

**Supplementary Table S1.** The association between PD-L1 expression and the clinicopathological factors in adenocarcinoma.

Variables	N	1% Cutoff		P*	5% Cutoff		P*	10% Cutoff		P
		PD-L1, N (%)			PD-L1, N (%)			PD-L1, N (%)		
		Negative	Positive		Negative	Positive		Negative	Positive	
<b>Age (years)</b>										
< 60	111	54 (48.6)	57 (51.4)	0.347	68 (61.3)	43 (38.7)	0.901	75 (67.6)	36 (32.4)	0.33
≥ 60	95	40 (42.1)	55 (57.9)		59 (62.1)	36 (37.9)		70 (73.7)	25 (26.3)	
<b>Gender</b>										
Male	110	53 (48.2)	57 (51.8)	0.431	72 (65.5)	38 (34.5)	0.229	79 (71.8)	36 (32.4)	0.63
Female	96	41 (42.7)	55 (57.3)		55 (57.3)	41 (42.7)		66 (68.8)	30 (31.3)	
<b>Smoking Index (SI)</b>										
SI < 400	133	78 (58.6)	55 (41.4)	< 0.001	95 (71.4)	38 (28.6)	< 0.001	104 (78.2)	29 (21.8)	< 0.001
SI ≥ 400	73	16 (21.9)	57 (78.1)		32 (43.8)	41 (56.2)		41 (56.2)	32 (43.8)	
<b>Clinical stage</b>										
I	105	53 (50.5)	52 (49.5)	0.363	68 (64.8)	37 (35.2)	0.547	76 (72.4)	29 (27.6)	0.49
II	32	13 (40.6)	19 (59.4)		20 (62.5)	12 (37.5)		24 (75.0)	8 (25.0)	
IIIA	69	28 (40.6)	41 (59.4)		39 (56.5)	30 (43.5)		45 (65.2)	24 (34.8)	
<b>Tumor size</b>										
≤ 3 cm	126	59 (46.8)	67 (53.2)	0.666	83 (65.9)	43 (34.1)	0.118	93 (73.8)	33 (26.2)	0.17
> 3 cm	80	35 (43.8)	45 (56.2)		44 (55.0)	36 (45.0)		52 (65.0)	28 (35.0)	
<b>Regional LN metastasis</b>										
No	109	55 (50.0)	54 (49.5)	0.140	72 (66.1)	37 (33.9)	0.168	81 (74.3)	28 (25.7)	0.19
Yes	97	39 (40.2)	58 (59.8)		55 (56.7)	42 (43.3)		64 (66.0)	33 (34.0)	
<b>Solid type adenocarcinoma</b>										
no	185	86 (46.5)	99 (53.5)	0.464	116 (62.7)	69 (37.3)	0.357	133 (71.9)	52 (28.1)	0.16
yes	21	8 (38.1)	13 (61.9)		11 (52.4)	10 (47.6)		12 (57.1)	9 (42.9)	
<b>EGFR mutation</b>										
No	146	68 (46.6)	78 (53.4)	0.671	92 (63.0)	54 (37.0)	0.530	107 (73.7)	39 (26.7)	0.15
Yes	60	26 (43.3)	34 (56.7)		35 (58.3)	25 (41.7)		38 (63.3)	22 (36.7)	
<b>NSE</b>										
≤15.2 ng/ml	159	73 (45.9)	86 (54.1)	0.671	98 (61.6)	61 (38.4)	0.993	112 (70.4)	47 (29.6)	0.97
>15.2 ng/ml	47	21 (44.7)	26 (55.3)		29 (61.7)	18 (38.3)		33 (70.2)	14 (29.8)	
<b>CEA</b>										
≤ 5.0 ng/ml	128	62 (48.4)	66 (51.6)	0.300	79 (61.7)	49 (38.3)	0.979	92 (71.9)	36 (28.1)	0.54
> 5.0 ng/ml	78	32 (41.0)	46 (59.0)		48 (61.5)	30 (38.5)		53 (67.9)	25 (23.1)	
<b>Cyfra21-1</b>										
≤ 3.3 ng/ml	142	59 (41.5)	83 (58.5)	0.080	76 (53.5)	66 (46.5)	< 0.001	93 (65.5)	49 (34.5)	0.02
> 3.3 ng/ml	64	35 (54.7)	29 (45.3)		51 (79.7)	13 (20.3)		52 (81.3)	12 (18.8)	
<b>SCCA</b>										
≤ 1.5 ng/ml	186	88 (47.3)	98 (52.7)	0.140	120 (64.5)	66 (35.5)	0.010	136 (73.1)	50 (26.9)	0.00
> 1.5 ng/ml	20	6 (30.0)	14 (70.0)		7 (35.0)	13 (65.0)		9 (45.0)	11 (55.0)	

LN: lymph node. SI: smoking index = (number of cigarettes per day) × (duration in years). \* P values <0.05 in bold.

**Supplementary Table S2.** The association between PD-L1 expression and the clinicopathological factors in squamous cell carcinoma.

Variables	1% Cutoff		5% Cutoff		10% Cutoff		50% Cutoff	
	N	PD-L1, N	P*	PD-L1, N	P*	PD-L1, N	P*	PD-L1, N

	N		P		N		P		N		P		
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	
<b>Age (years)</b>													
< 60	7	33	44	0.9	46	31	0.1	51	26	0.2	62	15	0.0
	7	(42.9	(57.1)	64	(59.7	(40.3)	91	(66.2	(23.8)	23	(80.5	(19.5)	71
≥ 60	8	35	46		40	41		46	35		55	26	
	1	(43.2	(56.8)		(49.4	(50.6)		(56.8	(43.2)		(67.9	(32.1)	
<b>Gender</b>													
Male	1	17	9	<b>0.0</b>	19	7	<b>0.0</b>	20	6	0.0	95	37	0.1
	3	(65.4	(34.6)	<b>12</b>	(73.1	(26.9)	<b>37</b>	(76.9	(23.1)	75	(72.0	(28.0)	29
Female	2	51	81		67	65		77	55		22	4	
	6	(38.6	(61.4)		(50.8	(49.2)		(58.3	(41.7)		(84.6	(15.4)	
<b>Smoking Index (SI)</b>													
SI < 400	7	43	27	< <b>0.001</b>	53	17	< <b>0.001</b>	55	15	< <b>0.001</b>	58	12	<b>0.024</b>
	0	(61.4	(28.6)		(75.7	(24.3)		(78.6	(21.4)		(82.9	(17.1)	
SI ≥ 400	8	25	63		33	55		42	46		59	29	
	8	(28.4	(71.6)		(37.5	(62.5)		(47.7	(52.3)		(67.0	(33.0)	
<b>Clinical stage</b>													
I	7	30	40	0.8	40	30	0.8	47	23	0.3	56	14	0.2
	0	(42.9	(57.1)	59	(57.1	(42.9)	29	(67.1	(32.9)	95	(80.0	(20.0)	59
II	4	16	24		21	19		22	18		29	11	
	0	(40.0	(60.0)		(52.5	(47.5)		(55.0	(45.0)		(72.5	(27.5)	
IIIA	4	22	26		25	23		28	20		32	16	
	8	(45.8	(54.2)		(52.1	(47.9)		(58.3	(41.7)		(66.7	(33.3)	
<b>Tumor size</b>													
≤ 3 cm	4	16	31	0.1	26	21	0.8	28	19	0.7	33	14	0.4
	7	(34.0	(66.0)	37	(55.3	(44.7)	84	(59.6	(40.4)	60	(70.2	(29.8)	74
> 3 cm	1	52	59		60	51		69	42		84	27	
	1	(46.8	(53.2)		(54.1	(45.9)		(62.2	(37.8)		(75.7	(24.3)	
<b>Regional LN metastasis</b>													
No	9	39	56	0.5	53	42	0.6	61	34	0.3	76	19	<b>0.036</b>
	5	(41.1	(58.9)	36	(55.8	(44.2)	74	(64.2	(35.8)	72	(80.0	(20.0)	
Yes	6	29	34		33	30		36	27		41	22	
	3	(46.0	(54.0)		(52.4	(47.6)		(57.1	(42.9)		(65.1	(34.9)	
<b>EGFR mutation</b>													
No	1	64	90	<b>0.033<sup>a</sup></b>	82	72	0.1	93	61	0.1	113	41	0.5
	5	(41.6	(58.4)		(53.2	(46.8)	26 <sup>a</sup>	(60.4	(39.6)	60 <sup>a</sup>	(73.4	(26.6)	73 <sup>a</sup>
Yes	4	4	0 (0)		4	0 (0)		4	0 (0)		4	0 (0)	
		(100.0)			(100.0)			(100.0)			(100.0)		
<b>NSE</b>													
≤15.2ng/ml	9	39	51	0.9	49	41	0.9	55	35	0.9	70	20	0.2
	0	(41.6	(56.7)	31	(54.4	(45.6)	97	(61.1	(38.9)	33	(77.8	(22.2)	19
>15.2ng/ml	6	29	39		37	31		42	26		47	21	

g/ml	8	(42.6 )	(57. 74)		(54.4 )	(45. 6)		(61.8 )	(38. 2)		(69.1 )	(30. 9)	
<b>CEA</b>													
≤ 5.0 ng/ml	1	42 (38.2 )	68 (61. 8)	0.0 62	56 (50.9 )	54 (49. 1)	0.1 78	63 (57.3 )	47 (42. 7)	0.1 07	80 (72.7 )	30 (27. 3)	0.5 66
> 5.0 ng/ml	4	26 (54.2 )	22 (45. 8)		30 (62.5 )	18 (37. 5)		34 (70.8 )	14 (29. 2)		37 (72.1 )	11 (22. 9)	
<b>Cyfra21-1</b>													
≤ 3.3 ng/ml	5	25 (47.2 )	28 (52. 8)	0.4 56	33 (32.6 )	20 (37. 7)	0.1 60	35 (66.0 )	18 (34. 0)	0.3 94	44 (83.0 )	9 (17. 0)	0.0 68
> 3.3 ng/ml	1	43 (41.0 )	62 (59. 0)		53 (50.5 )	52 (49. 5)		62 (59.0 )	43 (41. 0)		73 (69.5 )	32 (30. 5)	
<b>SCCA</b>													
≤ 1.5 ng/ml	9	43 (44.3 )	54 (55. 7)	0.6 79	57 (58.8 )	40 (41. 2)	0.1 78	63 (57.3 )	47 (42. 7)	0.4 11	77 (79.4 )	20 (20. 6)	0.0 54
> 1.5 ng/ml	6	25 (41.0 )	36 (59. 0)		29 (47.5 )	32 (52. 5)		34 (70.8 )	14 (29. 2)		40 (65.6 )	21 (34. 4)	

LN: lymph node. AD: adenocarcinoma. SCC: squamous cell carcinoma. SI : smoking index = (number of cigarettes per day) × (duration in years). \*P values < 0.05 in bold.

<sup>a</sup> Fisher exact test.

**Supplementary Table S3.** The association between PD-L2 expression and the clinicopathological factors.

Variables	Number of patients	PD-L2 expression (%)		P
		Negative	Positive	
<b>Age (years)</b>				
< 60	188	93 (49.5)	95 (50.5)	0.520
≥ 60	176	93 (52.8)	83 (42)	
<b>Gender</b>				
Male	228	114 (50.0)	114 (50.0)	0.587
Female	136	72 (52.9)	64 (47.1)	
<b>Smoking Index (SI)</b>				
SI < 400	203	108 (53.2)	95 (46.8)	0.308
SI ≥ 400	161	77 (47.8)	84 (52.2)	
<b>Clinical stage</b>				
I	175	82 (46.9)	93 (53.1)	0.178
II	72	43 (59.7)	29 (40.3)	
IIIA	177	61 (52.1)	56 (47.9)	
<b>Tumor size</b>				
≤ 3 cm	167	86 (51.5)	81 (48.5)	0.813
> 3 cm	197	99 (50.3)	98 (49.7)	
<b>Regional LN metastasis</b>				
No	204	102 (50.0)	102 (50.0)	0.722
Yes	160	83 (51.9)	77 (48.1)	

<b>Histology</b>				
AD	206	102 (49.5)	104 (50.4)	0.490
SCC	158	84 (53.2)	74 (46.8)	
<b>EGFR mutation</b>				
No	300	155 (51.7)	145 (48.3)	0.639
Yes	64	31 (48.4)	33 (51.6)	
<b>NSE</b>				
≤ 15.2 ng/ml	249	124 (49.8)	125 (50.2)	0.465
> 15.2 ng/ml	115	62 (53.9)	53 (46.1)	
<b>CEA</b>				
≤ 5.0 ng/ml	238	120 (50.4)	118 (49.6)	0.722
> 5.0 ng/ml	126	66 (52.4)	60 (47.6)	
<b>Cyfra21-1</b>				
≤ 3.3 ng/ml	195	96 (49.2)	99 (50.8)	0.444
> 3.3 ng/ml	169	90 (53.3)	79 (46.7)	
<b>SCCA</b>				
≤ 1.5 ng/ml	283	102 (50.0)	102 (50.0)	0.722
> 1.5 ng/ml	81	83 (51.9)	77 (48.1)	

LN: lymph node. AD: adenocarcinoma. SCC: squamous cell carcinoma. SI, smoking index = (number of cigarettes per day) × (duration in years).

**Supplementary Table S4.** Multivariate analysis for PD-L1 expression.

Variables	1% Cutoff		5% Cutoff		10% Cutoff	
	OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P
<b>Regional LN metastasis</b>						
No						
Yes						
<b>SCCA</b>						
≤ 1.5 ng/ml			2.402 (1.358-4.249)	<b>0.003</b>	1.761 (1.039-2.984)	<b>0.035</b>
> 1.5 ng/ml						
<b>Smoking Index (SI)</b>						
SI < 400	4.319 (2.748-6.787)	< <b>0.001</b>	3.925 (2.502-6.156)	< <b>0.001</b>	3.270 (2.068-5.171)	< <b>0.001</b>
SI ≥ 400						
<b>Cyfra21-1</b>						
≤ 3.3 ng/ml			0.558 (0.342-0.909)	<b>0.019</b>		
> 3.3 ng/ml						

OR: odd ratio. CI: confidence interval. LN: lymph node. SI: smoking index = (number of cigarettes per day) × (duration in years).

**Supplementary Table S5.** Summary of recent studies investigating PD-L1 expression in surgically resected non-small cell lung cancers.

Author	Cell type	I/II/III/IV	IHC evaluation	Percentage of tumors with positive PD-L1 expression	clinicopathological factors associated with positive PD-L1 protein expression
Takada et al.	417AD	305/63/49/0	1%	34.5%	Male gender, smoking, higher tumor grade, advanced T status, advanced N status, advanced stage, the presence of pleural and vessel invasions, micropapillary or solid predominant histological subtypes, and wild-type EGFR
			5%	20.4%	Male gender, smoking, higher tumor grade, advanced T status, advanced N status, advanced stage, the presence of pleural and vessel invasions, micropapillary or solid predominant histological subtypes, and wild-type EGFR
Uruga et al.	109AD	0/82/27/0	> 1%	51%	Higher N stage, solid dominant histology according to the IASLC/ATS/ERS classification, higher nuclear grade, and the presence of tumor island, necrosis, vascular

			>5%	39%	invasion and CD8+ T cells Higher T stage, higher N stage, solid dominant histology according to the IASLC/ATS/ERS classification, higher nuclear grade, and the presence of tumor island, necrosis, vascular invasion, STAS (Spread tumor alveolar space) and CD8+ T cells
			>50%	17%	Solid dominant histology according to the IASLC/ATS/ERS classification, the presence of necrosis, vascular invasion, and CD8+ T cells
Takada et al.	205SCC	108/73/24/0	>1%	51.7%	None
			>5%	35.1%	None
			>10%	29.7%	Higher N stage
			>50%	18.0%	Older age
Shimoji et al.	165AD 55SCC	145/44/33/22	Intensity× extent	22% of AD and 60% of SCC	AD: younger age, Smoking, high expression of P53, Vimentin, Ki-67 and P-glycoprotein, low expression of E-cadherin and ALDH1A1 SCC: none
Ameratunga et al.	282AD 182SCC	not available	Intensity Moderate to strong>5%	43.6%	Not available
			Intensity Moderate to strong≥50%	23.8%	Younger age
Sun et al.	644AD 299SC 58LC 49others	I/II/IIIA/IIIB- IV 520/284/201/65	≥1%	38%	Older age, male gender, smoking, poorer ECOG performance status (≥1 versus 0), squamous cell carcinoma, and advanced tumor stage
			≥50%	6%	
Huynh et al.	261AD	201/34/22/4	≥1%	49%	Smoking, solid dominant histology according to the IASLC/ATS/ERS classification, high nuclear grade, presence of lymphatic invasion and venous invasion, CD8+ TILs
			≥5%	36.5%	Smoking, solid dominant histology according to the IASLC/ATS/ERS classification, high nuclear grade, presence of lymphatic invasion and venous, invasion, positive lymph node metastasis, CD8+ TILs
			≥50%	24%	Smoking, solid dominant histology according to the IASLC/ATS/ERS classification, high nuclear grade, presence of lymphatic invasion and venous, invasion, higher T stage, CD8+ TILs
Takada et al.	417AD 82SCC	354/82/63/0	>1%	37.9%	male sex, smoking, higher tumor grade, higher T stage, higher N stage, advanced stage, the presence of Pleural invasion and vascular invasion, squamous cell carcinoma, and wild-type EGFR
			>5%	23.8%	male sex, smoking, higher tumor grade, higher T stage, higher N stage, advanced stage, the presence of Pleural invasion and vascular invasion, squamous cell carcinoma, and wild-type EGFR
			>10%	14.2%	male sex, smoking, higher tumor grade, higher T stage, advanced stage, the presence of Pleural invasion and vascular invasion, squamous cell carcinoma, and wild-type EGFR
			>50%	7.8%	male sex, smoking, higher tumor grade, advanced stage, the presence of vascular invasion, squamous cell carcinoma, and wild-

Wu et al.	133AD	65/16/42/10	>25%	13.5%	type EGFR male sex, smoking, solid, papillary or micropapillary dominant histology according to the IASLC/ATS/ERS classification
Okita et al. [12][12][12][ 12][12][12][ 12][12][12][ 12]	71AD 20SCC	IA/IB-III A 35/56	Intensity× extent	14%	Male gender, smoking, SUVmax on FDG-PET/CT scan, higher tumor grade, adenocarcinoma, higher N stage, advanced stage, EGFR expression

DFS: disease-free survival. OS: overall survival. RFS: recurrence-free survival. AD: adenocarcinoma. SCC: squamous cell carcinoma.

**Supplementary Figure S1.**

Kaplan-Meier survival curves of DFS (A, C, E) and OS (B, D, F) according to PD-L1 expression at 1% (A, B), 5% (C, D) and 10% (E, F) cutoff values (negative vs. positive) in NSCLC patients. Kaplan-Meier survival curves of DFS (G) and OS (H) according to PD-L2 expression (negative vs. positive) in NSCLC patients.

**Supplementary Figure S1.**

