

Figure S1. Expression of (A) BEX1, (B) BEX2, (C) BEX3, (D) BEX4 and (E) BEX5 was significantly downregulated in lung adenocarcinoma tissues in The Cancer Genome Atlas cohort compared with tissues obtained from healthy controls. The Mann Whitney U test was used to analyze differences in expression. BEX, brain-expressed X-linked.

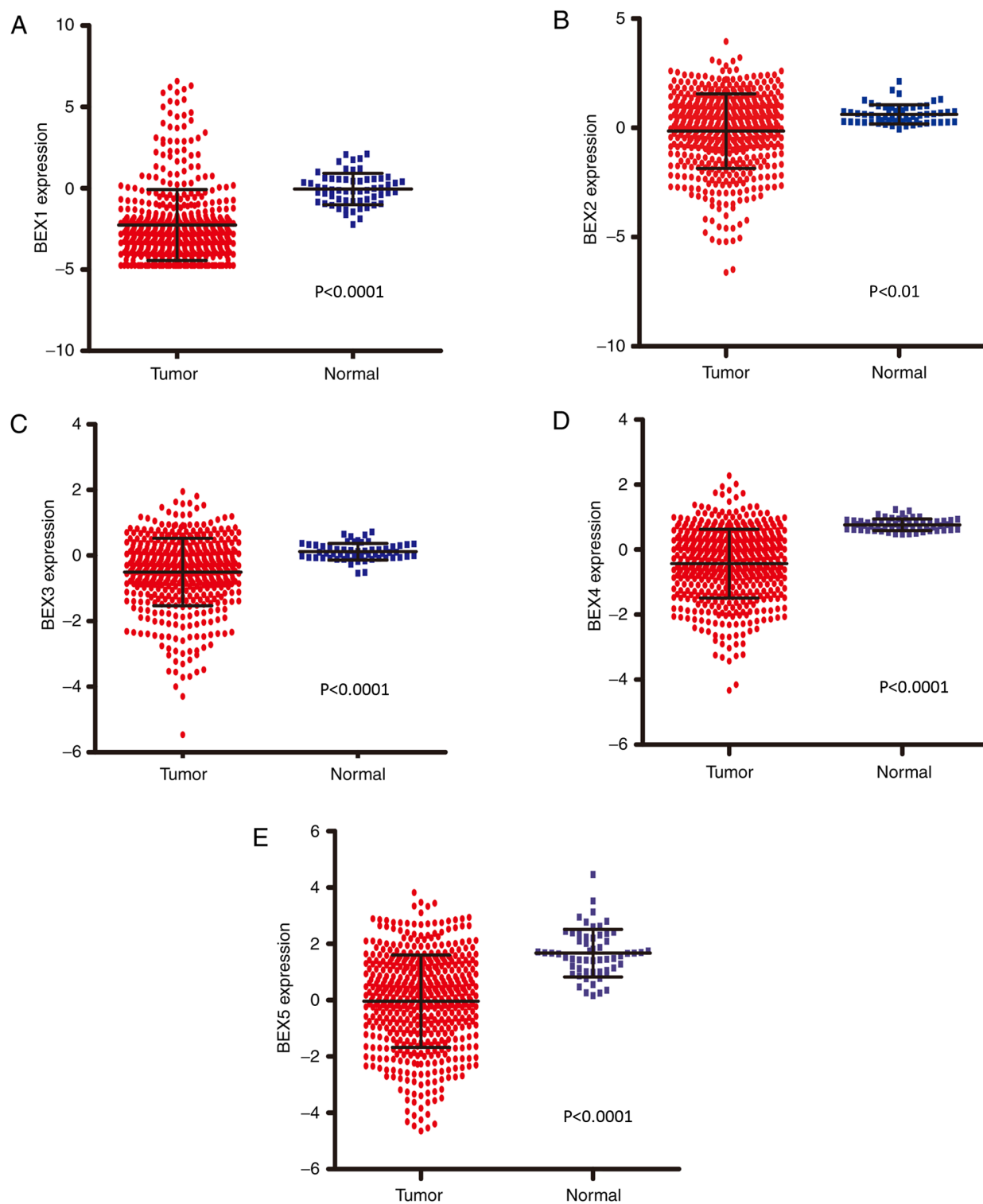


Figure S2. Low expression of BEX4 and BEX5 was significantly associated with poor survival in patients with LUAD AJCC stage I and II. Kaplan-Meier survival curve of (A) BEX1, (B) BEX2, (C) BEX3, (D) BEX4 and (E) BEX5 high- and low-expression levels in patients with LUAD AJCC stage I and II. Survival curves were compared using the log rank test and $P < 0.05$ was considered to indicate a statistically significant difference. BEX, brain-expressed X-linked; LUAD, lung adenocarcinoma; AJCC, American Joint Committee on Cancer.

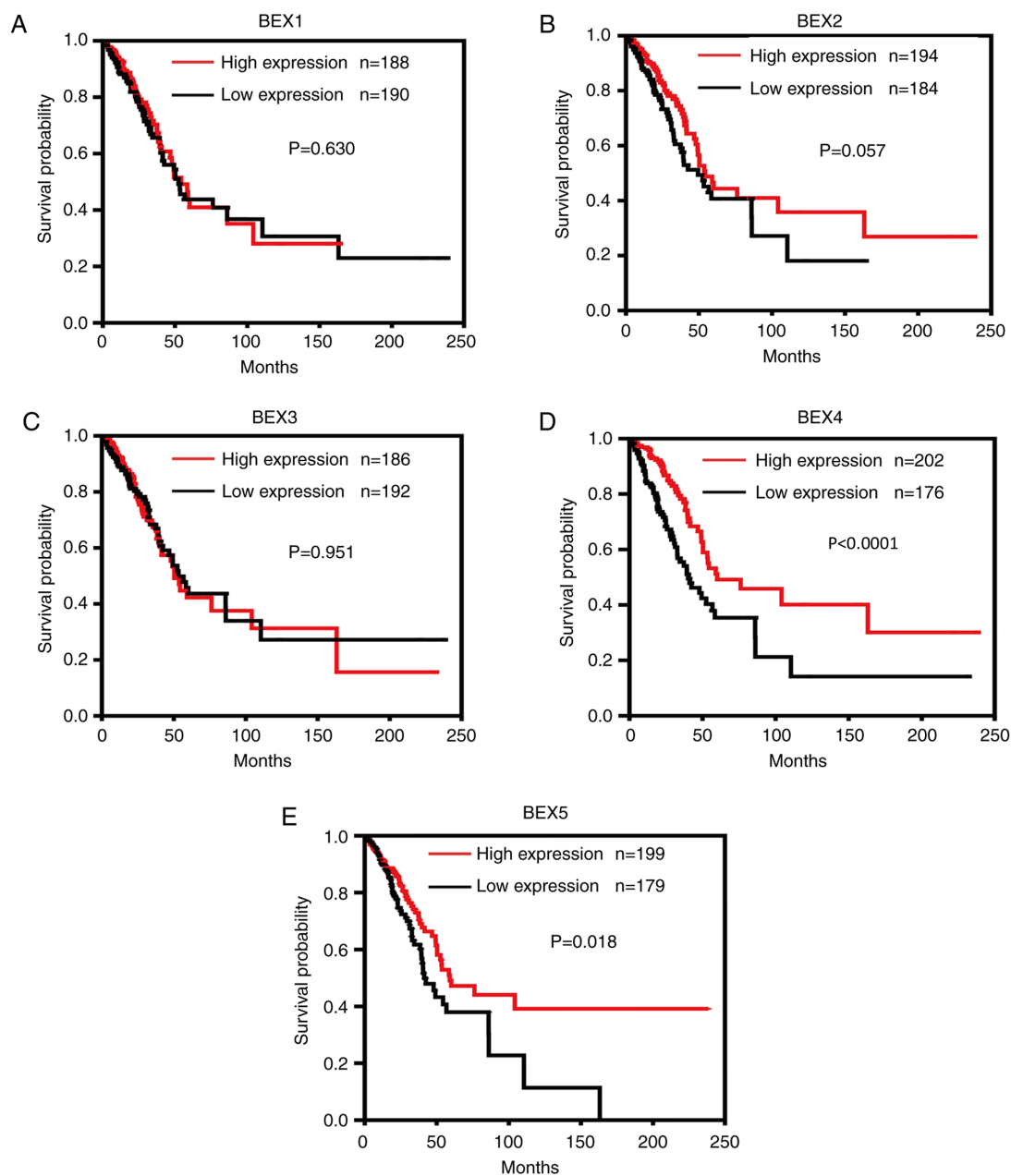


Figure S3. Effect of BEX family expression levels on the survival time patients with LUAD AJCC stage III and IV. Kaplan-Meier survival curve of (A) BEX1, (B) BEX2, (C) BEX3, (D) BEX4 and (E) BEX5 high- and low-expression levels in patients with LUAD AJCC stage III and IV. Survival curves were compared using the log rank test and $P < 0.05$ was considered to indicate a statistically significant difference. BEX, brain-expressed X-linked; LUAD, lung adenocarcinoma; AJCC, American Joint Committee on Cancer.

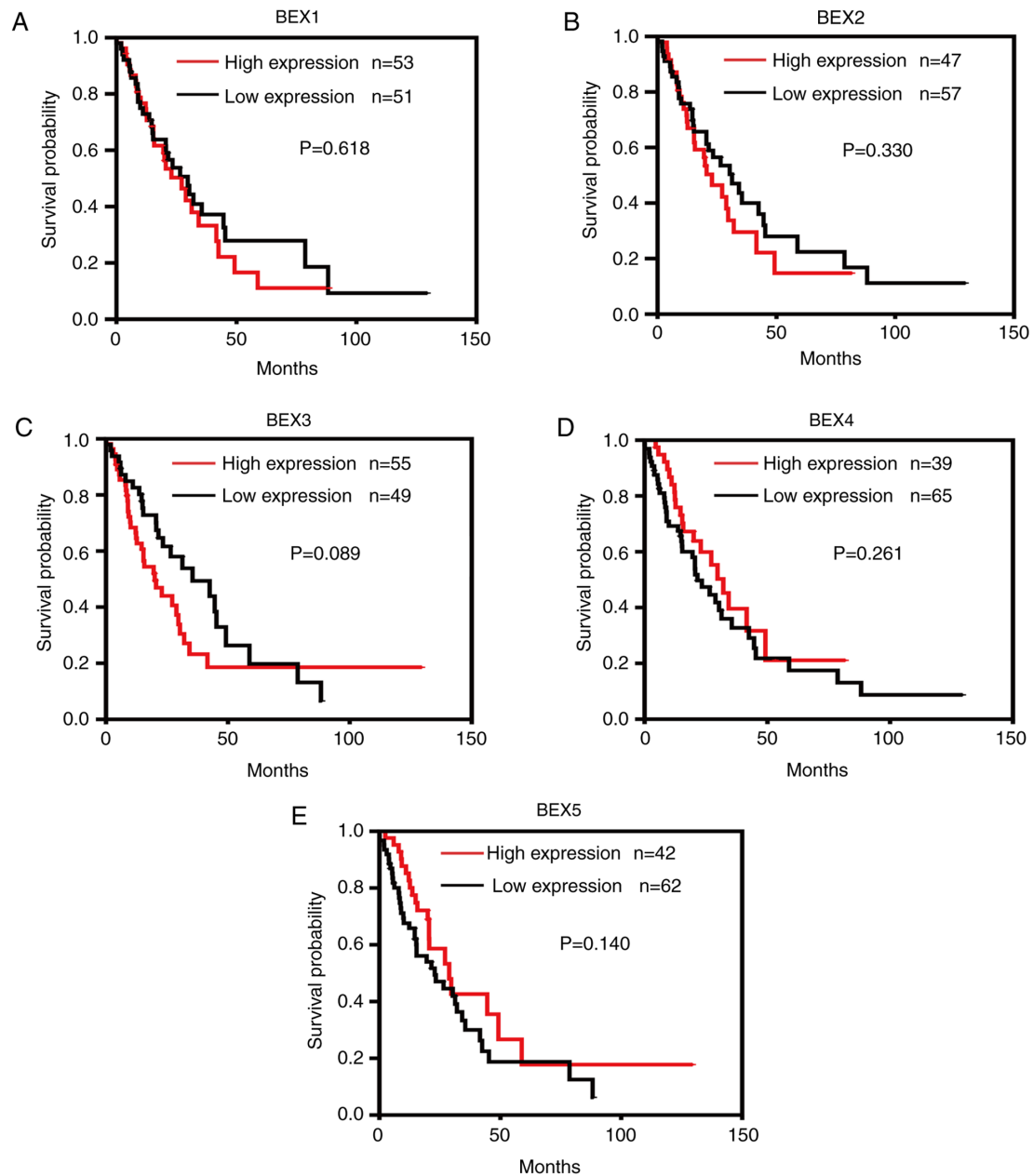


Figure S4. Analysis of mutations and copy number variations of the BEX family in patients with lung adenocarcinoma. The alteration frequency of (A) BEX1, (B) BEX2, (C) BEX3, (D) BEX4 and (E) BEX5 in different cohorts. BEX, brain-expressed X-linked; TCGA, The Cancer Genome Atlas.

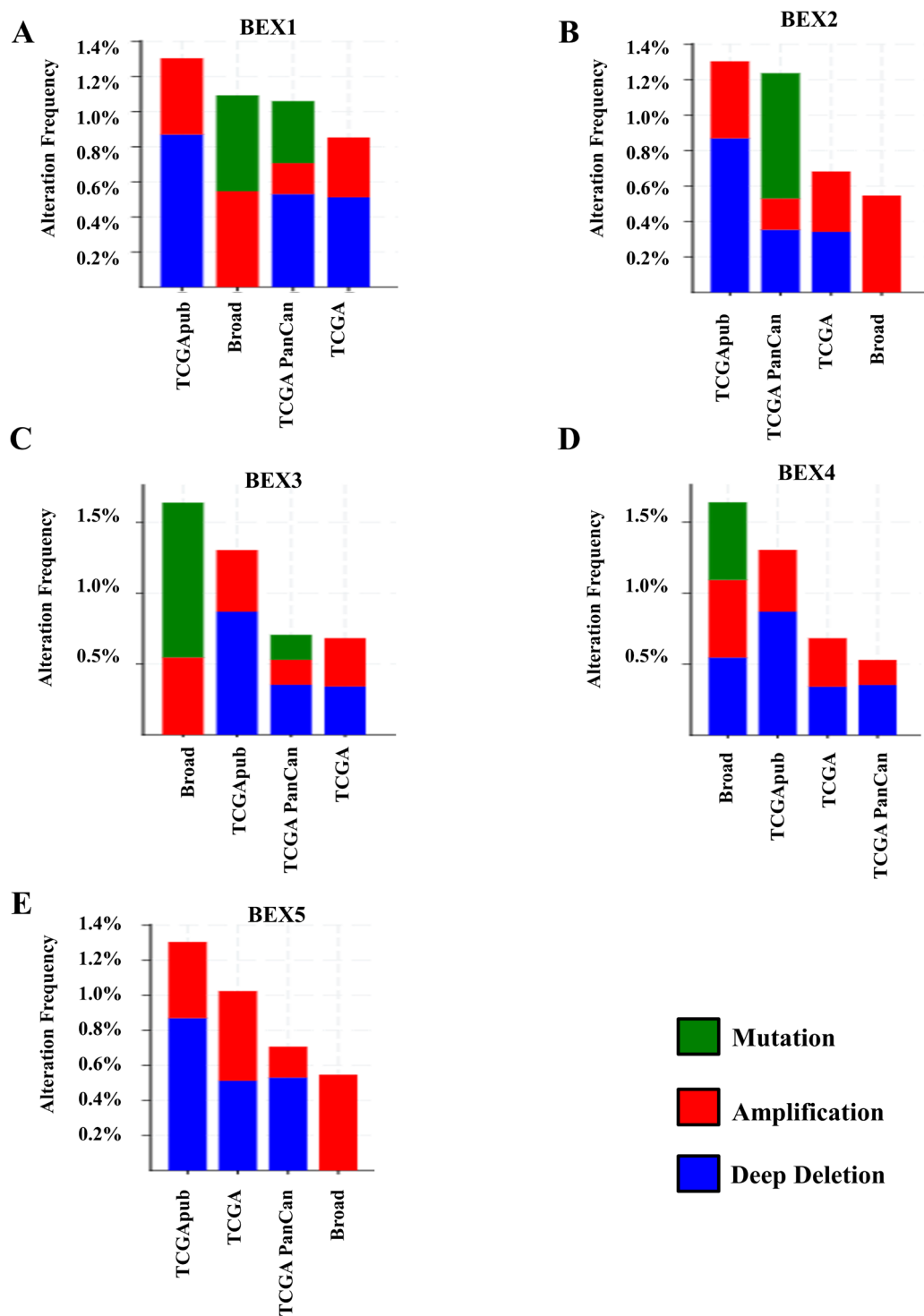


Figure S5. Promoter methylation average value of BEX members between tumor tissues and normal tissues obtained from healthy controls from the MethHC database. (A) BEX1 promoter methylation was significantly upregulated in LUAD tissues. (B) BEX2 promoter methylation was similar in LUAD and normal tissues. (C) BEX3 promoter methylation was significantly upregulated in LUAD tissues. (D) BEX4 promoter methylation was similar in LUAD and normal tissues. (E) BEX5 promoter methylation was similar in LUAD and normal tissues. Analysis was performed using a two-tailed Wilcoxon test with a cut-off of $P < 0.05$ with stringent false discovery rate control based on Bonferroni's method. BEX, brain-expressed X-linked; LUAD, lung adenocarcinoma.

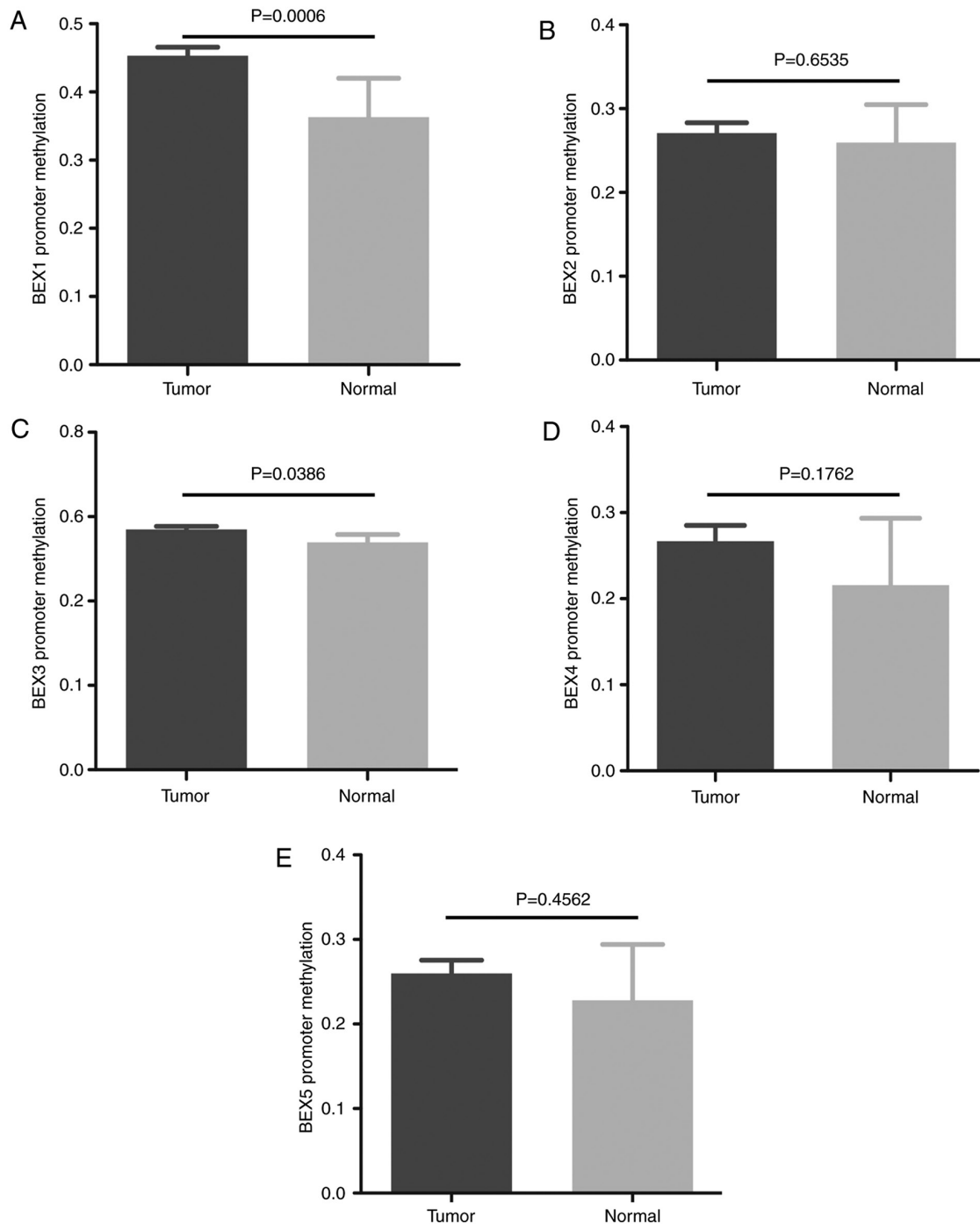


Table SI. Sequence of primers used in the quantitative polymerase chain reaction.

Gene	Forward primer (5'→3')	Reverse primer (5'→3')
Actin	CATGTACGTTGCTATCCAGGC	CTCCTTAATGTCACGCACGAT
BEX1	ACAAGGATAGGCCCAGGAGTAA	TTCGAAAGCAGGGGTCTGTT
BEX2	TGGTACCTGTTCCCGGTGT	CCCCTCCGGGTCCCTTAC
BEX3	CCTTCGGTGCAGTCGTCAC	TGGTTGTTTTTCTGCTCCGCT
BEX4	GCGTCAAGAATCCGGAGGAG	TTGCCATGCTGACCGTAACT
BEX5	TGCAGTCTGGTAGTTGTCGC	ACGCACTTAAAGACCTGCCA

BEX, brain-expressed X-linked.

Table SII. Associations between BEX1 expression and patient clinical characteristics in The Cancer Genome Atlas lung adenocarcinoma cohort.

Characteristic	n	BEX1 expression		χ^2	P-value
		High	Low		
Age at diagnosis (years)				0.262	0.609
<60	131	68	63		
≥60	351	173	178		
Sex				0.677	0.411
Male	221	106	115		
Female	261	135	126		
Clinical stage				0.049	0.825
I+II	378	188	190		
III+IV	104	53	51		
T (primary tumor)				9.485	0.023
T1	165	98	67		
T2	252	111	141		
T3	44	21	23		
T4	18	9	9		
TX	3	2	1		
N (regional lymph nodes)				0.000	0.998
N0	312	155	157		
N1-3	161	80	81		
NX	9	6	3		
M (distant metastases)				0.000	0.988
M0	319	160	159		
M1	24	12	12		
MX	139	69	70		

A total of 482 samples were analyzed, 241 with low-expression and 241 with high expression. BEX, brain-expressed X-linked.

Table SIII . Associations between BEX2 expression and patient clinical characteristics in The Cancer Genome Atlas lung adenocarcinoma cohort.

Characteristic	n	BEX2 expression		χ^2	P-value
		High expression	Low expression		
Age at diagnosis (years)				1.268	0.260
<60	131	60	71		
≥60	351	181	170		
Sex				9.100	0.003
Male	221	94	127		
Female	261	147	114		
Clinical stage				1.226	0.268
I+II	378	194	184		
III+IV	104	47	57		
T (primary tumor)				4.857	0.183
T1	165	90	75		
T2	252	126	126		
T3	44	16	28		
T4	18	8	10		
TX	3	1	2		
N (regional lymph nodes)				0.269	0.604
N0	312	153	159		
N1-3	161	83	78		
NX	9	5	4		
M (distant metastases)				0.037	0.847
M0	319	166	153		
M1	24	12	12		
MX	139	63	76		

A total of 482 samples were analyzed, 241 with low-expression and 241 with high expression. BEX, brain-expressed X-linked.

Table SIV. Associations between BEX3 expression and patient clinical characteristics in The Cancer Genome Atlas lung adenocarcinoma cohort.

Characteristic	n	BEX3 expression		χ^2	P-value
		High	Low		
Age at diagnosis (years)				0.010	0.918
<60	131	66	65		
≥60	351	175	176		
Sex				1.880	0.170
Male	221	118	103		
Female	261	123	138		
Clinical stage				0.441	0.506
I+II	378	186	192		
III+IV	104	55	49		
T (Primary tumor)				3.125	0.373
T1	165	83	82		
T2	252	119	133		
T3	44	26	18		
T4	18	11	7		
TX	3	2	1		
N (Regional lymph nodes)				1.351	0.245
N0	312	161	151		
N1-3	161	74	87		
NX	9	6	3		
M (Distant metastases)				0.257	0.612
M0	319	169	150		
M1	24	14	10		
MX	139	58	81		

A total of 482 samples were analyzed, 241 with low-expression and 241 with high expression. BEX, brain-expressed X-linked.