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The expression of indoleamine 2,3-dioxygenase (IDO) by tumor cells has been considered as a major tumor immune escape mechanism ². The aim of this study was to investigate the expression of IDO in lung cancer cell lines as well as in surgically resected lung cancer specimens comparing the latter, to the expression in autologous samples from the corresponding non malignant lung tissue. Correlations of IDO expression with clinicopathological parameters of the disease were performed.

MATERIALS AND METHODS

Nine human lung cancer cell lines and 28 patients with various types of primary lung cancer were enrolled in the study. IDO expression was determined by quantitative real-time PCR using a sample of lung hamartoma as reference ³.

RESULTS

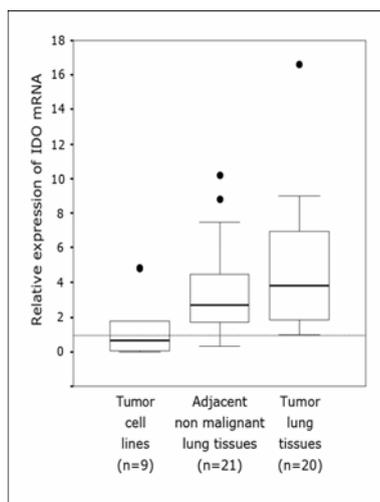
IDO expression was detected in all but three patients' tumor samples, in all but 4 autologous non malignant lung tissues and in three out of the nine cell lines that were examined. The relative expression of IDO in lung cancer cell lines (4.7 ± 11.1) was significantly lower than that of all patients' tumor samples ($p = 0.006$) as well as than that of the autologous non affected lung tissues ($p = 0.027$). No statistically significant differences were noted between ADC and SCC regarding either the tumor samples or the autologous non affected samples. No significant correlations between IDO expression and clinicopathological parameters were found.

PATIENT'S CHARACTERISTICS

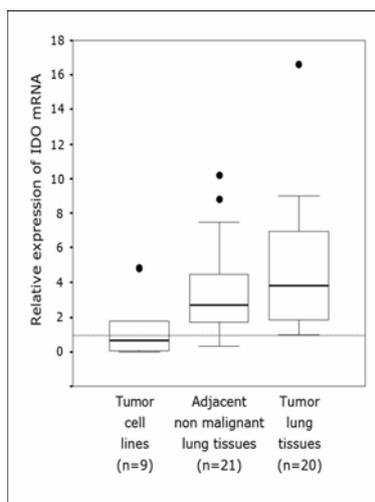
Patient no	Gender	Age (years)	Histology	Differentiation	TNM status	Stage	Tumor volume (mm ³)	IDO expression by Tumor ^a	IDO expression by Normal ^b
1	F	56	ADC	poor	T1N1M0	IA	15	16.6	10.2
2	M	65	ADC	moderate	T2N0M0	IB	56	6.5	4.4
3	M	65	ADC	poor	T1N2M0	IIA	15	2.6	7.5
4	F	48	ADC	moderate	T1N0M0	IA	27	3.8	2.3
5	F	59	ADC	well	T2N2M0	IIIA	120	3.3	1.7
6	M	73	ADC	moderate	T2N0M0	IB	52	1.0	3.0
7	M	55	ADC	moderate	T2N2M0	IIIB	57	8.5	2.1
8	M	60	ADC	poor	T2N1M0	IB	35	6.8	4.1
9	M	65	ADC	poor	T3N0M0	IB	55	37.5	2.7
10	M	74	ADC	poor	T2N0M0	IB	26	3.9	3.8
11	M	48	ADC	poor	T3N1M0	IIIA	1189	4.7	1.2
12	M	71	ADC	poor	T2N2M0	IIIA	361	7.1	0.9
13	M	61	SCC	poor	T2N0M1	IV	54	6.5	4.5
14	M	67	SCC	moderate	T1N0M0	IA	8	1.8	0.3
15	M	55	SCC	poor	T2N1M0	IB	42	1.0	N/A ^b
16	M	79	SCC	moderate	T2N0M0	IB	14	1.0	1.4
17	M	70	SCC	moderate	T2N0M0	IB	12	N/A	8.8
18	M	63	SCC	moderate	T3N1M0	IIIA	27	9.0	4.9
19	M	79	SCC	poor	T2N0M0	IB	37	2.9	2.2
20	M	59	SCC	moderate	T2N1M0	IB	23	N/A	5.2
21	M	62	SCC	poor	T2N0M0	IB	14	N/A	N/A
22	M	59	SCC	moderate	T1N1M0	IB	13	N/A	N/A
23	M	58	SCC	poor	T2N0M0	IB	29	1.9	0.6
24	F	76	SCC	moderate	T2N0M0	IB	428	1.6	2.0
25	M	40	SCC	poor	T3N1M0	IIIA	225	1.1	2.2
26	F	75	BAC	moderate	T2N0M0	IB	120	70.0	2.4
27	M	74	BAC	moderate	T2N1M0	IB	150	2.4	0.8
28	M	59	BAC	poor	T4N0M1	IV	31	1.5	2.7

^aRelative expression of IDO in tumor samples and adjacent non-affected lung tissues. ^bNot available.

RESULTS



Boxplot diagram of the relative expression of IDO mRNA in the lung cancer cell lines, the neighboring to the tumors non malignant tissues and the lung cancer tissues. An extreme value equal to 33.9 has been omitted from the group of cell lines and another one equal to 37.5 from the group of cancer tissues. The dotted line represents the expression level of the reference tissue.



Boxplot diagram of the relative expression of IDO mRNA in adenocarcinomas and squamous cell carcinomas. The gray boxes represent the neighboring to the tumors non malignant tissues and the open boxes the corresponding lung cancer tissues.

	Relative expression of IDO mRNA ^a		P-value
	Low (<3.3)	High (>3.3)	
Age (range; years) (mean±SD; years)	40-79 64.6±10.4	48-75 61.8±9.0	0.225
Sex (M/F)	14/2	9/3	0.206
Histotype			0.024
ADC	3	9	
SCC	10	2	
SCLC	1	-	
BAC	2	1	
Tumor status			0.143
T1	3	2	
T2	11	5	
T3	1	4	
T4	1	1	
N status			0.359
N0	9	6	
N1	5	4	
N2	2	2	
M status			0.420
M0	15	11	
M1	1	1	
Staging			0.125
I	8	3	
II	4	4	
III	3	4	
IV	1	1	
Differentiation			0.111
poor	6	7	
moderate	9	5	
well	1	-	
Tumor volume: mm ³	75.8±111.9	168.4±334.6	0.155
IDO expression			0.015
Tumor tissue	1.8±0.8	15.1±19.6	
Adjacent non-affected lung tissue	2.9±2.6	3.6±2.4	0.251

Clinical characteristics and distribution of patients according to their relative expression of IDO. ^aPatients were grouped according to the mean relative expression of IDO of adjacent non affected lung tissues.

Direct evidence is provided demonstrating that IDO mRNA can be constitutively expressed by lung cancer cells. The higher IDO expression observed in patients' samples can be attributed to the production of the enzyme by other cells recruited in the tumor microenvironment and the peri-tumoral lung area and/or to its induction by soluble factors of tumor origin.

References:

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