

KAI 1

Immunohistochemical Study of KAI1, a Tumor Metastasis Suppressor Gene, Expression in Rectal Cancer

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Purpose: KAI1/CD82 gene is a recently identified metastasis suppressor gene on human chromosome 11p11. Alteration to or reduction of this molecule may tumor cells to invade the surrounding tissue and vessels. Decreased KAI1 expression seems to be involved in the progression of human prostate, lung and po breast cancer, and recently has been demonstrated in several colorectal cell lines. The aim of this study is to determine whether the gene is altered to investigate its progression and metastatic process of rectal carcinoma. In addition, its prognostic significance is also evaluated. **Methods:** Total 108 tumor samples from primary, metastatic rectal carcinoma were prepared for immunohistochemical study with an anti-KAI1 polyclonal antibody to analyze the correlation between KAI1 expression and clinicopathological parameter and to evaluate for relationship between expression and survival.

Results: Decrease of KAI1 protein expression was associated with the depth of invasion of tumor (P<0.000) and lymph node metastasis (P<0.05). Liver metastasis showed decreased KAI1 expression when compared with their corresponding primary tumor. Although there was a trend of deteriorating survival from patients with KAI1-positive tumors to those with KAI1-decreased and -negative tumors,

it was not significant statistically (P=0.05). **Conclusions:** KAI1 may play a role in the malignant progression of rectal carcinoma through the down-regulation of expression. KAI1 might influence the metastatic process of human rectal cancer. And its prognostic significance needs further investigation with a larger number of patients. **J Korean Soc Coloproctol 2002;18:22-29**

Key Words: Rectal carcinoma, Metastasis suppressor gene, KAI1 gene, Immunohistochemical study

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2000

2001 6 28 29

2 ,
3
4 가
5 가
가
가
가
KAI1
가
KAI1
3-5 KAI1

KAI1

. Tris-

KAI1

HCl biotinylated rabbit anti-mouse immunoglobulin 15

KAI1

streptavidine-biotin complex 15

PBS biotinyl tyramide 가

amplification reagent 15

Horseshadish peroxide streptavidine

1990 1 1996 12 6

2)

0

133 가

4

90%

가

108

0

, 75%

가

1) KAI1

1 , 50%

2 , 25%

3

25%

4

가

KAI1 (C1-6, Santa Cruz Biotechnology, Santa Cruz, CA. USA) 1 : 200

3)

SPSS+ 8.0 version for Window

catalyzed signal amplification (CSA) system (Dako, CA. USA) 0.05 M Tris-HCl pH 7.6 0.3 M NaCl 0.1% Tween 20 TBST

KAI1 chi-square test

P < 0.05

Kaplan-Meier

, log rank test

KAI1

P 0.05

가

KAI1

4 μm xylene 10 가(2)

graded alcohol

1)

3%

5

0.015 M sodiumazide

55.1

60

phosphate-buffered saline (PBS) 5

가 가

1 : 1.2

1 : 200

3 6 cm가 60 , 6 cm 36

120

가 80 (74.1%) 가

14

12

가 10

(9.2%),

9 (8.3%),

89 (82.4%)

Duke B C가

Table 1. Clinical characteristics of patients

Characteristics	No (%)
Age	55.1±12.57
Sex (male : female)	51 : 57
Histologic grade	
Well	16 (14.8)
Moderate	80 (74.1)
Poor	12 (11.1)
Depth of invasion	
Mucosa/submucosa	1/9 (9.2)
Muscle	9 (8.3)
Perirectal fat	89 (82.4)
Metastasis	
LN metastasis	
N0	53 (46.2)
N1/N2	46/9 (42.5/8.3)
Liver metastasis	5 (4.6)
Stage (Duke's)	
A	1 (0.9)
B1	18 (16.6)
B2	33 (30.5)
C1	0 (0)
C2	51 (47.2)
D	5 (4.6)
Recurrence	
No	61 (55.5)
Local/Systemic	13/34 (12.0/31.5)

51 51

(Table 1).

2) KAI1

(1)

KAI1

:

KAI1

(Table 2).

KAI1

KAI1

0

(Fig. 1).

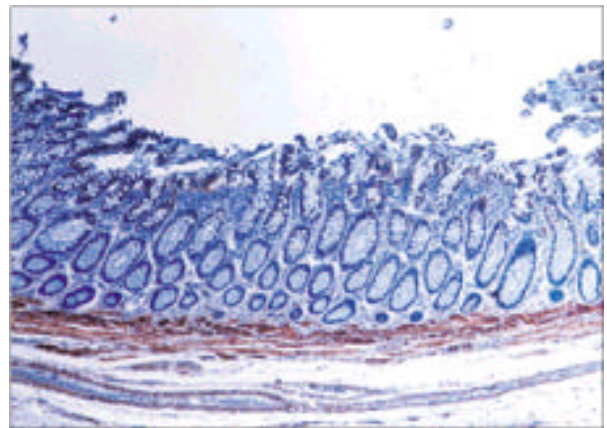


Fig. 1. The immunohistochemical stain for KAI1 of the normal colonic mucosa shows positivity in the cytoplasm of epithelium and muscularis mucosa (H&E, ×100).

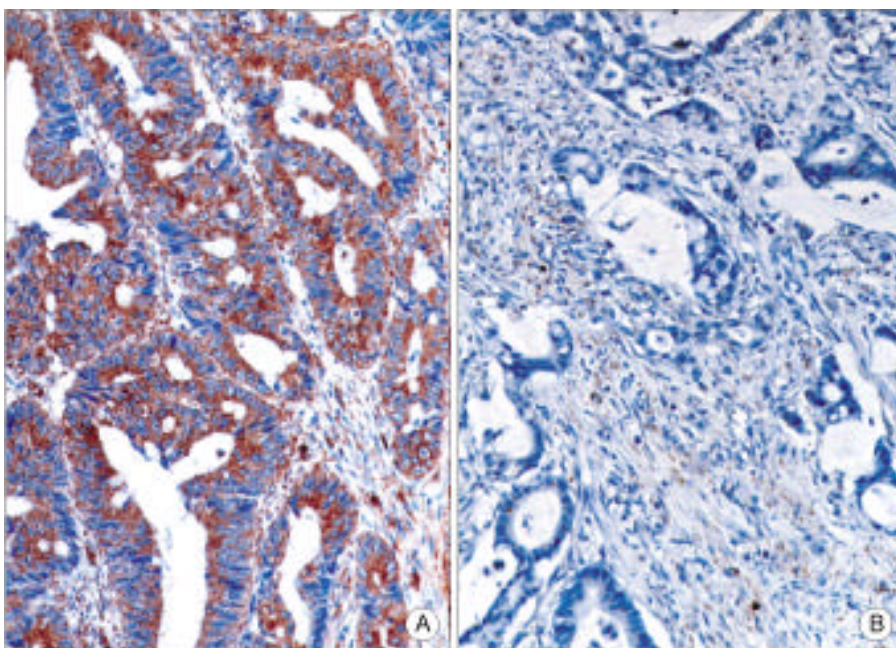


Fig. 2. The photomicrographs show the tumor with KAI1 immunoreactivity of KAI1 grade 0 (A) and that of grade 4 (B) (H&E, ×100).

Table 2. Relation between the grade of KAI1 expression and the clinicopathologic parameters

Parameter	No of cases	Grade of KAI1 expression				
		0	1	2	3	4
Age*						
39	12	1	4	4		3
40-49	27	1	3	10	8	5
50-59	26	2	6	5	8	5
60-69	29	2	7	11	6	3
70	14	2	3	6	2	1
Gender*						
Male	51	3	9	23	10	6
Female	57	5	14	13	14	11
Size of tumor*						
3 cm	12	2	1	3	5	1
3-6 cm	60	5	14	18	14	9
6 cm	36	1	8	15	5	7
Histologic Grade*						
Well	16	2	2	7	4	1
Moderate	80	5	21	26	15	13
Poor	12	1		3	5	3

*P > 0.05.

Table 3. Relation between the grade of KAI1 expression and the depth of invasion*

Depth of invasion	No of cases	Grade of KAI1 expression				
		0	1	2	3	4
Mucosa	1		1			
Submucosa	9	3	4	1	1	
Muscle	9	3	3	3		
Perirectal fat	89	2	15	32	23	17
Total	108	8	23	36	24	17

*P=0.0001.

, 4 (Fig. 2).
 80%가 1, ,
 67%가 1 KAI1
 가 .
 0 2.2%, 1 16.9%, 2 36%,
 3 25.8%, 4 19.1% 80.9%가 2
 , , KAI1
 가 (Table 3)(P <

Table 4. Relation between the grade of KAI1 expression in primary tumor and lymph node or liver metastasis

Parameter	No of cases	Grade of KAI1 expression				
		0	1	2	3	4
LN metastasis*						
N0, n=0	53	6	16	18	8	5
N1, n=1 3	46		6	14	15	11
N2, n= 4	9	2	1	4	1	1
Liver metastasis						
	5	0	0	1	0	4

*P=0.016

0.0001).

(2) KAI1 :
 가 55 KAI1

가 53
 가 (P=0.016), 가

KAI1 (Table 4).

KAI1

(Fig. 3).

가 5 KAI1

2 1 , 4 4

, 4 KAI1

(Fig. 4).

(3) KAI1 : Duke Stage A B

3 13.0% stage C D

3 50.9%, 80% stage C

D KAI1 stage A B

가 (P=0.0017)(Table 5).

(4) KAI1 :

56.8 (7 126)

47 13

(12%), 34 (31.4%)

KAI1

. KAI1 49%가 3

36%가 3 KAI1

53.8%가 3

47.0%

(Table 6).

(5) KAI1 : KAI1

5 0 50.0%, 1 69.5%,

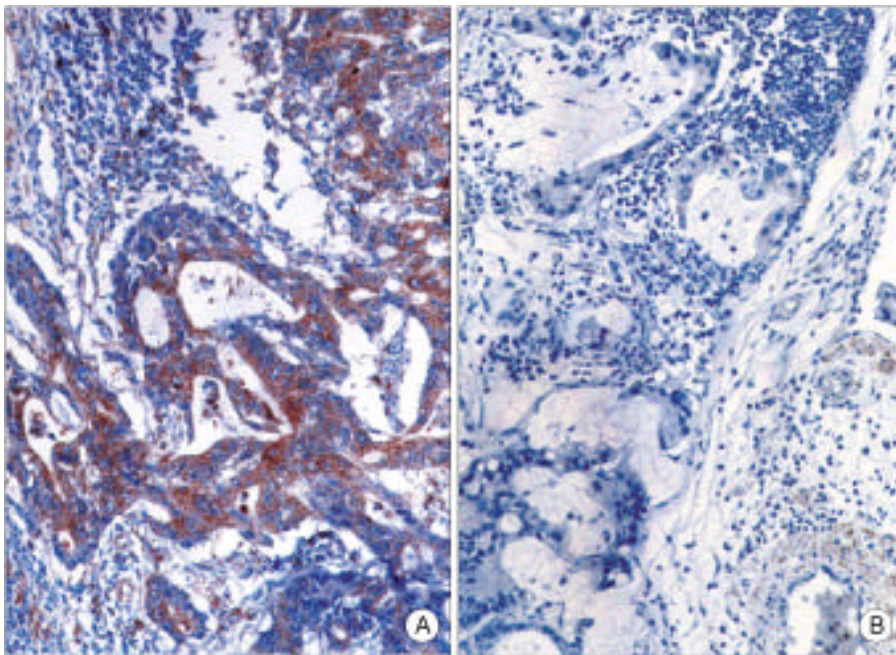


Fig. 3. The photomicrographs show the metastatic tumors with lymph node with KAI1 immunoreactivity of grade 0 (A) and that of grade 4 (B) (H&E, × 100).

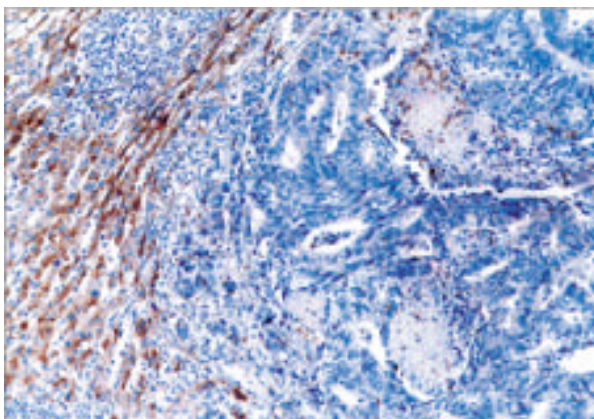


Fig. 4. The metastatic tumor in the liver show markedly decreased immunoreactivity for KAI1 (H&E, × 100).

Table 5. Relation between the grade of KAI1 expression and modified Astller-Coller stage of tumor*

MAC stage	No of cases	Grade of KAI1 expression				
		0	1	2	3	4
A	1	0				
B1	18	6	7	4	1	0
B2	33	1	7	14	8	4
C1	0					
C2	51	1	7	16	15	11
D	5				1	4

*P=0.0017.

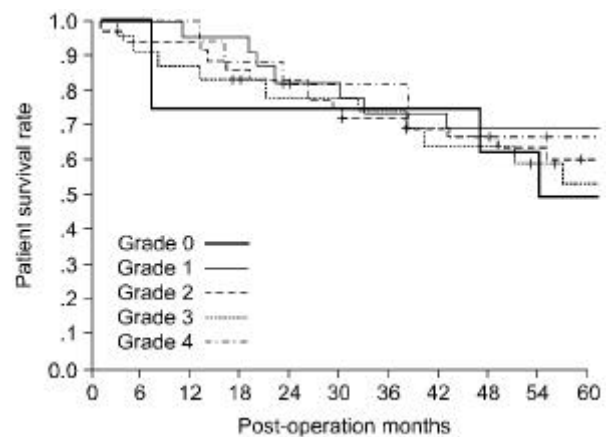


Fig. 5. Survival curve of rectal carcinoma in according to grade of KAI1 expression (P=0.899).

Table 6. Relation between the grade of KAI1 expression and recurrence*

Recurrence	No of cases	Grade of KAI1 expression				
		0	1	2	3	4
No	61	4	16	19	12	10
Yes						
Local	13		1	5	3	4
Systemic	34	4	6	8	9	7

*P=0.495.

2 60.5%, 3 53.5%, 4 67.0% KAI1
 (P=0.899)(Fig. 5).

70%가 가 20
 25% 가
 30 60% 가
 가
 가
 가 (oncogene)
 (tumor suppressor gene)가

CD82 KAI1
 가 가 2
 KAI1 267
 11 11.2 locus
 2,3 KAI1 (CD82) tetraspanins
 . Tetraspanins 4 membrane-spanning domains
 가 integrins,
 tetraspanins
 Maecker 9 tetraspanins molecular facilitators
 (group specific cell-surface proteins)
 가
 . Tetraspanins 가
 CD9/MRP-1, CD63/ME49 1, CD82/KAI1
 . CD9 가

,
 .¹⁰ CD63 melano-
 noma
 .¹¹
 Adachi¹² KAI1
 가 , Guo¹³ KAI1
 가 가
 ,¹⁴ ¹⁵ ¹⁶
 가
 KAI1¹⁷
 KAI1 가
 ,^{3,18}
 .⁶⁻⁸
 KAI1 KAI1 가
 Takaoka⁷ KAI1
 가
 . KAI1
 가
 ,¹⁹
 KAI1
 .^{2,20}
 Tetraspanin motility-related peptide-1
 (MRP-1 or CD9) melanoma-derived antigen (ME49 1 or
 CD63)^{10,11} tetra-
 spanin 가
 .^{7,8}
 p53
 KAI1 p53
 Mashimo²² KAI1 가
 topoisomerase II inhibitor etoposide가
 KAI1
 , p53 c-jun
 . Duriez²³ KAI1
 p53 transcriptional target gene
 .
 KAI1 KAI mRNA KAI1

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