

SUPPLEMENTARY MATERIAL

Supplementary Table 1. Targeted genes in the CORE sequencing assay.

Supplementary Table 2. Variants of unknown significance (VUS) of pancreatic ITPN and concomitant invasive carcinoma.

Supplementary Table 3. Differentially expressed genes based on the transcriptomic analysis.

Supplementary Figure 1. Representative immunohistochemical images of p53 staining in cases harboring *TP53* mutations (10x magnification; A: case #5; B: case #11; C: case #12; D: case #13). All cases showed diffuse nuclear positivity (>90% of neoplastic cells).

Supplementary Figure 2. Representative images of the adenocarcinoma harboring *ERBB2* fusion and amplification. (A) Hematoxylin-eosinstained histological slides (20x magnification). (B) Immunohistochemistry for Her2 showing a heterogeneous staining pattern, from a weak to a focally strong positivity.

Supplementary Figure 3. Summarizing figure of the pancreatic ITPN case with associated adenocarcinoma and liver metastasis. Upper panel: Heatmap showing the statistically significant similarities in the transcriptomic profiles of the different tumor components (TUB: intraductal tubular component; PAP: intraductal papillary; AC: adenocarcinoma; LM: liver metastasis) with the existing molecular subgroups of pancreatic ductal adenocarcinoma (Moffit's, Collisson's and Bailey's subgroups). Lower panel: Hematoxylin-eosin images illustrating the (A) intraductal component (10x magnification); (B) papillary component (10x magnification); (C) invasive adenocarcinoma (4x magnification); and (D) liver metastasis (10x magnification). Asterisk indicates the normal liver parenchyma, and hash symbol indicates the metastatic lesion.

Supplementary Table 1. Targeted genes in the CORE sequencing assay

AKT1	B2M	CDKN1A	ERG	HIST1H3B	KMT2A	MYB	PDGFRB	RHOA	STAT5B
AKT2	BAP1	CDKN1B	ESR1	HIST1H3C	KRAS	MYC	PHF6	RNF43	STK11
AKT3	BCL2	CDKN2A	ETV6*	HIST2H3C	MAP2K1	MYCN	PIK3CA	ROS1	SYK
ALK	BLM	CDKN2B	EZH2	HLA-A	MAP2K2	NBN	PIK3CB	RPL5	TERT
AMER1	BRAF	CHEK2	FAS	HLA-B	MAP2K4	NF1	PIK3R1	RUNX1	TGFBR2
APC	BRCA1	CIITA	FBXW7	HLA-C	MAP3K1	NF2	PMS2	SETBP1	TP53
APLNLR	BRCA2	CREBBP	FGF19	HNF1A	MAPK1	NFE2L2	POLE	SETD2	TSC1
AR	CBL	CTCF	FGFR1	HRAS	MAX	NOTCH1	POLQ	SF3B1	TSC2
ARAF	CCND1	CTNNB1	FGFR2	IDH1	MCL1	NOTCH2	PPP2R1A	SMAD4	U2AF1
ARID1A	CCND2	DAXX	FGFR3	IDH2	MDM2	NOTCH3	PTCH1	SMARCA4	VHL
ARID1B	CCND3	DICER1	FGFR4	IGF1R	MED12	NOTCH4	PTEN	SMARCB1	WT1
ARID2	CCNE1	DNMT3A	GATA3	JAK1	MEN1	NPM1	PTPN11	SMO	YAP1
ASXL1	CD274	EGFR	GNA11	JAK2	MET	NRAS	RAC1	SOCS1	
ATM	CD58	EP300	GNAQ	JAK3	MLH1	NTRK1	RAD21	SPOP	
ATR	CDK12	EPHA3	GNAS	JUN	MSH2	PALB2	RAD50	SRC	
ATRX	CDK2	ERBB2	H3F3A	KDR	MSH6	PBRM1	RAF1	STAG1	
AURKA	CDK4	ERBB3	H3F3B	KIT	MTOR	PDCD1LG2	RB1	STAG2	
AXL	CDK6	ERBB4	HGF	KLF4	MUTYH	PDGFRA	RET	STAT3	

Coding exons | [Coding and copy number](#) | [Copy number only](#) | [Full gene footprint for structural variants](#) | **Fusions detected**

* ETV6 reports NTRK3 fusions

Supplementary Table 2: Variants of unknown significance (VUS) of pancreatic ITPN and concomitant invasive carcinoma

ID case	Histology	Variants of unknown significance (VUS)				
		Gene	Variation	Mutation type	Freq (%)	Class
1	Tubular	<i>CREBBP</i>	p.L795F	Substitution - missense	36	3
		<i>PBRM1</i>	L693_P694InsM	Inframe insertion	16	3
		<i>RNF43</i>	p.T64P	Substitution - missense	75	3
	Papillary	<i>CREBBP</i>	p.L795F	Substitution - missense	35	3
		<i>PBRM1</i>	L693_P694InsM	Inframe insertion	51	3
		<i>RNF43</i>	p.T64P	Substitution - missense	71	3
2	Tubular	<i>NBN</i>	c.171+4T>C	Substitution - splice site	46	3
		<i>WT1</i>	p.Q410H	Substitution - missense	18	3
	Papillary	<i>NBN</i>	c.171+4T>C	Substitution - splice site	58	3
		<i>WT1</i>	p.Q410H	Substitution - missense	16	3
3	Tubular	<i>ESR1</i>	p.V392I	Substitution - missense	44	3
		<i>FGFR4</i>	p.N624T	Substitution - missense	47	3
		<i>GNAS</i>	p.V636I	Substitution - missense	53	3
		<i>NOTCH3</i>	p.V2202I	Substitution - missense	32	3
		<i>NOTCH4</i>	p.G1790A	Substitution - missense	44	3
		<i>PALB2</i>	p.I922V	Substitution - missense	40	3
		<i>RPL5</i>	p.A148G	Substitution - missense	32	3
	Papillary	<i>ESR1</i>	p.V392I	Substitution - missense	40	3
		<i>FGFR4</i>	p.N624T	Substitution - missense	52	3
		<i>GNAS</i>	p.V636I	Substitution - missense	46	3
		<i>NOTCH3</i>	p.V2202I	Substitution - missense	29	3
		<i>NOTCH4</i>	p.G1790A	Substitution - missense	31	3
		<i>PALB2</i>	p.I922V	Substitution - missense	35	3
		<i>RPL5</i>	p.A148G	Substitution - missense	26	3
4	Tubular	<i>GNAS</i>	p.S313R	Substitution - missense	19	3
	Papillary	<i>GNAS</i>	p.S313R	Substitution - missense	17	3
5	Tubular	<i>MTOR</i>	p.R1611Q	Substitution - missense	36	3
		<i>POLE</i>	p.V1426I	Substitution - missense	29	3
	Papillary	<i>MTOR</i>	p.R1611Q	Substitution - missense	13	3
		<i>POLE</i>	p.V1426I	Substitution - missense	15	3
6	Tubular	<i>ATM</i>	p.R1489C	Substitution - missense	80	3
		<i>NOTCH1</i>	p.A585T	Substitution - missense	50	3
		<i>RAD21</i>	p.E495D	Substitution - missense	44	3
		<i>MEN1</i>	p.D597A	Substitution - missense	91	3
		<i>MED12</i>	p.P1860H	Substitution - missense	35	3
	Papillary	<i>ATM</i>	p.R1489C	Substitution - missense	66	3
		<i>NOTCH1</i>	p.A585T	Substitution - missense	50	3
		<i>RAD21</i>	p.E495D	Substitution - missense	45	3
		<i>MEN1</i>	p.D597A	Substitution - missense	84	3
7a*	Tubular	<i>ATM</i>	p.A2040G	Substitution - missense	26	3
		<i>GNAS</i>	p.R246H	Substitution - missense	34	3

		<i>JAK1</i>	p.F837L	Substitution - missense	37	3
		<i>MUTYH</i>	p.C262Y	Substitution - missense	78	3
		<i>PTCH1</i>	p.R1113C	Substitution - missense	48	3
	Papillary	<i>ARID1A</i>	p.F1720L	Substitution - missense	5	3
		<i>ATM</i>	p.A2040G	Substitution - missense	53	3
		<i>GNAS</i>	p.R246H	Substitution - missense	35	3
		<i>MUTYH</i>	p.C262Y	Substitution - missense	72	3
		<i>PTCH1</i>	p.R1113C	Substitution - missense	47	3
7b*	AC	<i>ATM</i>	p.A2040G	Substitution - missense	47	3
		<i>GNAS</i>	p.R246H	Substitution - missense	26	3
		<i>MUTYH</i>	p.C262Y	Substitution - missense	62	3
		<i>PTCH1</i>	p.R1113C	Substitution - missense	47	3
8	Tubular	<i>JAK2</i>	p.R923H	Substitution - missense	29	3
		<i>RAD50</i>	p.R83G	Substitution - missense	50	3
		<i>SMARCA4</i>	p.V343A	Substitution - missense	50	3
	AC	<i>JAK2</i>	p.R923H	Substitution - missense	27	3
		<i>RAD50</i>	p.R83G	Substitution - missense	49	3
		<i>SMARCA4</i>	p.V343A	Substitution - missense	48	3
9	Tubular	<i>ERBB2</i>	c.226-5C>T	Substitution - intronic	42	3
		<i>NOTCH1</i>	p.A683T	Substitution - missense	49	3
		<i>MET</i>	p.I662V	Substitution - missense	59	3
		<i>NFE2L2</i>	p.A51Rfs*7	Substitution - frameshift	9	3
	Papillary	<i>ERBB2</i>	c.226-5C>T	Substitution - splice site	43	3
		<i>NOTCH1</i>	p.A683T	Substitution - missense	41	3
		<i>MET</i>	p.I662V	Substitution - missense	58	3
	AC	<i>ERBB2</i>	c.226-5C>T	Substitution - intronic	49	3
		<i>NOTCH1</i>	p.A683T	Substitution - missense	35	3
		<i>MET</i>	p.I662V	Substitution - missense	73	3
10	Tubular	<i>MET</i>	p.A8T	Substitution - missense	37	3
		<i>SETD2</i>	p.T1220N	Substitution - missense	36	3
		<i>AR</i>	c.1886-4A>G	Substitution - splice site	65	3
	Papillary	<i>MET</i>	p.A8T	Substitution - missense	43	3
		<i>SETD2</i>	p.T1220N	Substitution - missense	41	3
		<i>AR</i>	c.1886-4A>G	Substitution - splice site	72	3
	AC	<i>MET</i>	p.A8T	Substitution - missense	35	3
		<i>SETD2</i>	p.T1220N	Substitution - missense	43	3
		<i>AR</i>	c.1886-4A>G	Substitution - splice site	58	3
11	Tubular	<i>MSH6</i>	p.A1302T	Substitution - missense	54	3
	Papillary	<i>CCNE1</i>	p.Q197H	Substitution - missense	27	3
		<i>MSH6</i>	p.A1302T	Substitution - missense	49	3
	AC	<i>MSH6</i>	p.A1302T	Substitution - missense	30	3
12	Tubular	<i>DAXX</i>	c.815-5C>T	Substitution - splice site	49	3
		<i>KDR</i>	p.Q441E	Substitution - missense	26	3
		<i>PDGFRA</i>	p.A7V	Substitution - missense	23	3
		<i>SF3B1</i>	p.R238C	Substitution - missense	59	3

	Papillary	<i>DAXX</i>	c.815-5C>T	Substitution - splice site	49	3
		<i>PDGFRA</i>	p.A7V	Substitution - missense	16	3
		<i>SF3B1</i>	p.R238C	Substitution - missense	32	3
	AC	<i>DAXX</i>	c.815-5C>T	Substitution - splice site	49	3
		<i>KDR</i>	p.Q441E	Substitution - missense	5	3
		<i>PDGFRA</i>	p.A7V	Substitution - missense	30	3
		<i>SF3B1</i>	p.R238C	Substitution - missense	57	3
13	Tubular	<i>AR</i>	p.G416S	Substitution - missense	53	3
		<i>CDKN2A</i>	p.D153N	Substitution - missense	29	3
	Papillary	<i>AR</i>	p.G416S	Substitution - missense	48	3
		<i>CDKN2A</i>	p.D153N	Substitution - missense	45	3
	AC	<i>AR</i>	p.G416S	Substitution - missense	50	3
		<i>CDKN2A</i>	p.D153N	Substitution - missense	9	3
14	Tubular	<i>POLE</i>	p.E1963Q	Substitution - missense	41	3
	Papillary	<i>POLE</i>	p.E1963Q	Substitution - missense	37	3
	AC	<i>POLE</i>	p.E1963Q	Substitution - missense	7	3
15	Tubular	<i>EZH2</i>	p.R213H	Substitution - missense	36	3
		<i>KRAS</i>	p.V112I	Substitution - missense	52	3
		<i>POLQ</i>	p.V1701I	Substitution - missense	46	3
	AC	<i>EZH2</i>	p.R213H	Substitution - missense	36	3
		<i>KRAS</i>	p.V112I	Substitution - missense	43	3
		<i>POLQ</i>	p.V1701I	Substitution - missense	41	3
16	Tubular	<i>ALK</i>	p.F270L	Substitution - missense	47	3
		<i>ATR</i>	p.H453Q	Substitution - missense	42	3
		<i>DAXX</i>	p.R19H	Substitution - missense	30	3
		<i>ATM</i>	p.L2492R	Substitution - missense	53	3
		<i>NOTCH3</i>	p.T411K	Substitution - missense	50	3
	Papillary	<i>ALK</i>	p.F270L	Substitution - missense	48	3
		<i>ATR</i>	p.H453Q	Substitution - missense	46	3
		<i>DAXX</i>	p.R19H	Substitution - missense	23	3
		<i>ATM</i>	p.L2492R	Substitution - missense	48	3
		<i>NOTCH3</i>	p.T411K	Substitution - missense	50	3
	AC	<i>NTRK1</i>	p.V475M	Substitution - missense	11	3
		<i>ALK</i>	p.F270L	Substitution - missense	45	3
		<i>ATR</i>	p.H453Q	Substitution - missense	45	3
		<i>ATM</i>	p.L2492R	Substitution - missense	49	3
		<i>ERBB3</i>	p.D628Y	Substitution - missense	13	3
		<i>NOTCH3</i>	p.T411K	Substitution - missense	49	3
	Liver met.	<i>ALK</i>	p.F270L	Substitution - missense	51	3
		<i>ATR</i>	p.H453Q	Substitution - missense	53	3
		<i>ATM</i>	p.L2492R	Substitution - missense	63	3
		<i>NOTCH3</i>	p.T411K	Substitution - missense	60	3

Legend and abbreviations: AC: adenocarcinoma; met: metastasis. Class: clinical Impact class according to AMGP/AMP guidelines (3: variant of unknown significance; Richards *et al.* Genet Med 2015).

Notes: *7a pancreatic resection for ITPN; 7b: local relapse as adenocarcinoma.

Supplementary Table 3. Differentially expressed genes based on the transcriptomic analysis.**1. MAIN CLUSTERS**

Differentially expressed (DE) genes characterizing cluster A (alphabetical order) and reaching the statistical significance. No statistically significant DE genes characterized clusters B and C.

Genes	Cluster A vs. Cluster B		Cluster A vs. Cluster C	
	Log ₂ Fold Change	Adjusted p-value	Log ₂ Fold Change	Adjusted p-value
<i>ANXA13</i>	4,105672515	0,020614	5,532819	0,029647
<i>C12orf36</i>	3,150162369	0,048935	4,676995	0,038844
<i>CEACAM7</i>	3,852888982	0,039507	5,355246	0,039809
<i>CTSE</i>	5,136971578	0,01653	5,056455	0,028476
<i>CXCL14</i>	3,371983358	0,016614	5,476291	0,028272
<i>CYP2C18</i>	3,38683818	0,04137	6,35483	0,028272
<i>CYP2C19</i>	2,716559126	0,048335	5,410179	0,028272
<i>DPP4</i>	2,565562139	0,049221	5,492023	0,028272
<i>DUOXA2</i>	3,413054335	0,02298	4,415131	0,03202
<i>EDIL3</i>	2,736805436	0,024268	3,39782	0,037501
<i>F5</i>	3,987278528	0,026648	4,800849	0,044896
<i>HTRA3</i>	2,940371002	0,032754	4,693601	0,028518
<i>KRT23</i>	4,357223902	0,019445	5,913799	0,028549
<i>MB21D2</i>	2,680463846	0,024279	3,150186	0,044142
<i>MMP1</i>	4,106308926	0,016717	5,58348	0,028272
<i>MMP11</i>	2,997766866	0,01653	3,349507	0,032352
<i>MMP7</i>	3,02699049	0,019788	3,231568	0,048495
<i>MS4A8B</i>	2,992302058	0,036891	4,299446	0,034597
<i>NPC1L1</i>	3,873110425	0,02004	4,686681	0,033787
<i>SYT13</i>	3,075534174	0,036906	4,210573	0,039686
<i>XDH</i>	3,16347316	0,032215	4,55949	0,031892

2. CASE WITH INTRADUCTAL COMPONENTS, INVASIVE ADENOCARCINOMA AND LIVER METASTASIS

A. DE genes between the intraductal components and the adenocarcinoma (in decreasing order of log Fold Change coefficient of association) and reaching the statistical significance.

Up-regulated genes in the adenocarcinoma	Log ₂ Fold Change	Adjusted p-value	Down-regulated genes in the adenocarcinoma	Log ₂ Fold Change	Adjusted p-value
<i>CFTR</i>	4,621954	0,048338	<i>HLA-C</i>	-1,17734	0,048338
<i>INS</i>	2,672997	0,048338	<i>HLA-A</i>	-1,17981	0,048338
<i>SERPINE1</i>	2,499296	0,048338	<i>LRMP</i>	-1,27573	0,048338
<i>C7</i>	2,240478	0,048338	<i>HPD</i>	-1,52255	0,048338
<i>CTGF</i>	2,133908	0,048338	<i>APOL3</i>	-1,56139	0,048338
<i>CCL2</i>	2,005431	0,048338	<i>CYP2C8</i>	-1,68489	0,048338
<i>HSD3BP4</i>	1,946557	0,048338	<i>APOL6</i>	-1,8179	0,048338
<i>IGFBP7</i>	1,808263	0,048338	<i>BST2</i>	-1,83024	0,048338
<i>HBA2</i>	1,789848	0,048338			
<i>PFN1P2</i>	1,693262	0,048338			
<i>UG0898H09</i>	1,691375	0,048338			
<i>OR10R2</i>	1,691375	0,048338			
<i>FBN1</i>	1,611955	0,048338			

<i>GAS5</i>	1,539741	0,048338			
<i>SULF1</i>	1,53657	0,048338			

B. DE genes between the intraductal components and the liver metastasis (in decreasing order of log Fold Change coefficient of association) and reaching the statistical significance.

Up-regulated genes in the metastasis	Log ₂ Fold Change	Adjusted p-value	Down-regulated genes in the metastasis	Log ₂ Fold Change	Adjusted p-value
<i>HP</i>	7,017802	0,005943	<i>SNORA23</i>	-1,64489	0,013022
<i>APOA1</i>	6,0387	0,005943	<i>ZFP36</i>	-1,7306	0,015592
<i>ALB</i>	5,51791	0,009977	<i>ATF3</i>	-1,73175	0,047397
<i>APOA2</i>	5,318341	0,005943	<i>SNORD15A</i>	-1,75088	0,009977
<i>FGB</i>	5,190086	0,016441	<i>SNORA50</i>	-1,76231	0,018358
<i>TF</i>	5,102526	0,009927	<i>DUOX1</i>	-1,80858	0,008987
<i>FGG</i>	4,759302	0,011371	<i>SNORA5A</i>	-1,89194	0,044767
<i>APOH</i>	4,596138	0,005943	<i>DUSP1</i>	-1,93142	0,017044
<i>ALDOB</i>	4,586933	0,005943	<i>SNORD15B</i>	-1,93231	0,01775
<i>CYP3A4</i>	4,45091	0,006448	<i>SNORA46</i>	-1,93317	0,007609
<i>APOC2</i>	4,370468	0,009977	<i>ST8SIA3</i>	-1,981	0,048067
<i>PLG</i>	4,336711	0,005943	<i>FOS</i>	-2,15996	0,037161
<i>CYP2E1</i>	4,289854	0,008176	<i>IFI6</i>	-2,19958	0,025494
<i>ITIH3</i>	4,009893	0,005943	<i>PDZK1IP1</i>	-2,24968	0,033056
<i>HRG</i>	4,005914	0,008987	<i>SLC28A3</i>	-2,26334	0,027096
<i>APOC3</i>	3,92186	0,00596	<i>SUCNR1</i>	-2,49888	0,017882
<i>CPS1</i>	3,67548	0,00596	<i>S100A1</i>	-2,89604	0,005943
<i>APOB</i>	3,648244	0,016441	<i>PI3</i>	-3,10463	0,017882
<i>ACSM2B</i>	3,621242	0,005943	<i>GLT25D2</i>	-3,19635	0,016597
<i>ODAM</i>	3,604911	0,01973	<i>PIGR</i>	-3,32447	0,005943
<i>CFHR2</i>	3,511698	0,006448	<i>TFF1</i>	-3,53618	0,007447
<i>KNG1</i>	3,427344	0,035757	<i>TFF2</i>	-4,67091	0,03076
<i>APOC1</i>	3,406015	0,005943			
<i>CXCL6</i>	3,38009	0,006448			
<i>SERPINC1</i>	3,294735	0,005943			
<i>SERPIND1</i>	3,118743	0,007467			
<i>ADH4</i>	3,118613	0,005943			
<i>HPX</i>	3,114094	0,008751			
<i>C9</i>	3,1099	0,005943			
<i>HSD17B13</i>	3,058271	0,005943			
<i>MAT1A</i>	3,057807	0,007609			
<i>IGFBP1</i>	3,012305	0,005943			
<i>FABP1</i>	2,935021	0,034059			
<i>ADH1B</i>	2,916313	0,015592			
<i>HAO1</i>	2,900423	0,006448			
<i>HPR</i>	2,786892	0,005943			
<i>ANGPTL3</i>	2,785782	0,008176			
<i>AOX1</i>	2,731914	0,0192			
<i>TAT</i>	2,685163	0,006915			
<i>UGT2B4</i>	2,683203	0,008481			
<i>CFHR1</i>	2,60718	0,01514			
<i>ARG1</i>	2,598271	0,005943			
<i>CES1</i>	2,585309	0,008481			

<i>ITIH1</i>	2,50937	0,044767			
<i>F2</i>	2,508368	0,017882			
<i>SLCO1B1</i>	2,472614	0,009977			
<i>CRHBP</i>	2,463856	0,008481			
<i>GSTA1</i>	2,425822	0,01369			
<i>HAMP</i>	2,413042	0,025494			
<i>AFM</i>	2,41261	0,006448			
<i>A1BG</i>	2,405813	0,005943			
<i>F12</i>	2,389296	0,017882			
<i>OLFM4</i>	2,383347	0,021192			
<i>LAPTM4B</i>	2,367651	0,032758			
<i>CYP1A2</i>	2,324755	0,005943			
<i>CYP2A6</i>	2,302911	0,005943			
<i>SULT2A1</i>	2,302911	0,005943			
<i>SEMA3E</i>	2,297183	0,044767			
<i>DMBT1</i>	2,288829	0,035832			
<i>SERPINA11</i>	2,254855	0,005943			
<i>APOF</i>	2,228493	0,005943			
<i>CFHR5</i>	2,22182	0,005943			
<i>UGT2B15</i>	2,211883	0,00612			
<i>AQP9</i>	2,202645	0,017044			
<i>APOE</i>	2,181412	0,008442			
<i>TDO2</i>	2,179307	0,007467			
<i>HSD17B6</i>	2,179278	0,020018			
<i>PZP</i>	2,170526	0,008481			
<i>PON3</i>	2,129872	0,012932			
<i>AKR1C1</i>	2,117191	0,020194			
<i>SLC22A1</i>	2,115137	0,005943			
<i>ACSM2A</i>	2,104572	0,009977			
<i>GABRP</i>	2,101882	0,033056			
<i>UGT2B10</i>	2,080655	0,005943			
<i>UGT2A3</i>	2,070889	0,005943			
<i>FMO3</i>	2,067054	0,009464			
<i>UGT2B7</i>	2,050656	0,012822			
<i>LECT2</i>	1,971777	0,005943			
<i>PON1</i>	1,96918	0,019353			
<i>MT1G</i>	1,917408	0,009977			
<i>F13B</i>	1,905095	0,005943			
<i>CFHR4</i>	1,897272	0,009977			
<i>CCL16</i>	1,883508	0,005943			
<i>MTTP</i>	1,8571	0,005943			
<i>SPP2</i>	1,852643	0,005943			
<i>ANG</i>	1,835842	0,02332			
<i>AADAC</i>	1,834305	0,018358			
<i>C8B</i>	1,830118	0,016441			
<i>APOM</i>	1,82614	0,008481			
<i>ALDH1A2</i>	1,805242	0,03947			
<i>AKR1C2</i>	1,805194	0,02761			
<i>PLA2G2A</i>	1,804854	0,012882			
<i>GGH</i>	1,77894	0,011743			
<i>GLYAT</i>	1,769535	0,00596			

<i>MASP2</i>	1,769535	0,00596			
<i>SLC13A5</i>	1,730697	0,00612			
<i>KIAA0101</i>	1,729029	0,011823			
<i>ACAT1</i>	1,717924	0,044767			
<i>F9</i>	1,695653	0,00612			
<i>AKR1D1</i>	1,685448	0,00612			
<i>RDH16</i>	1,681386	0,014503			
<i>CDO1</i>	1,670928	0,036807			
<i>DPYS</i>	1,659547	0,006225			
<i>ADH1A</i>	1,656124	0,009977			
<i>CYP2B6</i>	1,646728	0,009977			
<i>BAALC</i>	1,646283	0,013011			
<i>C3P1</i>	1,618233	0,03521			
<i>PIPOX</i>	1,616108	0,025494			
<i>MASP1</i>	1,614454	0,028536			
<i>TFAP2A</i>	1,612567	0,007447			
<i>AGMO</i>	1,598069	0,033254			
<i>FCN2</i>	1,597922	0,021597			
<i>FGA</i>	1,57524	0,030464			

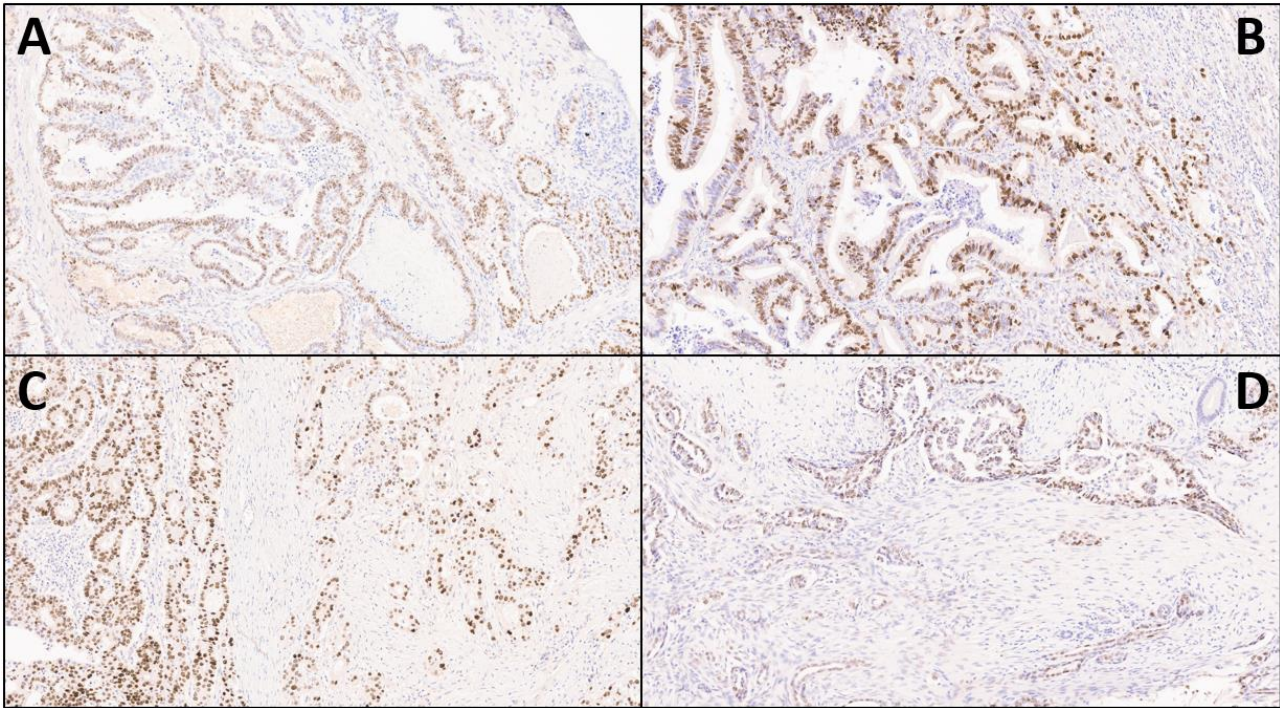
C. DE genes between the adenocarcinoma and the liver metastasis (in decreasing order of log Fold Change coefficient of association) and reaching the statistical significance.

Up-regulated genes in the metastasis	Log ₂ Fold Change		Down-regulated genes in the metastasis	Log ₂ Fold Change	
<i>HP</i>	6,813554	0,024068	<i>HLA-A</i>	-0,45948	0,041992
<i>APOA1</i>	5,86448	0,02049	<i>IGFBP7</i>	-0,67278	0,036014
<i>APOA2</i>	5,165234	0,034238	<i>HLA-C</i>	-0,74716	0,028795
<i>ALDOB</i>	4,812635	0,015876	<i>PFN1P2</i>	-0,77312	0,030448
<i>TF</i>	4,679343	0,029185	<i>UG0898H09</i>	-0,81351	0,026034
<i>CYP3A4</i>	4,594938	0,037447	<i>C7</i>	-0,8236	0,036357
<i>APOH</i>	4,520202	0,025666	<i>OR10R2</i>	-0,83688	0,026034
<i>PLG</i>	4,336711	0,015876	<i>HSD3BP4</i>	-0,89239	0,025666
<i>HRG</i>	4,335972	0,015961	<i>COL14A1</i>	-1,06461	0,045941
<i>KNG1</i>	4,05667	0,033566	<i>PTGIS</i>	-1,07581	0,036211
<i>APOC2</i>	4,040388	0,040233	<i>GOLM1</i>	-1,1372	0,024068
<i>CYP2E1</i>	3,992412	0,026034	<i>CASR</i>	-1,24446	0,043101
<i>ITIH3</i>	3,96069	0,015876	<i>LCN2</i>	-1,33966	0,042142
<i>APOC3</i>	3,711337	0,015876	<i>SIK1</i>	-1,36441	0,019229
<i>ACSM2B</i>	3,704603	0,028795	<i>AEBP1</i>	-1,37833	0,029194
<i>CPS1</i>	3,494854	0,017993	<i>CPXM2</i>	-1,48842	0,031693
<i>APOC1</i>	3,439309	0,028795	<i>F3</i>	-1,61732	0,027145
<i>FABP1</i>	3,423739	0,0468	<i>SNORD15A</i>	-1,70212	0,047862
<i>CFHR2</i>	3,301174	0,015876	<i>DUSP1</i>	-1,7034	0,015876
<i>SERPINC1</i>	3,294735	0,015876	<i>USP17L2</i>	-1,71201	0,028795
<i>CXCL6</i>	3,182959	0,017371	<i>DUOX1</i>	-1,72022	0,034227
<i>IGFBP1</i>	3,132712	0,017371	<i>SNORA23</i>	-1,74838	0,043162
<i>ODAM</i>	3,118929	0,033566	<i>MATN3</i>	-1,85243	0,045439
<i>ADH4</i>	3,118613	0,015876	<i>IFI6</i>	-1,85765	0,015876
<i>C9</i>	3,1099	0,015876	<i>RGS5</i>	-1,87514	0,045941

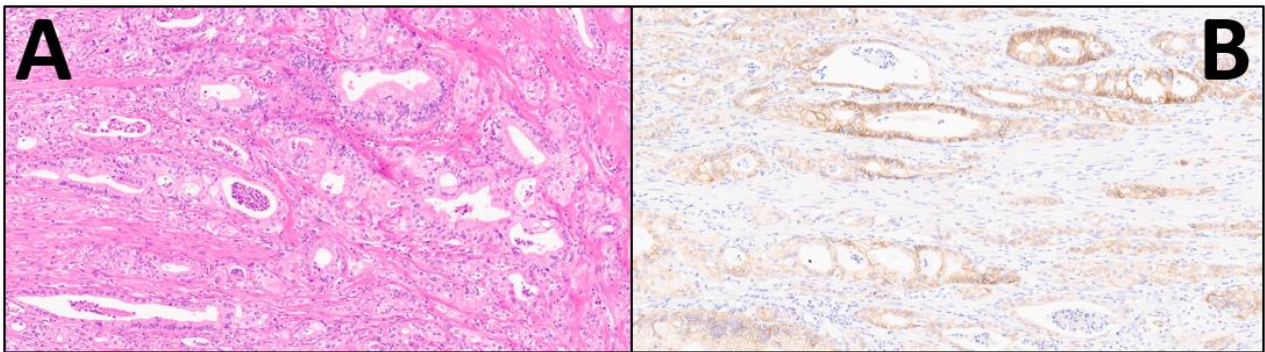
<i>HSD17B13</i>	3,058271	0,015876	<i>SLC28A3</i>	-1,91784	0,041992
<i>HAO1</i>	2,983785	0,034707	<i>GCNT3</i>	-1,94912	0,031987
<i>ANGPTL3</i>	2,974461	0,017993	<i>SNORA46</i>	-1,99044	0,032408
<i>HPX</i>	2,974257	0,045941	<i>RGCC</i>	-2,0703	0,017371
<i>SERPIND1</i>	2,90822	0,015876	<i>CFC1B</i>	-2,12718	0,045941
<i>UGT2B4</i>	2,874414	0,015901	<i>FOSB</i>	-2,15567	0,017993
<i>MAT1A</i>	2,847284	0,015876	<i>THBS4</i>	-2,25484	0,048871
<i>F2</i>	2,825845	0,015876	<i>ST8SIA3</i>	-2,37747	0,048871
<i>HPR</i>	2,786892	0,015876	<i>CST1</i>	-2,37855	0,017114
<i>APCS</i>	2,755943	0,025666	<i>SERPINE1</i>	-2,44186	0,015901
<i>HAMP</i>	2,739826	0,0468	<i>EMP1</i>	-2,46722	0,04426
<i>HPD</i>	2,707689	0,015876	<i>SNORA74A</i>	-2,54596	0,015876
<i>TAT</i>	2,619515	0,037873	<i>FOS</i>	-2,5757	0,015876
<i>ARG1</i>	2,598271	0,015876	<i>SPARCL1</i>	-2,68494	0,029185
<i>ADH1B</i>	2,584784	0,025666	<i>CTGF</i>	-2,70936	0,015876
<i>SLCO1B1</i>	2,580463	0,048449	<i>SNORD94</i>	-2,78056	0,037447
<i>CES1</i>	2,440309	0,036357	<i>GLT25D2</i>	-2,8032	0,016375
<i>AFM</i>	2,437653	0,035457	<i>IGJ</i>	-2,80874	0,026034
<i>A1BG</i>	2,405813	0,015876	<i>S100A1</i>	-2,81775	0,025666
<i>AOX1</i>	2,386859	0,039047	<i>HBA2</i>	-2,98706	0,015876
<i>CYP1A2</i>	2,324755	0,015876	<i>DUOX2</i>	-3,07071	0,037447
<i>CYP2A6</i>	2,302911	0,015876	<i>PIGR</i>	-3,17774	0,017993
<i>SULT2A1</i>	2,302911	0,015876	<i>APOD</i>	-3,17946	0,032408
<i>CRHBP</i>	2,291863	0,017993	<i>INS</i>	-3,27278	0,015901
<i>SAA4</i>	2,290103	0,019229	<i>IGLL5</i>	-3,50847	0,048871
<i>SERPINA11</i>	2,254855	0,015876	<i>TFF1</i>	-3,66612	0,037873
<i>UGT2B7</i>	2,239335	0,024068	<i>TFF2</i>	-3,88718	0,046129
<i>UGT2B15</i>	2,235146	0,029194	<i>GCG</i>	-5,90701	0,041992
<i>APOF</i>	2,228493	0,015876			
<i>CFHR5</i>	2,22182	0,015876			
<i>ACSM2A</i>	2,187933	0,045439			
<i>GSTA1</i>	2,16824	0,015876			
<i>SLC22A1</i>	2,130207	0,015876			
<i>UGT2A3</i>	2,110521	0,015876			
<i>ANG</i>	2,095057	0,025607			
<i>TDO2</i>	2,085072	0,029185			
<i>UGT2B10</i>	2,080655	0,015876			
<i>APOE</i>	2,053837	0,026034			
<i>PCK1</i>	2,05048	0,043341			
<i>C8B</i>	2,027775	0,025666			
<i>PZP</i>	2,021515	0,015876			
<i>LECT2</i>	1,971777	0,015876			
<i>AQP9</i>	1,943838	0,026444			
<i>FMO3</i>	1,927009	0,02651			
<i>PON3</i>	1,919349	0,015876			
<i>F13B</i>	1,905095	0,015876			
<i>C3P1</i>	1,892188	0,037729			
<i>CCL16</i>	1,883508	0,015876			
<i>HSD17B6</i>	1,882142	0,015876			
<i>DKK1</i>	1,862571	0,049074			
<i>MTTP</i>	1,8571	0,015876			

<i>SPP2</i>	1,852643	0,015876			
<i>PIPOX</i>	1,852441	0,024309			
<i>CYP2C8</i>	1,770427	0,016375			
<i>GLYAT</i>	1,769535	0,015876			
<i>MASP2</i>	1,769535	0,015876			
<i>MT1G</i>	1,768397	0,015876			
<i>CYP2B6</i>	1,751085	0,026945			
<i>APOM</i>	1,750478	0,034107			
<i>CFHR4</i>	1,748261	0,015876			
<i>SLC13A5</i>	1,730697	0,015876			
<i>GABRP</i>	1,728674	0,024068			
<i>F9</i>	1,695653	0,015876			
<i>AKR1D1</i>	1,685448	0,015876			
<i>TFAP2A</i>	1,662726	0,016375			
<i>DPYS</i>	1,659547	0,015876			
<i>H19</i>	1,554439	0,025666			
<i>ADH1A</i>	1,550198	0,025666			
<i>BAALC</i>	1,497272	0,016375			
<i>FN1</i>	1,343733	0,041992			
<i>C4BPB</i>	1,199459	0,036357			
<i>NT5DC2</i>	1,088281	0,037729			
<i>CXCL12</i>	0,915005	0,041992			
<i>BST2</i>	0,912483	0,025666			
<i>BCHE</i>	0,81596	0,026034			
<i>APOL6</i>	0,783419	0,026801			
<i>FOXQ1</i>	0,76549	0,027145			
<i>PTGR1</i>	0,724359	0,036014			

Supplementary Figure 1.



Supplementary Figure 2.



Supplementary Figure 3.

