

Supplementary Information

Additional file 1:

Supplementary Table 1. Characteristics of resected PDAC patients.

Characteristic	Italian Cohort N° of patients (%) – n=42	Spanish Cohort N° of patients (%) – n=49
Gender		
Male	26 (61.9)	30 (61.2)
Female	16 (38.1)	19 (38.8)
Sugery		
Duodenopancreatectomy	28 (66.7)	44 (89.8)
Distal pancreatectomy	14 (33.3)	5 (10.2)
Site		
Head	35 (83.3)	45 (91.8)
Body	5 (11.9)	1 (2.0)
Tail	2 (4.8)	3 (6.1)
Grade of differenciation		
1	2 (4.9)	4 (8.2)
2	23 (56.1)	28 (57.1)
3	16 (39.0)	17 (34.7)
Tumor (pT)		
1	4 (9.5)	0 (0.0)
2	29 (69.0)	1 (2.0)
3	9 (21.4)	48 (98.0)
Nodes (pN)		
0	17 (40.5)	15 (30.6)
1	12 (28.6)	34 (69.4)
2	13 (31.0)	0 (0.0)
Surgical margins		
R0	37 (90.2)	22 (44.9)
R1	4 (9.8)	27 (55.1)
Vascular Invasioin (pV)		
No	7 (23.3)	33 (68.8)
Yes	23 (76.7)	15 (31.2)
NA		0 (0.0)
Perineural Invasion (pPn)		
No	5 (14.3)	16 (33.3)
Yes	30 (85.7)	32 (66.7)
NA		
PDAC Relapse		
No	7 (16.7)	12 (24.5)
Yes	35 (83.3)	37 (75.5)
End of Surveillance		
Death	35 (83.3)	44 (89.8)
Alive	7 (16.7)	1 (2.0)
Alive (lost to follo-up)	0 (0.0)	4 (8.2)

Supplementary Table 2. IHQ tumor expression of G9a, DNMT1 and UHRF1 in Italian PDAC patient's cohort according to a semi-quantitative scoring system.

Scoring	G9a N°/n (%) n=42	DNMT1 N°/n (%) n=42	UHRF1 N°/n (%) n=42
0	0 (0)	5 (11,9)	0 (0)
1+	2 (4,5)	13 (30,9)	6 (14,2)
2+	2 (4,5)	9 (21,4)	3 (7,1)
3+	37 (88)	9 (21,4)	32 (76,1)

Supplementary Table 3. G9a, DNMT1 and UHRF1 expression (3+) versus (2+/1+/0) in cancer tissue versus normal pancreatic ducts in the entire cohort (n=91) and in specific Italian and Spanish cohorts.

Whole Cohort	Normal duct n=91	Cancer n=91	OR (95% CI)	p-value
DNMT1				
0/+1/+2	70	44		
3	7	39	8.86 (3.65,21.55)	<0.001
G9a				
0/+1/+2	57	27		
3	12	63	11.08 (5.14, 23.90)	<0.001
UHRF1				
0/+1/+2	69	46		
3	1	44	66 (8.78, 496)	<0.001
Italian Cohort	Normal duct n=42	Cancer n=42	OR (95% CI)	p-value
DNMT1				
0/+1/+2	27	27		
3	4	9	2.25 (0.62, 8.20)	0.21
G9a				
0/+1/+2	18	4		
3	3	37	55.5 (11.21, 274.73)	<0.001
UHRF1				
0/+1/+2	20	9		
3	1	32	71.11 (8.36, 604.52)	<0.001
Spanish Cohort	Normal duct n=49	Cancer n=49	OR (95% CI)	p-value
DNMT1				
0/+1/+2	43	17		
3	3	30	125.36 (24.59, 639.12)	<0.001
G9a				
0/+1/+2	39	23		
3	9	26	4.904 (1.96, 12.25)	<0.001
UHRF1				
0/+1/+2	49	37		
3	0	12		

Supplementary Table 4. Correlation of DNMT1, G9a and UHRF1 expression in cancer and normal pancreatic ducts with clinicopathological variables.

Variables	DNMT1			G9a			UHRF1		
	0/+1/+2 (n=44)	3 (n=39)	p-value	0/+1/+2 (n=27)	3 (n=63)	P Value	0/+1/+2 (n=46)	3 (n=44)	p-value
Gender			0.8243			0.8135			0.7006
Male	27 (54.0)	23 (46.0)		17 (30.9)	38 (69.1)		29 (52.7)	26 (47.3)	
Female	17 (51.5)	16 (48.5)		10 (28.6)	25 (71.4)		17 (48.6)	18 (51.4)	
Site			0.6735			0.8610			0.6261
Head	38 (52.8)	34 (47.2)		23 (29.1)	56 (70.9)		41 (51.9)	38 (48.1)	
Body	4 (66.7)	2 (33.3)		2 (33.3)	4 (66.7)		2 (33.3)	4 (66.7)	
Tail	2 (40.0)	3 (60.0)		2 (40.0)	3 (60.0)		3 (60.0)	2 (40.0)	
Surgery			0.4366			0.6932			0.7133
Duodenopancreatectomy	33 (50.8)	32 (49.2)		22 (31.0)	49 (69.0)		37 (52.1)	34 (47.9)	
Distal pancreatectomy	11 (61.1)	7 (38.9)		5 (26.3)	14 (73.7)		9 (47.4)	10 (52.6)	
Grade of differentiation			0.9593			0.0499			0.2008
G1	17 (54.8)	14 (45.2)		13 (40.6)	19 (59.4)		20 (62.5)	12 (37.5)	
G2	19 (51.4)	18 (48.6)		7 (17.1)	34 (82.9)		17 (41.5)	24 (58.5)	
G3	8 (53.3)	7 (46.7)		7 (41.2)	10 (58.8)		9 (52.9)	8 (47.1)	
Tumor (pT)			0.0092			0.0114			0.0002
T1	2 (50.0)	2 (50.0)		0	4 (100)		1 (25.0)	3 (75.0)	
T2	19 (79.2)	5 (20.8)		4 (13.3)	26 (86.7)		7 (23.3)	23 (76.7)	
T3	23 (41.8)	32 (58.2)		23 (41.1)	33 (58.9)		38 (67.9)	18 (32.1)	
Nodes (pN)			0.0590			0.2232			0.0380
N0	18 (60.0)	12 (40.0)		8 (25.0)	24 (75.0)		15 (46.9)	17 (53.1)	
N1	18 (41.9)	25 (58.1)		17 (37.8)	28 (62.2)		28 (62.2)	17 (37.8)	
N2	8 (80.0)	2 (20.0)		2 (15.4)	11 (84.6)		3 (23.1)	10 (76.9)	
pM			0.9158			0.0003			0.2157
M0	16 (36.4)	28 (63.6)		20 (44.4)	25 (55.6)		35 (77.8)	10 (22.2)	
M1	1 (33.3)	2 (66.7)		3 (75.0)	1 (25.0)		2 (50.0)	2 (50.0)	
Vascular Invasion (pV)			0.0440			0.0210			0.0067
No	14 (37.8)	23 (62.2)		18 (45.0)	22 (55.0)		28 (70.0)	12 (30.0)	
Yes	21 (61.8)	13 (38.2)		7 (18.4)	31 (81.6)		15 (39.5)	23 (60.5)	
Lymphatic Invasion			0.8944			0.0020			0.7139
No	5 (38.5)	8 (61.5)		7 (50.0)	7 (50.0)		11 (78.6)	3 (21.4)	
Yes	12 (36.4)	21 (63.6)		15 (44.1)	19 (55.9)		25 (73.5)	9 (26.5)	
Perineural Invasion (pPn)			0.7393			0.3364			0.1148
No	10 (52.6)	9 (47.4)		9 (42.9)	12 (57.1)		14 (66.7)	7 (33.3)	
Yes	27 (48.2)	29 (51.8)		16 (25.8)	46 (74.2)		29 (46.8)	33 (53.2)	
Adjuvant			0.9574			0.9153			0.6194
No	10 (52.6)	9 (47.4)		7 (33.3)	14 (66.7)		10 (47.6)	11 (52.4)	
Yes	32 (53.3)	28 (46.7)		19 (29.2)	46 (70.8)		35 (53.8)	30 (46.2)	