

**Table S1.** Basic characteristics of patients

Variables		Training cohort	Validation cohort
		(n=206)	(n=197)
		Number of cases (%)	Number of cases (%)
Age	54(19-84)		
(y, Median	<53	90(43.7%)	102(51.8%)
range)	≥53	116(56.3%)	95(48.2%)
Gender	Male	134(65.0%)	141(71.6%)
	Female	72(35.0%)	56(28.4%)
T stage	T1	116(56.3%)	118(59.9%)
	T2	48(23.3%)	39(19.8%)
	T3	32(15.5%)	33(16.8%)
	T4	10(4.9%)	7(3.6%)
N stage	N0	187(90.8%)	181(91.9%)
	N1	19(9.2%)	16(8.1%)
M stage	M0	181(87.9%)	185(93.9%)
	M1	25(12.1%)	12(6.1%)
Necrosis	Absent	149(72.3%)	151(76.6%)
	Present	57(27.7%)	46(23.4%)
MVI	Absent	179(86.9%)	169(85.8%)
	Present	27(13.1%)	28(14.2%)
Fuhrman grade	G1	42(20.4%)	44(22.3%)
	G2	94(45.6%)	85(43.1%)
	G3	55(26.7%)	49(24.9%)
	G4	15(7.3%)	19(9.6%)
HHLA2	Negative	115(55.8%)	116(58.9%)
	Positive	91(44.2%)	81(41.1%)
PD-L1	Negative	138(67.0%)	134(68.0%)
	Positive	68(33.0%)	63(32.0%)

Abbreviations: MVI, microvascular invasion, HHLA2: Human endogenous retrovirus-H long terminal repeat-associating protein 2, PD-L1: Programmed death 1 ligand 1

**Table S2.** The association of PD-L1 expression level with clinicopathological characteristics

Variables	Training cohort(n=206)				Validation cohort(n=197)			
	Patients NO.	PD-L1 expression		<i>p</i> -value	Patients NO.	PD-L1 expression		<i>p</i> -value
		Negative	Positive			Negative	Positive	
Age(y)				0.268				0.301
<53	90	64	26		102	66	36	
≥53	116	74	42		95	68	27	
Gender				0.702				0.479
Male	134	91	43		141	98	43	
Female	72	47	25		56	36	20	
Necrosis				<b>0.041</b>				<b>0.001</b>
Absent	149	106	43		151	112	39	
Present	57	32	25		46	22	24	
MVI				<b>&lt;0.001</b>				0.077
Absent	179	128	51		169	119	50	
Present	27	10	17		28	15	13	
Fuhrman grade				<b>0.002</b>				<b>0.003</b>
Low (1,2)	136	101	35		129	97	32	
High (3,4)	70	37	33		68	37	31	
TNM stage				<b>0.003</b>				<b>0.002</b>
Low (I, II)	146	107	39		146	108	38	
High (III, IV)	60	31	29		51	26	25	

Abbreviations: MVI microvascular invasion; *p*-value <0.05 marked in bold font shows statistical significance.

**Table S3.** The association of HHLA2/PD-L1 co-expression level with clinicopathological characteristics in training cohort and validation cohort.

Variables	Training cohort					Validation cohort				
	Patients NO.	HHLA2/PD-L1 co-expression				Patients NO.	HHLA2/PD-L1 co-expression			
		Group I	Group II	Group III	<i>p</i> -value		Group I	Group II	Group III	<i>p</i> -value
Age(y)					0.229					0.885
<53	90	44	30	16		102	47	34	21	
≥53	116	43	29	24		95	46	32	17	
Gender					0.698					0.051
Male	134	54	54	26		141	74	41	26	
Female	72	33	25	14		56	19	25	12	
Necrosis					<b>0.001</b>					<b>&lt;0.001</b>
Absent	149	75	51	23		151	83	46	22	
Present	57	12	28	17		46	10	20	16	
MVI					<b>&lt;0.001</b>					0.385
Absent	179	82	70	27		169	82	57	30	
Present	27	5	9	13		28	11	9	8	
Fuhrman grade					<b>&lt;0.001</b>					0.310
Low (1,2)	136	75	50	19		129	66	40	23	
High (3,4)	70	12	35	23		68	27	26	15	
TNM stage					<b>&lt;0.001</b>					<b>0.011</b>
Low (I, II)	146	77	77	59		146	78	42	26	
High (III, IV)	60	10	29	21		51	15	24	12	

**Table S4.** Distribution of types of microenvironment in renal cell carcinoma based on HHLA2/PD-L1 co-expression of tumor cells and density of CD4 plus CD8-positive TILs

Intra-tumoral TILs	Training cohort			Validation cohort		
	HHLA2/PD-L1 co-expression			HHLA2/PD-L1 co-expression		
	Group I (%)	Group II (%)	Group III (%)	Group I (%)	Group II (%)	Group III (%)
Negative	41(19.9)	26(12.7)	4(1.9)	45(22.8)	28(14.2)	5(2.5)
Positive	45(21.8)	53(25.7)	37(18.0)	44(22.4)	44(22.4)	31(15.7)

*Group I, both negative (HHLA2(-)/PD-L1(-)); Group II, single positive (HHLA2 (+)/PD-L1(-) or HHLA2(-)/PD-L1(+)); and Group III, both positive (HHLA2 (+)/PD-L1(+)).*

**Figure Legends**

**Figure S1.** Kaplan Meier survival curves for PFS and OS of patients with ccRCC according to HHLA2/PD-L1 co-expression in training cohort(a) and validation cohort(b).

**Figure S2.** Kaplan Meier survival curves for PFS and OS of patients with ccRCC according to HHLA2/PD-L1 co-expression in training cohort(a) and validation cohort(b).