

Supplementary Table 1. Hereditary cancer predisposition genes included in Illumina TruSight Cancer panel

Gene number	Gene symbol	Established pancreatic cancer susceptibility gene
1	<i>AIP</i>	
2	<i>ALK</i>	
3	<i>APC</i>	
4	<i>ATM</i>	X
5	<i>BAP1</i>	
6	<i>BLM</i>	
7	<i>BMPR1A</i>	
8	<i>BRCA1</i>	X
9	<i>BRCA2</i>	X
10	<i>BRIP1</i>	
11	<i>BUB1B</i>	
12	<i>CDC73</i>	
13	<i>CDH1</i>	
14	<i>CDK4</i>	
15	<i>CDKN1C</i>	
16	<i>CDKN2A</i>	X
17	<i>CEBPA</i>	
18	<i>CEP57</i>	
19	<i>CHEK2</i>	
20	<i>CYLD</i>	
21	<i>DDB2</i>	
22	<i>DICER1</i>	
23	<i>DIS3L2</i>	
24	<i>EGFR</i>	
25	<i>EPCAM</i>	
26	<i>ERCC2</i>	
27	<i>ERCC3</i>	
28	<i>ERCC4</i>	
29	<i>ERCC5</i>	
30	<i>EXT1</i>	
31	<i>EXT2</i>	
32	<i>EZH2</i>	
33	<i>FANCA</i>	
34	<i>FANCB</i>	
35	<i>FANCC</i>	
36	<i>FANCD2</i>	
37	<i>FANCE</i>	
38	<i>FANCF</i>	
39	<i>FANCG</i>	
40	<i>FANCI</i>	
41	<i>FANCL</i>	
42	<i>FANCM</i>	
43	<i>FH</i>	
44	<i>FLCN</i>	
45	<i>GATA2</i>	
46	<i>GPC3</i>	
47	<i>HNF1A</i>	
48	<i>HRAS</i>	
49	<i>KIT</i>	
50	<i>MAX</i>	
51	<i>MEN1</i>	
52	<i>MET</i>	
53	<i>MLH1</i>	X
54	<i>MSH2</i>	X
55	<i>MSH6</i>	X
56	<i>MUTYH</i>	
57	<i>NBN</i>	

58	<i>NF1</i>	
59	<i>NF2</i>	
60	<i>NSD1</i>	
61	<i>PALB2</i>	X
62	<i>PHOX2B</i>	
63	<i>PMS1</i>	
64	<i>PMS2</i>	X
65	<i>PRF1</i>	
66	<i>PRKAR1A</i>	
67	<i>PTCH1</i>	
68	<i>PTEN</i>	
69	<i>RAD51C</i>	
70	<i>RAD51D</i>	
71	<i>RB1</i>	
72	<i>RECQL4</i>	
73	<i>RET</i>	
74	<i>RHBDF2</i>	
75	<i>RUNX1</i>	
76	<i>SBDS</i>	
77	<i>SDHAF2</i>	
78	<i>SDHB</i>	
79	<i>SDHC</i>	
80	<i>SDHD</i>	
81	<i>SLX4</i>	
82	<i>SMAD4</i>	
83	<i>SMARCB1</i>	
84	<i>STK11</i>	X
85	<i>SUFU</i>	
86	<i>TMEM127</i>	
87	<i>TP53</i>	
88	<i>TSC1</i>	
89	<i>TSC2</i>	
90	<i>VHL</i>	
91	<i>WRN</i>	
92	<i>WT1</i>	
93	<i>XPA</i>	
94	<i>XPC</i>	

Supplementary Table 2. Primers used to validate germline mutations

Mutation	Forward primer	Reverse primer
g.chr10:104268965_CA>C	TCTGGAGAGATGTGGCCTCT	CAGGCCGAAGCTGATGTAGT
g.chr11:108098600_G>A	TGATGTGTGTTCTGAAATTGTGA	TGCCAAATTCATATGCAAGG
g.chr11:108117812_CAAAG>C	GGAGCTAGCAGTGTAAACAGAG	CATGACCTACTTACTGTACCTGG
g.chr11:108137985_C>T	GTGCCCAGCCTGATTAGGTA	GCTCTCTCCAGGTTTCGTTTG
g.chr11:108175549_C>T	ACTTTTGTGCACTGTACTTCCA	ATCCAAGTTTGCAGGGGTTG
g.chr11:108206686_A>T	TGTCATGCAACAGGTCTTCC	CATGAGCCACTTCACCCAAC
g.chr11:32456755_GC>G	CACGTCCGAGCCCATTTG	GGACTTCTCTTGCTGCAGG
g.chr13:32907014_A>T	TACCGTCTTTGGCCTGTGAA	ACCCTGAAATGAAGAAGCCAC
g.chr13:32914437_GT>G	GCACGCATTACATAAGGTTTT	TGCGTTTTGTAATGAAGCATCTG
g.chr13:32972346_TTGTA>T	AGTTAGGGGAGGGAGACTGT	AAGTCATCTGGGCTGAGACA
g.chr13:48922000_G>A	AAAGCATGAGAAACTACTATGACT	GCCTGCTATAATCGATCAAAC
g.chr14:45645855_G>T	TCGTGATCAGAGAGGTGTACAG	TGCACTGGTAAAGAAAACAGAGA
g.chr15:40462282_C>T	AAGTGTCGGGATTACAGGCA	CCAGAGGGTCATTTCCAGTG
g.chr15:89838165_C>T	GGGTGCTGCTGTTCTGAAC	TTCTGGGTTTTGGCCATCAG
g.chr15:89843584_C>CA	AGAGTGGCTGGAAAATGGAA	CCTGAAATTGCCGGATCTGG
g.chr16:23649206_GACAA>G	AAAGCAGGCATAAGTGAATGG	TTTCTGGGGCTGTTTTTGTCT
g.chr16:68771344_C>A	GGAAGTCAAAGCACCTGTG	CTTGGAAGAAGGGAAGCGGT
g.chr16:89871687_C>G	AAATGCAACCCACAACAGG	TCTGTGCTGCCTTTGTGAAC
g.chr17:59871059_C>A	TGGGAAAAGTAGCAGTGGTGA	AGGATGATACTGGTTGACACAA
g.chr2:29436851_G>A	TCTGAAGGGGGAAATGTGAG	CCCTCTCTACTGACAAGC
g.chr2:48033791_GTAAC>G	AGGCTTGCTAATCTCCAGA	TGCATCATCCCTTCCCCTTT
g.chr3:10083368_C>T	ATTGTCTGCCAGCTCTGTT	CCAAGGCAATGACTGACTGA
g.chr8:145739410_G>A	CGTGGAGGTCAGGCTCTT	TGGTCCCACAACCTCCGG
g.chr8:90960063_T>A	GGCACAATCATGAAGTAAGCC	TGGGAAGAAACGTGAACTCA
g.chr9:98279098_TC>T	TCTTCTCCTCCTCCTCCGTC	CCTCGAGTTTACTTTGCTTTCCT

Primer sequences are given 5' to 3'. M13F sequencing primer (5'-GTAAAACGACGGCCAG-3') was added 5'

Supplementary Table 3. Characteristics of patients with surgically resected IPMN and invasive carcinoma

Characteristic	Number	Percent	
<i>Diagnosis</i>	Adenosquamous PDAC	1	1.4
	Anaplastic carcinoma of the pancreas	1	1.4
	Colloid carcinoma	11	15.3
	Colloid carcinoma and PDAC	1	1.4
	PDAC	57	79.2
	Signet ring cell carcinoma	1	1.4
<i>Grade of invasive carcinoma</i>			
G1	7	9.7	
G2	43	59.7	
G3	17	23.6	
G4	3	4.2	
NR	2	2.8	
<i>Size of invasive carcinoma</i>			
<1	7	9.7	
≥1 and <2	10	13.9	
≥2 and <3	18	25.0	
≥3 and <4	19	26.4	
≥4 and <5	8	11.1	
≥5	9	12.5	
NR	1	1.4	
<i>Stage</i>			
T1N0	12	16.7	
T1N1	3	4.2	
T2N0	11	15.3	
T2N1	17	23.6	
T3N0	5	6.9	
T3N1	21	29.2	
T4N0	1	1.4	
T4N1	1	1.4	
NR	1	1.4	

IPMN - intraductal papillary mucinous neoplasm; PDAC - pancreatic adenocarcinoma; NR - not reported.

Supplementary Table 4. Number of germline mutations identified in pancreatic cancer susceptibility genes in patients with surgically resected IPMN compared to unselected pancreatic cancer patients

Gene	IPMN patients			Shindo <i>et al.</i>				Hu <i>et al.</i>			
	AC	AN	AF	AC	AN	AF	<i>P</i> value	AC	AN	AF	<i>P</i> value
<i>ATM</i>	5	630	0.008	10	1708	0.006	0.5657	69	6060	0.011	0.5500
<i>BRCA1</i>	0	630	0.000	3	1708	0.002	0.5683	18	6060	0.003	0.4052
<i>BRCA2</i>	3	630	0.005	12	1708	0.007	0.7717	59	6060	0.010	0.2766
<i>CDKN2A</i>	0	630	0.000	1	1708	0.001	1.0000	10	6060	0.002	0.6130
<i>MLH1</i>	0	630	0.000	2	1708	0.001	1.0000	5	6060	0.001	1.0000
<i>MSH2</i>	0	630	0.000	0	1708	0.000	1.0000	1	6060	0.000	1.0000
<i>MSH6</i>	1	630	0.002	0	1708	0.000	0.2695	7	6060	0.001	0.5469
<i>PALB2</i>	1	630	0.002	2	1708	0.001	1.0000	12	6060	0.002	1.0000
<i>PMS2</i>	0	630	0.000	0	1708	0.000	1.0000	2	6060	0.000	1.0000
<i>TP53</i>	0	630	0.000	1	1708	0.001	1.0000	6	6060	0.001	1.0000

IPMN - intraductal papillary mucinous neoplasm; AC - germline mutation allele count, AN - assessed allele number; AF - frequency of germline mutations.

Supplementary Table 5. Comparison of patients with surgically resected IPMN with and without concurrent invasive carcinoma

Variable	Concurrent invasive carcinoma ¹		
	+	-	
Patients with family history of pancreatic cancer (n)	8 (50)	32 (195)	1.0000
Patients with personal history of cancer (n)	11 (64)	43 (237)	1.0000
Mean age at surgery (years)	69.3 (72)	67.6 (243)	0.2403
Male patients (n)	46 (72)	116 (243)	0.4041
Patients with high-grade dysplasia (n)	45 (55)	93 (235)	< 0.0001
Mean longest diameter of IPMN (cm)	2.9 (61)	2.6 (236)	0.3751
Patients with multifocal IPMN (n)	9 (72)	53 (243)	0.0924
Patients with main duct involvement (n)	33 (55)	79 (203)	0.0059

¹Not all patients had data for each variable. Number of patients with data used for analysis indicated in parentheses.