

## Supplementary Materials for

### Recurrent *GNAS* Mutations Define an Unexpected Pathway for Pancreatic Cyst Development

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Table S1. Genes analyzed by massively parallel sequencing in IPMN cyst fluids.

<b>Gene symbol</b>	<b>Accession Number</b>	<b>Oncogene or Tumor Suppressor Gene</b>
ABL1	X16416	Oncogene
ARHGAP29	NM_004815.2	Suppressor Gene
AKT1	NM_005163	Oncogene
ALK	NM_004304	Oncogene
JARID1C	NM_004187.1	Suppressor Gene
APC	NM_000038	Suppressor Gene
ATM	NM_000051	Suppressor Gene
UBR4	NM_020765.1	Suppressor Gene
BRAF	NM_004333	Oncogene
BRCA1	NM_007294.1	Suppressor Gene
BRCA2	NM_000059.1	Suppressor Gene
CBL	NM_005188.1	Oncogene
CDC73	NM_024529.3	Suppressor Gene
CDH1	NM_004360.2	Suppressor Gene
CDKN2A	NM_000077	Suppressor Gene
CEBPA	NM_004364.2	Suppressor Gene
CSF1R	NM_005211	Oncogene
CTNNA1	NM_001903.2	Suppressor Gene
CTNNB1	NM_001904	Oncogene
ATR	NM_001184	Suppressor Gene
CYLD	NM_015247.1	Suppressor Gene
LRRK2	SU_LRRK2	Suppressor Gene
KIAA1409	ENST00000256339	Suppressor Gene
SPTAN1	ENST00000372731	Suppressor Gene
ATRX	NM_138271.1	Suppressor Gene
SPEG	SU_SPEG	Suppressor Gene
MAST4	SU_MAST4	Suppressor Gene
DPYSL4	ENST00000338492	Oncogene
EGFL6	NM_015507.2	Oncogene
EGFR	NM_005228	Oncogene
WNK2	SU_WNK2	Suppressor Gene
CAD	NM_004341.2	Suppressor Gene
SORL1	ENST00000260197	Suppressor Gene
NUP214	NM_005085.2	Suppressor Gene
ERBB2	NM_004448	Oncogene
TECTA	ENST00000392793	Suppressor Gene
ADAMTS20	NM_025003.2	Suppressor Gene
TRIP11	ENST00000267622	Suppressor Gene
FAM123B	NM_152424.1	Suppressor Gene
FBXW7	NM_033632.1	Suppressor Gene
TAF1	NM_138923	Suppressor Gene
FGFR3	NM_000142	Oncogene
FLT3	Z26652	Oncogene

COL14A1	NM_021110.1	Suppressor Gene
FOXL2	NM_023067.2	Oncogene
NUP98	NM_016320.2	Suppressor Gene
GATA1	NM_002049.2	Suppressor Gene
CDC42BPB	NM_006035	Suppressor Gene
LTBP1	NM_206943.1	Suppressor Gene
TAF1L	NM_153809	Suppressor Gene
GNAQ	NM_002072.2	Oncogene
GNAS	NM_000516.3	Oncogene
ITSN2	NM_006277.1	Suppressor Gene
N4BP2	NM_018177.2	Suppressor Gene
JARID1A	NM_005056.1	Suppressor Gene
DEPDC2	NM_024870.2	Suppressor Gene
HNF1A	NM_000545.3	Suppressor Gene
HRAS	NM_005343	Oncogene
IDH1	NM_005896.2	Oncogene
IDH2	NM_002168.2	Oncogene
GLI3	NM_000168.2	Suppressor Gene
CENTD3	NM_022481.4	Suppressor Gene
BAZ1A	NM_013448.2	Suppressor Gene
MAP4K4	NM_145686	Suppressor Gene
COL1A1	ENST00000225964	Suppressor Gene
ASXL1	ENST00000358956	Suppressor Gene
JAK2	NM_004972	Oncogene
JAK3	NM_000215	Oncogene
ROCK2	NM_004850	Suppressor Gene
ROCK1	NM_005406	Suppressor Gene
IKBKAP	NM_003640.2	Suppressor Gene
KIT	NM_000222	Oncogene
IGF1R	NM_000875	Suppressor Gene
KRAS	NM_004985	Oncogene
STK36	NM_015690	Suppressor Gene
RAD50	NM_133482.1	Suppressor Gene
MAP3K6	NM_004672	Suppressor Gene
PER1	ENST00000317276	Suppressor Gene
WNK4	NM_032387	Suppressor Gene
MAP2K4	NM_003010	Suppressor Gene
ADAMTS18	NM_199355.1	Suppressor Gene
MGA	XM_031689.7	Suppressor Gene
ABL2	NM_005158	Suppressor Gene
TSC1	NM_000368.2	Suppressor Gene
MEN1	ENST00000312049	Suppressor Gene
MET	NM_000245	Oncogene
TNKS2	AF264912.1	Suppressor Gene
TNK2	NM_005781	Suppressor Gene
TRIM33	NM_015906	Suppressor Gene

MLH1	NM_000249.2	Suppressor Gene
ULK2	NM_014683	Suppressor Gene
GUCY2F	NM_001522	Suppressor Gene
HDAC4	NM_006037.2	Suppressor Gene
MPL	NM_005373.1	Oncogene
MSH2	NM_000251.1	Suppressor Gene
MSH6	NM_000179.1	Suppressor Gene
ERN2	NM_033266.1	Suppressor Gene
USP24	XM_371254.3	Suppressor Gene
NF1	ENST00000358273	Suppressor Gene
NF2	NM_000268.2	Suppressor Gene
NFKB1	NM_003998.2	Suppressor Gene
EPHB1	NM_004441	Suppressor Gene
NOTCH1	NM_017617.2	Suppressor Gene
NOTCH2	NM_024408.2	Suppressor Gene
NPM1	NM_002520.4	Suppressor Gene
NRAS	NM_002524	Oncogene
PHF14	NM_001007157.1	Suppressor Gene
ROR2	NM_004560	Suppressor Gene
TNPO1	NM_002270.2	Suppressor Gene
PDGFRA	NM_006206	Oncogene
AXL	NM_001699	Suppressor Gene
PRKD2	NM_016457	Suppressor Gene
TTK	NM_003318	Suppressor Gene
PIK3CA	NM_006218.1	Oncogene
TNNI3K	NM_015978	Suppressor Gene
PRKAR1A	NM_212472.1	Suppressor Gene
VEPH1	ENST00000392832	Suppressor Gene
HIF1A	NM_001530.2	Suppressor Gene
PTCH1	NM_000264.2	Suppressor Gene
PTEN	NM_000314.4	Suppressor Gene
PTPN11	NM_002834.3	Oncogene
PTPRC	NM_002838.2	Oncogene
RPS6KA2	NM_021135	Suppressor Gene
BRD2	NM_005104	Suppressor Gene
ITGB3	NM_000212.2	Suppressor Gene
RB1	NM_000321	Suppressor Gene
RET	NM_020975	Oncogene
ADAM29	NM_014269.2	Suppressor Gene
ANAPC5	NM_016237.3	Suppressor Gene
ITGB2	NM_000211.1	Suppressor Gene
CHUK	NM_001278	Suppressor Gene
TCF12	NM_207037.1	Suppressor Gene
PDZRN4	NM_013377.2	Suppressor Gene
RUNX1	ENST00000300305	Suppressor Gene
SETD2	ENST00000330022	Suppressor Gene

SMAD2	NM_005901.3	Suppressor Gene
SMAD4	NM_005359.3	Suppressor Gene
SMARCA4	NM_003072.2	Suppressor Gene
SMARCB1	NM_003073.2	Suppressor Gene
PAK7	NM_020341	Suppressor Gene
SMO	NM_005631.3	Oncogene
APBB1IP	NM_019043.3	Suppressor Gene
SOCS1	NM_003745.1	Suppressor Gene
PRKCA	NM_002737	Suppressor Gene
NEK11	NM_024800.2	Suppressor Gene
TCF7L2	ENST00000369397	Suppressor Gene
STK11	NM_000455	Suppressor Gene
ITK	NM_005546	Suppressor Gene
MAP3K2	NM_006609	Suppressor Gene
ACVR1B	NM_020328	Suppressor Gene
CDC7	NM_003503.2	Suppressor Gene
TGFBR2	NM_003242	Suppressor Gene
SRC	NM_005417	Suppressor Gene
TNFAIP3	NM_006290.2	Suppressor Gene
BMPR1A	NM_004329	Suppressor Gene
ACVR2A	NM_001616	Suppressor Gene
RAD18	NM_020165.2	Suppressor Gene
SUFU	NM_016169.2	Suppressor Gene
TP53	NM_000546	Suppressor Gene
MAP2K7	NM_005043	Suppressor Gene
STK32B	NM_018401	Suppressor Gene
TSHR	NM_000369.1	Oncogene
MGC42105	NM_153361	Suppressor Gene
STK19	NM_032454	Suppressor Gene
UTX	NM_021140.1	Suppressor Gene
VHL	NM_000551.2	Suppressor Gene
LDHB	NM_002300.3	Suppressor Gene
WT1	NM_024426.2	Suppressor Gene
PHOX2B	ENST00000381741	Suppressor Gene

Table S2. Characteristics of patients with IPMNs analyzed in this study, including *GNAS* and *KRAS* mutation status.

IPMN #	KRAS mutation	GNAS mutation	Age at surgery	Sex	History of smoking	Post-operative diagnosis	Cyst Grade	Cyst diameter (cm)	Duct type	IPMN :Subtype	Cyst location	Sample type
1	G12V	R201C	71	M	No	IPMN	intermediate	3.0	mixed	gastric	body/tail	Cyst wall
2	G12D	R201H	68	M	unknown	IPMN	high	2.0	branch	gastric	body/tail	Cyst wall
3	G12D	R201H	69	M	unknown	IPMN	intermediate	2.0	branch	gastric	head	Cyst wall
4	G12R	R201H	73	F	unknown	IPMN	high	3.2	main	pancreatobiliary	head	Cyst wall
5	G12D & G12R	No mutation detected	66	F	No	IPMN	intermediate	4.0	branch	gastric	entire pancreas	Cyst fluid
6	G12R	R201C	63	M	unknown	IPMN	high	8.0	mixed	intestinal	head	Cyst wall
7	No mutation detected	R201H	64	F	No	IPMN	high	2.0	branch	intestinal	body/tail	Cyst wall
8	G12V	No mutation detected	80	M	No	IPMN	high	2.0	main	gastric	body/tail	Cyst wall
9	G12V & G12D	R201C & R201H	74	M	No	IPMN	high	6.5	main	pancreatobiliary	entire pancreas	Cyst wall
10	G12D	R201C	39	F	No	IPMN	low	2.0	branch	gastric	head	Cyst wall
11	G12D	R201C	67	F	No	IPMN	low	2.0	main	gastric	head	Cyst wall
12	G12V	No mutation detected	70	M	No	IPMN	high	2.0	main	gastric	head	Cyst wall
13	G12V	R201H	78	M	No	IPMN	high	3.0	branch	gastric	head	Cyst wall
14	G12V	R201H	79	M	No	IPMN	high	5.0	branch	gastric	head	Cyst wall
15	G12D	R201C	84	M	No	IPMN	low	1.5	branch	gastric	head	Cyst wall
16	G12D	R201C	66	F	No	IPMN	intermediate	1.8	branch	gastric	head	Cyst wall
17	G12D	R201C	63	F	Yes	IPMN	high	1.8	branch	gastric	body/tail	Cyst wall
18	G12D	R201C	81	F	Yes	IPMN	intermediate	3.0	not determined	gastric	head	Cyst wall
19	G12D	R201H	69	M	Yes	IPMN	low	2.5	not determined	gastric	head	Cyst wall
20	G12V	R201C	70	M	unknown	IPMN	high	5.0	mixed	not determined	body/tail	Cyst wall
21	No mutation detected	R201H	80	M	unknown	IPMN	high	0.7	main	gastric	body/tail	Cyst wall
22	No mutation detected	R201C	50	F	unknown	IPMN	low	1.2	mixed	intestinal	body/tail	Cyst wall
23	No mutation detected	R201C	81	M	unknown	IPMN	high	2.5	main	intestinal	body/tail	Cyst wall
24	G12V	R201C	51	F	unknown	IPMN	intermediate	1.0	mixed	gastric	head	Cyst wall
25	No mutation detected	R201H	78	M	unknown	IPMN	high	3.0	mixed	intestinal	head	Cyst wall
26	G12D	R201H	70	F	unknown	IPMN	intermediate	1.4	branch	not determined	head	Cyst wall
27	G12D	R201C	66	F	unknown	IPMN	low	2.7	mixed	gastric	head	Cyst wall
28	G12D	No mutation detected	62	M	unknown	IPMN	intermediate	3.5	branch	gastric	head	Cyst wall
29	G12D & G12V	No mutation detected	88	M	Yes	IPMN	high	3.5	main	pancreatobiliary	body/tail	Cyst fluid
30	No mutation detected	R201C	65	M	Yes	IPMN	high	6.5	main	gastric	head	Cyst fluid
31	G12D & G12V & G12R	R201H	79	M	unknown	IPMN	high	2.5	branch	not determined	head	Cyst fluid
32	G12R	No mutation detected	74	F	unknown	IPMN	high	5.0	mixed	pancreatobiliary	head	Cyst wall
33	G12V	R201H	82	F	unknown	IPMN	high	0.5	main	not determined	head	Cyst wall
34	G12V	R201C	75	M	No	IPMN	high	2.8	main	gastric	body/tail	Cyst fluid
35	G12V & G12D	R201H	58	F	No	IPMN	low	1.5	branch	gastric	head	Cyst fluid
36	G12D	R201H	69	M	Yes	IPMN	intermediate	2.8	branch	gastric	head	Cyst fluid
37	G12V	No mutation detected	73	M	unknown	IPMN	intermediate	2.0	branch	gastric	body/tail	Cyst fluid
38	No mutation detected	No mutation detected	48	M	No	IPMN	high	2.5	main	not determined	head	Cyst wall
39	G12D	No mutation detected	69	F	Yes	IPMN	low	1.1	mixed	not determined	head	Cyst fluid
40	G12R	R201C	76	F	Yes	IPMN	low	4.0	branch	not determined	tail	Cyst fluid
41	G12D	R201C	72	M	Yes	IPMN	intermediate	1.9	branch	not determined	head	Cyst fluid
42	G12D	R201C	68	M	Yes	IPMN	high	2.0	mixed	not determined	head	Cyst fluid
43	G12D	R201H	76	F	Yes	IPMN	high	0.8	mixed	not determined	body	Cyst fluid
44	G12D	No mutation detected	70	F	No	IPMN	low	5.6	branch	not determined	head	Cyst fluid
45	No mutation detected	R201H	85	F	No	IPMN	intermediate	4.5	mixed	not determined	neck	Cyst fluid
46	No mutation detected	R201H	72	F	No	IPMN	low	2.0	branch	not determined	tail	Cyst fluid
47	G12D	No mutation detected	62	M	No	IPMN	low	2.9	branch	not determined	tail	Cyst fluid
48	G12R	R201C & R201H	84	F	No	IPMN	low	3.2	branch	not determined	tail	Cyst fluid
49	G12D	No mutation detected	71	M	unknown	IPMN	high	1.5	main	not determined	body	Cyst fluid
50	G12D	R201C	70	M	unknown	IPMN	intermediate	3.0	branch	not determined	body	Cyst fluid
51	G12V	No mutation detected	76	F	unknown	IPMN	low	3.4	branch	not determined	body	Cyst fluid

52	G12V & G12R	No mutation detected	79	F	unknown	IPMN	intermediate	4.2	mixed	not determined	body	Cyst fluid
53	No mutation detected	No mutation detected	72	F	unknown	IPMN	high	6.7	main	not determined	body/tail	Cyst fluid
54	G12D	R201C	76	F	unknown	IPMN	high	8.5	not determined	not determined	body/tail	Cyst fluid
55	No mutation detected	No mutation detected	61	F	unknown	IPMN	intermediate	1.5	branch	not determined	head	Cyst fluid
56	G12V	R201H	86	M	unknown	IPMN	intermediate	1.5	branch	not determined	head	Cyst fluid
57	G12R	R201C	68	M	unknown	IPMN	intermediate	2.0	branch	not determined	head	Cyst fluid
58	G12D	No mutation detected	66	M	unknown	IPMN	high	2.0	main	not determined	head	Cyst fluid
59	G12V	R201C	81	M	unknown	IPMN	high	2.8	not determined	not determined	head	Cyst fluid
60	G12D & G12V	No mutation detected	68	M	unknown	IPMN	high	2.8	mixed	not determined	head	Cyst fluid
61	G12V	No mutation detected	80	M	unknown	IPMN	high	2.8	main	not determined	head	Cyst fluid
62	G12V	R201H	74	F	unknown	IPMN	intermediate	3.0	branch	not determined	head	Cyst fluid
63	G12V	R201C	65	F	unknown	IPMN	high	3.0	mixed	not determined	head	Cyst fluid
64	G12V	No mutation detected	72	F	unknown	IPMN	low	3.4	branch	not determined	head	Cyst fluid
65	G12D & G12R	R201C	65	F	unknown	IPMN	intermediate	3.5	branch	not determined	head	Cyst fluid
66	G12V	No mutation detected	76	F	unknown	IPMN	intermediate	3.9	branch	not determined	head	Cyst fluid
67	G12V	R201C & R201H	77	F	unknown	IPMN	intermediate	4.0	branch	not determined	head	Cyst fluid
68	No mutation detected	R201C	87	F	unknown	IPMN	intermediate	4.0	mixed	not determined	head	Cyst fluid
69	No mutation detected	R201C	70	M	unknown	IPMN	high	4.0	mixed	not determined	head	Cyst fluid
70	G12V	R201C	52	F	unknown	IPMN	high	4.2	mixed	not determined	head	Cyst fluid
71	G12V	No mutation detected	73	F	unknown	IPMN	intermediate	4.5	branch	not determined	head	Cyst fluid
72	G12D	R201H	74	F	unknown	IPMN	intermediate	5.0	branch	not determined	head	Cyst fluid
73	G12V	R201C	63	M	unknown	IPMN	high	6.0	main	not determined	head	Cyst fluid
74	No mutation detected	R201C	63	M	unknown	IPMN	high	6.5	mixed	not determined	head	Cyst fluid
75	No mutation detected	R201C	67	F	unknown	IPMN	high	7.0	main	not determined	head	Cyst fluid
76	G12D	No mutation detected	79	M	unknown	IPMN	low	13.0	main	not determined	head	Cyst fluid
77	G12V	No mutation detected	86	F	unknown	IPMN	intermediate	1.7	branch	not determined	tail	Cyst fluid
78	G12D & G12V	R201C & R201H	74	M	unknown	IPMN	intermediate	2.0	mixed	not determined	tail	Cyst fluid
79	G12V & G12R	R201H	70	M	unknown	IPMN	intermediate	2.2	branch	not determined	tail	Cyst fluid
80	No mutation detected	R201C	68	M	unknown	IPMN	high	2.5	main	not determined	tail	Cyst fluid
81	G12D	No mutation detected	77	F	unknown	IPMN	high	2.6	mixed	not determined	tail	Cyst fluid
82	G12V	R201C	67	M	unknown	IPMN	intermediate	2.7	branch	not determined	tail	Cyst fluid
83	G12D & G12V	No mutation detected	80	F	unknown	IPMN	intermediate	3.5	mixed	not determined	tail	Cyst fluid
84	G12D	No mutation detected	68	F	unknown	IPMN	intermediate	6.0	branch	not determined	tail	Cyst fluid
85	G12D & G12V	No mutation detected	68	F	unknown	IPMN	intermediate	6.0	branch	not determined	tail	Cyst fluid
86	G12D & G12V	R201C	69	M	unknown	IPMN	high	23.0	main	not determined	tail	Cyst fluid
87	G12D & G12V & G12R	R201C & R201H	69	M	unknown	IPMN	high	23.0	main	not determined	tail	Cyst fluid
88	No mutation detected	R201C	72	M	unknown	IPMN	high	1.4	main	not determined	head	Cyst wall
89	G12D	R201C	74	M	Yes	IPMN	intermediate	3.0	main	gastric	body/tail	Cyst fluid
90	G12V	No mutation detected	54	F	No	IPMN	low	2.0	branch	gastric	body/tail	Cyst fluid
91	No mutation detected	R201H	81	M	No	IPMN	high	1.8	main	intestinal	body/tail	Cyst fluid
92	G12V	R201H	63	F	No	IPMN	intermediate	1.9	branch	not determined	body/tail	Cyst fluid
93	G12D	R201C	73	M	No	IPMN	intermediate	3.2	branch	gastric	body/tail	Cyst fluid
94	G12V	No mutation detected	60	M	No	IPMN	high	4.0	branch	pancreatobiliary	head	Cyst fluid
95	G12D	No mutation detected	76	F	No	IPMN	high	1	branch	gastric	head	Cyst fluid
96	G12D & G12V	R201C	65	M	No	IPMN	intermediate	1.5	branch	gastric	head	Cyst fluid
97	G12V	R201H	67	F	No	IPMN	high	4	branch	gastric	head	Cyst fluid
98	No mutation detected	R201C	54	M	Yes	IPMN	intermediate	4.0	branch	gastric	body/tail	Cyst fluid
99	G12D	No mutation detected	72	M	Yes	IPMN	low	0.5	branch	gastric	body/tail	Cyst fluid
100	G12R	R201H	73	M	Yes	IPMN	intermediate	3.0	branch	gastric	head	Cyst fluid
101	No mutation detected	No mutation detected	79	F	Yes	IPMN	high	4.0	branch	gastric	head	Cyst fluid
102	G12V	No mutation detected	67	F	Yes	IPMN	intermediate	0.6	main	gastric	head	Cyst fluid
103	G12D	No mutation detected	60	F	Yes	IPMN	intermediate	1	branch	not determined	head	Cyst fluid
104	G12V	R201C	54	F	Yes	IPMN	intermediate	1.7	branch	gastric	head	Cyst fluid
105	G12V	R201H	57	M	Yes	IPMN	intermediate	4.5	branch	gastric	head	Cyst fluid
106	No mutation detected	No mutation detected	71	F	unknown	IPMN	low	1.7	branch	gastric	body/tail	Cyst fluid

107	G12D	No mutation detected	71	M	unknown	IPMN	low	6.0	branch	not determined	head	Cyst fluid
108	G12D	R201H	66	M	unknown	IPMN	intermediate	0.6	branch	intestinal	head	Cyst fluid
109	No mutation detected	R201H	65	F	unknown	IPMN	intermediate	1.8	mixed	gastric	head	Cyst fluid
110	G12V	R201C	56	M	unknown	IPMN	intermediate	2	main	gastric	head	Cyst fluid
111	G12D	No mutation detected	63	M	unknown	IPMN	intermediate	3.1	branch	gastric	head	Cyst fluid
112	G12R	R201C	62	M	unknown	IPMN	intermediate	3.5	branch	not determined	head	Cyst fluid
113	G12D	R201C	71	M	unknown	IPMN	low	3.5	branch	gastric	head	Cyst fluid
114	G12R	No mutation detected	60	M	No	IPMN	high	13.0	mixed	pancreatobiliary	entire pancreas	Cyst wall
115	G12D	R201H	70	M	No	IPMN	high	4.0	main	pancreatobiliary	head	Cyst wall
116	No mutation detected	R201C	62	F	No	IPMN	high	6.0	main	gastric	head	Cyst wall
117	G12D	R201C	75	M	unknown	IPMN	high	5.0	not determined	gastric	head	Cyst wall
118	G12D	No mutation detected	73	F	Yes	IPMN	high	2.8	branch	gastric	head	Cyst wall
119	G12R	No mutation detected	71	F	No	IPMN	low	4.0	branch	gastric	body/tail	Cyst wall
120	G12V	R201H	72	M	No	IPMN	high	7.0	main	intestinal	body/tail	Cyst wall
121	No mutation detected	R201H	77	M	No	IPMN	high	7.0	main	intestinal	entire pancreas	Cyst wall
122	G12V	R201H	35	M	No	IPMN	high	8.0	main	intestinal	head	Cyst wall
123	G12V	R201H	69	M	No	IPMN	high	5.1	mixed	intestinal	head	Cyst wall
124	G12V	No mutation detected	64	F	Yes	IPMN	low	2.0	branch	gastric	body/tail	Cyst wall
125	No mutation detected	R201C	76	F	Yes	IPMN	high	1.5	main	intestinal	body/tail	Cyst wall
126	G12D	No mutation detected	69	F	unknown	IPMN	intermediate	3.4	mixed	gastric	body/tail	Cyst wall
127	G12D	R201H	79	F	unknown	IPMN	high	14	main	not determined	entire pancreas	Cyst wall
128	G12D	No mutation detected	74	M	unknown	IPMN	intermediate	8.0	main	gastric	head	Cyst wall
129	G12D	No mutation detected	56	M	unknown	IPMN	intermediate	4	branch	gastric	head	Cyst wall
130	G12D & G12V	R201C	68	F	Yes	IPMN	intermediate	2.5	branch	gastric	body/tail	Cyst fluid
131	G12V	R201C	73	F	Yes	IPMN	high	6.0	mixed	intestinal	entire pancreas	Cyst fluid
132	G12V & G12R	R201H	71	M	No	IPMN	intermediate	3.0	mixed	gastric	body/tail	Cyst wall



Table S3. Characteristics of patients with cyst types other than IPMN, including GNAS and KRAS mutation status.

Cyst #	KRAS	GNAS	Age at surgery	Sex	History of smoking	Post-operative diagnosis	Cyst Grade	Cyst diameter (cm)	Cyst location	Sample type
OT01	No mutation detected	No mutation detected	57	F	unknown	SCA	NA	2.5	head	Cyst fluid
OT02	No mutation detected	No mutation detected	58	F	No	SCA	NA	1.5	Neck	Cyst fluid
OT03	No mutation detected	No mutation detected	54	M	unknown	SCA	NA	2	head	Cyst fluid
OT04	No mutation detected	No mutation detected	57	M	Yes	SCA	NA	2	body/tail	Cyst fluid
OT05	No mutation detected	No mutation detected	69	F	unknown	SCA	NA	3	tail	Cyst fluid
OT06	No mutation detected	No mutation detected	57	F	Yes	SCA	NA	3	body/tail	Cyst fluid
OT07	No mutation detected	No mutation detected	59	F	No	SCA	NA	3	head	Cyst fluid
OT08	No mutation detected	No mutation detected	64	F	No	SCA	NA	3	head	Cyst fluid
OT09	No mutation detected	No mutation detected	60	F	unknown	SCA	NA	3.1	head	Cyst fluid
OT10	No mutation detected	No mutation detected	56	M	Yes	SCA	NA	4	body	Cyst fluid
OT11	No mutation detected	No mutation detected	47	F	Yes	SCA	NA	4	head	Cyst fluid
OT12	No mutation detected	No mutation detected	49	F	unknown	SCA	NA	4	head	Cyst fluid
OT13	No mutation detected	No mutation detected	52	M	unknown	SCA	NA	4.5	tail	Cyst fluid
OT14	No mutation detected	No mutation detected	58	F	unknown	SCA	NA	4.8	tail	Cyst fluid
OT15	No mutation detected	No mutation detected	46	M	Yes	SCA	NA	5	head	Cyst fluid
OT16	No mutation detected	No mutation detected	81	M	unknown	SCA	NA	5	head	Cyst fluid
OT17	No mutation detected	No mutation detected	77	F	unknown	SCA	NA	6	body	Cyst fluid
OT18	No mutation detected	No mutation detected	61	F	unknown	SCA	NA	6	tail	Cyst fluid
OT19	No mutation detected	No mutation detected	72	M	Yes	SCA	NA	7	body/tail	Cyst fluid
OT20	No mutation detected	No mutation detected	61	F	unknown	SCA	NA	7.5	body	Cyst fluid
OT21	No mutation detected	No mutation detected	77	F	Yes	SCA	NA	8	body/tail	Cyst fluid
OT22	No mutation detected	No mutation detected	55	F	unknown	SCA	NA	10	tail	Cyst fluid
OT23	No mutation detected	No mutation detected	61	F	unknown	SCA	NA	13	tail	Cyst fluid
OT24	No mutation detected	No mutation detected	43	M	No	SCA	NA	1.5	head	Cyst fluid
OT25	No mutation detected	No mutation detected	63	M	unknown	SCA	NA	1.8	body/tail	Cyst fluid
OT26	No mutation detected	No mutation detected	62	F	No	SCA	NA	10.5	body/tail	Cyst fluid
OT27	No mutation detected	No mutation detected	57	F	No	SCA	NA	2.5	body/tail	Cyst fluid
OT28	No mutation detected	No mutation detected	86	F	No	SCA	NA	2.5	body/tail	Cyst fluid
OT29	No mutation detected	No mutation detected	58	M	Yes	SCA	NA	2.5	body/tail	Cyst fluid
OT30	No mutation detected	No mutation detected	68	F	unknown	SCA	NA	2.5	head	Cyst fluid
OT31	No mutation detected	No mutation detected	72	F	unknown	SCA	NA	2.8	body/tail	Cyst fluid
OT32	No mutation detected	No mutation detected	63	F	Yes	SCA	NA	3	body/tail	Cyst fluid
OT33	No mutation detected	No mutation detected	47	F	Yes	SCA	NA	3	head	Cyst fluid
OT34	No mutation detected	No mutation detected	64	M	Yes	SCA	NA	3.5	head	Cyst fluid
OT35	No mutation detected	No mutation detected	52	F	No	SCA	NA	3.5	body/tail	Cyst fluid
OT36	No mutation detected	No mutation detected	71	F	No	SCA	NA	3.7	body/tail	Cyst fluid
OT37	No mutation detected	No mutation detected	77	F	Yes	SCA	NA	4	body/tail	Cyst fluid
OT38	No mutation detected	No mutation detected	36	F	unknown	SCA	NA	4.1	head	Cyst fluid

OT39	No mutation detected	No mutation detected	74	F	unknown	SCA	NA	4.5	head	Cyst fluid
OT40	No mutation detected	No mutation detected	66	M	No	SCA	NA	5	body/tail	Cyst fluid
OT41	No mutation detected	No mutation detected	40	F	unknown	SCA	NA	5.4	body/tail	Cyst fluid
OT42	No mutation detected	No mutation detected	56	F	No	SCA	NA	5.9	body/tail	Cyst fluid
OT43	No mutation detected	No mutation detected	19	F	unknown	SCA	NA	6.6	head	Cyst fluid
OT44	No mutation detected	No mutation detected	69	M	unknown	SCA	NA	7.5	head	Cyst fluid
OT45	No mutation detected	No mutation detected	32	F	Yes	MCN	Not determined	2.3	body	Cyst fluid
OT46	No mutation detected	No mutation detected	51	F	Yes	MCN	Not determined	2.5	body	Cyst fluid
OT47	G12V	No mutation detected	65	F	No	MCN	Not determined	2.5	tail	Cyst fluid
OT48	G12V	No mutation detected	46	F	No	MCN	low	2.5	tail	Cyst fluid
OT49	G12V	No mutation detected	43	F	Yes	MCN	Not determined	3.2	body	Cyst fluid
OT50	No mutation detected	No mutation detected	46	F	No	MCN	Not determined	3.5	body	Cyst fluid
OT51	No mutation detected	No mutation detected	65	F	Yes	MCN	Not determined	4	tail	Cyst fluid
OT52	No mutation detected	No mutation detected	60	F	Yes	MCN	low	4	body/tail	Cyst fluid
OT53	No mutation detected	No mutation detected	59	F	No	MCN	Not determined	4.5	tail	Cyst fluid
OT54	No mutation detected	No mutation detected	52	F	No	MCN	Not determined	5	body / tail	Cyst fluid
OT55	No mutation detected	No mutation detected	24	F	unknown	MCN	low	5	body/tail	Cyst fluid
OT56	No mutation detected	No mutation detected	43	F	Yes	MCN	Not determined	5.5	body	Cyst fluid
OT57	No mutation detected	No mutation detected	59	F	Yes	MCN	low	7	body/tail	Cyst fluid
OT58	G12V	No mutation detected	42	F	No	MCN	Not determined	8.5	body / tail	Cyst fluid
OT59	No mutation detected	No mutation detected	34	F	unknown	MCN	low	16	head	Cyst fluid
OT60	G12D	No mutation detected	57	F	No	MCN	low	17	body	Cyst fluid
OT61	G12R	No mutation detected	66	F	Yes	MCN	low	1.5	head	Cyst fluid
OT62	G12R	No mutation detected	39	F	unknown	MCN	low	2.5	body/tail	Cyst fluid
OT63	No mutation detected	No mutation detected	36	F	unknown	MCN	low	3.5	head	Cyst fluid
OT64	No mutation detected	No mutation detected	54	F	unknown	MCN	low	5.5	body/tail	Cyst fluid
OT65	No mutation detected	No mutation detected	42	F	unknown	MCN	intermediate	7.4	head	Cyst fluid
OT66	G12D	No mutation detected	45	F	unknown	IOPN	high	3.1	head	Cyst fluid
OT67	No mutation detected	No mutation detected	36	M	unknown	IOPN	high	4.5	head	Cyst fluid
OT68	No mutation detected	No mutation detected	72	M	No	IOPN	high	6.0	head	Cyst fluid
OT69	No mutation detected	No mutation detected	74	M	Yes	IOPN	high	6.0	body/tail	Cyst fluid
OT70	No mutation detected	No mutation detected	55	F	unknown	IOPN	high	10.0	tail	Cyst fluid

Table S4. Quantification of mutations in selected IPMNs containing both *GNAS* and *KRAS* mutations.

IPMN #	<i>KRAS</i> mutant allele(s)	Major <i>KRAS</i> mutant allele	Major <i>KRAS</i> allele freq	Major <i>KRAS</i> allele fraction/total mutant alleles*
31	G12D & G12V & G12R	G12D	29%	97%
36	G12D	G12D	18%	Not applicable
41	G12D	G12D	3.0%	NA
42	G12D	G12D	17%	NA
43	G12D	G12D	33%	NA
48	G12R	G12S	1.6%	NA
57	G12R	G12S	0.8%	NA
65	G12D & G12R	G12D	27%	88%
67	G12V	G12V	8.0%	NA
72	G12D	G12D	36%	NA
78	G12D & G12V	G12V	0.9%	65%
79	G12V & G12R	G12V	11%	60%
86	G12D & G12V	G12V	18%	50%
87	G12D & G12V & G12R	G12V	8%	46%
100	G12R	G12S	1.4%	NA
105	G12V	G12V	1.0%	NA
130	G12D & G12V	G12V	4.0%	56%

\* NA = Not applicable because there was only a single mutation identified in the IPMN.

Table S5. Comparison of mutational status in DNA from IPMNs and pancreatic adenocarcinomas from the same patients.

<b>IPMN #</b>	<b>Lesion</b>	<b>KRAS mutation</b>	<b>GNAS mutation</b>
9	IPMN	G12V & G12D	R201H & R201C
	Cancer	G12V	R201H
11	IPMN	No mutation detected	R201C
	Cancer	No mutation detected	R201C
20	IPMN	G12V	R201C
	Cancer	G12V	R201C
33	IPMN	G12V	R201H
	Cancer	G12R	No mutation detected
122	IPMN	G12V	R201H
	Cancer	G12V	R201H
125	IPMN	No mutation detected	R201C
	Cancer	No mutation detected	R201C
127	IPMN	G12D	R201H
	Cancer	G12D	R201H
131	IPMN	G12V	R201C
	Cancer	G12V	R201C

Table S6. Oligonucleotide primer and probe sequences.

Gene	Used for:	5'-Modification	Mutation	Sequence (5'-3')*
<b>PCR Amplification Primers</b>				
<i>GNAS</i>	GNAS Forward Primer	None	<b>GNAS 201 R201C, R201H</b>	GGCTTTGGTGAGATCCATTG
<i>GNAS</i>	GNAS Reverse Primer	None	<b>GNAS 201 R201C, R201H</b>	TCCACCTGGAACCTGGTCTC
<i>KRAS</i>	PCR forward primer	None	<b>KRAS G12D, G12R, G12V</b>	GATCATATTCGTCCACAAAATGATTC
<i>KRAS</i>	PCR Reverse Primer	None	<b>KRAS G12D, G12R, G12V</b>	TGACTGAATATAAACTTGTGGTAGTTG
<b>Ligation probes</b>				
<i>GNAS</i>	WT-specific probe	6-FAM	R201H	ATG GAG AAC TTG ACG TCC TG TTC GCT GCC G
<i>GNAS</i>	Mutant-specific probe	HEX	R201H	TTCGCTGCCA
<i>GNAS</i>	Common anchoring probe	Phosphate	R201H	TGT CCT GAC TTC <b>GG TGT CCA CTA GTC ATG CTT</b>
<i>GNAS</i>	WT-specific probe	6-FAM	R201C	ATG GAG AAC TTG ACG TCC AC CTT CGC TGC C
<i>GNAS</i>	Mutant-specific probe	HEX	R201C	CTT *CGC T*G*C T
<i>GNAS</i>	Common anchoring probe	Phosphate	R201C	GTG TCC TGA CTT <b>GG TGT CCA CTA GTC ATG CTT</b>
<i>KRAS</i>	WT-specific probe	6-FAM	G12D	ATG GAG AAC TTG ACG TCC T C CTA CGC CAC
<i>KRAS</i>	Mutant-specific probe	HEX	G12D	TGCCT*ACGC*C*AT
<i>KRAS</i>	Common anchoring probe	Phosphate	G12D	CAG CTC CAA CTA <b>GG TGT CCA CTA GTC ATG CTT</b>
<i>KRAS</i>	WT-specific probe	6-FAM	G12R	TCC CGC GAA ATT AAT ACG AG <b>CTA CGC CACC</b>
<i>KRAS</i>	Mutant-specific probe	HEX	G12R	CTA CGC CAC G
<i>KRAS</i>	Common anchoring probe	Phosphate	G12R	AGC TCC AAC TAC CAC <b>GG TGT CCA CTA GTC ATG CTT</b>
<i>KRAS</i>	WT-specific probe	6-FAM	G12V	ATG GAG AAC TTG ACG TCC T C CTA CGC CAC
<i>KRAS</i>	Mutant-specific probe	HEX	G12V	CCT ACG CCA A
<i>KRAS</i>	Common anchoring probe	Phosphate	G12V	CAG CTC CAA CTA <b>GG TGT CCA CTA GTC ATG CTT</b>
<b>BEAMing probes</b>				
<i>GNAS</i>	Detecting beads containing either WT or mutant sequences	ROX	R201C	CTGAAACAAAATTGAGGT
<i>GNAS</i>	WT-specific probe	Cy3	R201C	AGGACACgGCAGCGA
<i>GNAS</i>	Mutant-specific probe	Cy5	R201C	AGGACACaGCAGCGA
<i>GNAS</i>	Detecting beads containing either WT or mutant sequences	ROX	R201H	CTGAAACAAAATTGAGGT
<i>GNAS</i>	WT-specific probe	Cy3	R201H	CAGGACACGGCAGCG
<i>GNAS</i>	Mutant-specific probe	Cy5	R201H	CAGGACATGGCAGCG
<i>KRAS</i>	Detecting beads containing either WT or mutant sequences	ROX	G12D	TGACGATACAGCTAATTCA
<i>KRAS</i>	WT-specific probe	Cy3	G12D	GGAGCTGGTGGCGTA
<i>KRAS</i>	Mutant-specific probe	Cy5	G12D	GGAGCTGATGGCGTA
<i>KRAS</i>	Detecting beads containing either WT or mutant sequences	ROX	G12V	TGACGATACAGCTAATTCA
<i>KRAS</i>	WT-specific probe	Cy3	G12V	GGAGCTGGTGGCGTA
<i>KRAS</i>	Mutant-specific probe	Cy5	G12V	GGAGCTGTTGGCGTA
<i>KRAS</i>	Detecting beads containing either WT or mutant sequences	ROX	G12R	TGACGATACAGCTAATTCA
<i>KRAS</i>	WT-specific probe	Cy3	G12R	TGGAGCTGGTGGCGT
<i>KRAS</i>	Mutant-specific probe	Cy5	G12R	TGGAGCTCGTGGCGT

\* indicates LNA linkages; red font indicates additional nucleotides used to discriminate WT from Mutant sequences in the ligation assays.