

Les curiosités dans les MICI

Patch caecal, quelle implication ?

Maxime Collard

Chirurgie digestive, Hôpital Saint-Antoine



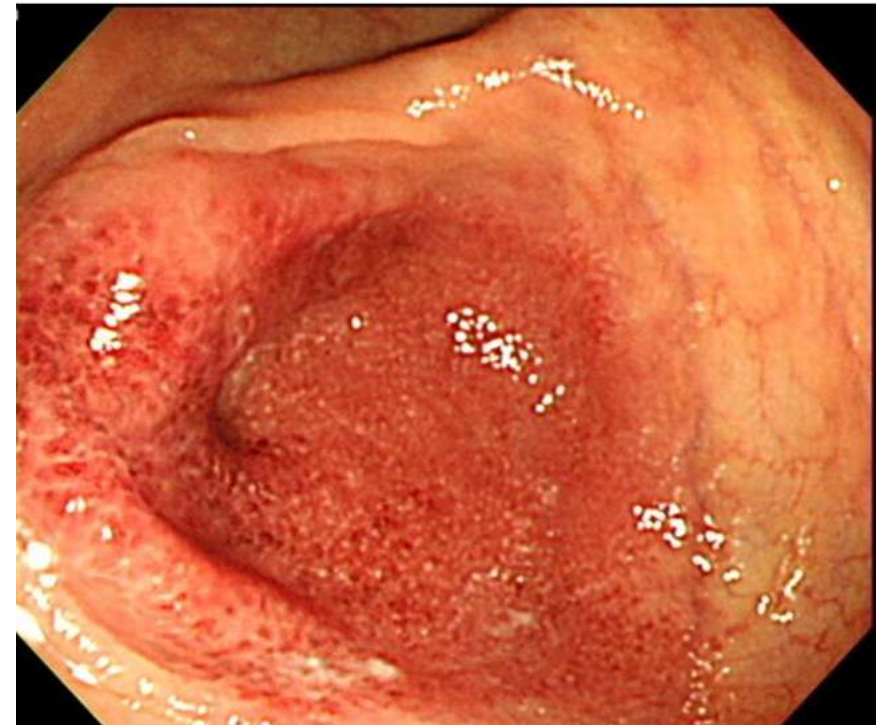
GETAID

Groupe d'Étude Thérapeutique
des Affections Inflammatoires du Tube Digestif

ReMind

Patch caecal: Définition

- Inflammation isolée en patch au niveau du caecum observée en endoscopie
- Cas spécifique: Inflammation localisée autour de l'orifice appendiculaire = ***Peri-appendiceal red patch***



Patch caecal chez la souris (et autres mammifères): le faux ami de la littérature scientifique



Skip inflammation of the appendiceal orifice: A prospective endoscopic study

KARIN LADEFOGED¹, LARS KRISTIAN MUNCK¹, FRANK JORGENSEN¹ & PETER ENGEL²

Scandinavian Journal of Gastroenterology, 2005; 40: 1192–1196

Diagnosis	N	Appendectomy		Discontinuous inflammation of appendiceal orifice		Histological grading of the discontinuous inflammation				
		n	(%)	n	% Non-appendectomized	0	1	2	3	missing samples
Ulcerative colitis	83	8	10	20	27	4	9	6	1	
Crohn's disease	54	5	9	12	24	4	3	1	2	2
Indeterminate colitis	12	2	17	4	40	1	2	1		
Microscopic colitis*	15	2	13	1	8		1			
Irritable bowel syndrome	54	15	28	4	10	3	1			
Other diseases**	53	7	13	4	9	2	2			

- L'inflammation de l'orifice appendiculaire n'est pas spécifique de la RCH
- Corrélation imparfaite entre aspect macroscopique et inflammation histologique

Skip lesion dans la RCH

Incidence du patch caecal péri-appendiculaire dans la RCH: **très variable d'une étude à une autre**, estimations allant de **5% à 28%** dans la littérature

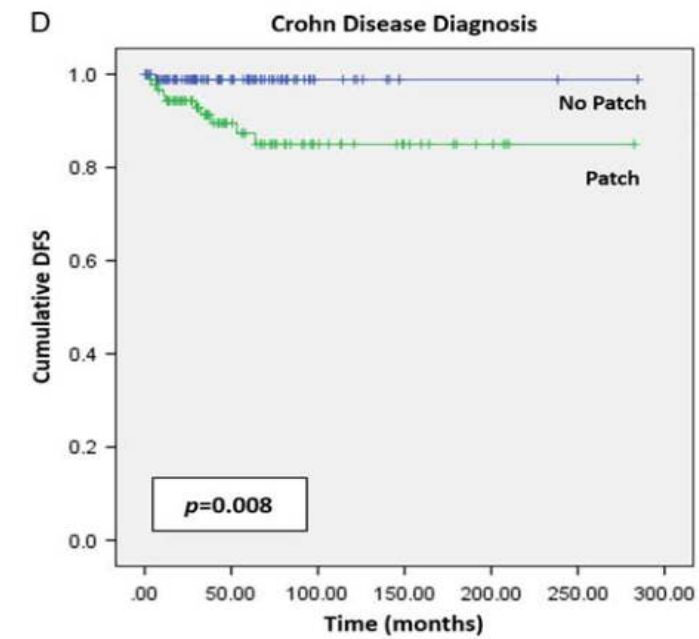
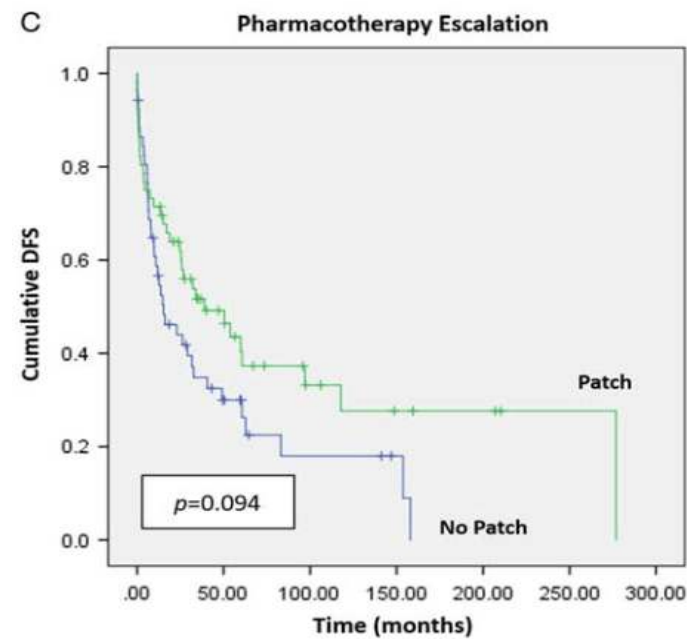
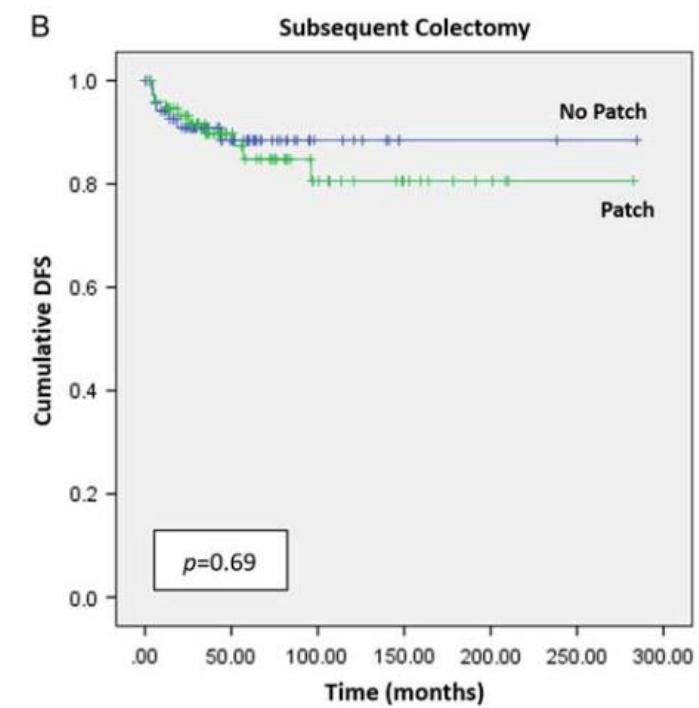
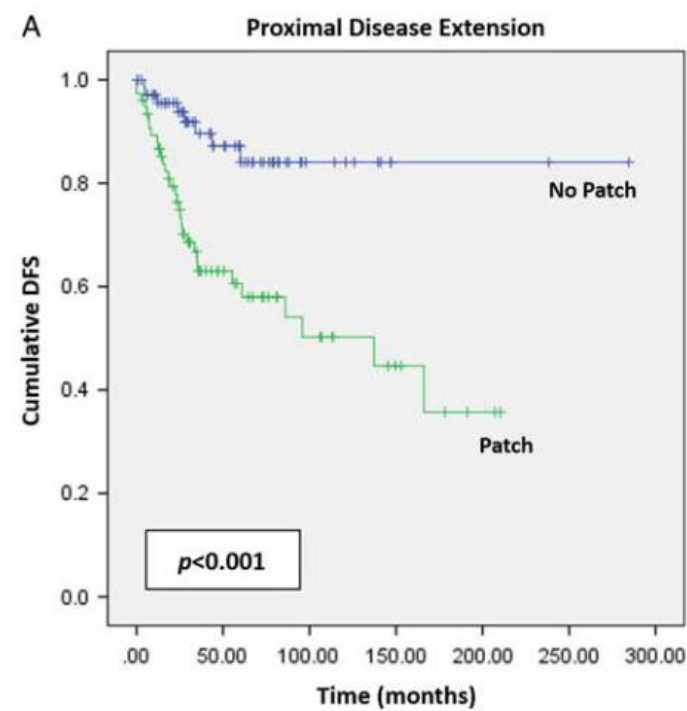
Characteristics and Outcomes of Left-sided Ulcerative Colitis With a Cecal/Periappendiceal Patch of Inflammation

Albayrak et al, Am J Surg Pathol, 2022

DEFINITION HISTOLOGIQUE ET NON ENDOSCOPIQUE

536 patients avec une RCH localisée au rectum +/- colon gauche: 102 patients avec inflammation d'un patch caecal soit une prévalence à **19%**

Patch caecal dans la RCH: conséquences à long terme ?



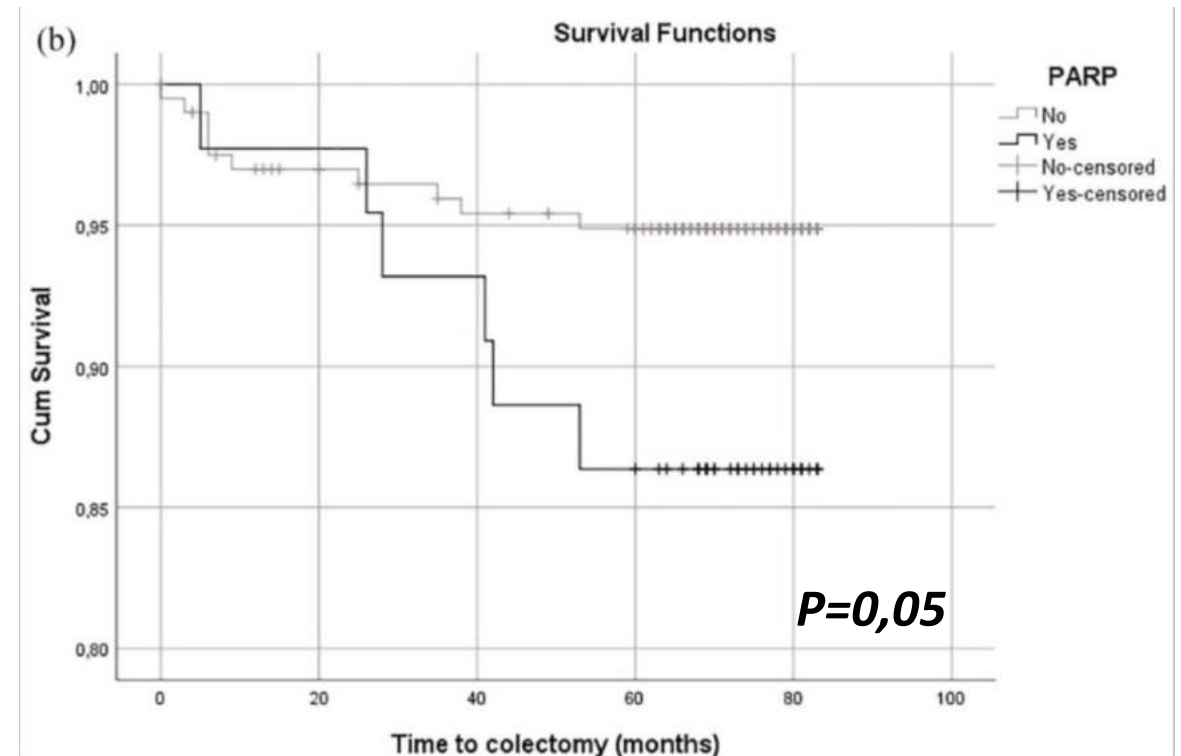
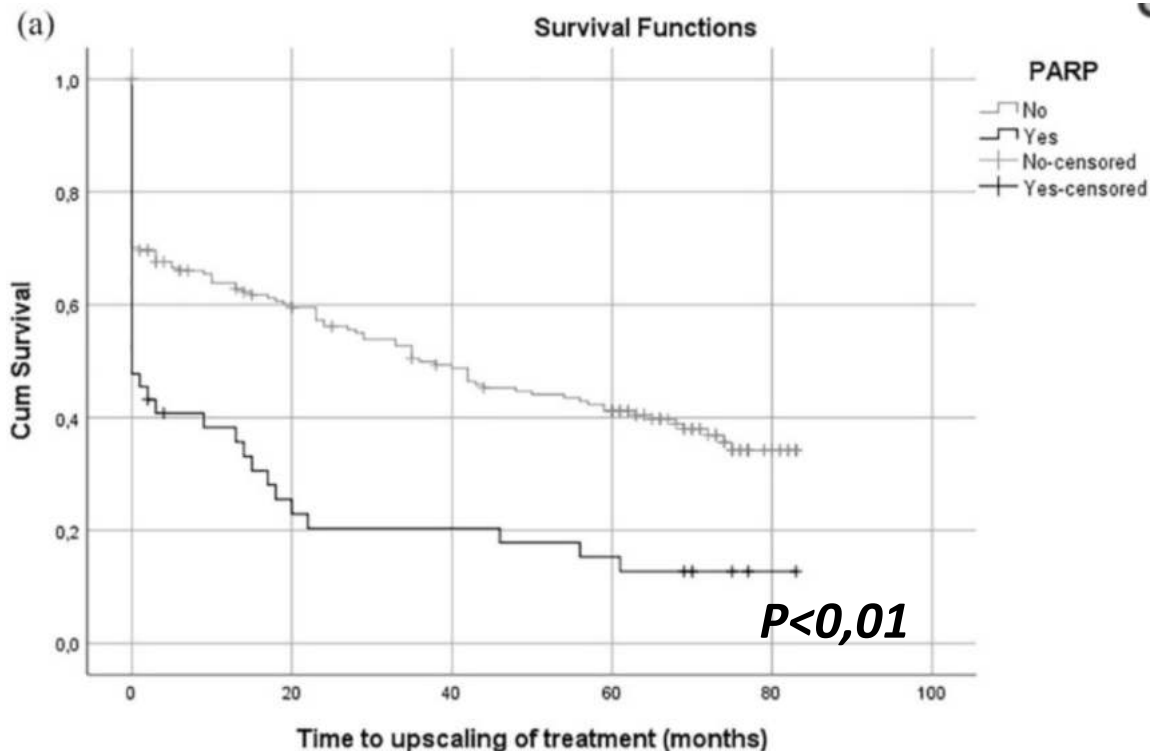
Patch caecal dans la RCH: conséquences à long terme ?

> Therap Adv Gastroenterol. 2022 Jun 28;15:17562848221098849. doi: 10.1177/17562848221098849.
eCollection 2022.

Clinical relevance of endoscopic peri-appendiceal red patch in ulcerative colitis patients

Maud A Reijntjes¹, Lianne Heuthorst¹, Krisztina Gecse², Aart Mookhoek³, Willem A Bemelman¹,
Christianne J Buskens⁴

249 patients dont 44 patients avec une inflammation pré-appendiculaire (17,7%)

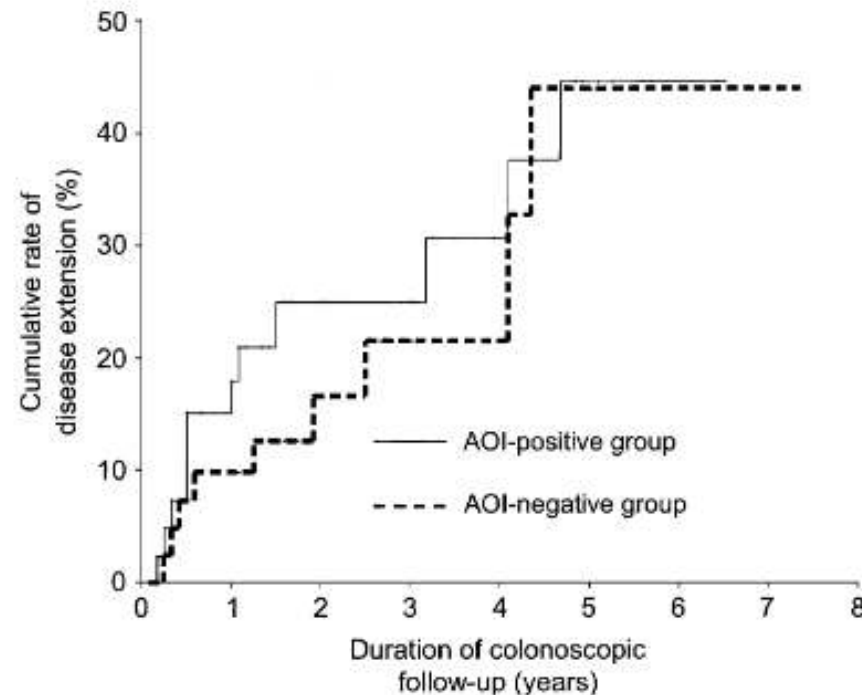
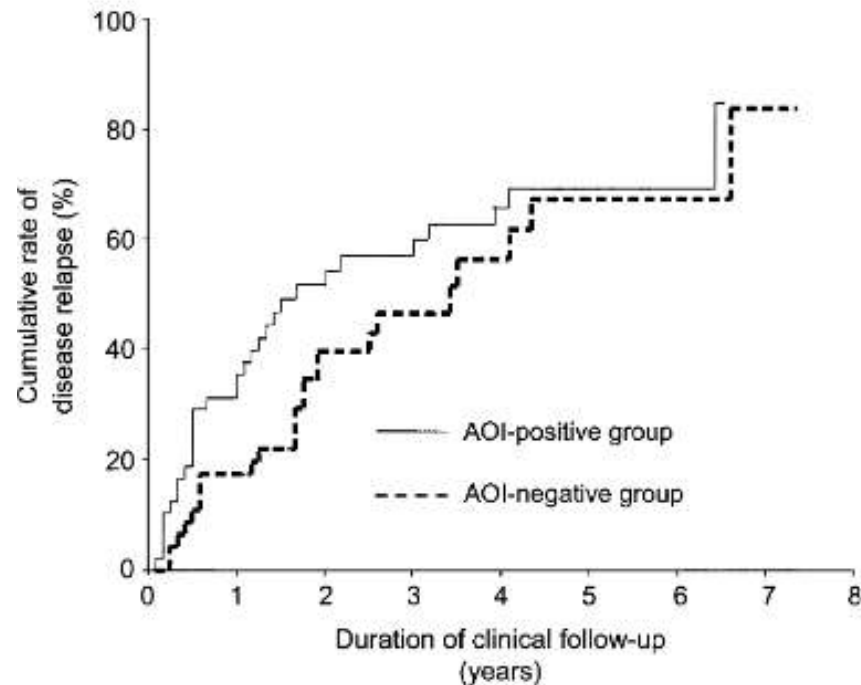


Patch caecal dans la RCH: conséquences à long terme ?

> *Inflamm Bowel Dis.* 2005 Apr;11(4):366-71. doi: 10.1097/01.mib.0000164018.06538.6e.

Clinical course of distal ulcerative colitis in relation to appendiceal orifice inflammation status

Jeong-Sik Byeon¹, Suk-Kyun Yang, Seung-Jae Myung, Seung Il Pyo, Hyun Ju Park, Young Min Kim, Yun Jung Lee, Seong Soo Hong, Kyu-Jong Kim, Gin Hyug Lee, Hwoon-Yong Jung, Weon-Seon Hong, Jin-Ho Kim, Young Il Min



Conclusions: In patients with distal UC, AOI may have no prognostic implications in terms of remission, relapse, or proximal disease extension.

Patch caecal sur colon normal, est-ce prédictif d'une RCH ?

> *Endoscopy*. 2012 Jan;44(1):95-8. doi: 10.1055/s-0031-1291443. Epub 2011 Dec 23.

Long term follow-up of appendiceal and distal right-sided colonic inflammation

Suivi endoscopique
médian: 18 mois

S H Park ¹, S K Yang, M J Kim, D H Yang, K W Jung, K J Kim, B D Ye, J S Byeon, S J Myung, J H Kim

19 patients avec une inflammation isolée de l'orifice péri-appendiculaire

**Evolution vers
une rectocolite
hémorragique**

5 patients

**Persistance d'une
inflammation
isolée**

7 patients

**Résolution
spontanée de
l'inflammation**

7 patients

Inflammation du patch caecal dans la RCH = endo-appendicite ?

> United European Gastroenterol J. 2021 Dec;9(10):1148-1156. doi: 10.1002/ueg2.12171.

Epub 2021 Nov 9.

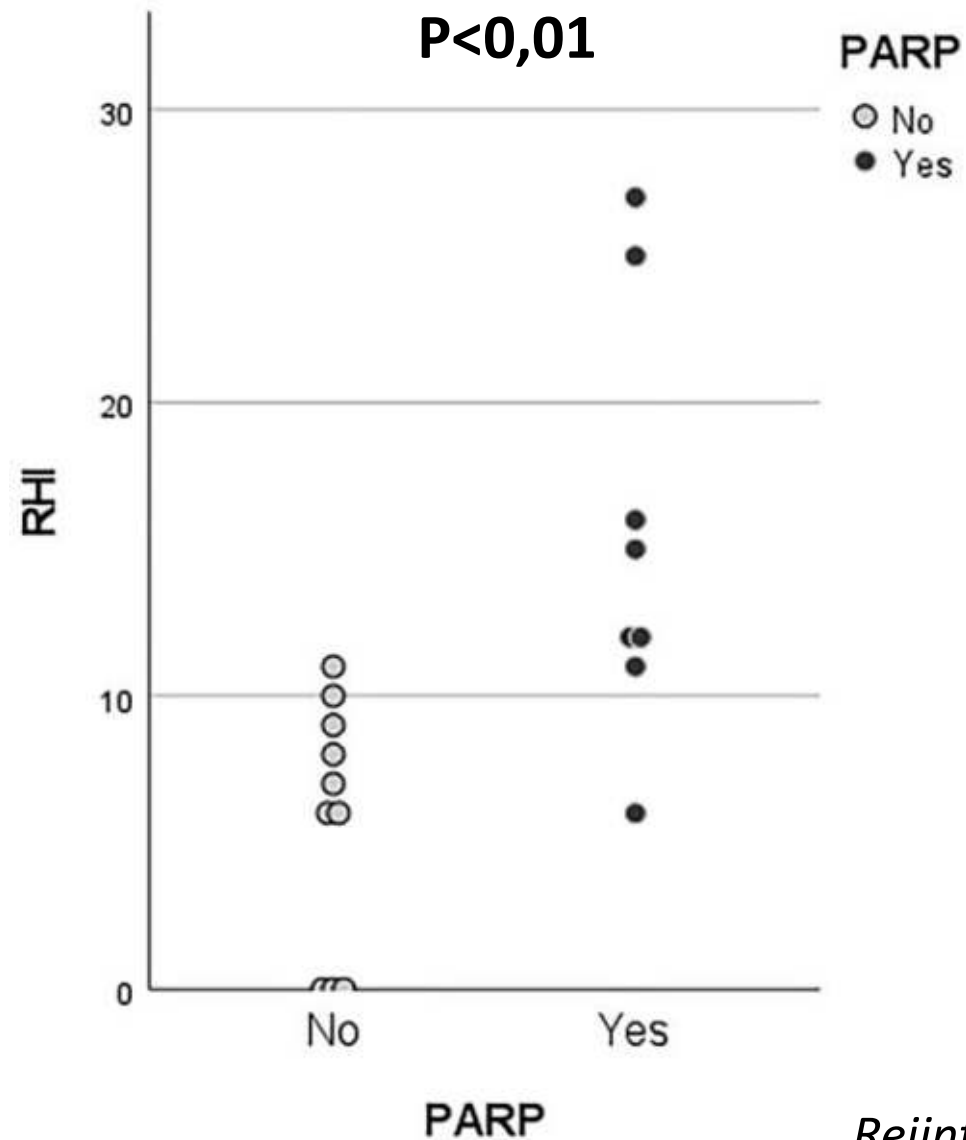
High prevalence of ulcerative appendicitis in patients with ulcerative colitis

Lianne Heuthorst ¹, Aart Mookhoek ², Manon E Wildenberg ³, Geert R D'Haens ⁴,
Willem A Bemelman ¹, Christianne J Buskens ¹

Analyse histologique de l'appendice après appendicectomie: 35 patients pour RCH active et 35 patients pour RCH en rémission

- 54% d'appendicite aiguë si RCH active versus 46% si RCH en rémission clinique (p=0,45)
- Sur le plan histologique: « Ulcerative appendicitis »
- Tous les patients avec une inflammation de l'orifice appendiculaire en endoscopie avaient une endo-appendicite intense (p<0,001 sur le score RHI)

Inflammation du patch caecal dans la RCH = endo-appendicite ?



Appendectomy and Protection against Ulcerative Colitis



The NEW ENGLAND
JOURNAL of MEDICINE

Roland E. Andersson, M.D., Ph.D., Gunnar Olaison, M.D., Ph.D., Curt Tysk, M.D., Ph.D., and Anders Ekblom, M.D., Ph.D.

2011

TABLE 3. THE INCIDENCE RATE OF ULCERATIVE COLITIS AMONG CASE PATIENTS AND CONTROLS.

VARIABLE	NO. OF PAIRS	PERSON-YEARS OF FOLLOW-UP*		NO. OF PATIENTS WITH ULCERATIVE COLITIS		INCIDENCE OF ULCERATIVE COLITIS PER 100,000 PERSON-YEARS		INCIDENCE-RATE RATIO (95% CI)†
		CASE PATIENTS	CONTROLS	CASE PATIENTS	CONTROLS	CASE PATIENTS	CONTROLS	
		All appendectomies	212,963	2,829,628	2,835,038	304	410	
Appendicitis	163,954	2,154,914	2,157,183	234	320	10.86	14.83	0.73 (0.62–0.87)
Perforated	22,879	284,916	285,842	24	41	8.42	14.34	0.59 (0.34–0.99)
Nonperforated	141,075	1,869,998	1,871,341	210	279	11.23	14.91	0.75 (0.62–0.90)
Lymphadenitis	19,362	277,991	278,410	20	42	7.19	15.09	0.48 (0.27–0.83)
Nonspecific abdominal pain	16,322	211,392	212,856	32	24	15.14	11.28	1.34 (0.77–2.38)
Other diagnoses	13,325	185,331	186,589	18	24	9.71	12.86	0.76 (0.39–1.45)

Appendicectomie thérapeutique et RCH

Bolin et al. Am J Gastroenterol, 2009

30 patients RCH limitée au rectum

Sahami et al. J Crohns Colitis, 2019

30 patients RCH réfractaire (rectite n=6, rectocolite gauche n=13, pan-colite n=11)

Appendicectomie programmée

- 90% des patients amélioration des symptômes durant le suivi
- 40% disparition des symptômes avec arrêt de tout traitement à 3 mois
- **97% inflammation appendiculaire chronique**

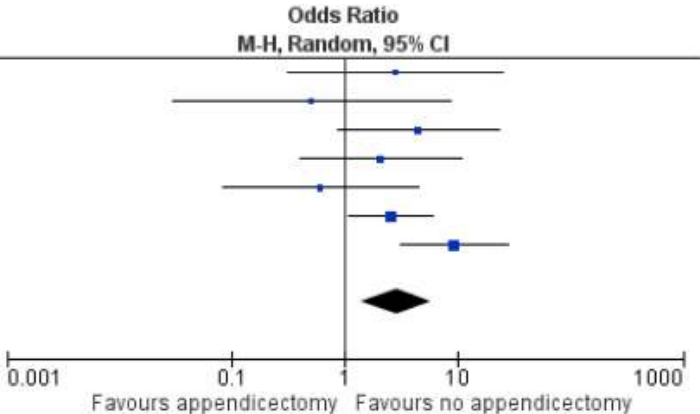
- 53% réponse clinique à 3 mois
- 46% réponse histologique
- **85% réponse histologique si inflammation appendiculaire**

Essai randomisé contrôlé en cours (ACCURE-trial)
Traitement envisageable dans un futur proche

The risk of colectomy and colorectal cancer after appendectomy in patients with ulcerative colitis: a systematic review and meta-analysis

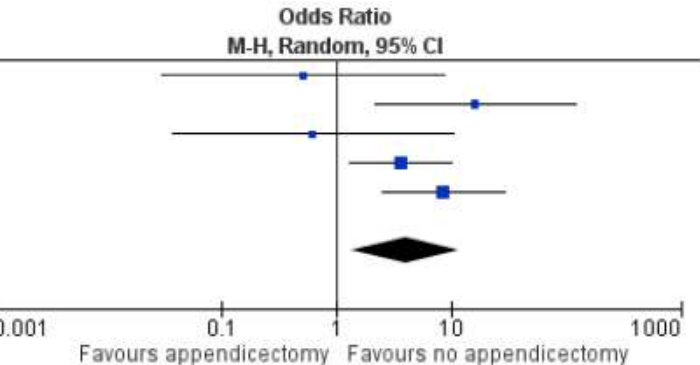
Stellingwerf M. et Al, JCC, 2019

Study or Subgroup	Appendectomy		No appendectomy		Weight	Odds Ratio M-H, Random, 95% CI	Year
	Events	Total	Events	Total			
Radford-Smith 2002	1	21	5	286	8.5%	2.81 [0.31, 25.22]	2002
Cosnes 2002	0	49	11	589	5.5%	0.51 [0.03, 8.75]	2002
Florin 2004	2	19	7	275	13.2%	4.50 [0.87, 23.36]	2004
Picazo-Ferrera 2011	3	38	3	76	13.2%	2.09 [0.40, 10.86]	2011
Lee 2014	1	104	40	2544	9.9%	0.61 [0.08, 4.46]	2014
Gordillo 2015	7	60	38	771	27.8%	2.55 [1.09, 5.98]	2015
Harnoy 2016	9	15	30	217	21.9%	9.35 [3.10, 28.16]	2016
Total (95% CI)		306		4758	100.0%	2.85 [1.40, 5.78]	
Total events	23		134				
Heterogeneity: Tau ² = 0.28; Chi ² = 8.87, df = 6 (P = 0.18); I ² = 32%							
Test for overall effect: Z = 2.90 (P = 0.004)							



Sur-risque de cancer ou dysplasie de haut-grade:
OR 2,85
[1,40-5,78]

Study or Subgroup	Appendectomy		No appendectomy		Weight	Odds Ratio M-H, Random, 95% CI	Year
	Events	Total	Events	Total			
Cosnes 2002	0	49	11	589	10.9%	0.51 [0.03, 8.75]	2002
Florin 2004	2	19	2	275	17.5%	16.06 [2.13, 121.09]	2004
Lee 2014	0	104	19	2544	11.1%	0.62 [0.04, 10.33]	2014
Gordillo 2015	5	60	19	771	32.0%	3.60 [1.29, 10.00]	2015
Harnoy 2016	5	15	12	217	28.5%	8.54 [2.52, 28.97]	2016
Total (95% CI)		247		4396	100.0%	3.97 [1.35, 11.70]	
Total events	12		63				
Heterogeneity: Tau ² = 0.68; Chi ² = 7.72, df = 4 (P = 0.10); I ² = 48%							
Test for overall effect: Z = 2.51 (P = 0.01)							



Sur-risque de cancer:
OR 3,97
[1,35-11,70]

The Appendix Orchestrates T-Cell Mediated Immunosurveillance in Colitis-Associated Cancer

Appendectomy



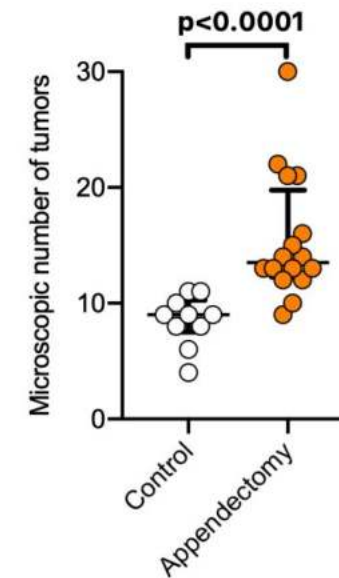
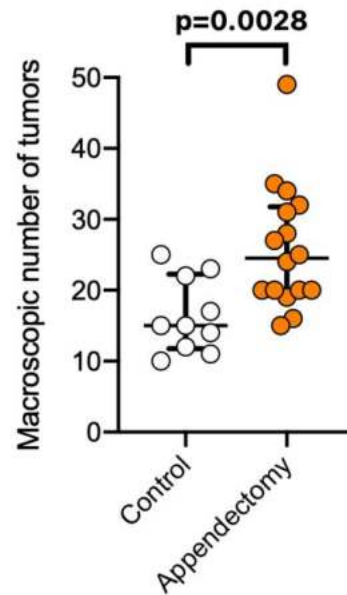
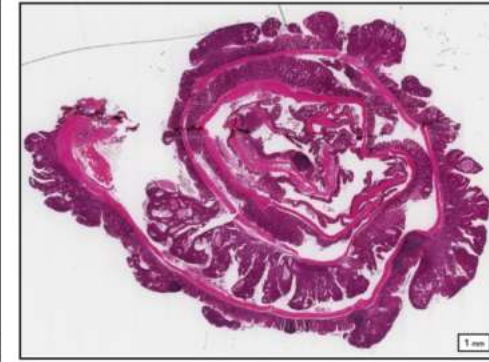
Control



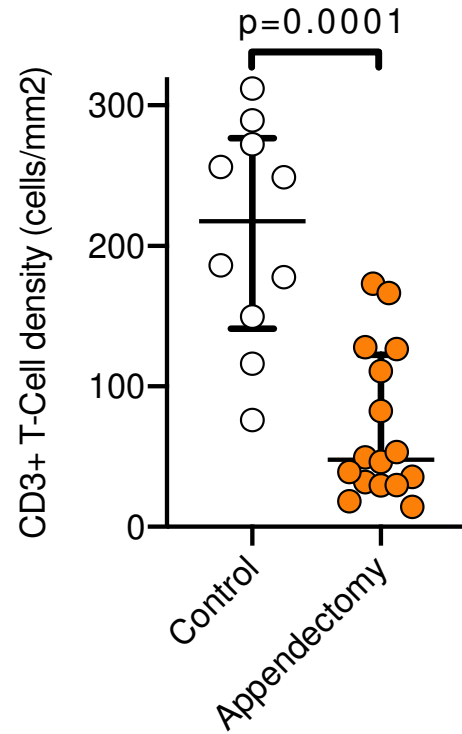
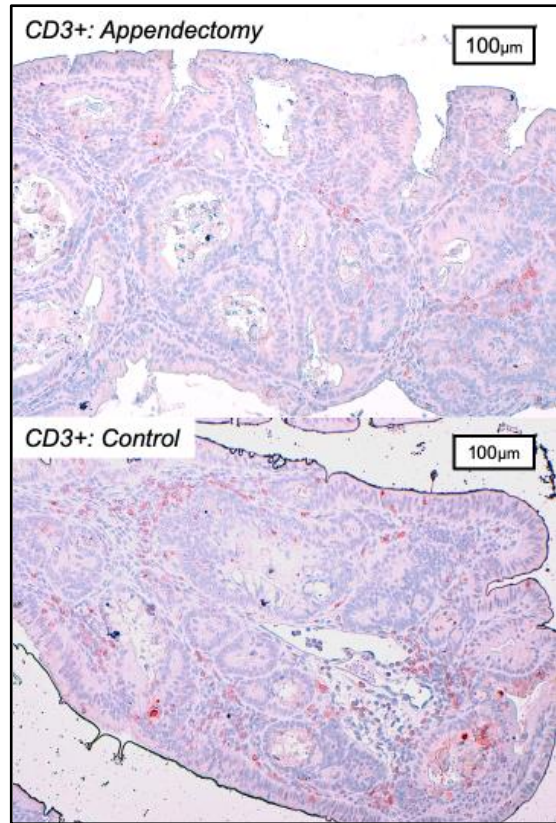
Control



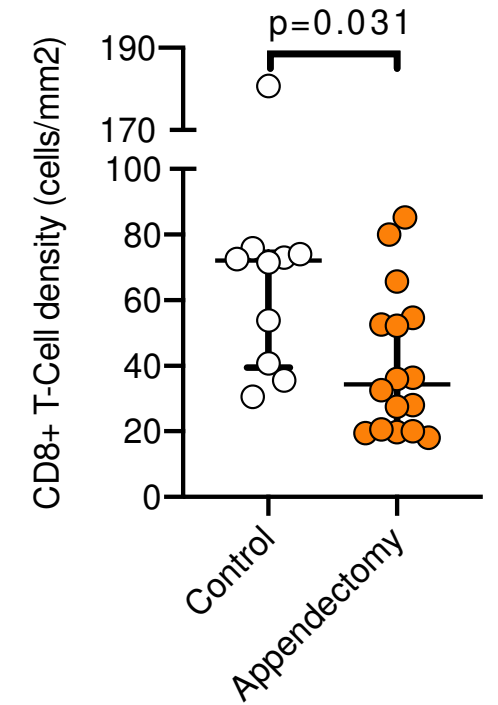
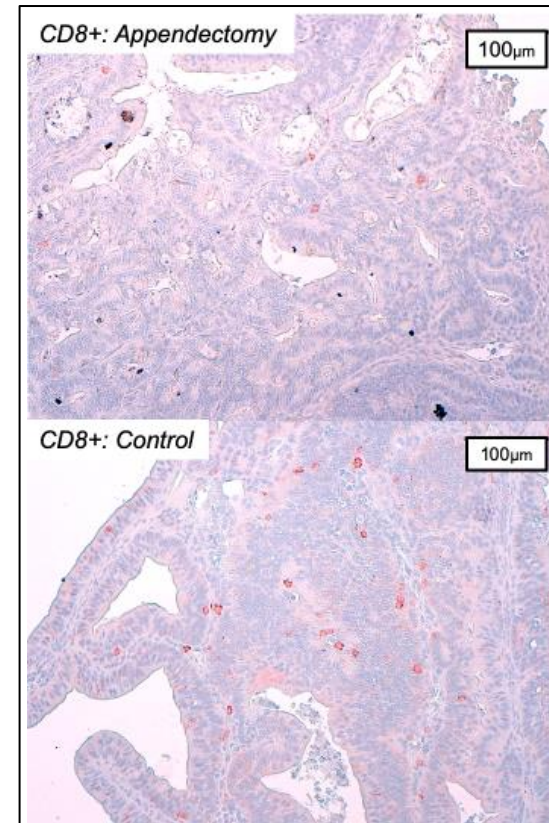
Appendectomy



Infiltration lymphocytaire T intra-tumorale

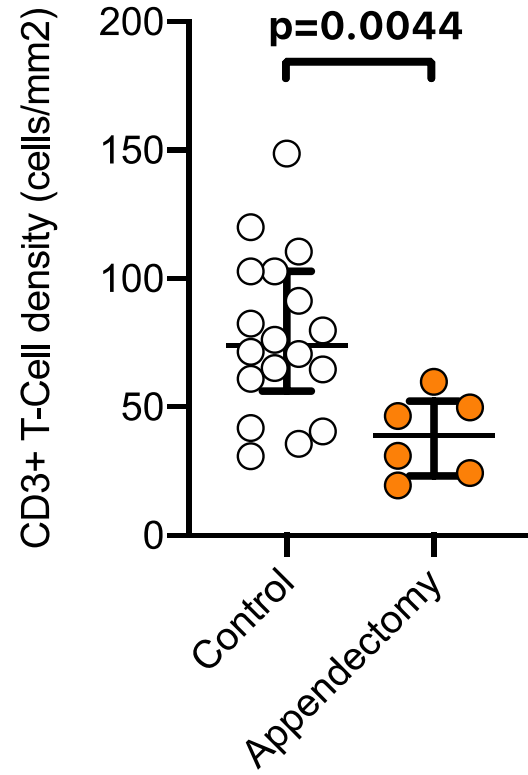
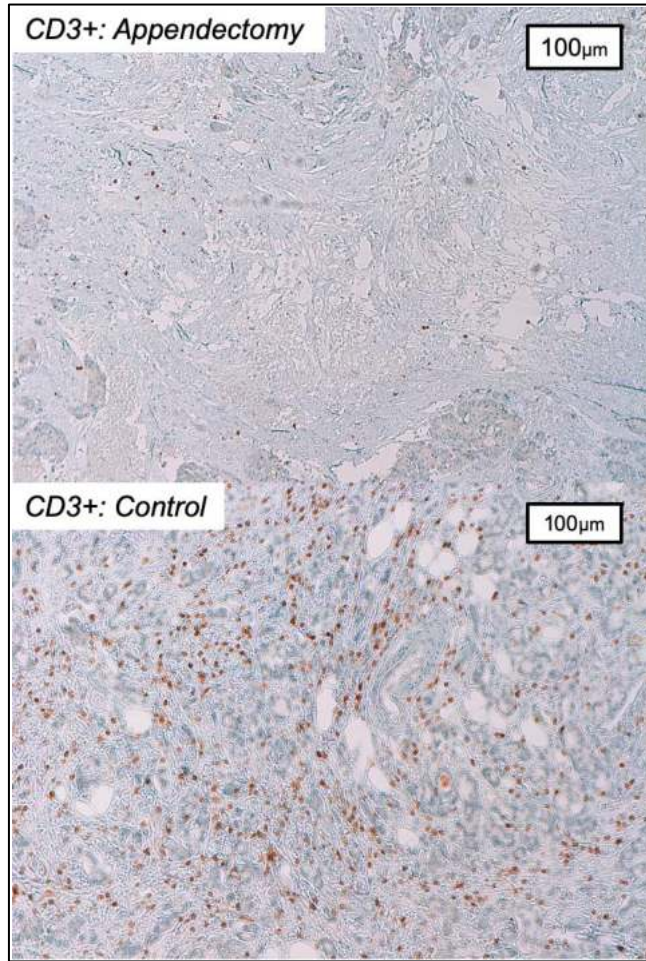


Lymphocytes T

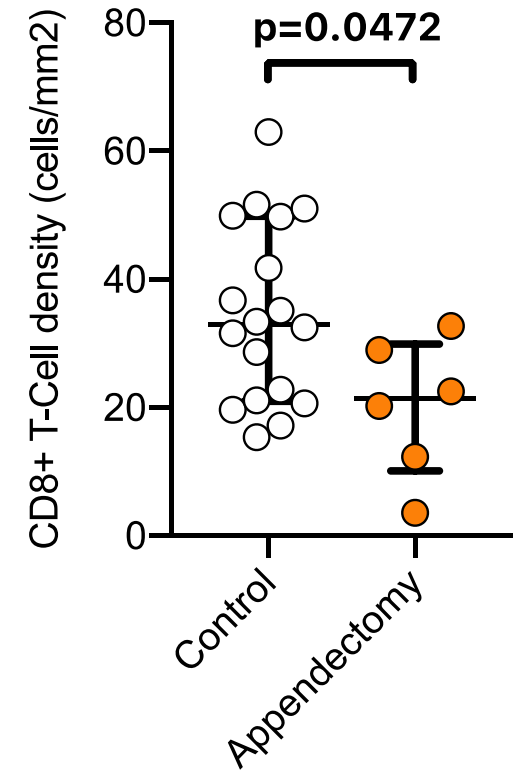
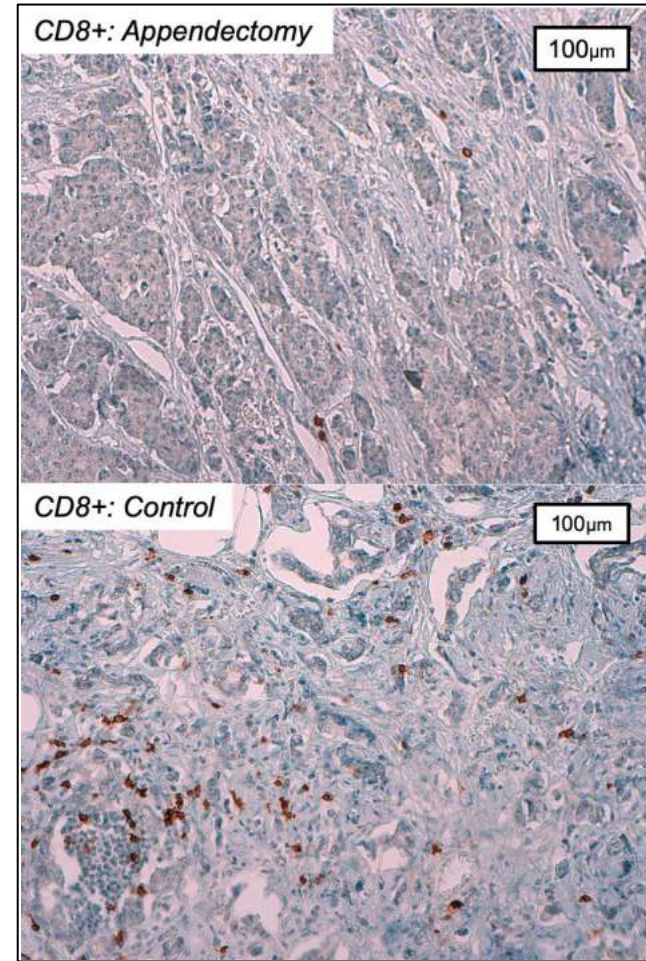


Lymphocytes T-8

Et chez l'Homme ?

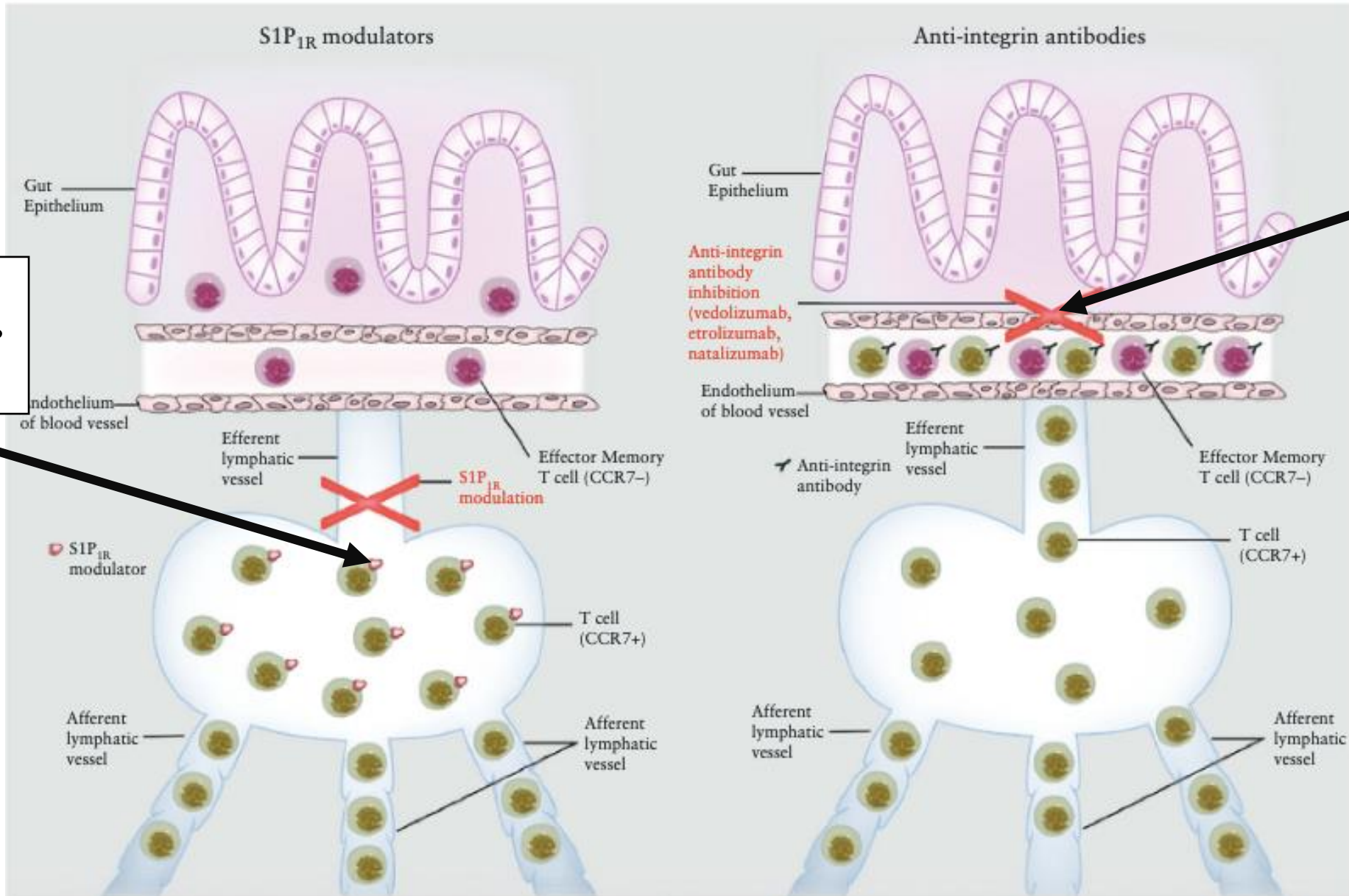


Lymphocytes T



Lymphocytes T-8

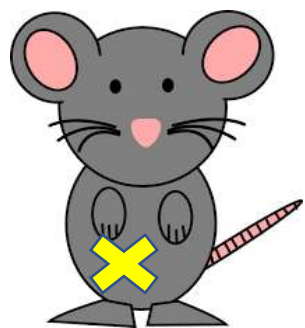
Blocage circulation lymphocytaire = appendicectomie chimique ?



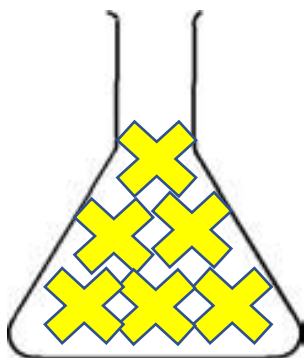
FTY720
Antagoniste
du S1PR

Vedolizumab
Anti-integrine
 $\alpha 4\beta 7$

Thérapie cellulaire à partir des lymphocytes appendiculaires après appendicite



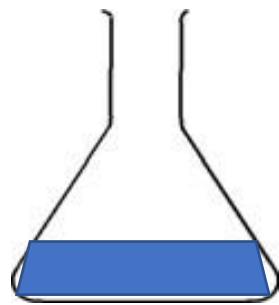
Induction
d'une
appendicite
(27 souris)



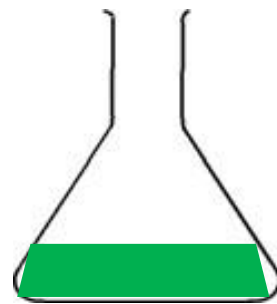
J7
Prélèvement des
appendices



*Tri cellulaire:
billes magnétiques*



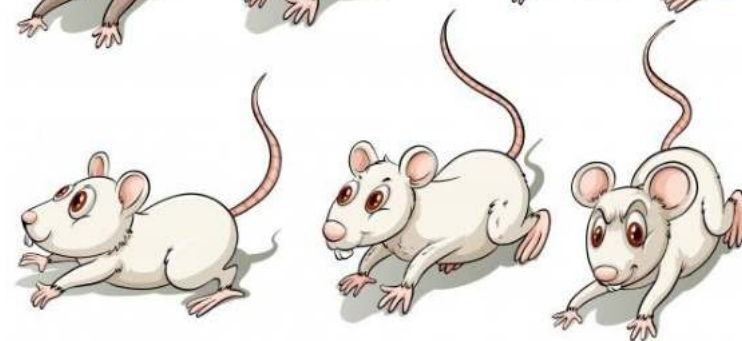
CD45+ CD3-



CD3+

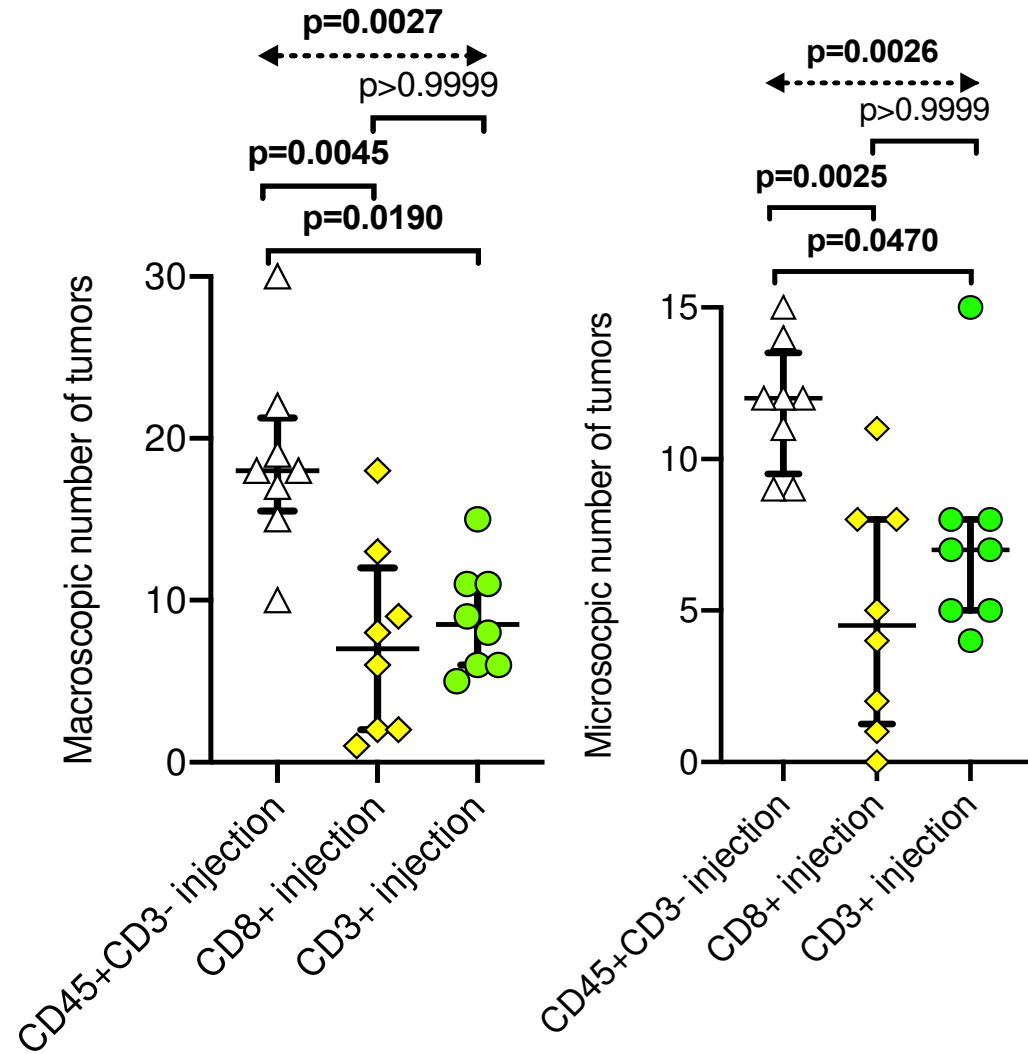


CD8+

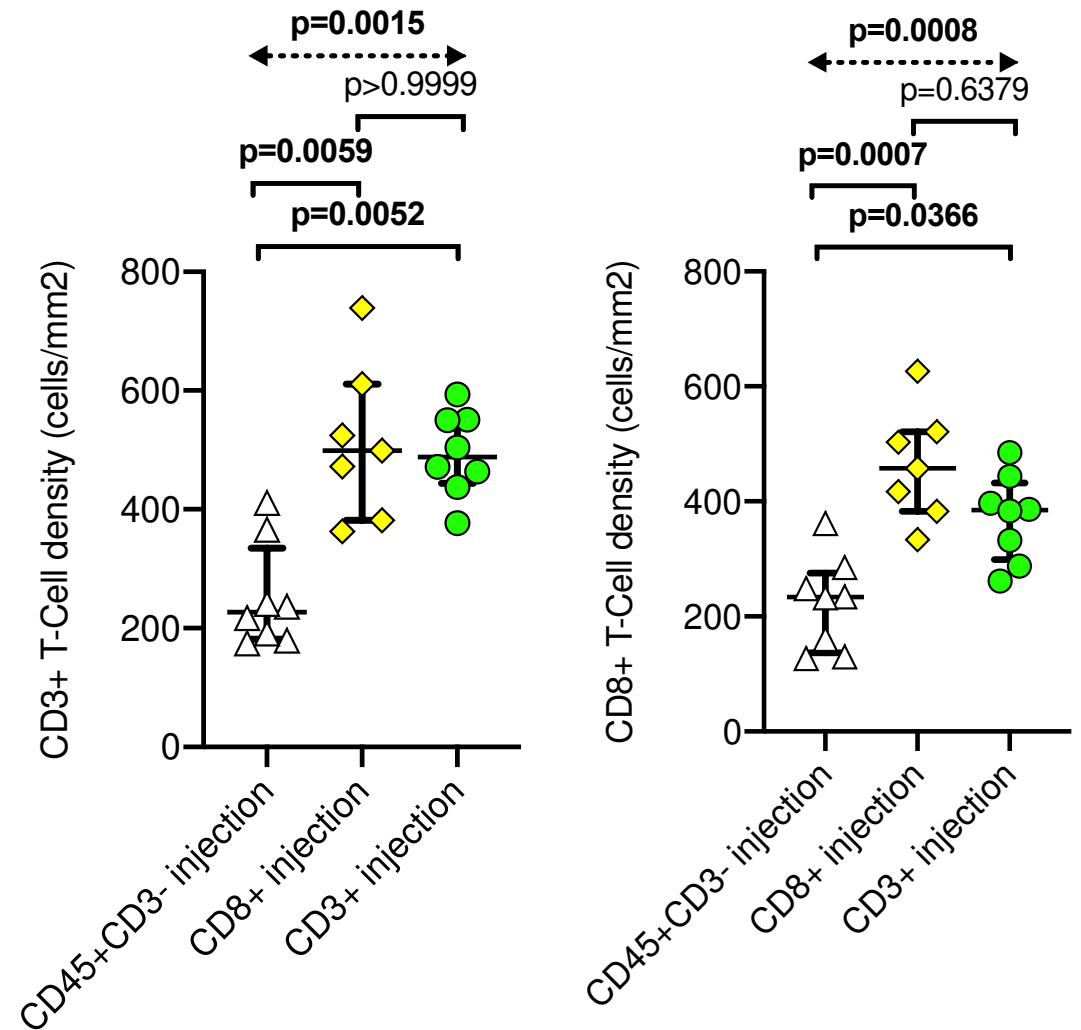


Thérapie cellulaire à partir des lymphocytes appendiculaires après appendicite

Phénotype tumoral



Phénotype lymphocytaire



Injection de lymphocytes T-8 issus d'un appendice inflammatoire protège du cancer colorectal associé aux colites

Patch caecal: take home message

- Fréquent dans la RCH: **environ 20%**
- Ce signe n'est pas pathognomonique de la RCH
- Les conséquences sur la RCH lorsque ce signe est retrouvé sont débattues: Profil plus agressif de la maladie ?
- L'inflammation de l'orifice appendiculaire serait le témoin d'une endo-appendicite
- Ce signe pourrait être prédictif du succès de l'appendicectomie prophylactique

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Maxime Collard

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ReMind

Patch caecal dans la RCH

	Cecal/Periappendiceal Patch, n (%)		<i>P</i>	
	Absent (N = 102)	Present (N = 102)	Univariate	Multivariate
Patient age (y)				
Median (IQR)	41 (31.3-52.8)	31 (25-55)	< 0.001	0.004
Patient sex				
Female	50 (49.0)	48 (47.1)	0.78	0.97
Male	52 (51.0)	54 (52.9)		
Disease duration (y)				
Median (IQR)	12.9 (6.6-21.4)	9.8 (5.6-17.3)	0.084	0.99
Colitis extent				
Rectum/sigmoid	29 (28.4)	60 (58.8)	< 0.001	< 0.001
More proximal	73 (71.6)	42 (41.2)		
Histologic inflammation				
Inactive/mild	54 (52.9)	48 (47.1)	0.40	0.26
Moderate/severe	48 (47.1)	54 (52.9)		
Neoplasia (all grades)				
Present	11 (10.8)	8 (7.8)	0.47	0.68
Absent	91 (89.2)	94 (92.2)		
Baseline pharmacotherapy*				
Level 1 (salicylates)	13 (16.3)	24 (32.0)	0.022	0.006
Level 2 (immunomodulators)	28 (35.0)	17 (22.7)		
Level 3 (biologics)	39 (48.8)	34 (45.3)		
Eventual CD				
Present	1 (1.0)	10 (9.8)	0.005	0.022
Absent	101 (99.0)	92 (90.2)		