Les colites inflammatoires associées à la CSP

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MICI associées à la CSP

Association à une MICI
Europe du Nord 60-80%
Eur.Sud et Asie 30-50%

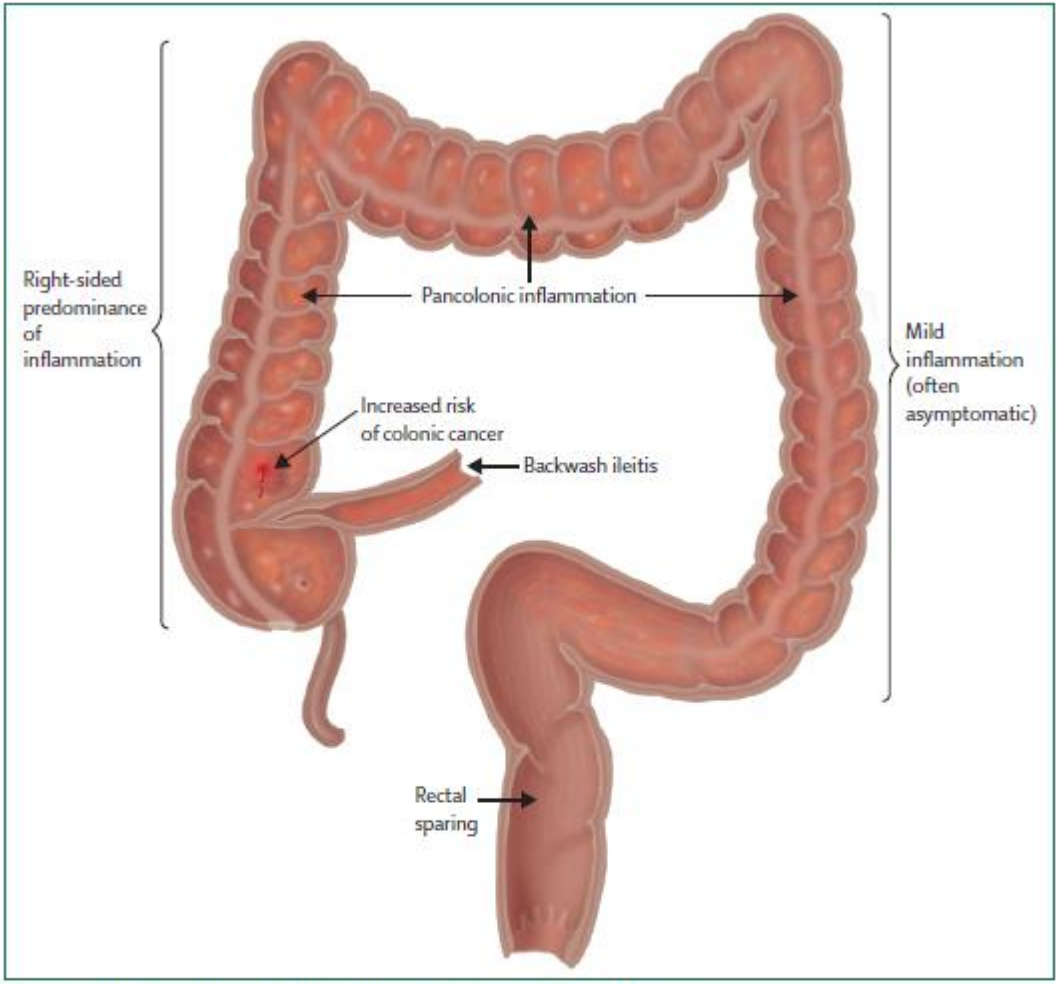

Figure 2: **Inflammatory bowel disease in primary sclerosing cholangitis**
Inflammatory bowel disease presents earlier in patients with primary sclerosing cholangitis than in those who do not have primary sclerosing cholangitis. Usually primary sclerosing cholangitis is diagnosed in patients with pre-existing inflammatory bowel disease. The colitis is usually total but symptomatically mild, often with no rectal bleeding and inflammation (rectal sparing), and characterised by prolonged remissions. Inflammation is more pronounced in the right colon than in the left, and colon cancer in patients with inflammatory bowel disease who also have primary sclerosing cholangitis is typically right-sided. In some patients, the terminal ileum is slightly inflamed (backwash ileitis), but by definition does not show features of Crohn's ileitis. Reproduced with permission of Kari C Toverud.

Epidémiologie: littérature

Table 1 Epidemiology primary sclerosing cholangitis - inflammatory bowel disease *n* (%)

Ref.	Country	Period	Incidence[1]	PSC	Male Gender
Rabinovitz *et al*[100], 1990	United States	NA	NA	66	NA
Farrant *et al*[19], 1991	United Kingdom	1972-1989	NA	126	78 (61.9)
Schrumpf *et al*[18], 1994	Norway	1975-1989	NA	77	51 (66.2)
Escorsell *et al*[17], 1994	Spain	1984-1988	0.07	43	26 (60.5)
Broomé *et al*[2], 1996	Sweden	? - 1992	NA	305	195 (63.9)
Boberg *et al*[4], 1998	Norway	1986-1995	1.31	17	12 (70.6)
Ponsioen *et al*[20], 2002	The Netherlands	1979-1999	NA	174	105 (60.3)
Bambha *et al*[5], 2003	United States	1976-2000	0.90	22	15 (68.3)
Kingham *et al*[101], 2004	United Kingdom	1984-2003	0.91	53	33 (62.3)
Bergquist *et al*[102], 2005	Sweden	1984-1999	NA	145	100 (69.0)
Tischendorf *et al*[103], 2007	Germany	1978-2004	NA	273	195 (71.4)
Bergquist *et al*[104], 2007	Sweden	1984-2004	NA	246	165 (67.1)
Kaplan *et al*[14], 2007	Canada	2000-2005	0.92	49	27 (55.1)
Card *et al*[3], 2008	United Kingdom	1987-2002	0.41	223	141 (63.2)
Lindkvist *et al*[105], 2010	Sweden	1992-2005	1.22	199	142 (71.4)
Bowlus *et al*[106], 2010	United States	1995-2009	NA	6767	4475 (66.1)
Toy *et al*[107], 2011	United States	2000-2006	0.41	169	101 (59.8)
Boonstra *et al*[22], 2013	The Netherlands	2000-2007	0.50	590	375 (63.6)

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Epidémiologie: quelle MICI ?

Table 1 Epidemiology primary sclerosing cholangitis - inflammatory bowel disease *n* (%)

Ref.	PSC-IBD	PSC-UC	PSC-CD
Rabinovitz *et al*[100], 1990	47 (71.2)	39 (83.0)	8 (17.0)
Farrant *et al*[19], 1991	85 (67.5)	83 (97.6)	2 (2.4)
Schrumpf *et al*[18], 1994	76 (98.7)	58 (76.3)	11 (14.5)
Escorsell *et al*[17], 1994	20 (46.5)	19 (95.0)	1 (5.0)
Broomé *et al*[2], 1996	249 (81.6)	220 (88.4)	20 (8.0)
Boberg *et al*[4], 1998	12 (70.6)	9 (75.0)	2 (16.7)
Ponsioen *et al*[20], 2002	114 (65.5)	83 (72.8)	28 (24.6)
Bambha *et al*[5], 2003	16 (72.7)	12 (75.0)	3 (18.8)
Kingham *et al*[101], 2004	33 (62.3)	30 (90.9)	3 (19.1)
Bergquist *et al*[102], 2005	126 (86.9)	107 (84.9)	19 (15.1)
Tischendorf *et al*[103], 2007	172 (63.0)	141 (82.0)	29 (16.9)
Bergquist *et al*[104], 2007	195 (79.3)	166 (85.1)	21 (10.8)
Kaplan *et al*[14], 2007	36 (73.5)	17 (47.2)	19 (52.8)
Card *et al*[3], 2008	108 (48.4)	67 (62.0)	13 (12.0)
Lindkvist *et al*[105], 2010	152 (76.4)	129 (84.9)	17 (11.2)
Bowlus *et al*[106], 2010	4637 (68.5)	3067 (66.1)	1090 (23.5)
Toy *et al*[107], 2011	109 (64.5)	95 (87.2)	13 (11.9)
Boonstra *et al*[22], 2013	402 (68.1)	308 (76.6)	78 (19.4)

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Epidémiologie: localisation de la MICI

Table 2 Phenotypic features primary sclerosing cholangitis - inflammatory bowel disease *n* (%)

Ref.	IBD (*n*)	PSC-IBD (*n*)	Proctitis		Leftsided		Pancolitis		Rectal Sparing	
			IBD	PSC-IBD	IBD	PSC-IBD	IBD	PSC-IBD	IBD	PSC-IBD
Olsson *et al*[9], 1991	1445	55	552 (38.2)	3 (5.5)	NA	NA	893 (61.8)	52 (94.5)	NA	NA
Loftus *et al*[11], 2005	142	71	NA	NA	NA	NA	76 (53.5)	60 (84.5)	8 (5.6)	34 (47.9)
Kaplan *et al*[14], 2007	0	36	NA	NA	NA	NA	NA	17 (47.2)	NA	2 (5.6)
Sokol *et al*[15], 2008	150	75	138 (92.0)	68 (90.7)	130 (86.7)	68 (90.7)	91 (60.7)	49 (65.3)	20 (13.3)	15 (20.0)
Joo *et al*[31], 2009	40	40	0	0	14 (35.0)	3 (7.5)	18 (45.0)	34 (85.0)	10 (25.0)	11 (27.5)
Sano *et al*[32], 2010	60	20	18 (30.0)	1 (5.0)	19 (31.7)	1 (5.0)	21 (35.0)	7 (35.0)	NA	NA
Ye *et al*[25], 2011	63	21	NA	NA	NA	NA	35 (55.6)	20 (95.2)	1 (1.6)	8 (38.1)
Jørgensen *et al*[33], 2012	0	110	NA	NA	NA	3 (2.7)	NA	60 (54.5)	NA	73 (66.4)
O'toole *et al*[35], 2012	2649	103	209 (7.9)	1 (1.0)	649 (24.5)	23 (22.3)	663 (25.0)	56 (54.4)	NA	NA
Boonstra *et al*[12], 2012	0	380	NA	9 (2.4)	NA	34 (8.9)	NA	219 (57.6)	NA	NA
Boonstra *et al*[12], 2012[3]	80	80	4 (5.0)	2 (2.5)	16 (20.0)	2 (2.5)	35 (43.8)	52 (65.0)	1 (1.3)	8 (10.0)
Schaeffer *et al*[34], 2013	0	97	NA	0	NA	17 (17.5)	NA	42 (43.3)	NA	NA
Sinakos *et al*[30], 2013	0	129	NA	NA	NA	16 (12.4)	NA	76 (58.9)	NA	31 (24.0)
Mean			28.8%	13.4%	39.6%	18.8%	47.5%	64.7%	9.9%	30.9%

[1]IBD Endoscopic findings; [2]IBD Histological findings (biopsies); [3]Subgroup analysis. PSC: Primary sclerosing cholangitis; IBD: Inflammatory bowel disease; NA: Not available.

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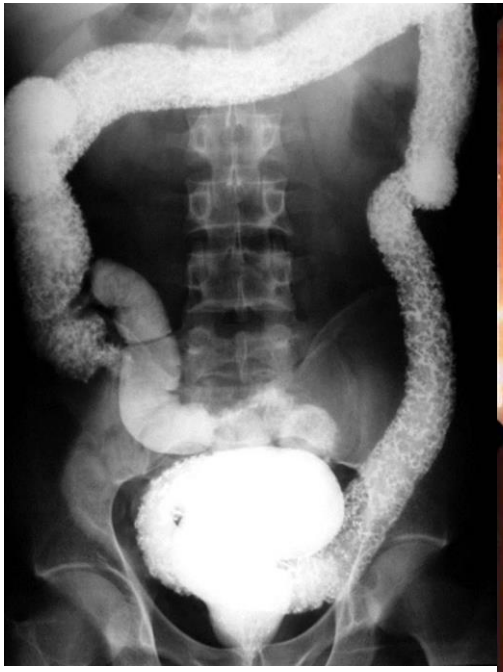
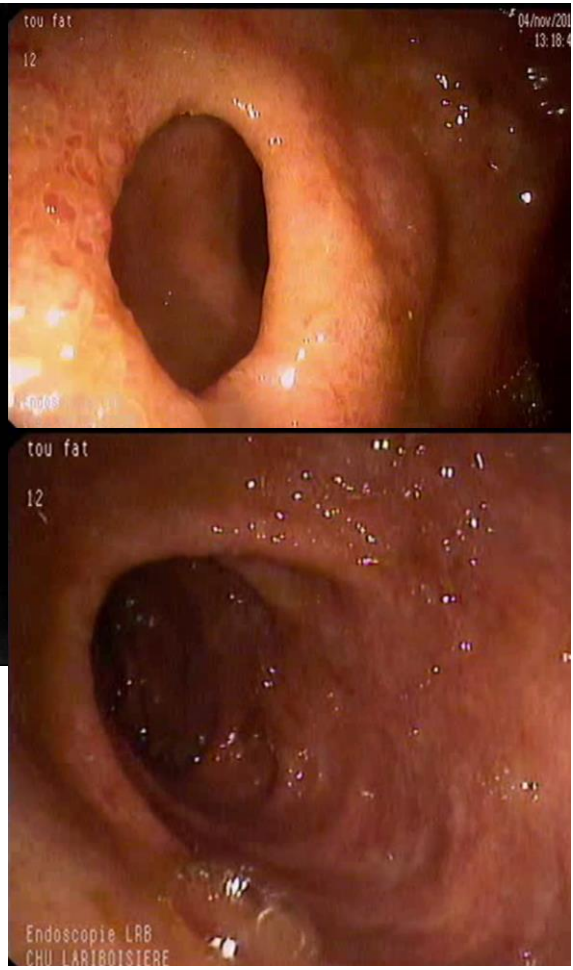
M. Crohn associée à la CSP

- Colique ou iléocolique
- Iléale très rare *Moussata D, et al. Isolated ileitis associated with primary sclerosing cholangitis in three patients with Crohn's disease. Scand J Gastroenterol 2016*

Epidémiologie: iléite de reflux

Ref.	IBD (*n*)	PSC-IBD (*n*)	Backwash	
			IBD	PSC-IBD
Olsson *et al*[9], 1991	1445	55	NA	NA
Loftus *et al*[11], 2005	142	71	10 (7.0)	20 (28.2)
Kaplan *et al*[14], 2007	0	36	NA	4 (11.1)
Sokol *et al*[15], 2008	150	75	36 (24.0)	14 (18.7)
Joo *et al*[31], 2009	40	40	3 (7.5)	4 (10.0)
Sano *et al*[32], 2010	60	20	NA	NA
Ye *et al*[25], 2011	63	21	2 (3.2)	9 (42.9)
Jørgensen *et al*[33], 2012	0	110	NA	17 (15.5)
O'toole *et al*[35], 2012	2649	103	NA	NA
Boonstra *et al*[12], 2012	0	380	NA	NA
Boonstra *et al*[12], 2012[3]	80	80	2 (2.5)	4 (5.0)
Schaeffer *et al*[34], 2013	0	97	NA	NA
Sinakos *et al*[30], 2013	0	129	NA	15 (11.6)
Mean			12.3%	16.7%





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Pochite après Anastomose iléo-anale

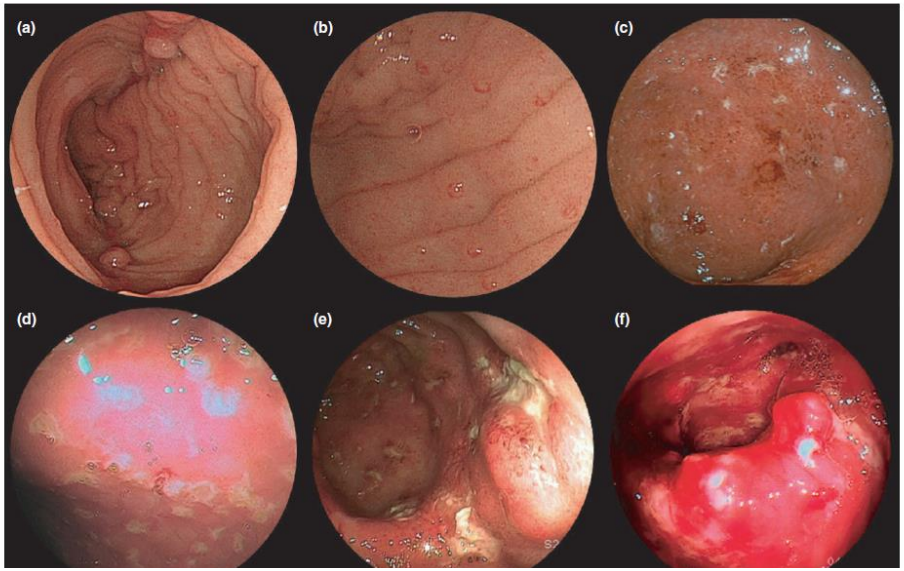

Table 5 Pouchitis in primary sclerosing cholangitis - inflammatory bowel disease *n* (%)

Ref.	Country	IBD (*n*)	PSC-IBD (*n*)	IPAA		Pouchitis		Chronic pouchitis		Pouch failure	
				IBD	PSC-IBD	IBD	PSC-IBD	IBD	PSC-IBD	IBD	PSC-IBD
Kartheuser *et al*[74], 1993	United States	NA	40	NA	40	NA	19 (47.5)	NA	NA	NA	NA
Penna *et al*[69], 1996	United States	1043	54	1043	54	336 (32.2)	34 (63.0)	? (15.0)[2]	? (60.0)[2]	NA	NA
Aitola *et al*[60], 1998	Finland	63	10	63	10	19 (30.2)	9 (90.0)	7 (11.1)	7 (70.0)	NA	NA
Gorgun *et al*[75], 2005	United States	260	65	260	65	31 (11.9)	9 (13.8)	31 (11.9)	9 (13.8)	19 (7.3)	1 (1.5)
Abdelrazeq *et al*[67], 2007	United Kingdom	182	16	182	16	53 (29.1)	11 (68.8)	18 (9.9)	9 (56.3)	NA	NA
Lepistö *et al*[59], 2008	Finland	389	52	389	52	101 (26.0)	25 (48.1)	NA	NA	13 (3.3)	2 (3.8)
Wasmuth *et al*[73], 2010	Norway	178	11	178	11	94 (52.8)	8 (72.0)	17 (9.6)	4 (36.4)	20 (11.2)	1 (9.1)
Mathis *et al*[70], 2011	United States	NA	100	NA	100	NA	64 (64.0)	NA	16 (16.0)	NA	3 (3.0)
Block *et al*[58], 2013	Norway	113	48	62	31	20 (32.3)	27 (87.1)	8 (12.9)	20 (64.5)	4 (6.5)	5 (16.1)

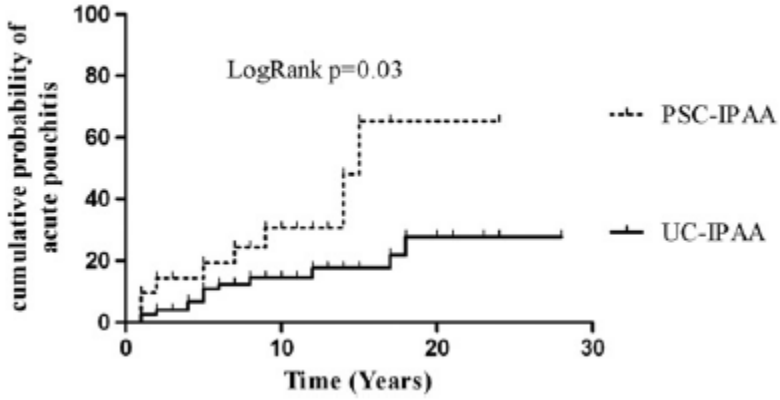

Table 3 Pouch related and surgical complications.

	PSC-IPAA n = 21 (%)	UC-IPAA n = 79 (%)	p value
Pouch dysfunction	15 (71%)	37 (47%)	0.053
Acute pouchitis	8 (38%)	16 (20%)	0.15
Immunomodulator/biologic for pouchitis	2 (9.5%)	4 (5.1)	0.6
Pelvic abscess	1 (4.8%)	9 (11%)	0.68
Fistulas	0	10 (13%)	0.11
Anastomotic strictures	3 (14%)	14 (18%)	1.0
Refashioning of temporary ileostomy post IPAA	1 (4.8%)	9 (11%)	0.68
Pouch excision	2 (9.5%)	5 (6.3%)	0.64
Second pouch formation	1 (4.8%)	3 (3.8%)	1.0
Pouch failure	1 (4.8%)	2 (2.5%)	0.51

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Dysplasie et cancers du colon

Table 3 Dysplasia or colorectal cancer in primary sclerosing cholangitis - inflammatory bowel disease *n* (%)

Ref.	IBD (*n*)	PSC-IBD (*n*)	Country	Dysplasia		Risk/incidence	
				IBD	PSC-IBD	IBD	PSC-IBD
Broomé *et al*[45], 1995	80	40	Sweden	7 (8.8)	11 (27.5)	CR = 10 yr: 2%	CR = 10 yr: 9%
Gurbuz *et al*[49], 1995	0	35	United States	NA	13 (37.1)	NA	CR = 10 yr: 0%
Brentnall *et al*[56], 1996	25	20	United States	4 (16)	9 (45)	NA	OR = 4.9
Loftus *et al*[29], 1996	0	143	United States	NA	27 (18.9)	NA	CR = 20 yr: 17%
Kornfeld *et al*[48], 1997	0	58	Sweden	NA	5 (8.6)	NA	NA
Leidenius *et al*[50], 1997	45	45	Finland	4 (8.9)	13 (28.9)	CR = 10 yr: 3%	CR = 10 yr: 11%
Marchesa *et al*[54], 1997[8]	1185	27	United States	145 (12.2)	18 (66.7)	NA	RR = 10.4
Shetty *et al*[84], 1999	196	132	United States	11 (5.6)	33 (25)	RR = 1	RR = 3.15
Lindberg *et al*[46], 2001	103	19	Sweden	31 (30.1)	12 (63.2)	CR = 20 yr: 16%	CR = 20 yr: 32%
Bergquist *et al*[108], 2002	0	477	Sweden	NA	35 (7.3)	NA	SIR = 10.3
Loftus *et al*[11], 2005	142	71	United States	15 (10.6)	18 (25.4)	CP = 10 yr: 20%	CP = 10 yr: 53%
Kaplan *et al*[109], 2007	0	45	Canada	NA	5 (11.1)	NA	IR = 3.1
Lepistö *et al*[16], 2008	389	52	Finland	63 (16.2)	17 (32.7)	CR = 20 yr: 0.39	CR = 20 yr: 0.43
Sokol *et al*[15], 2008	150	75	France	2 (1.3)	10 (13.3)	CR = 25 yr: 1.5%	CR = 25 yr: 25.6%
Terg *et al*[51], 2008	64	39	Argentina	2 (3.1)	7 (17.9)	CR = 10 yr: 2.0%	CR = 10 yr: 11%
Claessen *et al*[52], 2009	0	126	The Netherlands	NA	35 (27.8)	NA	CR = 10 yr: 9%
Lindström *et al*[38], 2011	46	28	Sweden	3 (6.5)	9 (32.1)	NA	OR = 6.78
Braden *et al*[58], 2012	216	166	United Kingdom	14 (6.5)	14 (8.4)	CIR = 2.9%	CIR = 7.5%
Imam *et al*[53], 2012	0	784	United States	NA	10 (1.3)	NA	I = 0.4/yr
Jess *et al*[55], 2012	47374	NA	Denmark	329 (0.7)	9 (?)[9]	RR = 1.07 (UC)	RR = 9.13
de Valle *et al*[79], 2012	0	152	Sweden	NA	3 (2.0)	NA	SIR = 4.31
Boonstra *et al*[22], 2013	722	402	The Netherlands	7 (1)	19 (4.7)	SIR = 1.2	SIR = 8.6

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Dysplasie et cancers du colon

Ref.	IBD (*n*)	PSC-IBD (*n*)	Proximal colon[1]		Age dysplasia diagnosis (yr)		IBD duration (yr)	
			IBD	PSC-IBD	IBD	PSC-IBD	IBD	PSC-IBD
Broomé *et al*[45], 1995	80	40	NA	NA	NA	NA	26.0[2]	18.0[2]
Gurbuz *et al*[49], 1995	0	35	NA	NA	NA	51.4[2]	NA	12.2[2]
Brentnall *et al*[56], 1996	25	20	NA	NA	NA	NA	NA	20.0[2]
Loftus *et al*[29], 1996	0	143	NA	42.9%[5]	NA	41.0[6]	NA	NA
Kornfeld *et al*[48], 1997	0	58	NA	NA	NA	NA	NA	NA
Leidenius *et al*[50], 1997	45	45	NA	NA	NA	NA	17.5[2]	11.0[6]
Marchesa *et al*[54], 1997[8]	1185	27	40.8%[5]	100.0%[5]	NA	NA	NA	NA
Shetty *et al*[84], 1999	196	132	20.0%[5]	76.5%[5]	NA	NA	NA	NA
Lindberg *et al*[46], 2001	103	19	32.3%	69.2%	NA	NA	NA	NA
Bergquist *et al*[108], 2002	0	477	NA	NA	NA	NA	NA	NA
Loftus *et al*[11], 2005	142	71	50%[5]	28.6%[5]	NA	NA	12.1[6]	12.7[6]
Kaplan *et al*[109], 2007	0	45	NA	NA	NA	NA	NA	NA
Lepistö *et al*[16], 2008	389	52	NA	NA	NA	NA	NA	NA
Sokol *et al*[15], 2008	150	75	0.0%[5]	100.0%[5]	NA	NA	44.4[2]	17.4[2]
Terg *et al*[51], 2008	64	39	NA	NA	NA	NA	NA	NA
Claessen *et al*[52], 2009	0	126	NA	63.0%[5]	NA	NA	NA	12.6[6]
Lindström *et al*[38], 2011	46	28	0.0%	66.0%	NA	NA	10.0[6]	12.0[6]
Braden *et al*[58], 2012	216	166	30.0%	35.7%	NA	NA	NA	NA
Imam *et al*[53], 2012	0	784	NA	60.0%	NA	37.4[2]	NA	NA
Jess *et al*[55], 2012	47374	NA	38.0%	100.0%	71.66	64.0[6]	NA	13.7[6]
de Valle *et al*[79], 2012	0	152	NA	NA	NA	NA	NA	NA
Boonstra *et al*[22], 2013	722	402	NA	NA	596	39.0[6]	4.0[6]	15.0[6]

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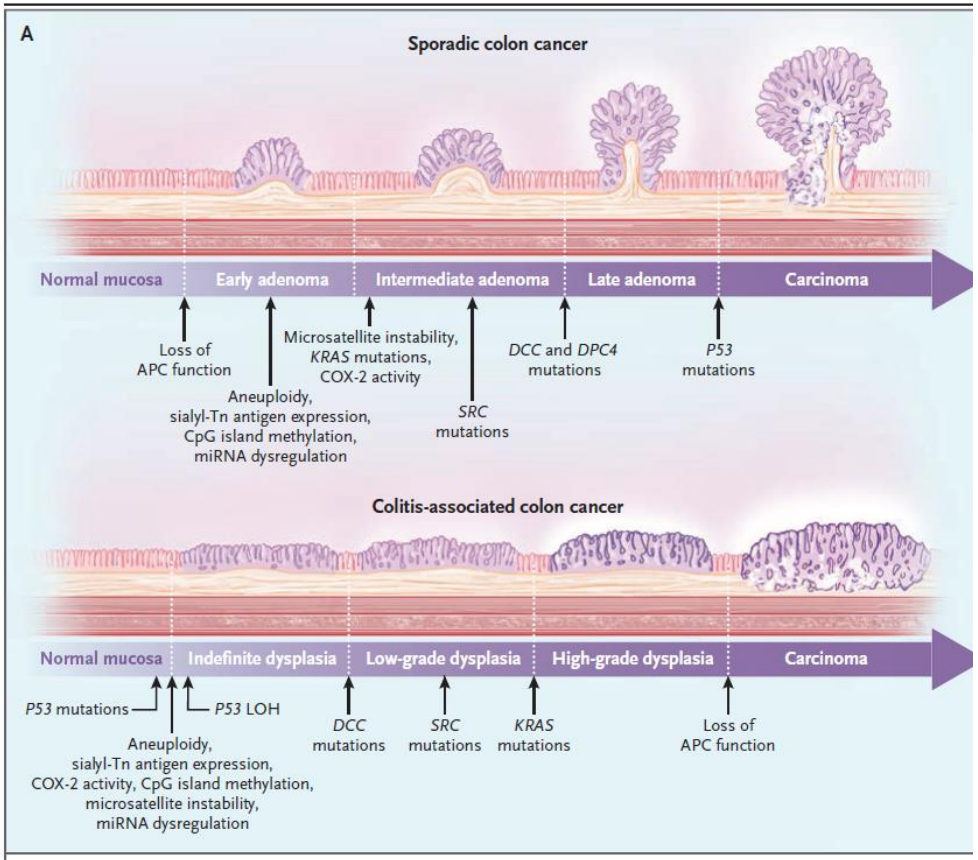
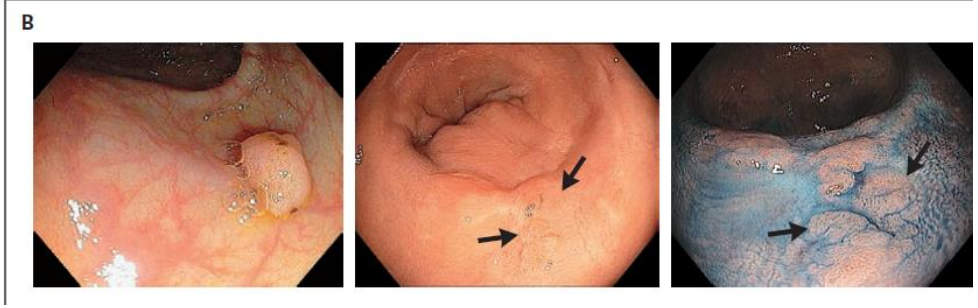
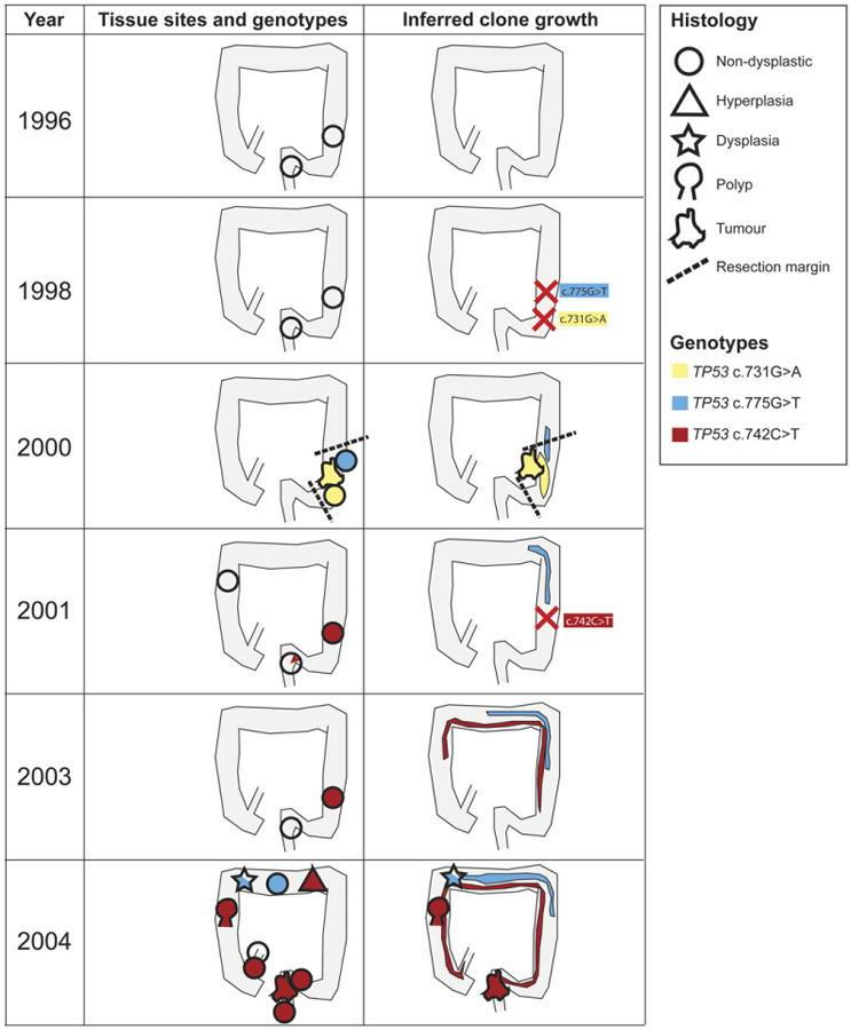
Cancérogénèse …

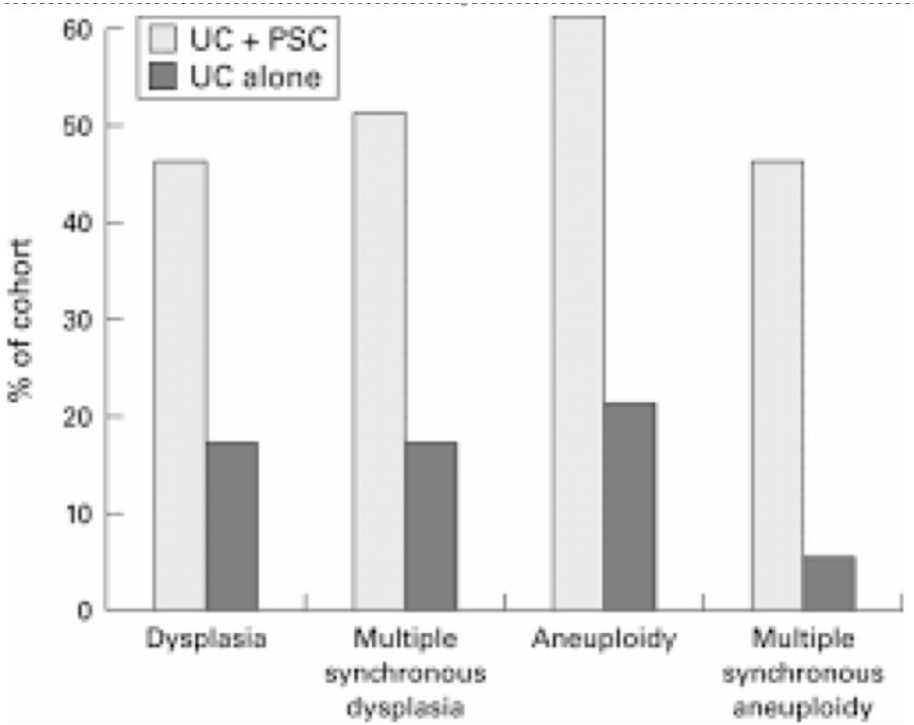
The NEW ENGLAND JOURNAL of MEDICINE







Dysplasie et cancers du colon



Recommandations de surveillance – dépistage

Coloscopie annuelle dès le Dg de CSP associée à une MICI
Chromoendoscopie conseillée
Biopsies ciblées et/ou systématiques

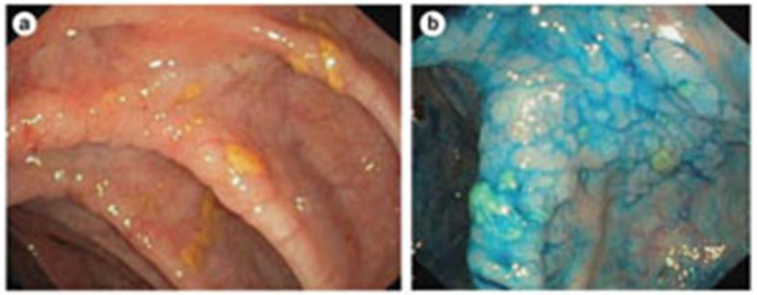


Figure 1 | Endoscopy image showing a nonadenoma-like dysplasia-associated lesion or mass. The slightly raised, poorly circumscribed dysplastic lesion was seen in a 53-year-old man with a 20-year history of extensive colitis and primary sclerosing cholangitis. Previously, multifocal indefinite dysplasia was found in random biopsy samples taken during surveillance colonoscopy. The histology of this lesion revealed the presence of high-grade dysplasia (Figure 2). **a** | Conventional endoscopy. **b** | Chromoendoscopy.

CSP + MICI: une maladie

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Analysis of five chronic inflammatory diseases identifies 27 new associations and highlights disease-specific patterns at shared loci

David Ellinghaus[1,49], Luke Jostins[2], Sarah L Spain[2], Adrian Cortes[3,4], Jörn Bethune[1], Buhm Han[5], Yu Rang Park[6], Soumya Raychaudhuri[7,8,9], Jennie G Pouget[10,11], Matthias Hübenthal[1], Trine Folseraas[12,13,14,15], Yunpeng Wang[16], Tonu Esko[17,18,19], Andres Metspalu[17], Harm-Jan Westra[7,8,9], Lude Franke[20], Tune H
D'Amato[24,25], Jonas Halfvarson[26]
Degenhardt[30,31], Andreas J Forstn
Consortium (IIBDGC)[32], Internatio
International PSC Study Group (IP
(GAPC)[32], Psoriasis Association G
Mrowietz[34], Brian D Juran[35], Kons

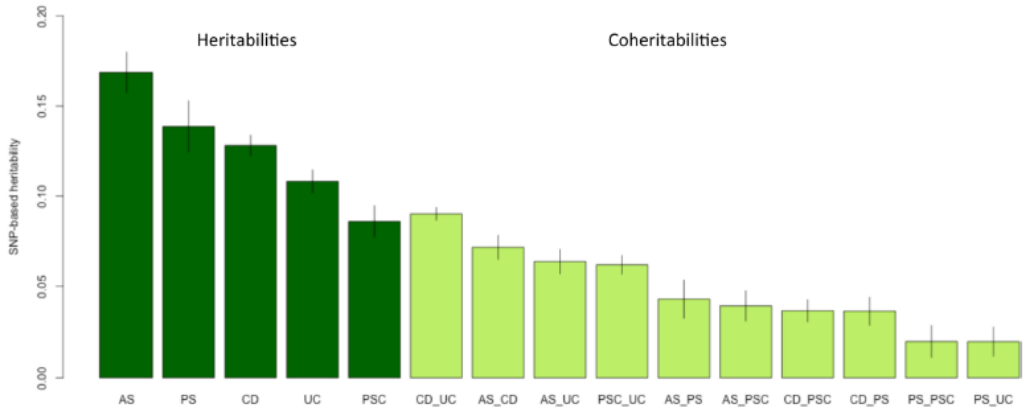

Figure 4. Estimation of Immunochip-wide pleiotropy (excluding the MHC region) between the five diseases under study

Proportion of genetic variance in liability (SNP-based heritability) and proportion of genetic covariance in liability between diseases (SNP-based coheritability) with 95% error bars (see **Supplementary Table 15a**; estimates including MHC SNPs see **Supplementary Table 15b**). Disease-associated SNP markers from Supplementary **Table 3a** (at a maximum of 244 independent signals from 169 non-MHC risk loci, see also **Supplementary Figure 6**) explain 42.2% of AS-, 79.63% of CD-, 39.6% of PS-, 29% of PSC- and 55% of UC-Immunochip-wide SNP-heritability (excluding the MHC region) on the liability scale, respectively. As the Immunochip densely tags common variants but at the cost of losing genome-wide coverage, the estimated SNP-heritabilities are lower bounds for genome-wide SNP-heritabilities.

the strong comorbidity between primary sclerosing cholangitis and inflammatory bowel disease is likely the result of a unique disease, which is genetically distinct from classical inflammatory bowel disease phenotypes.

ORIGINAL ARTICLE

Primary sclerosing cholangitis is characterised by intestinal dysbiosis independent from IBD

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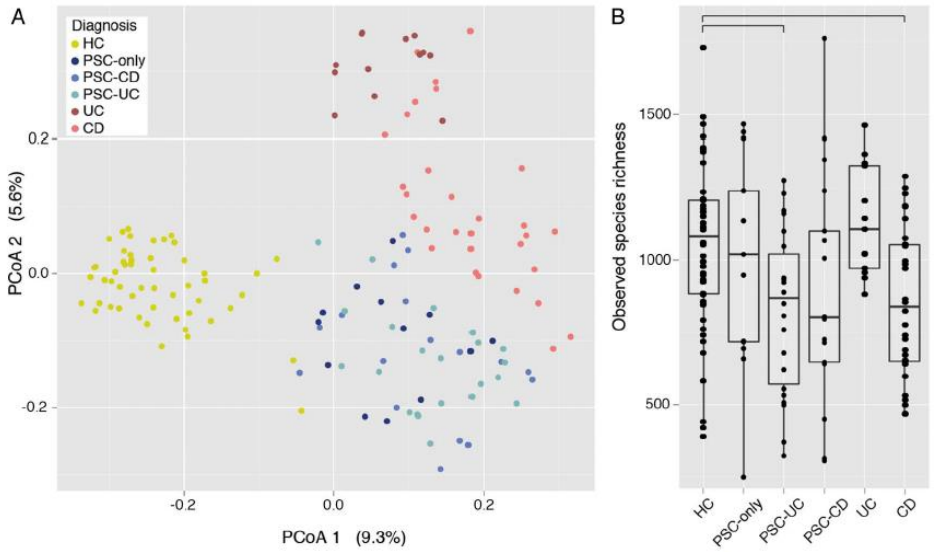

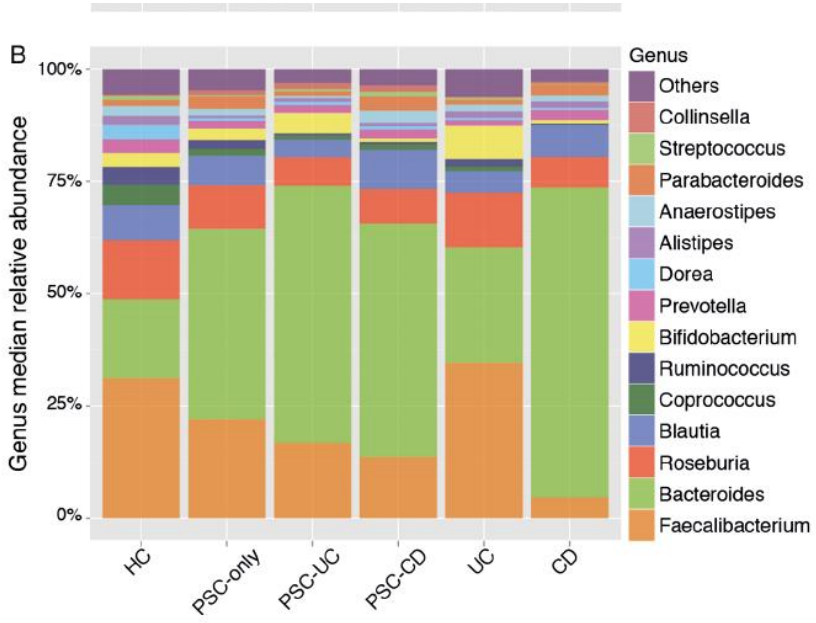

Faecal microbiota variation across healthy controls (HC) and patients with primary sclerosing cholangitis (PSC) and IBD (n=147).

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Original Article

Original Article

Characterization of Intestinal Microbiota in Ulcerative Colitis Patients with and without Primary Sclerosing Cholangitis

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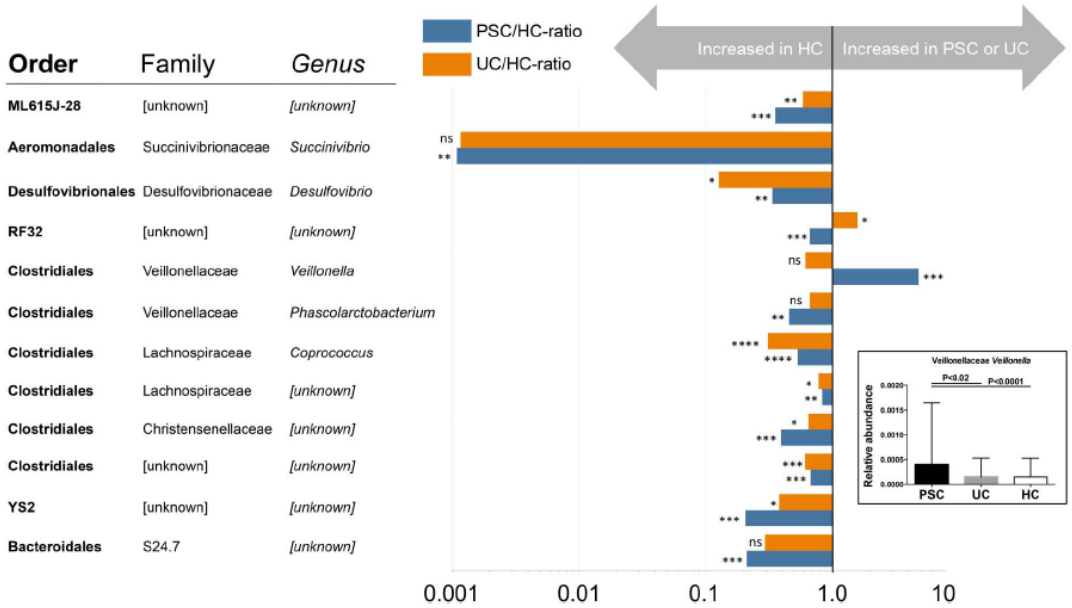
Table 2. Genera which showed a nominal association with primary sclerosing cholangitis [PSC] phenotype with p-value < 0.05.

Oslo Cohort		Calgary Cohort	
Organism	p-Value*	Organism	p-Value*
Acinetobacter	0.006	*Acinetobacter*	0.182
Lactobacillus	0.009	*Lactobacillus*	0.792
Corynebacterium	0.015	*Corynebacterium*	0.630
Veillonella	0.015	*Veillonella*	0.523
Ralstonia	0.018	*Ralstonia*	0.630
Rothia	0.030	*Rothia*	0.538
Sphingomonas	0.032	*Sphingomonas*	--
Lachnospira	0.453	***Lachnospira***	0.012
Oscillospira	0.908	***Oscillospira***	0.020
Roseburia	0.166	***Roseburia***	0.024
Ruminococcus	0.908	***Ruminococcus***	0.031
Collinsella	0.355	***Collinsella***	0.038

Conclusions: No strong PSC-specific microbial associations in UC patients consistent across different cohorts were identified. Recruitment centre had a strong effect on microbial composition. Future studies should include larger cohorts to increase power and the ability to control for confounding factors.

The gut microbial profile in patients with primary sclerosing cholangitis is distinct from patients with ulcerative colitis without biliary disease and healthy controls

Kummen M, *et al. Gut* 2017;**66**:611–619. doi:10.1136/gutjnl-2015-310500



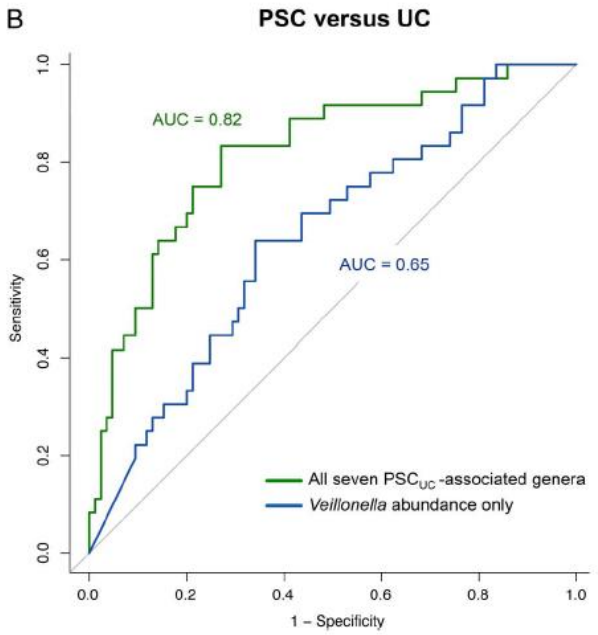


Figure 3 The 12 genera confirmed in the validation panel, differing between PSC and HC, illustrated by the ratio between PSC and HC on a logarithmic scale. The ratio between UC and HC is included for comparison. One genus, *Veillonella*, showed a significant increase in PSC compared with both HC and UC (framed box). The ML615J-28, RF32 and YS2 orders are part of the Tenericutes, Proteobacteria and Cyanobacteria phyla, respectively. All data in the chart are based on the combined panel. The ratios were calculated by dividing the mean relative abundance in the patients with PSC/patients with UC by the mean relative abundance in HC. Data in the framed box are shown as median and IQR. HC, healthy controls; PSC, primary sclerosing cholangitis. *Q_{FDR}<0.05, **Q_{FDR}<0.01, ***Q_{FDR}<0.001, ****Q_{FDR}<0.0001.

Conclusions Patients with PSC exhibited a gut microbial signature distinct from both HC and UC without liver disease, but similar in PSC with and without IBD. The *Veillonella* genus, which is also associated with other chronic inflammatory and fibrotic conditions, was enriched in PSC.

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The features of mucosa-associated microbiota in primary sclerosing cholangitis

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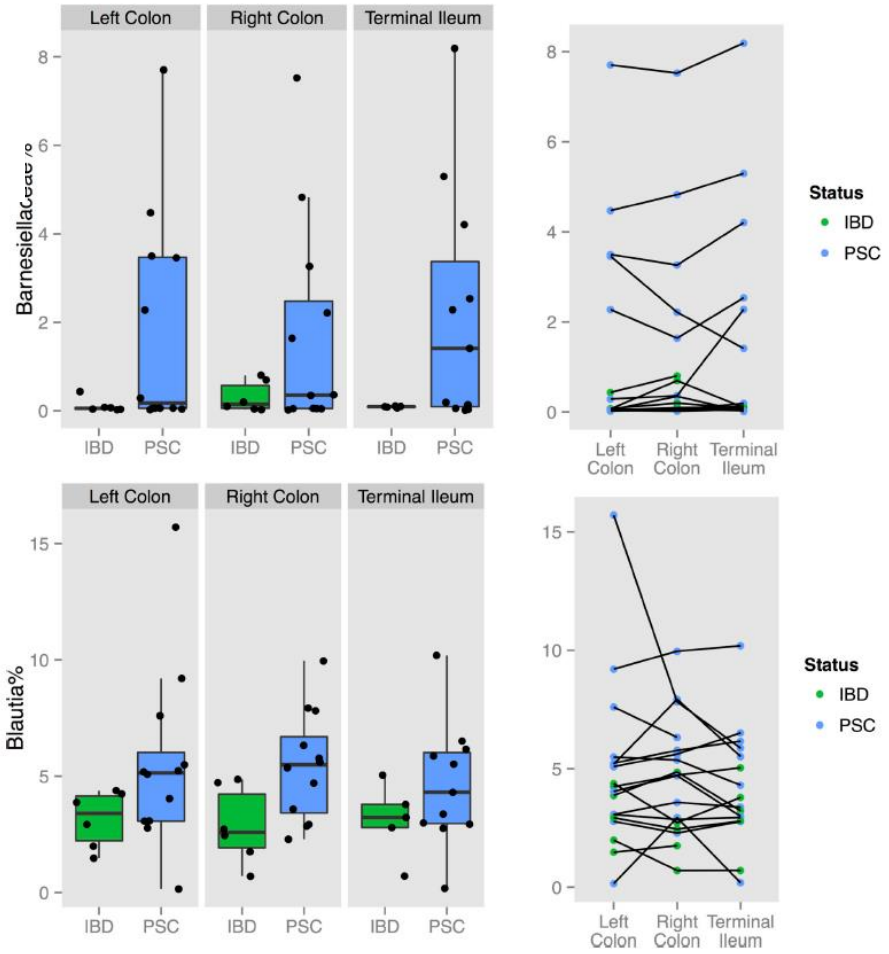
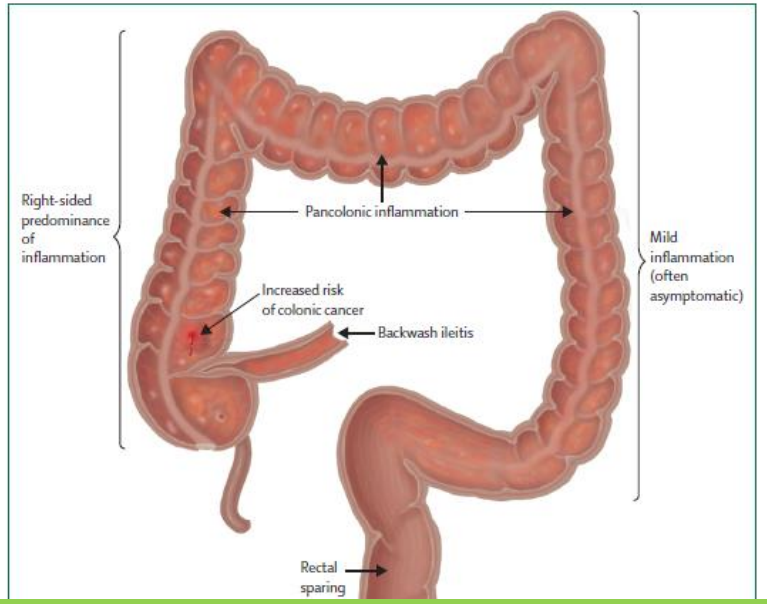


Figure 3. The relative abundance of *Barnesiellaceae* and *Blautia* in PSC and non-PSC-IBD at multiple locations

microbiota of PSC patients was characterized by enrichment of *Blautia* and *Barnesiellaceae* and by major shifts in OTUs within *Clostridiales* order.

MICI associées à la CSP



- Maladies rares
- Evidence clinique, génétique, écologique de spécificité
- Graves, notamment cancers
- Qui doivent se suivre différemment des autres MICI… et probablement se traiter