

Adjuvant Immunochemotherapy with Protein-Bound Polysaccharide K for Colon Cancer in Relation to Oncogenic β -Catenin Activation

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Due to a production error, uncorrected versions of Figure 1, Table 1, Table 2, Table 5, and Supplementary Tables 1 and 2 were included in the article published in this issue (DOI: 10.1007/s10350-006-0842-5). We reprint them here in their entirety on the following pages. In addition, line 3 of the first paragraph in the section “Statistical Analysis of the Data and Survival Rates” should read “chi-square test” not “chi-squared test.”

Springer regrets the error.

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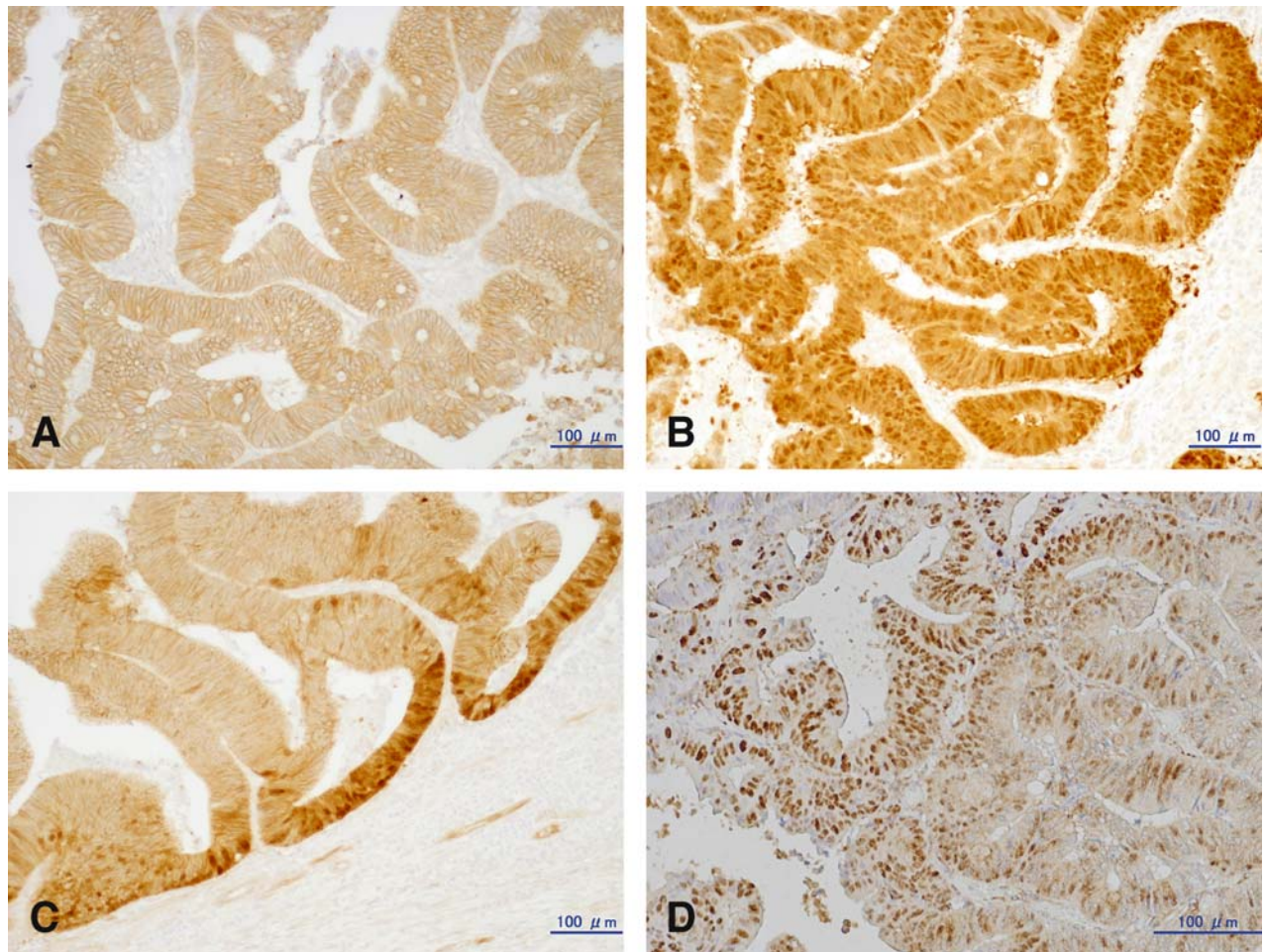


Figure 1. Representative expression patterns of β -catenin (A–C) and the active subunit (p65) of nuclear factor-kappaB (NF- κ B) (D) in colon cancer. A. Membranous expression. B. Diffuse nuclear accumulation-type β -catenin activation. C. Nuclear accumulation in the tumor invasion front-type β -catenin activation. D. Expression of the p65 subunit of NF- κ B in tumor cells' nuclei. Bar in each panel indicates a length of 100 μ M.

Table 1.
Comparison of Clinicopathologic Characteristics and Survival Rate Between the Groups of Patients with Regard to Different Forms of Adjuvant Therapy and Different Status of β -catenin Activation in the Primary Tumor

Variable/Category	All Patients		NA (-) (n=95)		NAd (n=89) ^b		NAinv (n=18)	
	PSK	5-FU	PSK	5-FU	PSK	5-FU	PSK	5-FU
Age (yr)								
≤65	55	70	35	23	16	39 ^c	4	8
>65	44	33	22	15	18	16	4	2
Male/female ratio	55/44	55/48	29/28	22/16	18/16	27/28	8/0	6/4
Gross type								
Expansive	82	86	45	33	30	46	7	7
Infiltrative	17	17	12	5	4	9	1	3
Histologic type								
W/D	55	55	26	23	23	28	6	4
M/D	40	47	27	15	11	26	2	6
P/D	4	1	4	0	0	1	0	0
Lymph vessel invasion								
Absent	22	34	10	13	9	18	3	3
Present	77	69	47	25	25	37	5	7
Venous invasion								
Absent	61	64	34	25	21	31	6	8
Present	38	39	23	13	13	24	2	2
TNM stage								
1	7	11	5	8	2	3	0	0
2	50	44	33	15	15	26	2	3
3	42	48	19	15	17	26	6	7
Lymph node dissection ^a								
D1	2	2	1	1	1	0	0	1
D2	40	37	22	18	13	17	5	2
D3	57	64	34	19	20	38	3	7
Survival rate (5-yr)								
RFS (%)	76.8	74.8	77.2	86.8	85.3	69.1 ^d	37.5	60
CDS (%)	86.6	81.4	87.4	92.1	94.1	77.9 ^e	50	60
OS (%)	82.8	80.6	82.5	92.1	91.2	76.4 ^f	50	60

PSK = polysaccharide K; 5-FU = 5-fluorouracil; W/D = well-differentiated adenocarcinoma; M/D = moderately differentiated adenocarcinoma; P/D = poorly differentiated adenocarcinoma; RFS = recurrence-free survival; CDS = cancer death survival; OS = overall survival; NA (-) = no β -catenin activation; NAd = diffuse nuclear accumulation-type β -catenin activation; NAinv = β -catenin activation in the tumor invasion front.

^a Level of lymph node dissection according to the Japanese Classification of Colorectal Carcinoma.²⁶

^b Survival curves of the patients with NAd-type β -catenin activation were shown in Figure 2.

^{c-f} Chi-square test: ^c $P=0.043$; Age adjusted log-rank test: ^d $P=0.027$; ^e $P=0.016$; ^f $P=0.02$.

Table 2.
Comparison of Survival Rates in Patients with NAd-type β -catenin Activation

Five-Year Survival Rate	Stage 1 and 2 (n=46)		Statistical Difference	Stage 3 (n=43)		Statistical Difference
	PSK	5-FU		PSK	5-FU	
RFS	100	80	NS: $P=0.077$	70.6	53.8	NS: $P=0.114$
CDS	100	96.2	NS: $P=0.265$	88.2	57.7	$P=0.019$
OS	100	92.3	NS: $P=0.175$	82.4	57.7	$P=0.038$

PSK = polysaccharide K; 5-FU = 5-fluorouracil; RFS = recurrence-free survival; CDS = cancer death survival; OS = overall survival; NS = not significant.

Data are percentages unless otherwise indicated.

Survival curves of the patients with tumor in Stage 3 were shown in Figure 2B.

Statistical difference was determined by an age-adjusted log-rank test.

Table 5. Influences of the Clinical and Histopathologic Characteristics and Types of Adjuvant Therapy on Survival of Patients with NAd-type β -catenin Activation in the Primary Tumor

Variable	Univariate analysis			RFS			CDS			OS		
	Category	HR (95% CI)	P Value	HR (95% CI)	P Value	HR (95% CI)	P Value	HR (95% CI)	P Value	HR (95% CI)	P Value	
Age (yr)	Older than 65 vs. 65 or younger	1.678 (0.727–3.873)	0.225	0.975 (0.354–2.682)	0.96	1.299 (0.512–3.291)	0.96	1.299 (0.512–3.291)	0.96	1.299 (0.512–3.291)	0.582	
Gender	Male vs. female	0.957 (0.415–2.208)	0.918	0.937 (0.352–2.496)	0.896	0.939 (0.373–2.365)	0.896	0.939 (0.373–2.365)	0.896	0.939 (0.373–2.365)	0.893	
Gross type	Infiltrative vs. expansive	0.975 (0.288–3.295)	0.967	1.499 (0.427–5.264)	0.528	1.297 (0.375–4.481)	0.528	1.297 (0.375–4.481)	0.528	1.297 (0.375–4.481)	0.681	
Histology	M/D + P/D vs. W/D	1.409 (0.611–3.251)	0.421	1.501 (0.560–4.020)	0.42	1.487 (0.587–3.764)	0.42	1.487 (0.587–3.764)	0.42	1.487 (0.587–3.764)	0.402	
Ly invasion	Present vs. absent	2.088 (0.707–6.171)	0.183	3.272 (0.743–14.403)	0.117	2.333 (0.675–8.064)	0.117	2.333 (0.675–8.064)	0.117	2.333 (0.675–8.064)	0.181	
V invasion	Present vs. absent	0.639 (0.26–1.566)	0.327	0.844 (0.307–2.322)	0.742	0.704 (0.264–1.875)	0.742	0.704 (0.264–1.875)	0.742	0.704 (0.264–1.875)	0.482	
TNM stage	Stage 3 vs. 1 + 2	4.217 (1.555–11.440)	0.005	9.508 (2.145–42.141)	0.003	6.694 (1.925–23.28)	0.003	6.694 (1.925–23.28)	0.003	6.694 (1.925–23.28)	0.003	
NF-kB	(+) vs. (-)	1.005 (0.393–2.567)	0.993	1.295 (0.45–3.731)	0.632	1.421 (0.533–3.788)	0.632	1.421 (0.533–3.788)	0.632	1.421 (0.533–3.788)	0.483	
Treatment	5-FU vs. PSK + 5-FU	2.416 (0.891–6.551)	0.083	4.796 (1.09–21.107)	0.038	3.427 (0.992–11.84)	0.038	3.427 (0.992–11.84)	0.038	3.427 (0.992–11.84)	0.051	
Multivariate Analysis												
RFS												
CDS												
OS												
Variable	Category	HR (95% CI)	P Value	HR (95% CI)	P Value	HR (95% CI)	P Value	HR (95% CI)	P Value	HR (95% CI)	P Value	
TNM stage	Stage 3 vs. 1 + 2	4.55 (1.574–13.148)	0.005	9.43 (2.018–44.068)	0.004	6.973 (1.877–25.903)	0.004	6.973 (1.877–25.903)	0.004	6.973 (1.877–25.903)	0.004	
Treatment	5-FU vs. PSK + 5-FU	3.544 (1.237–10.147)	0.018	6.213 (1.36–28.392)	0.019	4.567 (1.271–16.412)	0.019	4.567 (1.271–16.412)	0.019	4.567 (1.271–16.412)	0.02	

W/D = well-differentiated adenocarcinoma; M/D = moderately differentiated adenocarcinoma; P/D = poorly differentiated adenocarcinoma; Ly invasion = lymph vessel invasion; V invasion = venous invasion; PSK = polysaccharide K; 5-FU = 5-fluorouracil; RFS = recurrence-free survival; CDS = cancer death survival; OS = overall survival; NS = not significant; HR = hazard ratio; CI = confidence interval; NF- κ B = nuclear factor-kappaB; (-) = no activation or absence of nuclear accumulation; (+) = activated or presence of nuclear accumulation.

Supplementary Table 1.

Comparison of Clinicopathologic Characteristics and Survival Rates Between the Original Cohort of Patients in CIP Study and the Cohort of the Present Study

Variables/Categories	Original Cohort (n=441)	Present Cohort (n=202)	Statistical Difference
Age (yr)			
≤65	281 (63.7)	125 (61.9)	
>65	160 (36.3)	77 (38.1)	NS; <i>P</i> =0.719
Male/female ratio	244 (55.3)/197 (44.7)	110 (54.5)/92 (45.5)	NS; <i>P</i> =0.904
Gross type			
expansive	365 (82.8)	168 (83.2)	
infiltrative	76 (17.2)	34 (16.8)	NS; <i>P</i> =0.99
Histologic type			
W/D	225 (51)	110 (54.5)	
M/D	191 (43.3)	87 (43.1)	
P/D	25 (5.7)	5 (2.5)	NS; <i>P</i> =0.188
Lymph vessel invasion			
absent	117 (26.5)	56 (27.7)	
present	324 (73.5)	146 (72.3)	NS; <i>P</i> =0.825
Venous invasion			
absent	276 (62.6)	125 (61.9)	
present	165 (37.4)	77 (38.1)	NS; <i>P</i> =0.934
TNM stage			
Stage 1	36 (8.2)	18 (8.9)	
Stage 2	193 (43.8)	94 (46.5)	
Stage 3	212 (48.1)	90 (44.6)	NS; <i>P</i> =0.412
Adjuvant therapy			
PSK + 5-FU	220 (49.9)	99 (49)	
5-FU alone	221 (50.1)	103 (51)	NS; <i>P</i> =0.903
Survival rate (5-yr)			
RFS (%)	75.5	75.7	NS; <i>P</i> =0.664
CDS (%)	83.5	83.9	NS; <i>P</i> =0.85
OS (%)	81.9	81.7	NS; <i>P</i> =0.898

W/D = well-differentiated adenocarcinoma; M/D = moderately differentiated adenocarcinoma; P/D = poorly differentiated adenocarcinoma; 5-FU = 5-fluorouracil; PSK = protein-bound polysaccharide K; RFS = recurrence-free survival; CDS = cancer death survival; OS = overall survival; NS = not significant.

Data are numbers with percentages in parentheses unless otherwise indicated.

Supplementary Table 2.Comparison of Clinicopathologic Characteristics, Treatment Options, and β -catenin and NF- κ B Activation in the Tumor in the Respective Groups of Patients with Colon Cancer

Variable/Category	All Patients		NF- κ B (-) (n = 138)		NF- κ B (+) (n = 64)	
	NF- κ B (-)	NF- κ B (+)	PSK	5-FU	PSK	5-FU
Age (yr)						
\leq 65	83	42	36	47	19	23
$>$ 65	55	22	31	24	13	9
Male/female ratio	80/58	30/34	41/26	39/32	14/18	16/16
Gross type						
Expansive	118	50	57	61	25	25
Infiltrative	20	14	10	10	7	7
Histologic type						
W/D	77	33	43	34 ^a	12	21
M/D	59	28	22	37	18	10
P/D	2	3	2	0	2	1
Lymph vessel invasion						
Absent	40	16	15	25	7	9
Present	98	48	52	46	25	23
Venous invasion						
Absent	85	40	39	46	22	18
Present	53	24	28	25	10	14
TNM stage						
1	14	11	6	8	1	3
2	66	44	35	31	15	13
3	58	48	26	32	16	16
β -catenin status						
NA (-)	61	34	33	28	24	10
NAd	64	25	26	38	8	17
NAinv	13	5	8	5	0	5 ^b
Adjuvant therapy						
5-FU alone	67	32				
PSK + 5-FU	71	32				

W/D = well-differentiated adenocarcinoma; M/D = moderately differentiated adenocarcinoma; P/D = poorly differentiated adenocarcinoma; RFS = recurrence-free survival; CDS = cancer death survival; OS = overall survival; NA (-), no β -catenin activation; NAd = diffuse nuclear accumulation-type β -catenin activation; NAinv = β -catenin activation in the tumor invasion front; 5-FU = 5-fluorouracil; PSK = protein-bound polysaccharide K; NF- κ B = nuclear factor- κ B; (-) = no activation or absence of nuclear accumulation; (+) = activated or presence of nuclear accumulation.

^{a,b} Statistical difference determined by Chi-square test: ^a $P = 0.034$; ^b $P < 0.001$.