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SUPPLEMENTAL DATA

Tissue MICA/B expression and serum soluble MICA in cholangiocarcinoma: Associations with survival and advanced disease

Pornsinee Wilaikaew[1,2], Songpol Haohan[2], Malinee Thanee[3], Molin Wongwattanakul[2], Supakan Amontailak[2], Sutthiwan Janthamala[2], Attapol Titapun[4,5], Anchalee Techasen[2,4*]

[1]Medical Science Program, Faculty of Associated Medical Sciences, Khon Kaen University, Khon Kaen, Thailand;

[2]School of Medical Technology, Faculty of Associated Medical Sciences, Khon Kaen University, Khon Kaen, Thailand;

[3]Department of Pathology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand;

[4]Cholangiocarcinoma Research Institute, Khon Kaen University, Khon Kaen, Thailand;

[5]Department of Surgery, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand.

*Correspondence to **Anchalee Techasen**: anchte@kku.ac.th.

Full article is available at the following link: Tissue MICA/B expression and serum soluble MICA in cholangiocarcinoma: Associations with survival and advanced disease

Table S1. Performance of *MICA* mRNA expression in discriminating CCA from adjacent normal tissue: ROC analysis and YI-determined cut-off value

Group comparison	mRNA	AUC (95% CI)	Cut-off (Relative expression)	YI	Se (%)	Sp (%)	LR	*p* value
Adjacent normal vs CCA tissues	*MICA*	0.781 (0.63-0.93)	1.40	0.44	50.00	94.40	9.00	**<0.001**

Statistically significant *p* values are shown in bold. **Abbreviations**: AUC, area under the receiver operating characteristic curve; CCA, cholangiocarcinoma; CI, confidence interval; LR, likelihood ratio; MICA, major histocompatibility complex class I polypeptide-related sequence A; mRNA, messenger ribonucleic acid; ROC, receiver operating characteristic; Se, sensitivity; Sp, specificity; YI, Youden index.

Table S2. Association between *MICA* mRNA expression and clinicopathological characteristics and laboratory parameters

Characteristics*	Low *MICA* expression	High *MICA* expression	*p* value
Sex (*n*=30)			1.000
Female	6 (40.00%)	6 (40.00%)	
Male	9 (60.00%)	9 (60.00%)	
Age(median, years) (*n*=30)			1.000
<63	7 (46.70%)	7 (46.70%)	
≥63	8 (53.30%)	8 (53.30%)	
Location of tumor (*n*=30)			1.000
Intrahepatic (iCCA)	13 (86.70%)	12 (80.00%)	
Extrahepatic (eCCA)	2 (13.30%)	3 (20.00%)	
Tumor growth type (*n*=30)			1.000
Non-mixed type	6 (40.00%)	6 (40.00%)	
Mixed type	9 (60.00%)	9 (60.00%)	
Histological types (*n*=30)			0.682
Papillary	3 (20.00%)	5 (33.30%)	
Non-papillary	12 (80.00%)	10 (66.70%)	
Perineural invasion (*n*=30)			1.000
Invasion	6 (40.00%)	6 (40.00%)	
Non-invasion	9 (60.00%)	9 (60.00%)	
Lymph node metastasis (*n*=30)			0.715
Yes	6 (40.00%)	8 (53.30%)	
No	9 (60.00%)	7 (46.70%)	
OV infection (*n*=30)			0.598
Yes	1 (6.70%)	3 (20.00%)	
No	14 (93.30%)	12 (80.00%)	
Albumin (g/dl) (*n*=29)			1.000
<3.5	3 (21.40%)	3 (20.00%)	
≥3.5	11 (78.60%)	12 (80.00%)	
Total bilirubin (mg/dl)			0.648

(*n*=28)			
<1.2	12 (85.70%)	10 (71.40%)	
≥1.2	2 (14.30%)	4 (28.60%)	
Direct bilirubin (mg/dl)			1.000
(*n*=28)			
<0.3	7 (50.00%)	8 (57.10%)	
≥0.3	7 (50.00%)	6 (42.90%)	
ALT (U/l) (*n*=29)			1.000
<33	8 (57.10%)	8 (53.30%)	
≥33	6 (42.90%)	7 (46.70%)	
AST (U/l) (*n*=29)			0.715
<40	7 (50.00%)	6 (40.00%)	
≥40	7 (50.00%)	9 (60.00%)	
ALP (U/l) (*n*=29)			0.710
<129	5 (35.70%)	7 (46.70%)	
≥129	9 (64.30%)	8 (53.30%)	
CA19-9 (U/ml) (*n*=29)			0.710
<37	6 (42.90%)	5 (33.30%)	
≥37	8 (57.10%)	10 (66.70%)	
CEA (ng/ml) (*n*=28)			0.396
<2.5	2 (15.40%)	5 (33.30%)	
≥2.5	11 (84.60%)	10 (66.70%)	

p values were calculated using the chi-square test or Fisher's exact test, as appropriate. *Missing data were present for some clinicopathological and laboratory variables; therefore, denominators vary across variables. Data are presented as number (percentage), and percentages were calculated based on the number of patients with available data for each variable. **Abbreviations**: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CA19-9, carbohydrate antigen 19-9; CEA, carcinoembryonic antigen; eCCA, extrahepatic cholangiocarcinoma; iCCA, intrahepatic cholangiocarcinoma; MICA, major histocompatibility complex class I polypeptide-related sequence A; mRNA, messenger ribonucleic acid; OV, *Opisthorchis viverrini*.

Table S3. Univariate Cox proportional hazards analysis of *MICA* expression and clinicopathological factors for overall survival in CCA patient

Variables	Overall survival	
	Univariate analysis	
	HR (95% CI)	***p* value**
MICA expression (high)	1.00 (0.44, 2.28)	0.998
Sex (male)	1.06 (0.46, 2.46)	0.892
Age (≥63)	0.59 (0.26, 1.35)	0.212
Location of tumor (eCCA)	1.11 (0.38, 3.28)	0.849
Tumor growth type (mixed type)	1.81 (0.74, 4.46)	0.194
Histological type (non-papillary)	0.49 (0.21, 1.17)	0.107
Perineural invasion (invasion)	1.12 (0.49, 2.55)	0.796
Lymph node metastasis (yes)	1.59 (0.69, 3.68)	0.277
OV infection (positive)	0.53 (0.16, 1.81)	0.311
Albumin (g/dl) ≥3.5	0.53 (0.22, 1.43)	0.222
Total bilirubin (mg/dl) ≥1.2	1.14 (0.42, 3.09)	0.803
Direct bilirubin (mg/dl) ≥0.3	1.60 (0.69, 3.73)	0.273
ALT (U/l) ≥33	1.68 (0.72, 3.92)	0.229
AST (U/l) ≥40	1.79 (0.75, 4.28)	0.192
ALP (U/l) ≥129	1.99 (0.81, 4.93)	0.133
CA19-9 (U/ml) ≥37	1.18 (0.49, 2.83)	0.709
CEA (ng/ml) ≥2.5	3.21 (0.94, 10.97)	0.063

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CA19-9, carbohydrate antigen 19-9; CCA, cholangiocarcinoma; CEA, carcinoembryonic antigen; CI, confidence interval; eCCA, extrahepatic cholangiocarcinoma; HR, hazard ratio; MICA, major histocompatibility complex class I polypeptide-related sequence A; OV, *Opisthorchis viverrini*.

Table S4. Association between *MICB* mRNA expression and clinicopathological characteristics and laboratory parameters

Characteristics*	***MICB*-negative**	***MICB*-positive**	***p* value**
Sex (*n*=30)			0.193
Female	11 (47.80%)	1 (14.30%)	
Male	12 (52.20%)	6 (85.70%)	
Age (median, years) (*n*=30)			1.000
<63	11 (47.80%)	3 (42.90%)	
≥63	12 (52.20%)	4 (57.10 %)	
Location of tumor (*n*=30)			1.000
Intrahepatic (iCCA)	19 (82.60%)	6 (85.70%)	
Extrahepatic (eCCA)	4 (17.40%)	1 (14.30%)	
Tumor growth type (*n*=30)			0.666
Mixed type	14 (60.90%)	3 (42.90%)	
Non-mixed type	9 (39.10%)	4 (57.10%)	
Histological type (*n*=30)			0.306
Papillary	4 (17.40%)	3 (42.90%)	
Non-papillary	19 (82.60%)	4 (57.10%)	
Perineural invasion (*n*=30)			1.000
Invasion	11 (47.80%)	3 (42.90%)	
Non-invasion	12 (52.20%)	4 (57.10%)	
Lymph node metastasis (*n*=30)			0.399
Yes	12 (52.20%)	2 (28.60%)	
No	11 (47.80%)	5 (71.40%)	
OV infection (*n*=30)			0.128
Yes	1 (4.30%)	2 (28.60%)	
No	22 (95.70%)	5 (71.40%)	
Albumin (g/dl) (*n*=29)			0.253
<3.5	3 (13.60%)	2 (28.60%)	
≥3.5	19 (86.40%)	5 (71.40%)	
Total bilirubin (mg/dl) (*n*=28)			1.000
<1.2	16 (76.20%)	6 (85.70%)	
≥1.2	5 (23.80%)	1 (14.30%)	

Direct bilirubin (mg/dl) (*n*=28)			1.000
<0.3	10 (47.60%)	4 (57.10%)	
≥0.3	11 (52.40%)	3 (42.90%)	
ALT (U/l) (*n*=29)			1.000
<33	14 (63.60%)	4 (57.10%)	
≥33	8 (36.40%)	3 (42.90%)	
AST (U/l) (*n*=29)			0.667
<40	13 (59.10%)	3 (42.90%)	
≥40	9 (40.90%)	4 (57.10%)	
ALP (U/l) (*n*=29)			
<129	9 (40.90%)	2 (28.60%)	0.677
≥129	13 (59.10%)	5 (71.40%)	
CA19-9 (U/ml) (*n*=29)			1.000
<37	8 (34.80%)	2 (33.30%)	
≥37	15 (65.20%)	4 (66.70%)	
CEA (ng/ml) (*n*=28)			0.639
<2.5	6 (28.60%)	1 (14.30%)	
≥2.5	15 (71.40%)	6 (85.70%)	

p values were calculated using the chi-square test or Fisher's exact test, as appropriate. *Missing data were present for some clinicopathological and laboratory variables; therefore, denominators vary across variables. Data are presented as number (percentage), and percentages were calculated based on the number of patients with available data for each variable. **Abbreviations**: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CA19-9, carbohydrate antigen 19-9; CEA, carcinoembryonic antigen; eCCA, extrahepatic cholangiocarcinoma; iCCA, intrahepatic cholangiocarcinoma; MICB, major histocompatibility complex class I polypeptide-related sequence B; mRNA, messenger ribonucleic acid; OV, *Opisthorchis viverrini*.

Table S5. Association between MICA/B expression and clinicopathological characteristics and laboratory parameters

Characteristics*	Low MICA/B expression	High MICA/B expression	*p* value
Sex (*n*=101)			1.000
Female	17 (33.30%)	16 (32.00%)	
Male	34 (66.70%)	34 (68.00%)	
Age(median, years) (*n*=101)			0.427
<64	21 (41.20%)	25 (50.00%)	
≥64	30 (58.80%)	25 (50.00%)	
Location of tumor (*n*=96)			0.836
Intrahepatic (iCCA)	27 (57.40%)	30 (61.20%)	
Extrahepatic (eCCA)	20 (42.60%)	19 (38.80%)	
Tumor growth type (*n*=97)			0.837
Mixed type	29 (60.40%)	28 (57.10%)	
Non-mixed type	19 (39.60%)	21 (42.90%)	
Histological type (*n*=99)			1.000
Papillary	16 (32.00%)	16 (32.70%)	
Non-papillary	34 (68.00%)	33 (67.30%)	
Perineural invasion (*n*=101)			1.000
Invasion	24 (47.10%)	24 (48.00%)	
Non-invasion	27 (52.90%)	26 (52.00%)	
Lymph node metastasis (*n*=99)			0.687
Yes	24 (47.10%)	20 (41.70%)	
No	27 (52.90%)	28 (58.30%)	

OV infection (*n*=101)			0.577
Yes	9 (17.60%)	6 (12.00%)	
No	42 (82.40%)	44 (88.00%)	
Albumin (g/dl) (*n*=97)			
<3.5	10 (20.80%)	4 (8.20%)	0.090
≥3.5	38 (79.20%)	45 (91.80%)	
Total bilirubin (mg/dl) (*n*=97)			
<1.2	31 (62.00%)	28 (59.60%)	0.838
≥1.2	19 (38.00%)	19 (40.40%)	
Direct bilirubin (mg/dl) (*n*=97)			
<0.3	19 (38.00%)	19 (40.40%)	0.838
≥0.3	31 (62.00%)	28 (59.60%)	
ALT (U/l) (*n*=98)			
<33	21 (42.00%)	23 (47.90%)	0.685
≥33	29 (58.00%)	25 (52.10%)	
AST (U/l) (*n*=98)			
<40	21 (42.00%)	18 (37.50%)	0.684
≥40	29 (58.00%)	30 (62.50%)	
ALP (U/l) (*n*=98)			
<129	12 (24.00%)	18 (37.50%)	0.190
≥129	38 (76.00%)	30 (62.50%)	
CA19-9 (U/ml) (*n*=98)			
<37	17 (35.40%)	15 (30.00%)	0.668
≥37	31 (64.60%)	35 (70.00%)	
CEA (ng/ml) (*n*=85)			
<2.5	9 (23.10%)	15 (32.60%)	0.469
≥2.5	30 (76.90%)	31 (67.40%)	

p values were calculated using the chi-square test or Fisher's exact test, as appropriate. *Missing data were present for some clinicopathological and laboratory variables; therefore, denominators vary across variables. Data are presented as number

(percentage), and percentages were calculated based on the number of patients with available data for each variable. **Abbreviations**: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CA19-9, carbohydrate antigen 19-9; CEA, carcinoembryonic antigen; eCCA, extrahepatic cholangiocarcinoma; iCCA, intrahepatic cholangiocarcinoma; MICA/B, major histocompatibility complex class I chain-related molecules A and B; OV, *Opisthorchis viverrini*.