



Supplementary Figure 1. (A) Overall survival for the whole population cohort. Median OS is 38 months (95% CI 8-30 months) (B) Schematic of the TempO-Seq™ workflow. (C) Survival analysis of patients categorized as M_CL1, M_CL2, M_CL3 according to metabolic profile (p=0.0013 by log-rank test). (D) Schematic of the digital pathology approach used to annotate pancreatic tissue as stroma, adipose or pancreatic gland. (E) Enrichment pathway analysis of M_CL1 versus M_CL3 samples. Dot-plot shows top 10 enriched GO terms in M_CL1, ordered by gene ratio (percentage of DEGs in the GO term) and color-coded by p-value. The size of the dot represents the count of the genes in the GO term.

Metabolites	Fold Change PDAC vs non PDAC
Dihydrothymine	1.40
Lactic acid	1.62
3-Hydroxymethylglutaric acid	1.75
Uridine	1.99
Valine	2.02
Methionine sulfone	2.12
N8-Acetylspermidine	2.53
Butyrylcarnitine	2.96
Pantothenic acid	3.03
Cysteine-S-sulfate	3.19
Methionine sulfoxide	3.49
Galacturonic acid	3.60
Alanylisoleucine	4.05
Glycerophosphocholine	-5.14
N-Acetyl-L-aspartic acid	-2.12
Ethanolamine	-1.54
Isopentenyl pyrophosphate	-1.26
4-Guanidinobutanoic acid	-1.17

Supplementary Figure 2. Metabolites significantly different in PDAC versus non PDAC juices (by Wilcoxon-Mann-Whitney test), confirmed by MS/MS.

Variable	N	Overall, N = 26 ¹	Cluster 1, N = 8 ¹	Cluster 2, N = 9 ¹	Cluster 3, N = 9 ¹	p-value ²
Molecular subtype	26					0.004
Classical		10 (38%)	2 (25%)	6 (67%)	2 (22%)	
Intermediate		8 (31%)	6 (75%)	0 (0%)	2 (22%)	
Squamous		8 (31%)	0 (0%)	3 (33%)	5 (56%)	
Gender	26					0.2
Female		15 (58%)	5 (62%)	7 (78%)	3 (33%)	
Male		11 (42%)	3 (38%)	2 (22%)	6 (67%)	
Age at surgery	26	72.50 (45.00-85.00)	76.50 (45.00-85.00)	72.00 (59.00-78.00)	68.00 (56.00-82.00)	0.3
BMI	26	24.00 (20.00-34.00)	23.50 (21.00-27.00)	22.00 (20.00-34.00)	25.00 (23.00-27.00)	0.3
Diabetes	26	13 (50%)	3 (38%)	4 (44%)	6 (67%)	0.6
Neoadjuvant therapy	26	1 (3.8%)	0 (0%)	1 (11%)	0 (0%)	>0.9
Adjuvant therapy	26	13 (50%)	4 (50%)	3 (33%)	6 (67%)	0.4
Perineural invasion	26	24 (92%)	7 (88%)	8 (89%)	9 (100%)	0.8
Lymphovascular invasion	26	22 (85%)	6 (75%)	8 (89%)	8 (89%)	0.7
R status	26					0.092
R0		14 (54%)	7 (88%)	3 (33%)	4 (44%)	
R1		12 (46%)	1 (12%)	6 (67%)	5 (56%)	
MPD diameter, mm	19	5.00 (2.00-10.00)	6.00 (2.00-10.00)	5.00 (3.00-7.00)	4.50 (3.00-7.00)	0.8
(Missing)		7	1	3	3	
T	26					0.5
T1		4 (15%)	2 (25%)	1 (11%)	1 (11%)	
T2		11 (42%)	4 (50%)	5 (56%)	2 (22%)	
T3		11 (42%)	2 (25%)	3 (33%)	6 (67%)	
N	26					0.5
N0		5 (19%)	3 (38%)	1 (11%)	1 (11%)	
N1		9 (35%)	3 (38%)	2 (22%)	4 (44%)	
N2		12 (46%)	2 (25%)	6 (67%)	4 (44%)	
M	26					0.3
M0		23 (88%)	6 (75%)	8 (89%)	9 (100%)	
M1		3 (12%)	2 (25%)	1 (11%)	0 (0%)	
Stage	26					0.5
I		3 (12%)	1 (12%)	1 (11%)	1 (11%)	
II		10 (38%)	4 (50%)	2 (22%)	4 (44%)	
III		10 (38%)	1 (12%)	5 (56%)	4 (44%)	
IV		3 (12%)	2 (25%)	1 (11%)	0 (0%)	

¹ n (%); Median (Minimum-Maximum)² Fisher's exact test; Kruskal-Wallis rank sum test

Supplementary Table 1. Characteristics of the study population.

Characteristic	N (%)
Gender	
Female	35 (50)
Male	35 (50)
Age at surgery	
Median; range	70; 43-85
≤70 yrs/>70 yrs	35 (50)/35 (50)
Neoadjuvant therapy	
Yes/No	11 (16)/59 (84)
Diagnosis	
Ductal Adenocarcinoma	58 (83)
Pancreatitis	2 (3)
Papillary-Ampulla Tumor	7 (10)
Neuroendocrine	2 (3)
IPMN	1 (1)
BMI	
Median; range	23; 16-32
Perineural invasion*	
Yes/No	58 (83)/10 (15)
Lymphovascular invasion*	
Yes/No	55 (83)/13 (15)
R status*	
R0	30 (52)
R1	28 (48)
Nodal Status*	
N0	14 (24)
N1	19 (33)
N2	25 (43)
T status*	
T1	4 (7)
T2	33 (57)
T3	20 (35)
M*	
M0	51 (88)
M1	7 (12)
Tumor grade*	
G1-2	15 (26)
G3-4	40 (69)

Supplementary Table 2. Demographics and Clinicopathological Characteristics of 70 patients with pancreatic diseases (cohort 2).