Supplemental Tables and Figures

Supplemental Table 1. Clinical characteristics FFPE tissue patient subset

Parameters	FFPE subset (n = 25)	non-IPMN[§] (n=9)	IPMN (n = 10)	Cancer (n = 6)
Gender (F:M)	13:12	**8:1*†**	**2:8***	**2:4†**
Age (years) median (range)	66 (31 – 81)	**48*† (31 – 68)**	**66.5* (47 – 78)**	**70.5† (65 – 81)**
BMI (kg/m^2) median (range)	25.8 (20.2 – 35.0)	28.0 (23.0 – 35)	25.3 (21.5 – 30.6)	25.4 (20.2 – 29.4)
Smoking (%)	12	22.2	10	0
Alcohol (%)	40	44.4	40.0	33.3
Diabetes (%)	16	0	20.0	33.3
PPI use (%)	12	22	10.0	0
S-Ca 19-9 (kE/L) median (range) above normal [#] (%)	8.8 (<1.0 – 480) 28	**7.9† (5.9 – 34) 0†**	5.7 (<1.0 – 71) 10.0	**315† (63 – 480) 100†**
HbA1c (mmol/mol) median (range)	36 (30 – 64)	33.0 (30 – 43)	38.5 (32 – 64)	37.5 (31 – 52)
Amylase (µkat/L) median (range)	0.30 (<0.13 – 2.62)	0.31 (0.22 – 1.64)	0.25 (<0.13 – 2.62)	<0.13 (<0.13 – 0.34)
Albumin (g/L) median (range)	36 (28 – 42)	**38.0† (33 – 42)**	36.0 (30 – 42)	**28.5† (28 – 36)**
Bilirubin (µmol/L) median (range)	6 (<3 – 119)	**5† (<3 – 18)**	6 (<3 – 17)	**14† (5 – 119)**
CRP (mg/L) median (range)	2 (1 – 130)	2 (1 – 13)	1 (1 – 49)	17 (2 – 130)
Invasive endoscopic procedure (%) mean freq. (range)	48 0.8 (0 – 3)	**11.1† 0.11 (0 – 1) †**	50.0 1 (0 – 3)	**100† 1.5 (1 – 3) †**
Uni-/Multicystic (%)	68/32	88.8/11.1	40/60	83.3/16.6

[§] non-IPMN group comprises of MCN (n=3) and SCN (n=6)

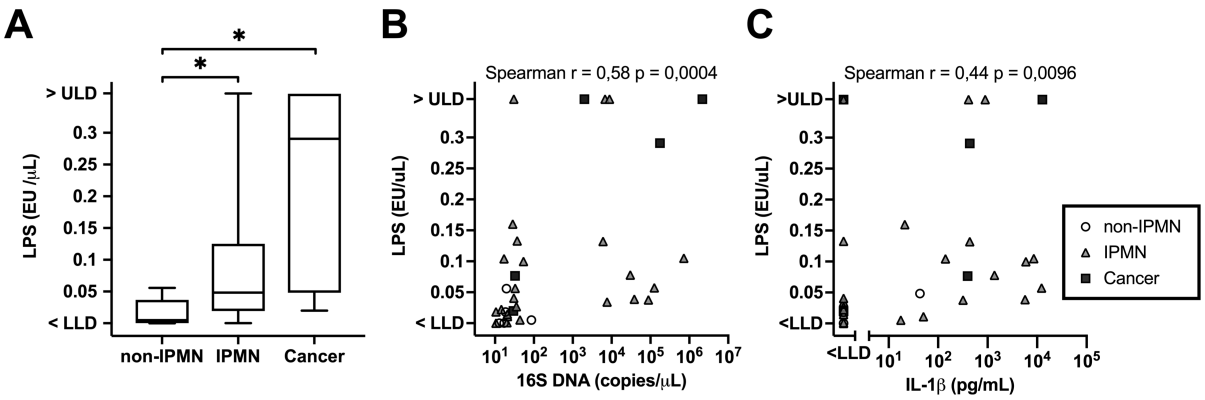
[#] normal S-Ca 19-9 < 34 kE/L

Pairwise comparisons between the diagnosis groups were made using Fisher's exact test (qualitative parameters) and Kruskal-Wallis test with Dunn's multiple comparisons correction (quantitative variables).

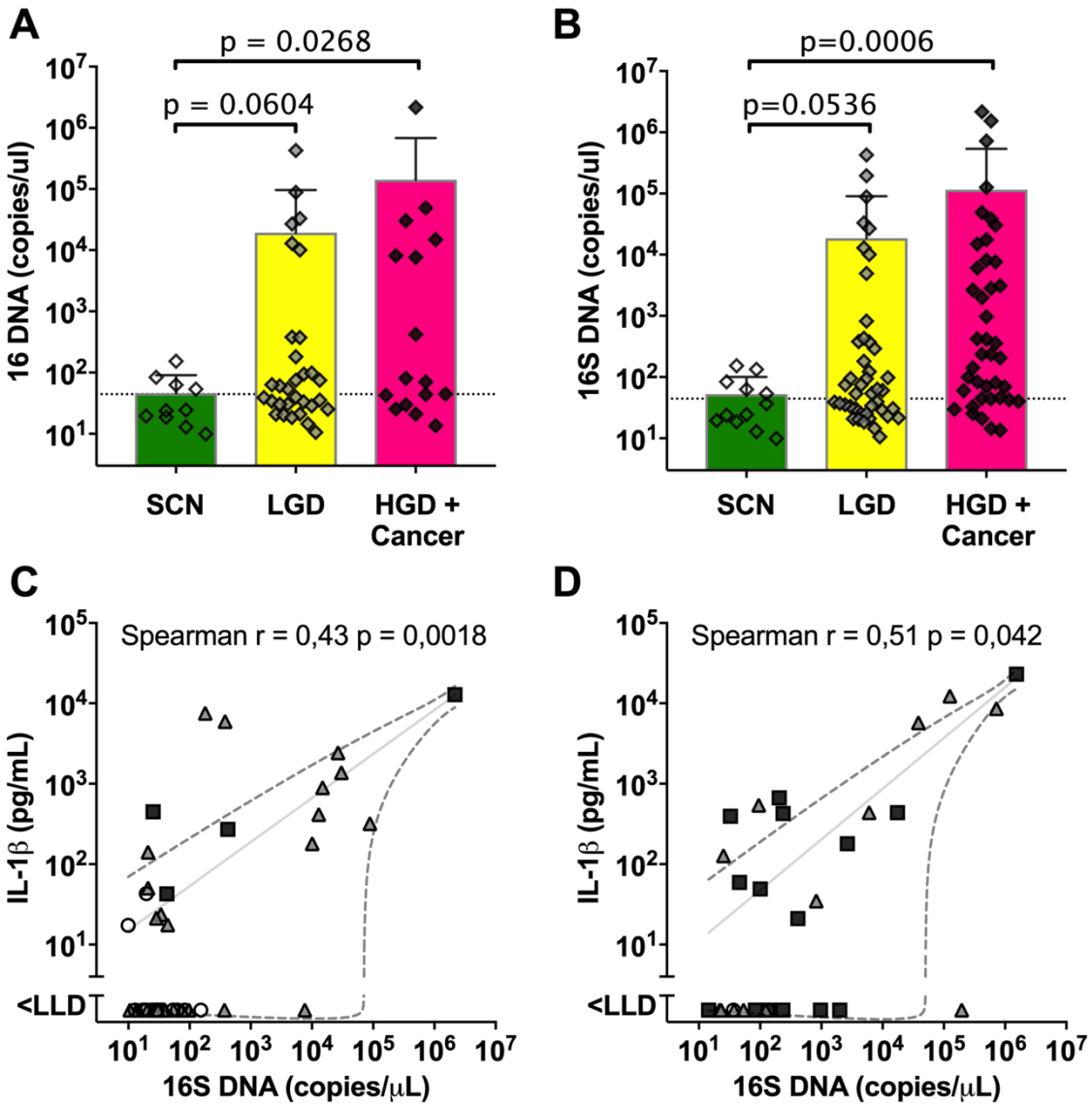
* indicates "non-IPMN cyst" vs "IPMN" $p < 0.05$ (two-tailed)

† indicates "non-IPMN cyst" vs "Cancer" $p < 0.05$ (two-tailed)

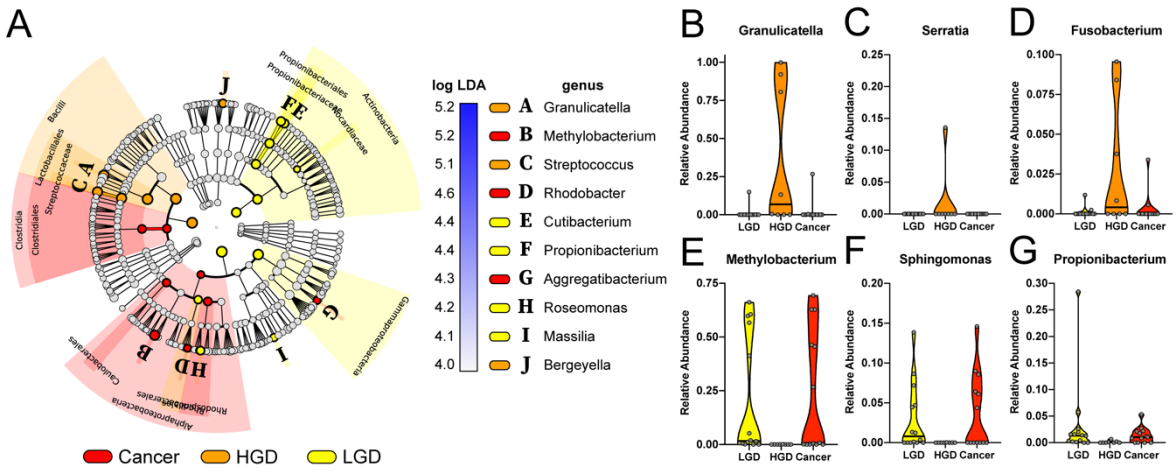
n.a. = not applicable



Supplemental Figure 1. A) Quantification of bacterial lipopolysaccharide (LPS) in cyst fluid from ”non-IPMN” (n=5), ”IPMN” (n=24), ”IPMN Cancer” (n=5) patients. **B)** Spearman correlation analysis on intracystic 16S DNA copies and LPS quantities. **C)** Spearman correlation analysis on intracystic IL-1β and LPS quantities. Statistically significant differences were determined using Kruskal-Wallis test with Dunn’s multiple comparison test with * $p < 0.05$. LLD = lower limit of detection, ULD = upper limit of detection.



Supplemental Figure 2. Intracystic quantity of bacterial 16S DNA in **A)** patients who never underwent IEP in "SCN" (n=10), "IPMN LGD" (n=31), "IPMN HGD and Cancer" (n=16) patient group, and (**B**) in all patients of "SCN" (n=12), "IPMN LGD" (n=43), "IPMN HGD and Cancer" (n=41) patient group. Bars indicate mean for 16S DNA quantity. Spearman correlation analysis on 16S DNA and IL-1β quantities in cyst fluid in **C)** patients who never underwent IEP, and **D**) patients that had history or prior IEP. Statistically significant differences were determined using Mann-Whitney test.



Supplemental Figure 3. Sub-analysis of microbial relative abundance data allowing one sample per patient (n=35) **A)** Cladogram representing LEfSe results which identified 10 features that are differentially abundant between the three diagnose classes (red = Cancer, orange = IPMN HGD, yellow = IPMN LGD). **B,C,D,E,F,G)** Violin plot showing relative abundance distribution and median of selected differentially abundant bacterial genera per diagnose group.