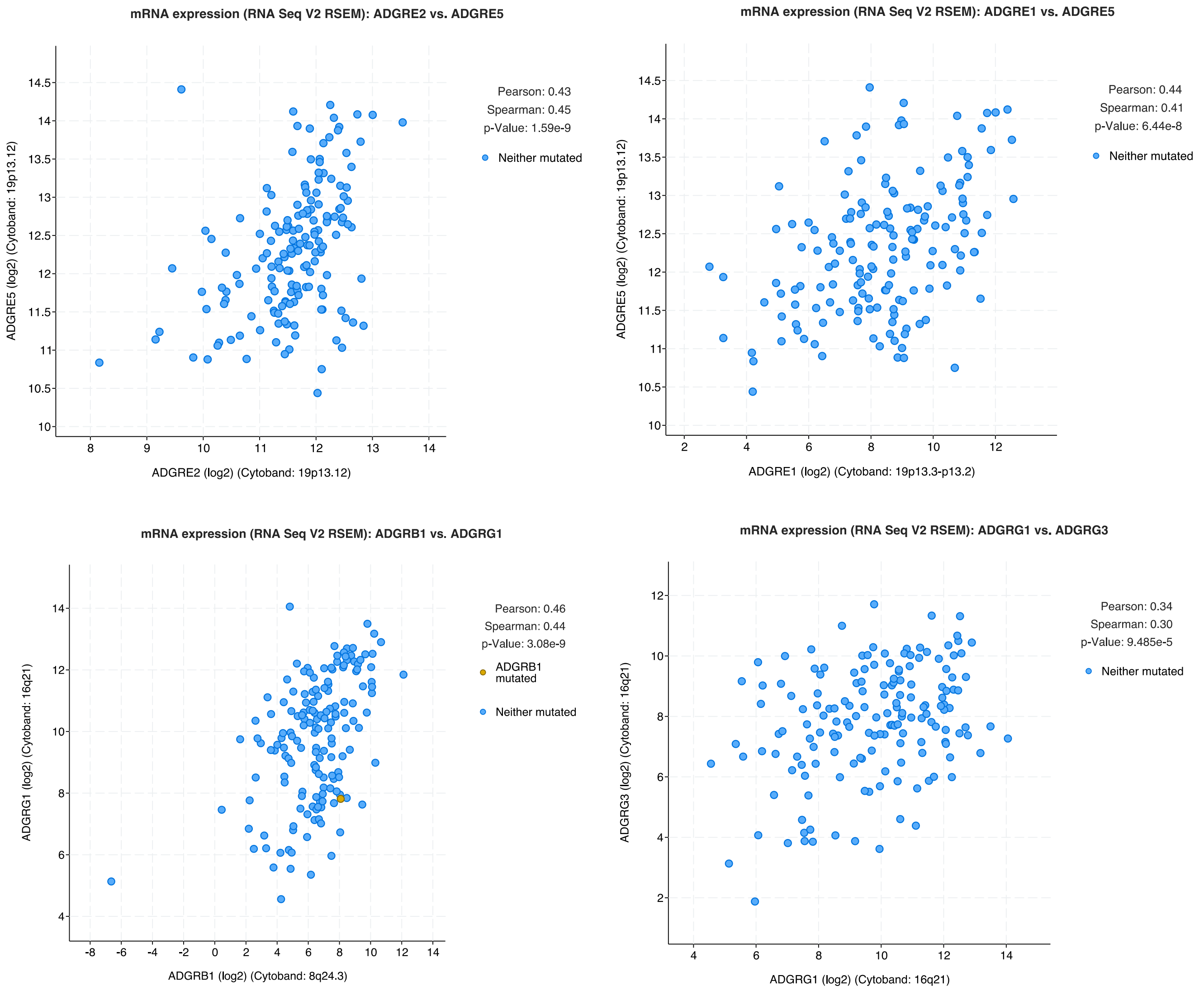


Figure S5. Correlation between expression levels of the eight adhesion GPCRs genes. Spearman's rho correlation analysis and Pearson correlation analysis between expression levels of the eight aGPCR genes are conducted. Scatter-plots showing a log2 transformed mRNA expression levels of *ADGRE5* and *ADGRE2*, *ADGRE5* and *ADGRE1*, *ADGRB1* and *ADGRG1*, *ADGRG1* and *ADGRG3*. Expression correlations are shown in four pairs of the eight genes.

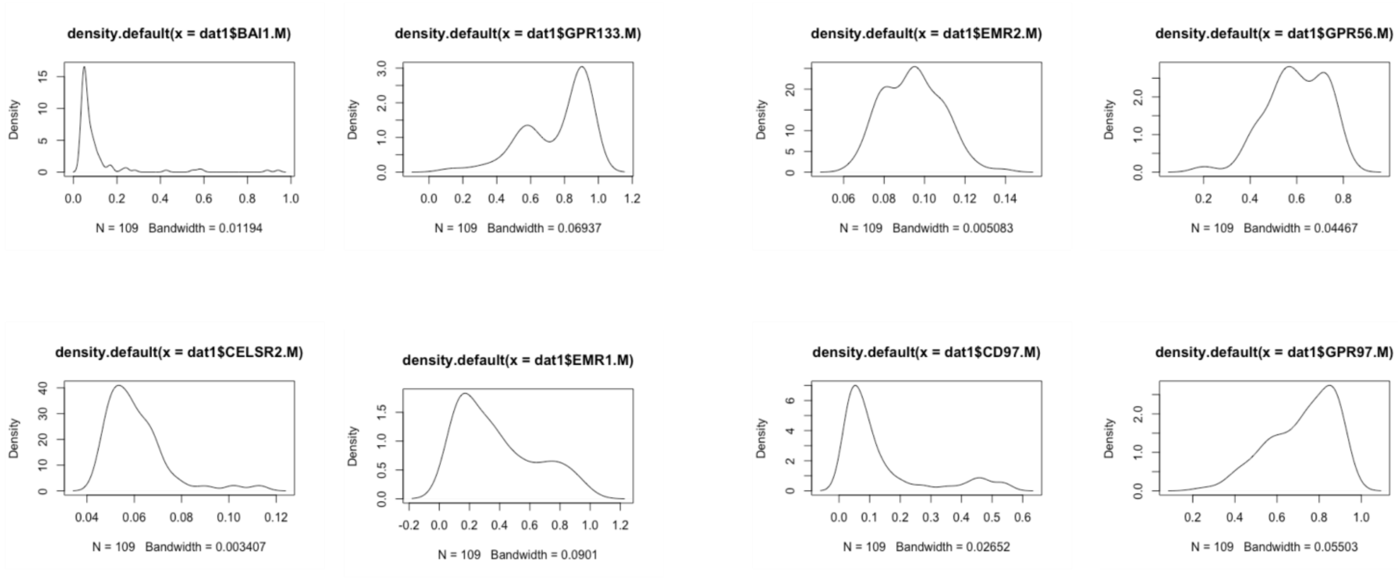


Figure S6. The methylation β value distribution of 109 patients in each of the eight adhesion GPCR genes. The 109 patients from the TCGA dataset whose methylation value are available were included in the analysis. The X-axis represent the methylation β-value, the Y-axis represent the distribution of the patients.

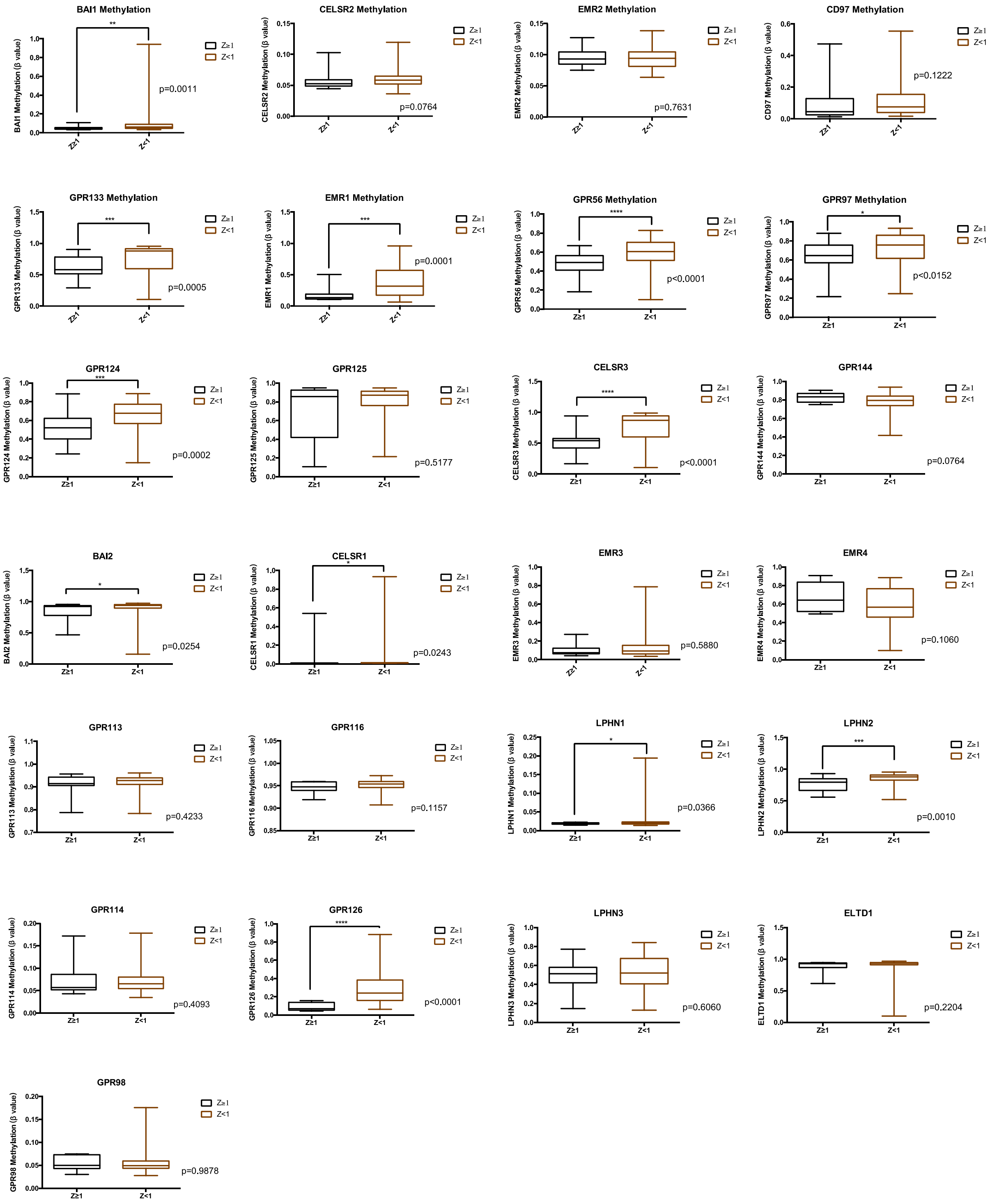
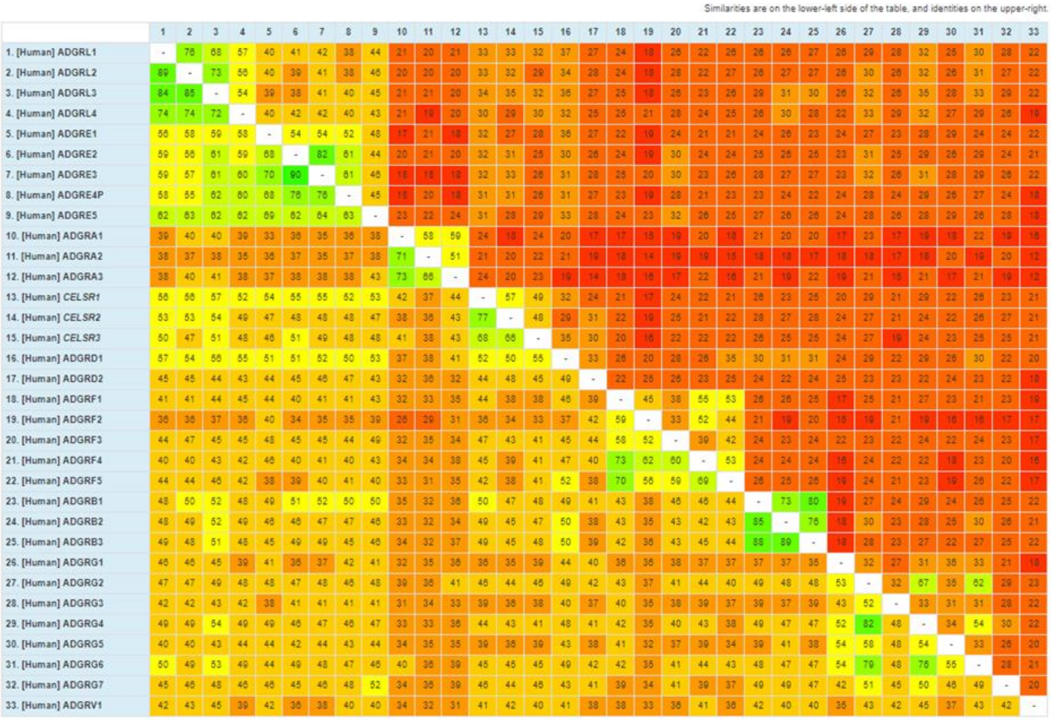


Figure S7. Associations between methylation and individual adhesion GPCR mRNA expression. *Adhesion GPCRs* methylation β value comparison between patients according to their expression (Z-score ≥ 1 and < 1). A non-parametric Mann–Whitney U test was used to compare the median of methylation β value between the groups.



Similarities are on the lower-left side of the table, and identities on the upper-right.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33
1. [Human] ADGRL1	-	76	68	57	40	41	42	38	44	21	20	21	33	33	32	37	27	24	18	26	22	26	26	26	27	26	29	28	32	25	30	28	22
2. [Human] ADGRL2	89	-	73	56	40	39	41	38	45	20	20	20	33	32	29	34	28	24	18	28	22	27	26	27	27	26	30	26	32	26	31	27	22
3. [Human] ADGRL3	84	85	-	54	39	38	41	40	45	21	21	20	34	35	32	36	27	25	18	26	23	26	29	31	30	26	32	26	35	28	33	29	22
4. [Human] ADGRL4	74	74	72	-	40	42	42	40	43	21	19	20	30	29	30	32	25	26	21	28	24	25	26	30	28	22	33	29	32	27	29	26	19
5. [Human] ADGRE1	56	58	59	58	-	54	54	52	48	17	21	18	32	27	28	36	27	22	19	24	21	21	24	26	23	24	27	23	28	29	24	24	22
6. [Human] ADGRE2	59	56	61	59	68	-	82	61	44	20	21	20	32	31	25	30	26	24	19	30	24	24	25	26	25	23	31	25	29	26	29	24	21
7. [Human] ADGRE3	59	57	61	60	70	90	-	61	46	18	18	18	32	33	26	31	28	25	20	30	23	26	28	27	27	23	32	26	31	28	29	26	22
8. [Human] ADGRE4P	58	55	62	60	68	76	76	-	45	18	20	18	31	31	26	31	27	23	19	28	21	23	23	24	22	24	28	24	29	26	27	24	18
9. [Human] ADGRE5	62	63	62	62	69	62	64	63	-	23	22	24	31	28	29	33	28	24	23	32	26	25	27	26	26	24	28	26	28	29	26	28	18
10. [Human] ADGRA1	39	40	40	39	33	36	35	36	38	-	58	59	24	18	24	20	17	17	15	19	20	18	21	20	20	17	23	17	19	18	22	19	16
11. [Human] ADGRA2	38	37	38	35	36	37	35	37	38	71	-	51	21	20	22	21	19	18	14	19	19	15	18	18	17	18	18	17	18	20	19	20	12
12. [Human] ADGRA3	38	40	41	38	37	38	38	38	43	73	66	-	24	20	23	19	14	18	16	17	22	16	21	19	22	19	21	15	21	17	21	19	12
13. [Human] *CELSR1*	56	56	57	52	54	55	55	52	53	42	37	44	-	57	49	32	24	21	17	24	22	21	26	23	25	20	29	21	29	22	26	23	21
14. [Human] *CELSR2*	53	53	54	49	47	48	48	48	47	38	36	43	77	-	48	29	31	22	19	25	21	22	26	27	26	24	27	21	24	22	26	27	21
15. [Human] *CELSR3*	50	47	51	48	46	51	49	48	48	41	38	43	68	66	-	35	30	20	16	22	22	22	26	25	25	24	27	19	24	23	25	25	21
16. [Human] ADGRD1	57	54	56	55	51	51	52	50	53	37	38	41	52	50	55	-	33	26	20	28	26	35	30	31	31	24	29	22	29	26	30	22	20
17. [Human] ADGRD2	45	45	44	43	44	45	46	47	43	32	36	32	44	48	45	49	-	22	25	26	23	25	24	22	24	25	23	23	22	24	23	22	18
18. [Human] ADGRF1	41	41	44	45	44	40	41	41	43	32	33	35	44	38	38	46	39	-	45	38	55	53	26	26	25	17	25	21	27	23	21	23	19
19. [Human] ADGRF2	36	36	37	36	40	34	35	35	39	26	29	31	36	34	33	37	42	59	-	33	52	44	21	19	20	15	19	21	19	16	16	17	17
20. [Human] ADGRF3	44	47	45	45	48	45	45	44	49	32	35	34	47	43	41	45	44	58	52	-	39	42	24	23	24	22	23	22	24	22	24	23	17
21. [Human] ADGRF4	40	40	43	42	46	40	41	40	43	34	34	38	45	39	41	47	40	73	62	60	-	53	24	24	24	16	24	22	22	18	23	20	16
22. [Human] ADGRF5	44	44	46	42	38	39	40	41	40	33	31	35	42	38	41	52	38	70	56	59	69	-	26	25	26	19	24	21	23	19	26	22	17
23. [Human] ADGRB1	48	50	52	48	49	51	52	50	50	35	32	36	50	47	48	49	41	43	38	46	46	44	-	73	80	19	27	24	29	24	26	25	22
24. [Human] ADGRB2	48	49	52	49	46	46	47	47	46	33	32	34	49	45	47	50	38	43	35	43	42	43	85	-	76	18	30	23	28	25	30	26	21
25. [Human] ADGRB3	49	48	51	48	45	49	49	45	46	34	32	37	49	45	48	50	39	42	36	43	45	44	88	89	-	18	28	23	27	22	27	25	22
26. [Human] ADGRG1	46	46	45	39	41	36	37	42	41	32	35	36	36	35	39	44	40	36	36	38	37	37	37	37	36	-	32	27	31	36	33	21	18
27. [Human] ADGRG2	47	47	49	48	48	47	48	46	48	39	36	41	46	44	46	49	42	43	37	41	44	40	49	48	48	53	-	32	67	36	62	29	23
28. [Human] ADGRG3	42	42	43	42	38	41	41	41	41	31	34	33	39	36	38	40	37	40	35	38	39	37	39	37	39	43	52	-	33	31	31	28	22
29. [Human] ADGRG4	49	49	54	49	49	46	47	46	47	33	33	36	44	43	41	48	41	42	35	40	43	38	49	47	47	52	82	48	-	34	54	30	22
30. [Human] ADGRG5	40	40	43	44	44	42	44	43	44	34	35	35	39	36	39	43	38	41	32	37	39	34	39	41	38	54	58	48	54	-	33	26	20
31. [Human] ADGRG6	50	49	53	49	44	49	48	47	46	40	36	39	45	45	45	49	42	42	35	41	44	43	48	47	47	54	79	48	76	55	-	28	21
32. [Human] ADGRG7	45	46	48	46	46	45	46	48	52	34	36	39	46	44	46	43	41	39	34	41	39	37	49	49	47	42	51	45	50	46	49	-	20
33. [Human] ADGRV1	42	43	45	39	42	36	38	40	40	34	32	31	41	42	40	41	38	38	33	36	41	36	42	40	40	36	43	42	45	37	43	42	-

Figure S8: A matrix of the structure similarity between members of the aGPCR family: Similarity are shown on the lower-left side of the table and identities on the upper-right. The color of each score ranged from red (the lowest) to green (the highest). The figure was generated on gpcrdb.org/similaritymatrix/ and selecting for structurally conserved positions for the sequence segment selection.