

Dual epigenetic changes in diabetes mellitus-associated pancreatic ductal adenocarcinoma correlate with downregulation of E-cadherin and worsened prognosis

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Supplementary Figure S1
Supplementary Tables S1 – S3

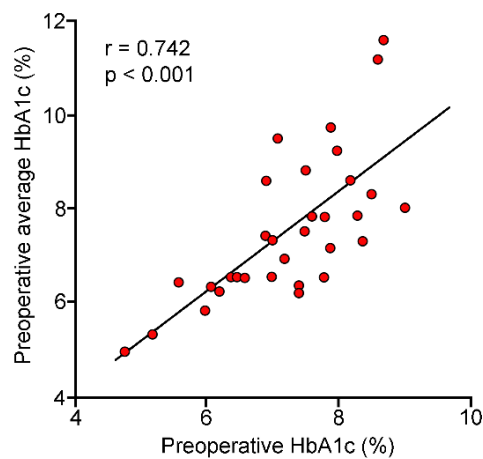


Figure S1. Preoperative HbA1c levels (within 1 month) showed a significant proportional correlation with average HbA1c levels 3-12 months before surgery in PDAC subjects ($r = 0.742$, $p < 0.001$). PDAC, pancreatic ductal adenocarcinoma.

Table S1. Clinicopathological characteristics of 132 subjects

	Control	DM	p-value
Number (male:female)	67 (28:39)	65 (36:29)	0.216
Age (year)*	70 (66 – 75)	70 (66 – 75)	0.868
Smoker	50.8% (34/67)	53.9% (35/65)	0.778
Body mass index (kg/m ²)*	21.8 (19.7 – 24.0)	23.5 (21.1 – 26.1)	< 0.01
Diabetes duration (years)	N.A.	3.0 (0 – 10)	-
Long-DM	N.A.	52.3% (34/65)	-
Diabetes therapy			
Diet only	N.A.	36.9% (24/65)	-
DPP4 inhibitor	N.A.	52.3% (34/65)	-
Metformin	N.A.	12.3% (8/65)	-
Insulin	N.A.	16.9% (11/65)	-
HbA1c (NGSP, %) (pre-operation)*	5.6 (5.3 – 6.0)	7.2 (6.5 – 7.9)	< 0.01
Tumor size (mm)*	30.0 (22.5 – 39.0)	30.0 (25.0 – 40.0)	0.388
T stage:			
T1-T2	68.7% (46/67)	63.1% (41/65)	
T3-T4	31.3% (21/67)	36.9% (24/65)	0.456
N stage:			
N0	46.3% (31/67)	43.1% (28/65)	
N1	53.7% (36/67)	56.9% (37/65)	0.776
Histological grade:			
Well-mod	77.6% (52/67)	69.2% (45/65)	
Poor	22.4% (15/67)	30.8% (20/65)	0.200
ly-factor			
0-1	26.9% (18/67)	35.4% (23/65)	
2-3	73.1% (49/67)	66.2% (43/65)	0.286
v-factor			
0-1	22.4% (15/67)	20.0% (13/65)	
2-3	77.6% (52/67)	80.0% (52/65)	0.862
ne-factor			
0-1	10.5% (7/67)	7.7% (5/65)	
2-3	89.6% (60/67)	92.3% (60/65)	0.806

Table S1 Continued

INF type			
a-b	23.9% (16/67)	23.1% (15/65)	
c	76.1% (51/67)	76.9% (50/65)	> 0.999
Location			
Ph	74.6% (50/67)	53.9% (35/65)	
Pb-t	25.4% (17/67)	38.5% (25/65)	
Phbt	0	7.7% (5/65)	< 0.01
Type of resection			
Pancreatico-duodenectomy	71.6% (48/67)	50.8% (33/65)	
Distal pancreatectomy	25.4% (17/67)	38.5% (25/65)	
Total pancreatectomy	3.0% (2/67)	10.8% (7/65)	< 0.05
Curative resection			
R0	92.5% (62/67)	93.9% (61/65)	
R1-2	7.5% (5/67)	6.2% (4/65)	> 0.999
Neo-adjuvant chemotherapy	6.0% (4/67)	13.9% (9/65)	0.097
Post-operative chemotherapy	86.6% (58/67)	80.0% (52/65)	0.253
Resectability			
Resectable	85.1% (57/67)	81.5% (53/65)	
Borderline resectable	14.9% (10/67)	18.5% (12/65)	0.704
CA19-9 (U/mL)	67.0 (11.5 – 220)	72.0 (25 – 322)	0.497

DM, diabetes mellitus; long-DM, long duration of DM; N.A., not applicable; DPP4, dipeptidyl peptidase4; well, well differentiated adenocarcinoma; mod, moderately differentiated adenocarcinoma; poor, poorly differentiated adenocarcinoma. *Values are expressed as median (range).

Table S2. Univariate analysis (Disease Free Survival)

Factor	Median DFS (date)	p-value
Age (years): < 65 vs \geq 65	418 vs 428	0.737
Male vs Female	369 vs 461	0.200
Location: Body-Tail vs Head	441 vs 407	0.306
Tumor size (mm): < 30 vs \geq 30	460 vs 287	< 0.05
T1-2 vs T3-4	433vs 365	0.306
N: N0 vs N1	632 vs 365	< 0.001
CA19-9 (U/mL): < 200 vs \geq 200	464 vs 282	< 0.01
Adjuvant chemotherapy: (-) vs (+)	244 vs 441	< 0.001
HbA1c (%): \geq 6.5 vs < 6.5	342 vs 441	< 0.05
DM: (+) vs (-)	365 vs 460	0.09
Long-DM: (+) vs (-)	341 vs 437	0.152
miR-100-5p expression: < 4.13 vs \geq 4.13	460 vs 365	< 0.05
<i>CDH1</i> promoter methylation: (-) vs (+)	461 vs 352	< 0.01

DFS, disease free survival; DM, diabetes mellitus; long-DM, long duration of DM.

Table S3. Multivariate analysis (Disease Free Survival)

Factor	Risk ratio	95%CI	p-value
Tumor size (mm): ≥ 30	1.58	1.03 – 2.43	< 0.05
N: N1	1.52	0.98 – 2.36	0.06
CA19-9 (U/mL): ≥ 200	1.58	1.02 – 2.45	< 0.05
Adjuvant chemotherapy: (+)	0.41	0.25 – 0.69	<0.01
miR-100-5p expression: ≥ 4.13	1.54	1.01 – 2.35	< 0.05
<i>CDH1</i> promoter methylation: (+)	1.71	1.13 – 2.58	< 0.05

CI, confidence interval