

Supplement Table 1 Clinical characteristics of lung cancer patients

		Research								Validate	
		Total	GSE31210	GSE8894	GSE30219	GSE37745	GSE50081	GSE3141	GSE31908	GSE29013	GSE157011
Study		Number (%)	Number (%)	Number (%)	Number (%)	Number (%)	Number (%)	Number (%)	Number (%)	Number (%)	Number (%)
Country			Japan	South Korea	France	Sweden	Canada	USA	USA	USA	USA
Sample Size		1251 (100.00)	246 (19.66)	138 (11.03)	307 (24.54)	196 (15.67)	181 (14.16)	111 (8.87)	17 (1.36)	55 (4.40)	482 (100.00)
Age	Mean ± SD (range)	62.68 ± 10.17 (13 ~ 89)	59.54 ± 8.08 (30 ~ 89)	60.78 ± 9.58 (13 ~ 82)	61.51 ± 11.58 (15 ~ 84)	63.77 ± 9.18 (39 ~ 84)	68.79 ± 9.4 (40 ~ 88)			63.58 ± 8.73 (32 ~ 76)	68.94 ± 8.63 (43 ~ 92)
Type	Normal	35 (2.80)	20 (8.13)		14 (4.56)				1 (5.88)		
	Tumor	1216 (97.20)	226 (91.87)	138 (100.00)	293 (95.44)	196 (100.00)	181 (100.00)	111 (100.00)	16 (94.12)	55 (0.00)	482 (100.00)
Gender	Male	716 (63.59)	116 (47.15)	104 (75.36)	250 (85.32)	107 (54.59)	98 (54.14)		3 (17.65)	38 (69.09)	313 (64.94)
	Female	410 (36.41)	130 (52.85)	34 (24.64)	43 (14.68)	89 (45.41)	83 (45.86)		14 (82.35)	17 (30.91)	169 (35.06)
Smoking	No	153 (32.08)	123 (50.00)				24 (15.00)		4 (25.00)	2 (3.64)	
	Yes	324 (67.92)	123 (50.00)				136 (85.00)		12 (75.00)	53 (96.36)	
Stage	1	612 (63.29)	168 (74.34)		152 (51.88)	130 (66.33)	127 (70.17)		11 (68.75)	24 (43.64)	186 (38.59)
	2	209 (21.61)	58 (25.66)		43 (14.68)	35 (17.86)	54 (29.83)		5 (31.25)	14 (25.45)	247 (51.24)
	3	131 (13.55)			87 (29.69)	27 (13.78)				17 (30.91)	49 (10.17)
	4	15 (1.55)			11 (3.75)	4 (2.04)					
EGFR mutation	No	107 (44.21)	99 (43.81)						8 (50.00)		
	Yes	135 (55.79)	127 (56.19)						8 (50.00)		
Histology	Adenocarcinoma	713 (57.97)	226 (100.00)	63 (45.65)	85 (27.69)	106 (54.08)	129 (71.27)	58 (52.25)	16 (100.00)	30 (54.55)	
	Squamous cell carcinoma	344 (27.97)		75 (54.35)	82 (26.71)	66 (33.67)	43 (23.76)	53 (47.75)		25 (45.45)	482 (100.00)
	Large cell carcinoma	92 (7.48)			59 (19.22)	24 (12.24)	9 (4.97)				
	Others	81 (6.59)			81 (26.38)						
Relapse	No	603 (61.16)	162 (71.68)	69 (50.00)	164 (58.99)	47 (48.96)	126 (71.19)		8 (50.00)	27 (49.09)	
	Yes	383 (38.84)	64 (28.32)	69 (50.00)	114 (41.01)	49 (51.04)	51 (28.81)		8 (50.00)	28 (50.91)	
Survival	Alive	545 (50.56)	191 (84.51)		93 (31.74)	51 (26.02)	106 (58.56)	53 (47.75)	14 (87.50)	37 (62.27)	219 (45.44)
	Dead	533 (49.44)	35 (15.49)		200 (68.26)	145 (73.98)	75 (41.44)	58 (52.25)	2 (12.50)	18 (32.73)	263 (54.56)

SD: standard deviation

Supplement Table 2 ROC analysis of gene expression of PD1 and PDL1 for predicting outcome in lung cancer patients

	Gene expression			
	PD1		PDL1	
	AUC (95%CI)	P-value ^a	AUC (95%CI)	P-value ^a
Non-relapse vs. relapse				
Adenocarcinoma stage 1	0.55 (0.48 ~ 0.62)	0.1377	0.54 (0.48 ~ 0.61)	0.2129
Adenocarcinoma stage 2+3+4	0.55 (0.46 ~ 0.65)	0.2565	0.51 (0.42 ~ 0.61)	0.7681
Squamous cell carcinoma stage 1	0.60 (0.49 ~ 0.72)	0.0839	0.59 (0.47 ~ 0.72)	0.1456
Squamous cell carcinoma stage 2+3+4	0.57 (0.43 ~ 0.70)	0.3272	0.59 (0.46 ~ 0.73)	0.1603
Alive vs. death				
Adenocarcinoma stage 1	0.72 (0.67 ~ 0.78)	<0.0001	0.74 (0.69 ~ 0.79)	<0.0001
Adenocarcinoma stage 2+3+4	0.77 (0.69 ~ 0.84)	<0.0001	0.77 (0.69 ~ 0.84)	<0.0001
Squamous cell carcinoma stage 1	0.55 (0.44 ~ 0.67)	0.3845	0.59 (0.48 ~ 0.70)	0.0964
Squamous cell carcinoma stage 2+3+4	0.79 (0.68 ~ 0.89)	<0.0001	0.78 (0.67 ~ 0.89)	<0.0001

ROC: receiver operating characteristic, AUC: areas under the ROC curves, CI: confidence interval

^a: P value for Mann-Whitney U test

Bold face: statistical significant (P value<0.05)

Supplement Table 3 PD1 and PDL1 gene Affymetrix probes gene expression at different study

	PD1							
	Raw data		Quantile normalization by mean		Quantile normalization by Median		Bayes' normalization	
	Mean ± SD	P-Value ^a	Mean ± SD	P-Value ^a	Mean ± SD	P-Value ^a	Mean ± SD	P-Value ^a
		<0.0001		<0.0001		<0.0001		0.9377
GSE50081	5.37 ± 0.35		66.18 ± 20.51		6.03 ± 0.27		5.32 ± 0.64	
GSE30219	5.69 ± 0.23		64.51 ± 10.6		6.02 ± 0.15		5.32 ± 0.63	
GSE31210	34.76 ± 20.69		15.21 ± 7.89		4.17 ± 0.64		5.32 ± 0.66	
GSE8894	2.33 ± 0.16		7.51 ± 7.05		3.49 ± 0.48		5.32 ± 0.58	
GSE37745	6.80 ± 0.24		79.01 ± 14.72		6.22 ± 0.19		5.32 ± 0.62	
GSE3141	102.39 ± 91.41		18.46 ± 15.31		4.27 ± 0.83		5.31 ± 0.66	
GSE31908	6.25 ± 0.20		47.32 ± 8.2		5.72 ± 0.19		5.32 ± 0.58	
GSE29013	5.34 ± 1.08		45.85 ± 54.47		5.11 ± 1.10		5.32 ± 0.65	
	PDL1							
	Raw data		Quantile normalization by mean		Quantile normalization by Median		Bayes' normalization	
	Mean ± SD	P-Value ^a	Mean ± SD	P-Value ^a	Mean ± SD	P-Value ^a	Mean ± SD	P-Value ^a
		<0.0001		<0.0001		0.1297		0.3560
GSE50081	5.35 ± 0.78		92.28 ± 111.50		6.06 ± 0.70		6.67 ± 0.93	
GSE30219	5.92 ± 1.02		120.52 ± 155.33		6.26 ± 0.95		6.67 ± 0.97	
GSE31210	628.08 ± 429.63		180.15 ± 112.16		6.82 ± 0.56		6.67 ± 0.89	
GSE8894	4.26 ± 1.45		150.85 ± 207.27		6.10 ± 1.21		6.67 ± 0.95	
GSE37745	7.22 ± 0.97		175.99 ± 193.27		6.73 ± 0.96		6.67 ± 0.96	
GSE3141	689.58 ± 508.63		193.57 ± 174.07		6.92 ± 0.89		6.67 ± 0.84	
GSE31908	6.47 ± 0.28		75.46 ± 24.18		5.90 ± 0.33		6.66 ± 0.76	
GSE29013	6.97 ± 0.75		222.37 ± 182.97		7.17 ± 1.10		6.67 ± 0.70	

SD: standard deviation

^a: P-value for homogeneity Levene's Test

Bold face: statistical significant (P value > 0.05)

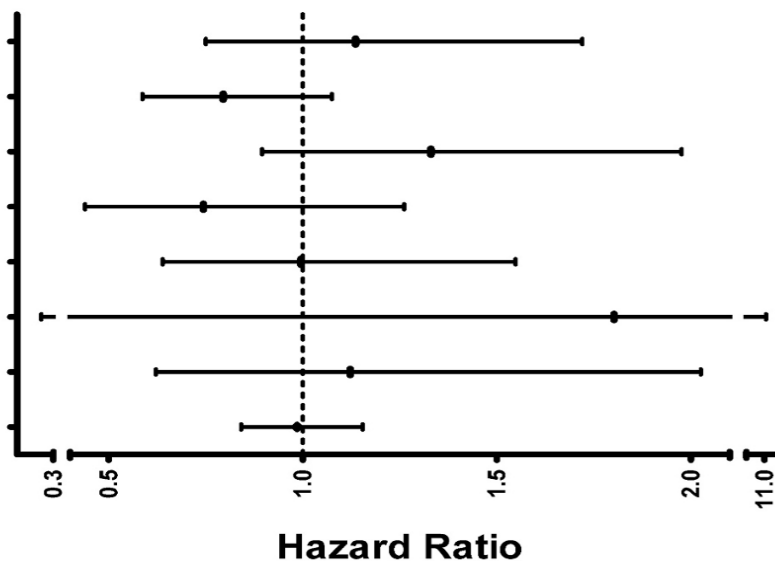
Supplement Figure 1 PD1 and PDL1 gene expression forest plot

A

Study	Hazard ratio (95% CI)
GSE50081	1.14 (0.75 ~ 1.72)
GSE30219	0.80 (0.59 ~ 1.08)
GSE31210	1.33 (0.90 ~ 1.98)
GSE8894	0.74 (0.44 ~ 1.26)
GSE37745	1.00 (0.64 ~ 1.55)
GSE31908	1.80 (0.30 ~ 11.00)
GSE29013	1.12 (0.62 ~ 2.03)
Total	0.99 (0.84 ~ 1.15)

GSE50081 (N=181)
GSE30219 (N=307)
GSE31210 (N=246)
GSE8894 (N=138)
GSE37745 (N=196)
GSE31908 (N=17)
GSE29013 (N=55)
Total (N=1140)

PD1 Forest plot



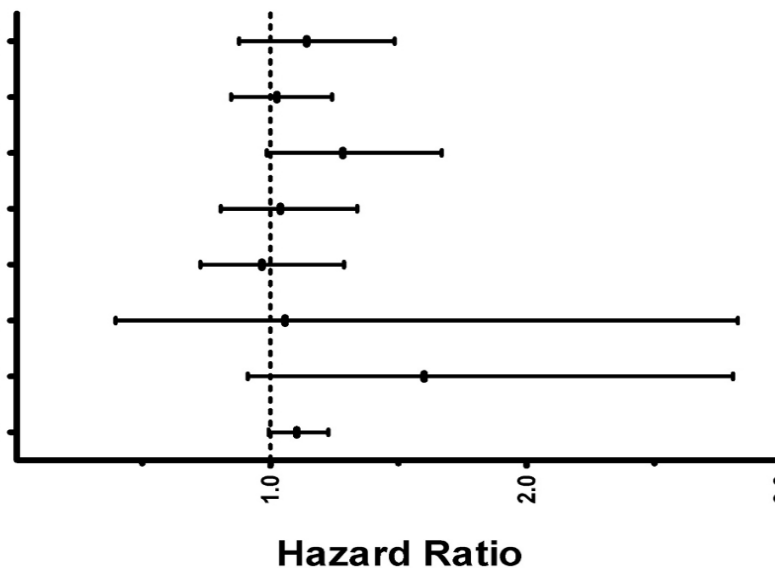
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30.01%
18.31%
10.60%
14.88%
0.93%
8.51%
100.00%

B

Study	Hazard ratio (95% CI)
GSE50081	1.14 (0.88 ~ 1.49)
GSE30219	1.03 (0.85 ~ 1.24)
GSE31210	1.28 (0.99 ~ 1.67)
GSE8894	1.04 (0.81 ~ 1.34)
GSE37745	0.97 (0.73 ~ 1.29)
GSE31908	1.06 (0.40 ~ 2.83)
GSE29013	1.60 (0.91 ~ 2.81)
Total	1.10 (0.99 ~ 1.23)

GSE50081 (N=181)
GSE30219 (N=307)
GSE31210 (N=246)
GSE8894 (N=138)
GSE37745 (N=196)
GSE31908 (N=17)
GSE29013 (N=55)
Total (N=1140)

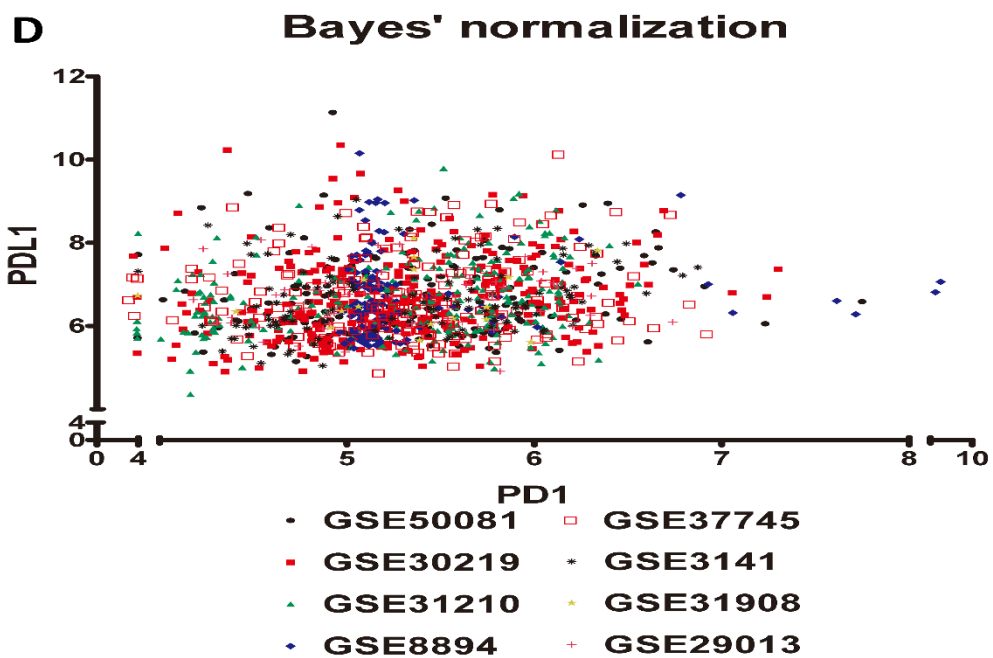
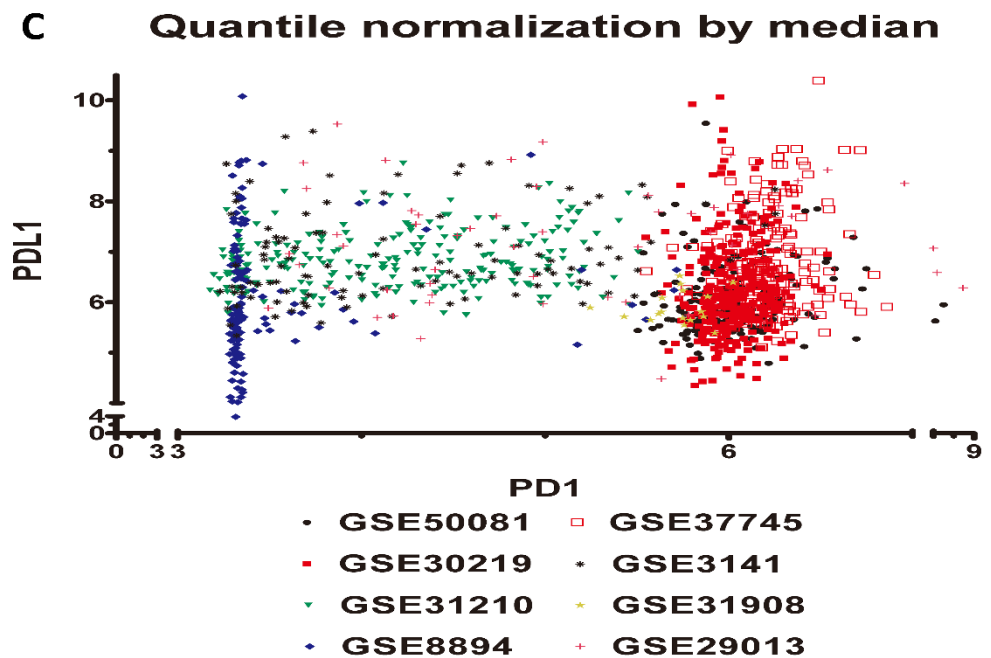
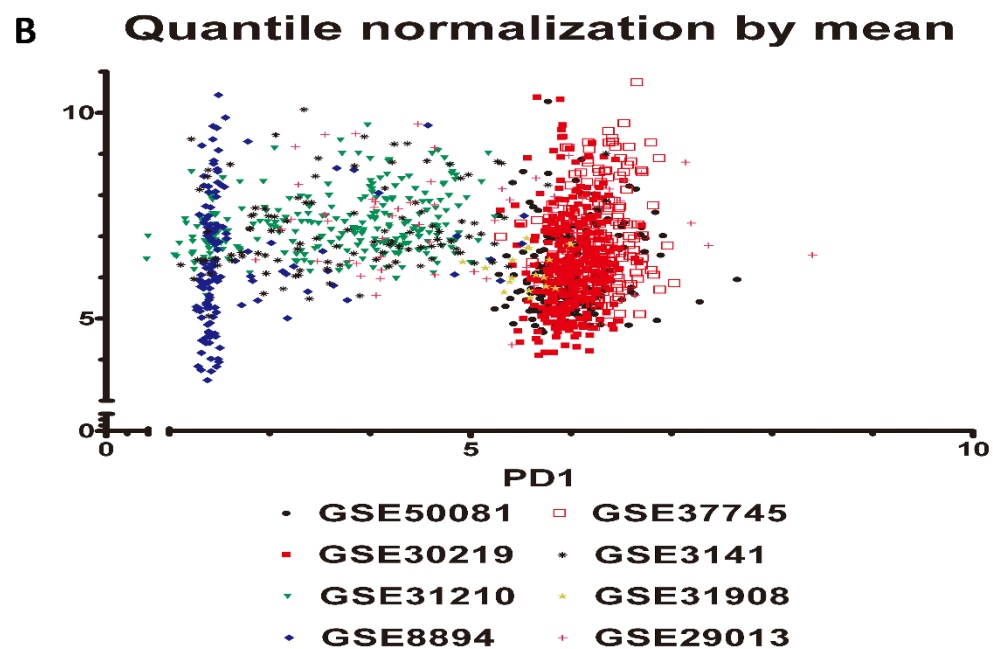
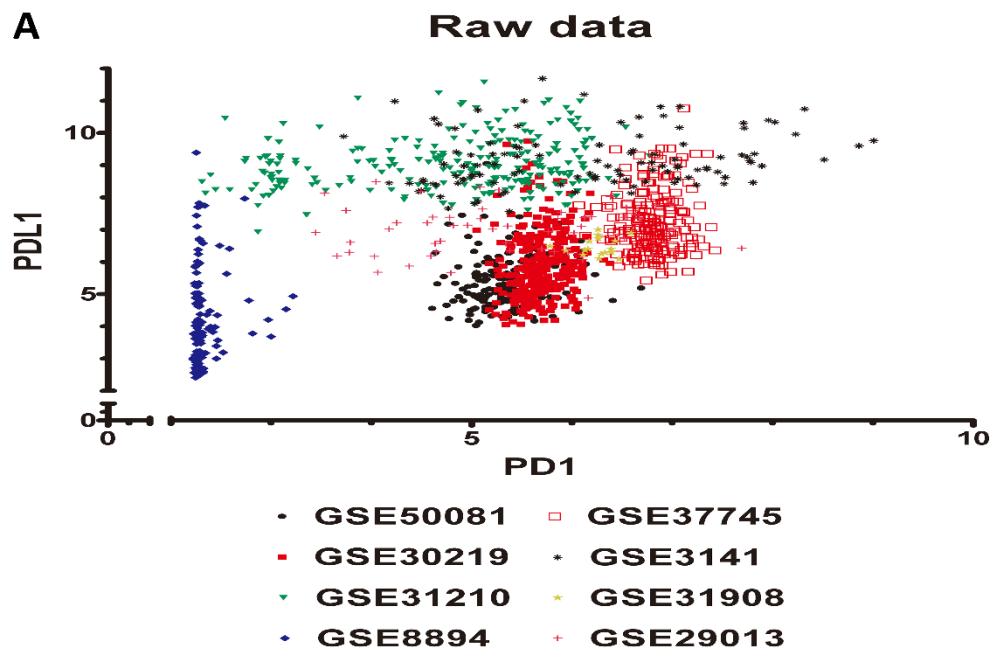
PDL1 Forest Plot



Weight (random)
16.37%
31.03%
16.34%
17.62%
13.88%
1.17%
3.59%
100.00%

Meta-analyses random effects model forest plot in PD1 (A), PDL1 (B).

Supplement Figure 2 PD1 and PDL1 gene expression in different normalized methods



Scatter plot of PD1 and PDL1 gene expression in raw data(A), quantile normalization by mean (B), quantile normalization by median (C), and Bayes' normalization (D).