

**Supplementary Table 1. Clinicopathologic characteristics of three cohorts of patients with hepatocellular carcinoma**

		Cohort 1 (224 cases)		Cohort 2 (380 cases)		Cohort 3 (461 cases)	
		N	%	N	%	N	%
Age(year)	≤50	95	42.4	150	39.5	222	48.2
	>50	129	57.6	230	60.5	239	51.8
Sex	Female	25	11.2	65	17.1	71	15.4
	Male	199	88.8	315	82.9	390	84.6
HBsAg	Negative	42	18.8	54	14.2	65	14.1
	Positive	182	81.2	326	85.8	396	85.9
HCV	Negative	222	99.1	377	99.2	457	99.1
	Positive	2	0.9	3	0.8	4	0.9
AFP(ng/ml)	≤20	91	40.6	145	38.2	157	34.1
	>20	133	59.4	235	61.8	304	65.9
GGT(U/L)	≤54	83	37.1	195	51.3	207	44.9
	>54	141	62.9	185	48.7	254	55.1
Liver cirrhosis	No	30	13.4	61	16.1	75	16.3
	yes	194	86.6	319	83.9	386	83.7
Tumor size(cm)	≤5	103	46.0	232	61.1	228	49.5
	>5	121	54.0	148	38.9	233	50.5
Tumor number	Single	192	85.7	337	88.7	394	85.5
	Multiple	32	14.3	43	11.3	67	14.5
Vascular invasion	No	144	64.3	261	68.7	268	58.1
	Yes	80	35.7	119	31.3	193	41.9
Tumor encapsulation	complete	103	46.0	211	55.5	256	55.5
	none	121	54.0	169	44.5	205	44.5
Tumor differentiation	I+II	152	67.9	285	75.0	308	66.8
	III+IV	72	32.1	95	25.0	153	33.2
TNM stage	I	124	55.4	234	61.6	236	51.2
	II+III	100	44.6	146	38.4	225	48.8

Abbreviations: AFP, alpha-fetoprotein; GGT, gamma glutamyl transferase; TNM, tumor-node-metastasis.

**Supplementary Table 2. The distribution of plasmacytoid dendritic cells (pDCs) in the whole tumor sections of HCC (cohort 1, n=224).**

Variable*	Mean	SE	Range	<i>p</i> <sup>#</sup>
BDCA2+ pDCs:				
Intratumoral	8.86	0.84	0-127	
Peritumoral stroma	23.43	1.70	0-145	<i>P</i> <0.001
Nontumoral	38.64	2.50	0-221	<i>P</i> <0.001

\* Number of BDCA2+ cells per mm<sup>2</sup>.

# Compared with intratumoral pDCs.

**Supplementary Table 3. Correlation between the ratio of intratumoral pDCs and/or pDCs of nontumor tissues and peritumor stromal tissues of whole tumor sections and clinicopathologic characteristics in HCC (cohort 1, n=224)**

Clinicopathological indexes		Intratumoral pDCs/Peritumor stromal pDCs (Cut-off 50%)			Nontumoral pDCs/Peritumor stromal pDCs (Cut-off 50%)		
		Low	High	P	Low	High	P
Age(year)	≤50	47	48	0.984	47	48	0.892
	>50	64	65		65	64	
Sex	Female	15	10	0.268	9	16	0.137
	Male	96	103		103	96	
HBsAg	Negative	26	16	0.076	22	20	0.732
	Positive	85	97		90	92	
HCV	Negative	109	113	†0.244	110	112	†0.498
	Positive	2	0		2	0	
AFP (ng/ml)	≤20	44	47	0.766	43	48	0.496
	>20	67	66		69	64	
GGT (U/L)	≤54	42	41	0.810	44	39	0.489
	>54	69	72		68	73	
Liver cirrhosis	No	17	13	0.402	15	15	1.000
	yes	94	100		97	97	
Tumor size(cm)	≤5	50	53	0.780	52	51	0.893
	>5	61	60		60	61	
Tumor number	Single	97	95	0.478	96	96	1.000
	Multiple	14	18		16	16	
Vascular invasion	absence	76	68	0.195	70	74	0.577
	present	35	45		42	38	
Tumor encapsulation	complete	55	48	0.288	52	51	0.893
	none	56	65		60	61	
Tumor differentiation	I+II	79	73	0.293	72	80	0.252
	III+IV	32	40		40	32	
TNM stage	I	69	55	<b>0.042</b>	61	63	0.788
	II+III	42	58		51	49	

Abbreviations: AFP, alpha-fetoprotein; GGT, gamma glutamyl transferase; TNM, tumor-node-metastasis.

†Fisher's exact tests; Chi-square tests for all the other analyses.

**Supplementary Table 4. Descriptive statistics of immunohistochemical variables of intratumoral lymphocytes in HCC and correlations with pDCs (cohort 1, n=224)**

Variable*	Mean	SE	Range	Correlations with pDCs#
CD3+	298.7	23.96	7-1779	r=0.078, p=0.217
CD4+	119.6	9.57	4-712	r=0.126, p=0.098
CD8+	108.1	8.85	5-636	r=0.025, p=0.537
Granzyme B+	33.98	3.42	0-256	r=0.092, p=0.188

\* Number of lymphocytes per mm<sup>2</sup>.

# Correlations of pDCs with intratumoral lymphocytes were tested using Spearman's rho coefficients tests

**Supplementary Table 5. Correlation between intratumoral Treg cells or IL-17<sup>+</sup> cells of whole tumor sections and clinicopathologic characteristics in HCC (cohort 1, n=224)**

Clinicopathological indexes		Intratumoral Treg cells (Cut-off 50%)			Intratumoral IL-17 <sup>+</sup> cells (Cut-off 50%)		
		Low	High	P	Low	High	P
Age(year)	≤50	50	45	0.740	43	52	0.383
	>50	65	64		66	63	
Sex	Female	14	11	0.621	11	14	0.621
	Male	101	98		98	101	
HBsAg	Negative	26	16	0.129	22	20	0.593
	Positive	89	93		87	95	
HCV	Negative	113	109	†0.498	108	114	†1.000
	Positive	2	0		1	1	
AFP (ng/ml)	≤20	46	45	0.845	51	40	0.067
	>20	69	64		58	75	
GGT (U/L)	≤54	45	38	0.509	47	36	0.067
	>54	70	71		62	79	
Liver cirrhosis	No	16	14	0.814	18	12	0.182
	yes	99	95		91	103	
Tumor size(cm)	≤5	54	49	0.764	58	45	<b>0.035</b>
	>5	61	60		51	70	
Tumor number	Single	95	97	0.172	94	98	0.827
	Multiple	20	12		15	17	
Vascular invasion	absence	81	63	<b>0.049</b>	79	65	<b>0.013</b>
	present	34	46		30	50	
Tumor encapsulation	complete	65	48	0.570	56	47	0.115
	none	60	61		53	68	
Tumor differentiation	I+II	84	68	0.088	76	76	0.560
	III+IV	31	41		33	39	
TNM stage	I	69	55	0.151	69	55	<b>0.020</b>
	II+III	46	54		40	60	

Abbreviations: AFP, alpha-fetoprotein; GGT, gamma glutamyl transferase; TNM, tumor-node-metastasis.

†Fisher's exact tests; Chi-square tests for all the other analyses.

**Supplementary Table 6. Univariate and multivariate analyses of prognostic factors in TMA of HCC**

**(cohort 2, n=380)**

Variable	TTR		OS	
	HR(95%CI)	P	HR(95%CI)	P
<b>Univariate analysis</b>				
Age, year (≤50 versus >50)	1.229(0.934-1.615)	.140	1.036(0.768-1.398)	.817
Sex (female versus male)	1.387(0.954-2.016)	.087	1.093(0.735-1.625)	.662
HBsAg (negative versus positive)	1.387(0.921-2.087)	.117	1.172(0.757-1.814)	.478
AFP,ng/ml (≤20 versus>20)	1.302(0.991-1.710)	.058	1.607(1.175-2.199)	<b>.003</b>
GGT,U/L (≤54 versus>54)	1.698(1.305-2.210)	<b>.000</b>	1.853(1.378-2.492)	<b>.000</b>
Liver cirrhosis (no versus yes)	1.647(1.101-2.463)	<b>.015</b>	1.466(0.939-2.290)	.092
Tumor size,cm(≤5 versus>5)	1.572(1.208-2.045)	<b>.001</b>	2.000(1.495-2.676)	<b>.000</b>
Tumor number (single versus multiple)	1.695(1.170-2.456)	<b>.005</b>	1.825(1.233-2.702)	<b>.003</b>
Vascular invasion (no versus yes)	1.767(1.349-2.313)	<b>.000</b>	1.855(1.378-2.496)	<b>.000</b>
Tumor encapsulation (complete vs none)	1.312(1.011-1.704)	<b>.041</b>	1.300(0.972-1.739)	.077
Tumor differentiation (I+II versus III+IV)	1.443(1.078-1.931)	<b>.014</b>	1.746(1.278-2.386)	<b>.000</b>
TNM stage (I versus II III)	1.739(1.337-2.262)	<b>.000</b>	2.017(1.508-2.699)	<b>.000</b>
Intra- pDCs (low versus high)	1.797(1.375-2.348)	<b>.000</b>	2.005(1.485-2.707)	<b>.000</b>
Intra- pDCs and IL-17+ cells (both low versus both high)	2.013(1.476-2.744)	<b>.000</b>	2.318(1.633-3.291)	<b>.000</b>
Intra- pDCs and Treg cells (both low versus both high)	2.178(1.597-2.969)	<b>.000</b>	2.466(1.734-3.505)	<b>.000</b>
Intra- pDCs and IL-17+, and Treg cells (all low versus all high)	2.407(1.721-3.367)	<b>.000</b>	2.832(1.932-4.151)	<b>.000</b>
<b>Multivariate analysis</b>				
AFP,ng/ml (≤20 versus>20)	NA	NA	1.343(0.969-1.861)	.077
GGT,U/L (≤54 versus>54)	1.577(1.205-2.063)	<b>.001</b>	1.689(1.247-2.288)	<b>.001</b>
Liver cirrhosis (no versus yes)	1.455(0.964-2.197)	.074	NA	NA
Tumor size,cm(≤5 versus>5)	1.288(0.977-1.700)	.073	1.604(1.186-2.170)	<b>.002</b>
Tumor number (single versus multiple)	1.457(0.995-2.132)	.053	1.593(1.064-2.386)	<b>.024</b>
Vascular invasion (no versus yes)	1.410(1.060-1.876)	<b>.018</b>	1.283(0.937-1.758)	.121
Tumor encapsulation (complete vs none)	1.199(0.917-1.569)	.185	NA	NA
Tumor differentiation (I+II versus III+IV)	1.408(1.067-1.937)	<b>.017</b>	1.658(1.198-2.294)	<b>.002</b>
Intra- pDCs (low versus high)	1.541(1.165-2.038)	<b>.002</b>	1.799(1.315-2.460)	<b>.000</b>
Intra- pDCs and IL-17+ cells (both low versus both high)	1.655(1.194-2.292)	<b>.002</b>	1.913(1.326-2.760)	<b>.001</b>
Intra- pDCs and Treg cells (both low versus both high)	1.721(1.238-2.393)	<b>.001</b>	2.096(1.453-3.024)	<b>.000</b>
Intra- pDCs and IL-17+, and Treg cells (all low versus all high)	1.867(1.305-2.671)	<b>.000</b>	2.219(1.484-3.317)	<b>.000</b>

NOTE: Cox proportional hazards regression model. Abbreviations: AFP, alpha-fetoprotein; GGT, gamma glutamyl transferase; TNM, tumor-node-metastasis. HR, hazard ratio; CI, confidential interval.

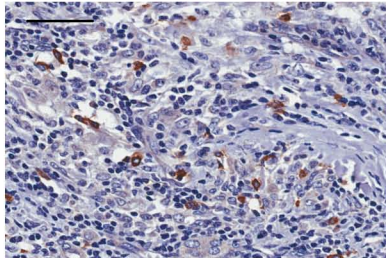
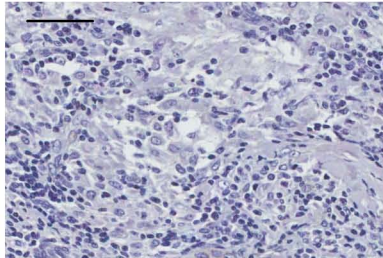
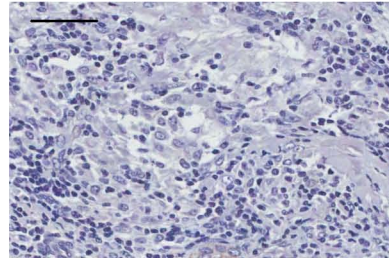
**Supplementary Table 7. Univariate and multivariate analyses of prognostic factors in TMA of HCC****(cohort 3, n=461)**

Variable	TTR		OS	
	HR(95%CI)	P	HR(95%CI)	P
<b>Univariate analysis</b>				
Age, year (≤50 versus >50)	0.981(0.783-1.229)	.869	1.042(0.815-1.332)	.741
Sex (female versus male)	1.011(0.739-1.384)	.945	1.024(0.728-1.441)	.890
HBsAg (negative versus positive)	1.347(0.947-1.917)	.097	1.100(0.767-1.578)	.606
AFP,ng/ml (≤20 versus>20)	1.646(1.285-2.109)	<b>.000</b>	1.505(1.152-1.967)	<b>.003</b>
GGT,U/L (≤54 versus>54)	1.928(1.525-2.438)	<b>.000</b>	2.148(1.657-2.784)	<b>.000</b>
Liver cirrhosis (no versus yes)	1.344(0.970-1.862)	.076	1.382(0.964-1.983)	.079
Tumor size,cm(≤5 versus>5)	1.802(1.434-2.264)	<b>.000</b>	1.976(1.538-2.539)	<b>.000</b>
Tumor number (single versus multiple)	1.623(1.206-2.185)	<b>.001</b>	1.547(1.124-2.131)	<b>.007</b>
Vascular invasion (no versus yes)	2.148(1.711-2.695)	<b>.000</b>	2.572(2.007-3.295)	<b>.000</b>
Tumor encapsulation (complete vs none)	1.503(1.199-1.883)	<b>.000</b>	1.695(1.326-2.167)	<b>.000</b>
Tumor differentiation (I+II versus III+IV)	1.506(1.192-1.902)	<b>.001</b>	1.568(1.218-2.019)	<b>.000</b>
TNM stage (I versus II III)	2.179(1.732-2.742)	<b>.000</b>	2.489(1.932-3.206)	<b>.000</b>
Intra- pDCs (low versus high)	1.705(1.357-2.142)	<b>.000</b>	1.837(1.430-2.360)	<b>.000</b>
Intra- pDCs and IL-17+ cells (both low versus both high)	1.826(1.407-2.371)	<b>.000</b>	2.030(1.523-2.706)	<b>.000</b>
Intra- pDCs and Treg cells (both low versus both high)	1.851(1.431-2.396)	<b>.000</b>	2.132(1.603-2.836)	<b>.000</b>
Intra- pDCs and IL-17+, and Treg cells (all low versus all high)	1.985(1.497-2.663)	<b>.000</b>	2.424(1.770-3.319)	<b>.000</b>
<b>Multivariate analysis</b>				
AFP,ng/ml (≤20 versus>20)	1.351(1.045-1.747)	<b>.022</b>	1.198(0.910-1.578)	.198
GGT,U/L (≤54 versus>54)	1.830(1.434-2.336)	<b>.000</b>	1.979(1.511-2.593)	<b>.000</b>
Tumor size,cm(≤5 versus>5)	1.297(1.019-1.651)	<b>.034</b>	1.428(1.099-1.855)	<b>.008</b>
Tumor number (single versus multiple)	1.561(1.156-2.107)	<b>.004</b>	1.542(1.115-2.133)	<b>.009</b>
Vascular invasion (no versus yes)	1.578(1.241-2.008)	<b>.000</b>	1.894(1.462-2.455)	<b>.000</b>
Tumor encapsulation (complete vs none)	1.282(1.017-1.616)	<b>.035</b>	1.461(1.138-1.877)	<b>.003</b>
Tumor differentiation (I+II versus III+IV)	1.174(0.923-1.492)	.192	1.191(0.919-1.543)	.187
Intra- pDCs (low versus high)	1.497(1.180-1.899)	<b>.000</b>	1.645(1.267-2.134)	<b>.000</b>
Intra- pDCs and IL-17+ cells (both low versus both high)	1.562(1.186-2.058)	<b>.000</b>	1.783(1.318-2.412)	<b>.000</b>
Intra- pDCs and Treg cells (both low versus both high)	1.602(1.220-2.104)	<b>.000</b>	1.927(1.425-2.605)	<b>.000</b>
Intra- pDCs and IL-17+, and Treg cells (all low versus all high)	1.685(1.250-2.273)	<b>.000</b>	2.190(1.571-3.052)	<b>.000</b>

NOTE: Cox proportional hazards regression model.

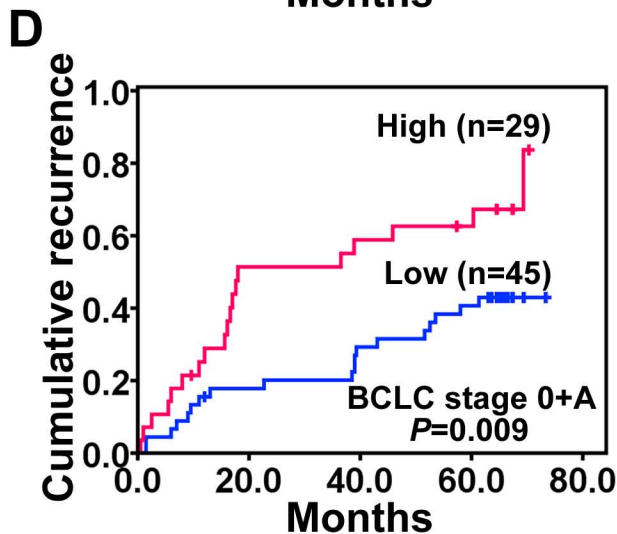
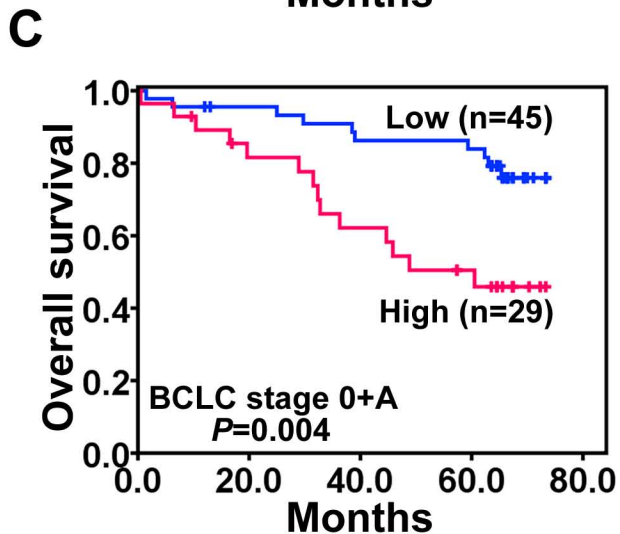
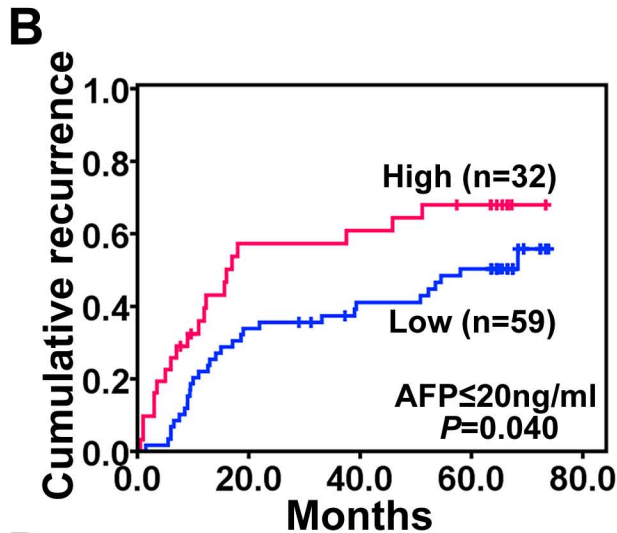
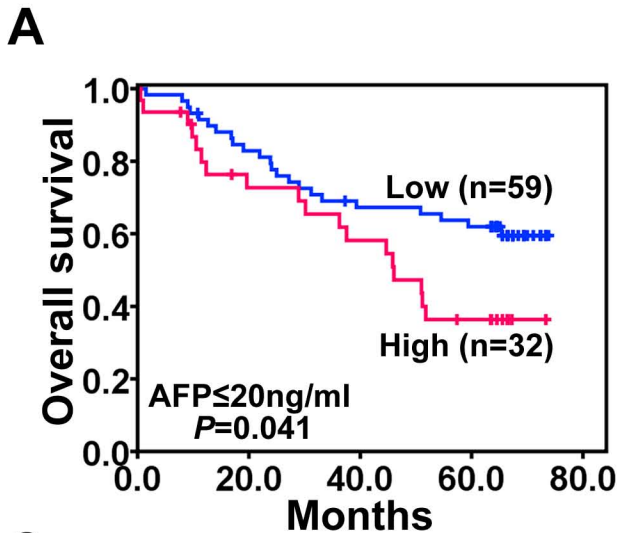
Abbreviations: AFP, alpha-fetoprotein; GGT, gamma glutamyl transferase; TNM, tumor-node-metastasis.

HR, hazard ratio; CI, confidential interval.

**A****BDCA2****B****Negative controls****C****Rabbit IgG**

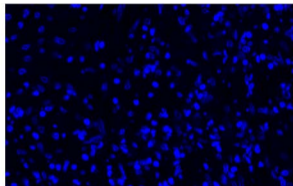
**Supplementary Figure 1. Immunohistochemistry staining showed (A) BDCA2, (B) Negative controls, and (C) Rabbit IgG. Scale bar=50 $\mu$ m.**



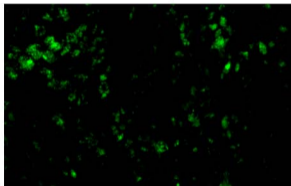


**Supplementary Figure 2. Kaplan–Meier analysis of intratumoral BDCA2+ pDCs in subgroups of HCC patients. The prognostic value of pDCs was significant in (A-B) the AFP  $\leq$  20 ng/mL and (C-D) BCLC stage 0+A.**

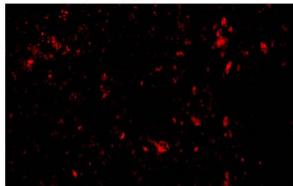
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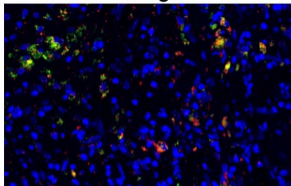
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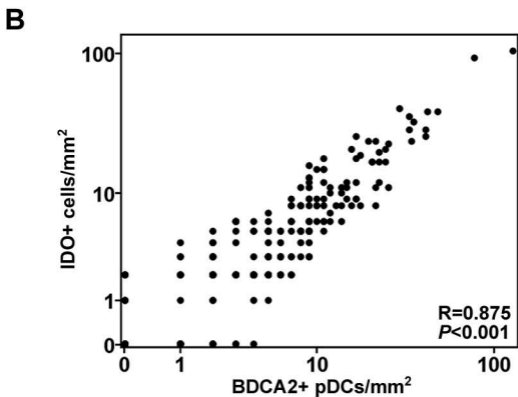
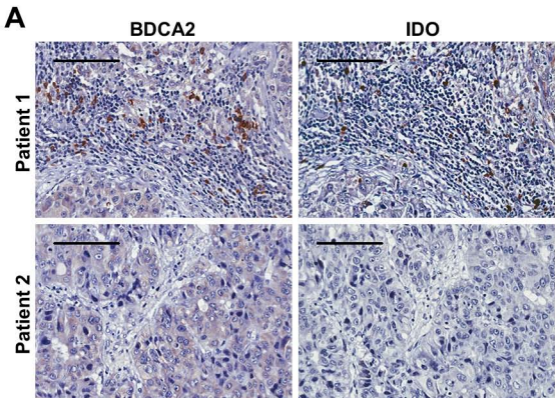
CD303



Merge



**Supplementary Figure 3. Fluorescence microscopy showed colocalization of BDCA2 and CD123 expression on cell surface.**



Supplementary Figure 4. High infiltration of intratumoral pDCs is associated with increased IDO+ cells. (A) High infiltration of intratumoral pDCs and IDO+ cells, and low infiltration of intratumoral pDCs and IDO+ cells. Scale bar=100 $\mu$ m. (C) Association between intratumoral pDCs and IDO+ cells.