



Microbiote et endométriose

Challenges et espoirs

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Conflits d'intérêts



Laboratoire Besins Healthcare : prise en charge, symposium

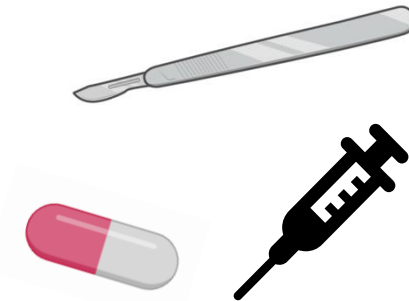
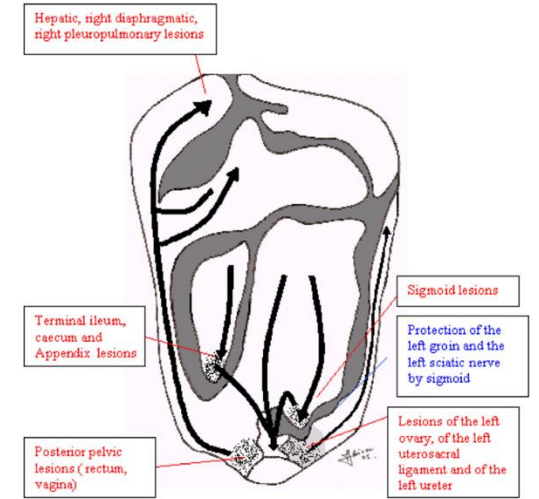
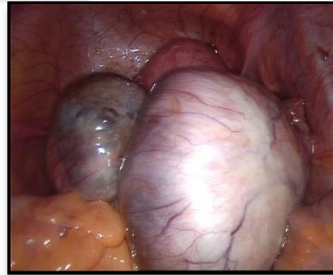
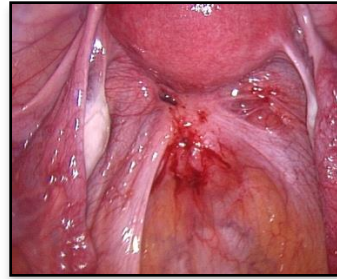
Bourses de recherche



Une maladie hétérogène



Menstruations rétrogrades
Reliquats embryonnaires
Métaplasie
Génétique



DYSMÉNORRHEES

DOULEURS NON CYCLIQUES

SYMPTÔMES DIGESTIFS

SENSIBILISATION CENTRALE

INFERTILITÉ

n = 290 patientes avec
endométriose / diagnostic
chirurgical

Endometriosis confirmed†

	No.	%†
Dysmenorrhoea	237	82.6
Dyspareunia	187	82.7
Pelvic pain	191	80.9
Back pain	214	80.1
Leg/thigh pain	143	82.2
Dyschezia	140	84.3
Premenstrual spotting	168	81.1
Infertility	80	89.9
Gastrointestinal symptoms	261	81.3
Diarrhoea	65	78.3
Constipation	88	86.3
Nausea	162	81.8
Vomiting	58	76.3
Rectal bleeding	52	82.5
Bloating	240	81.6
Bloating only	32	78.0

An inedit survey
including a large
sample:

→ **1 557***

women with
endometriosis



In France, 1.5 to 2.5 million of
women of childbearing age suffer
with endometriosis.



At the beginning, women feel in
average

4,6 different symptoms
associated to endometriosis.

Severe
dysmenorrhea



Other frequent symptoms:

- Pelvic pain: **66 %**
- Chronic fatigue: **54 %**
- Digestive disorders: **52 %**
- Dyspareunia: **50 %**
- Urinary disorders: **25 %**

endoVie



Are digestive symptoms in women presenting with pelvic endometriosis specific to lesion localizations?

A preliminary prospective study[†]

Horace Roman^{1,2,*}, Julie Ness¹, Nicolae Suciu³, Valérie Bridoux⁴,
Guillaume Gourcerol^{5,6}, Anne Marie Leroi^{5,6}, Jean Jacques Tuech⁴,
Philippe Ducrotté⁷, Céline Savoye-Collet⁸, and Guillaume Savoye^{6,7}

n = 116 patientes /
phénotypage chirurgical

	Superficielle	Rectal -	Rectal +	p
Défécation	8 (38%)	18 (43 %)	36 (68 %)	0.02
Nausées	8 (38%)	8 (19 %)	19 (36 %)	ns
Rectorragies	1 (5 %)	3 (7 %)	8 (15 %)	ns
Constipation	7 (33 %)	11 (26 %)	29 (55 %)	0.01
Diarrhées	8 (38 %)	18 (43 %)	25 (47 %)	ns
Ballonnements	9 (43 %)	25 (60 %)	27 (50 %)	ns

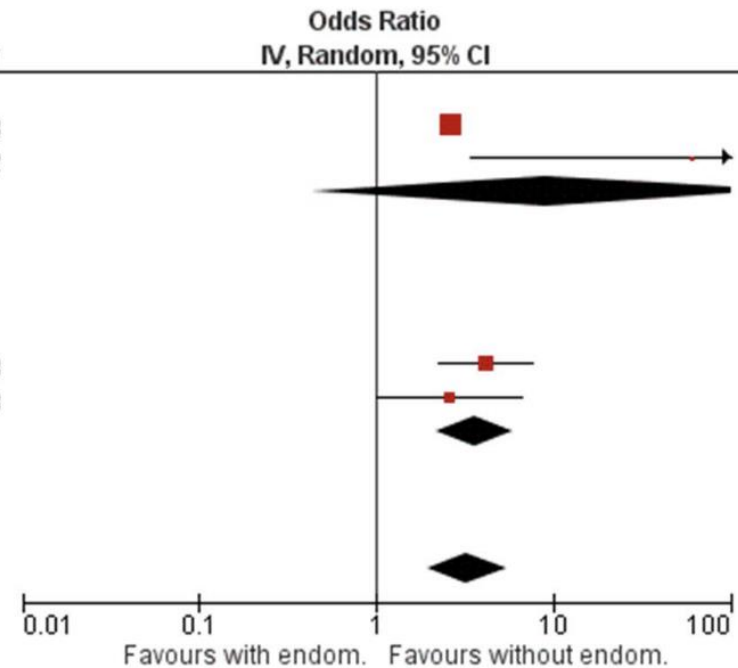
Syndrome de l'intestin irritable

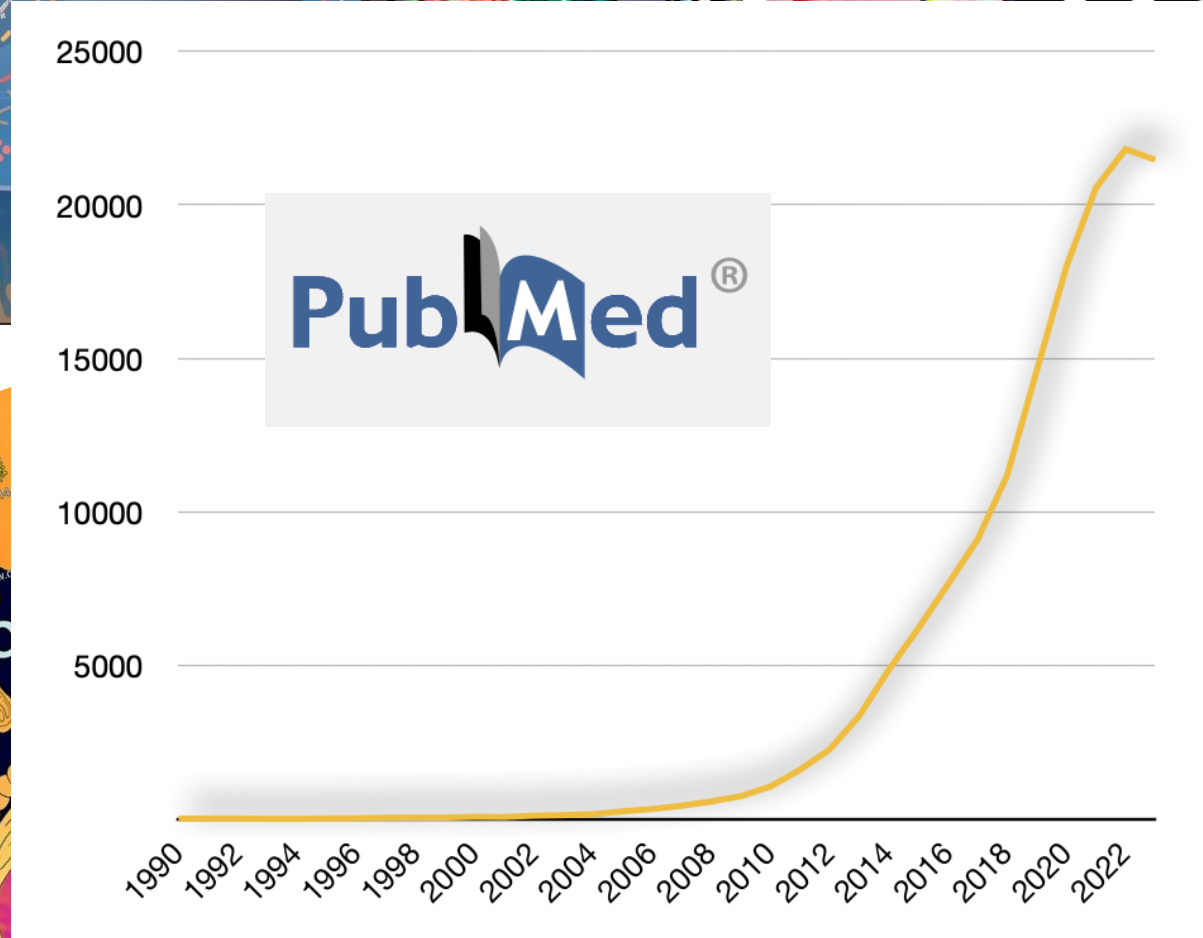
Prévalence de 10%

Touche préférentiellement les femmes jeunes...

n = 27 000
Diagnostic IBS par ROME III

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Year
1.7.1 Crude OR					
Seaman 2008	0.9555	0.0626	49.4%	2.60 [2.30, 2.94]	2008
Issa 2012	4.1089	1.4661	2.9%	60.88 [3.44, 1077.50]	2012
Subtotal (95% CI)			52.3%	8.95 [0.44, 183.00]	
Heterogeneity: $\text{Tau}^2 = 3.90$; $\text{Chi}^2 = 4.62$, $\text{df} = 1$ ($P = 0.03$); $I^2 = 78\%$					
Test for overall effect: $Z = 1.42$ ($P = 0.15$)					
1.7.2 Adjusted OR					
Schomacker 2018	1.4231	0.3078	29.3%	4.15 [2.27, 7.59]	2018
Ek 2018	0.9478	0.4785	18.3%	2.58 [1.01, 6.59]	2018
Subtotal (95% CI)			47.7%	3.61 [2.17, 6.00]	
Heterogeneity: $\text{Tau}^2 = 0.00$; $\text{Chi}^2 = 0.70$, $\text{df} = 1$ ($P = 0.40$); $I^2 = 0\%$					
Test for overall effect: $Z = 4.96$ ($P < 0.00001$)					
Total (95% CI)			100.0%	3.26 [1.97, 5.39]	
Heterogeneity: $\text{Tau}^2 = 0.13$; $\text{Chi}^2 = 6.78$, $\text{df} = 3$ ($P = 0.08$); $I^2 = 56\%$					
Test for overall effect: $Z = 4.62$ ($P < 0.00001$)					
Test for subgroup differences: $\text{Chi}^2 = 0.34$, $\text{df} = 1$ ($P = 0.56$), $I^2 = 0\%$					



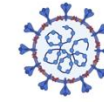


Le microbiote

L'ensemble des micro-organismes qui vivent dans un environnement spécifique



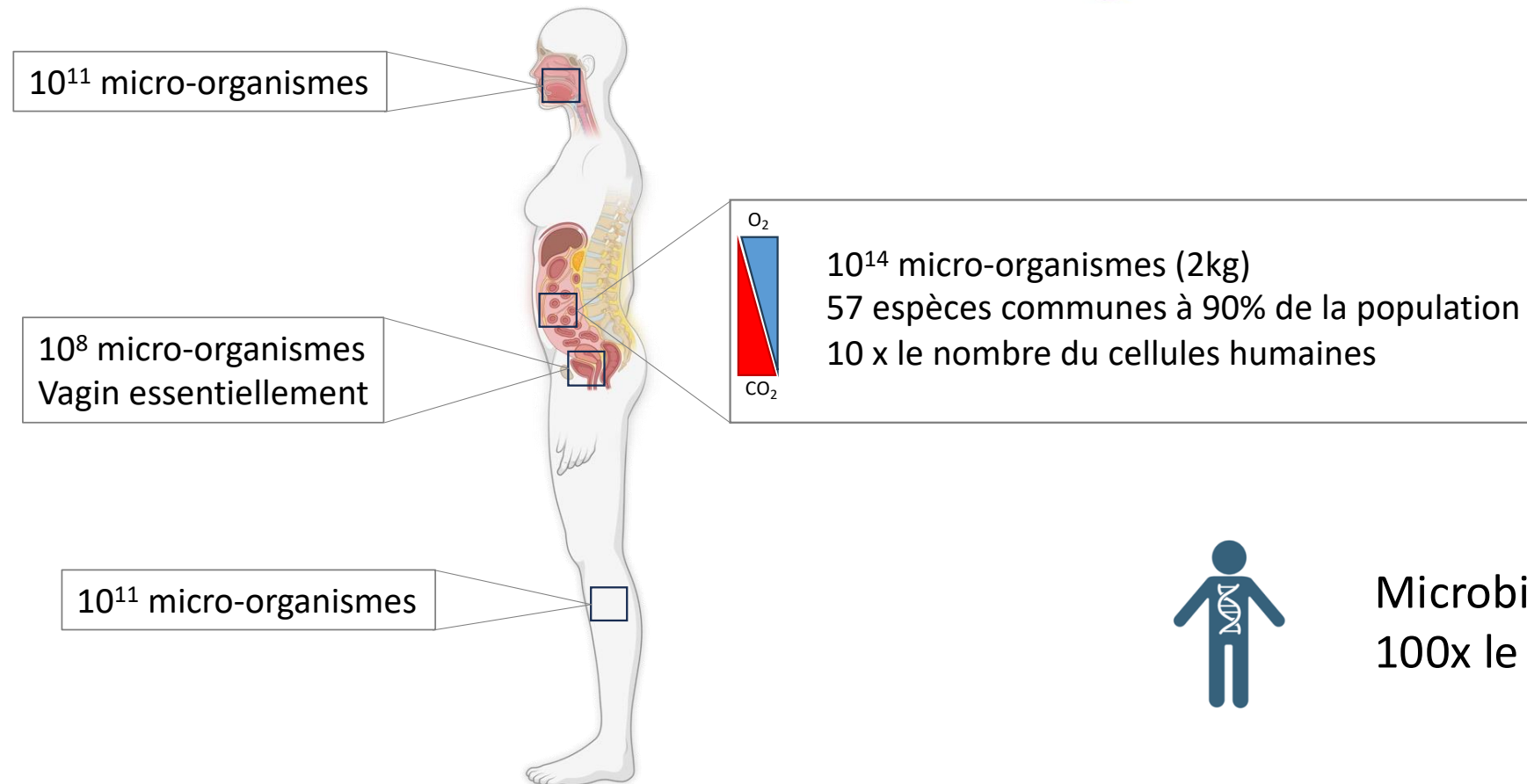
Bactéries



Virus

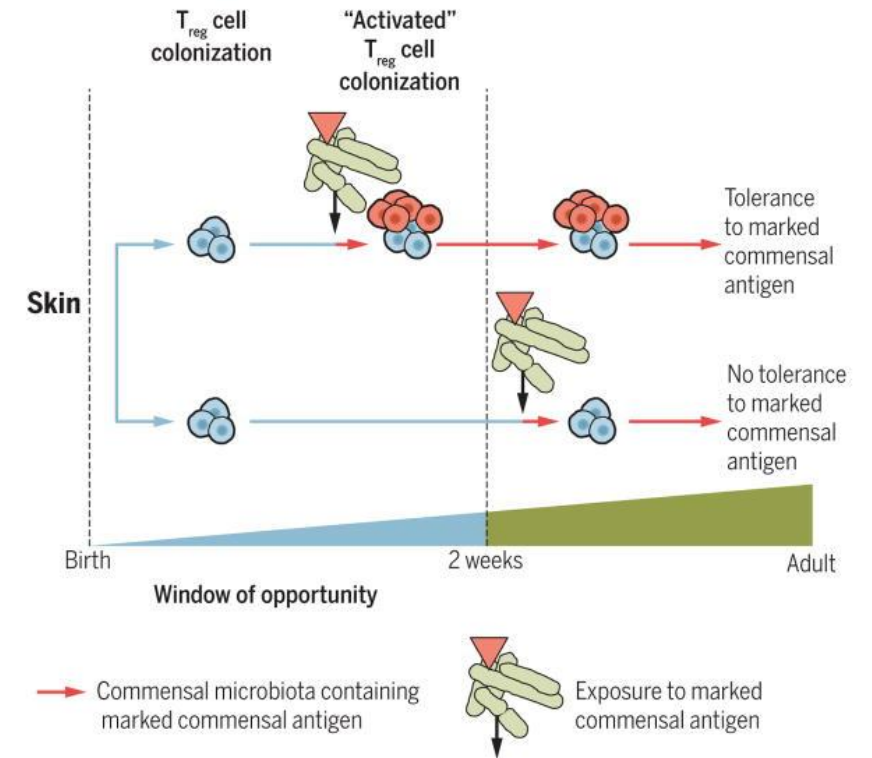
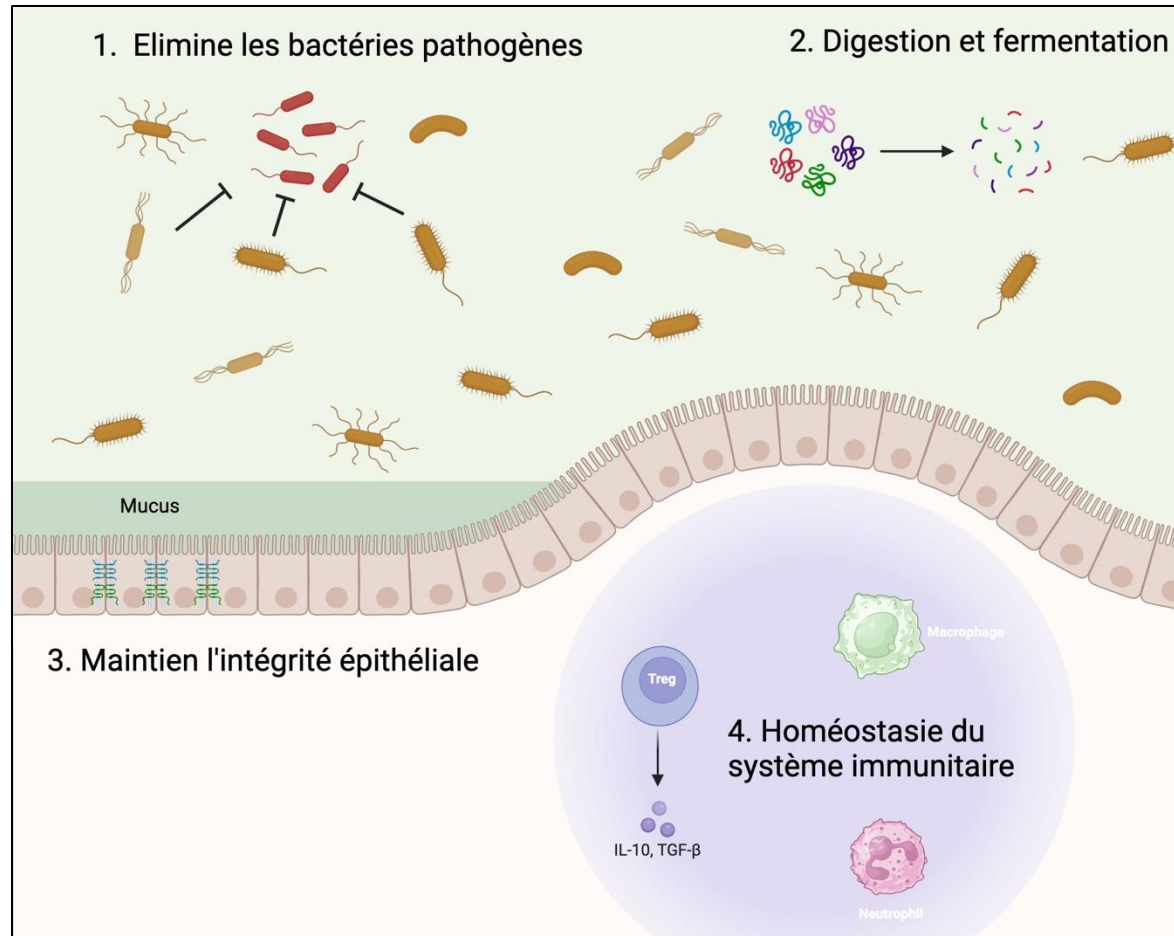


Champignons



Microbiome =
100x le génome humain

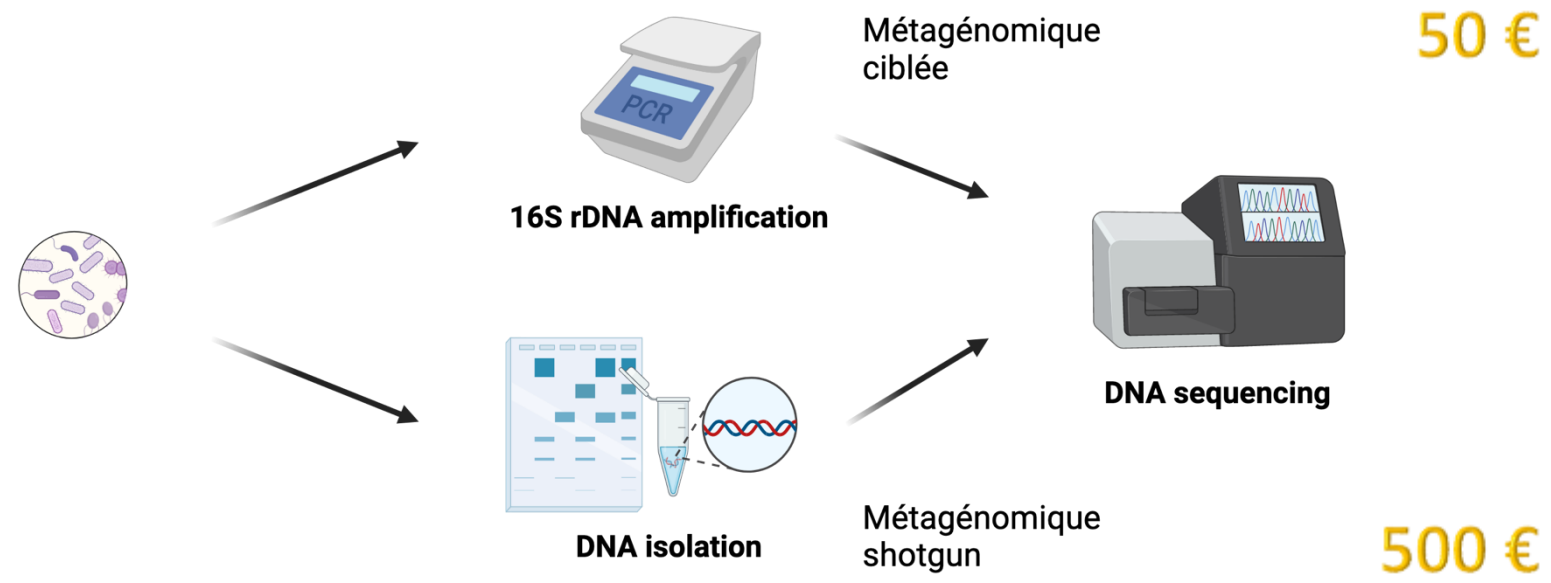
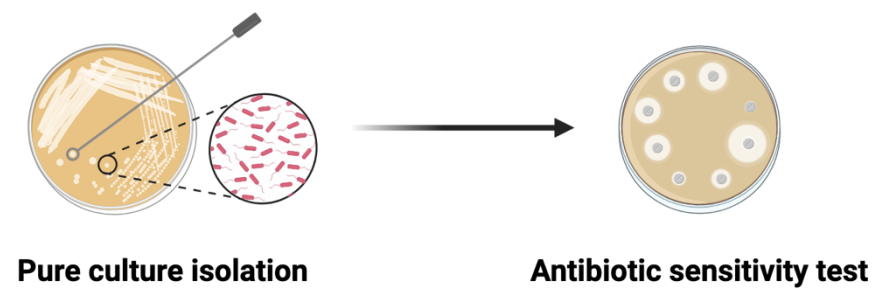
Fonctions d'interface



Gensollen T et al. *Science* 2016

Ses méthodes d'étude

Next
Generation
Sequencing



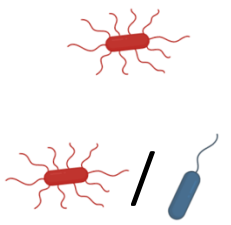
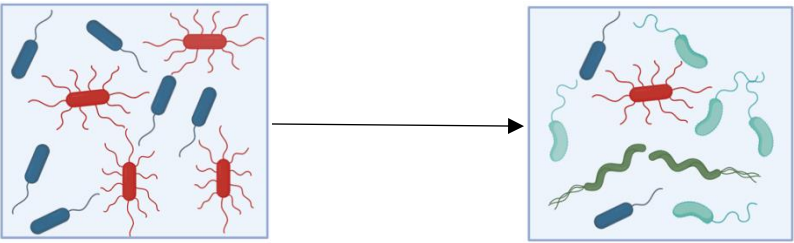
Ses résultats



Diversité α

<<

Diversité α

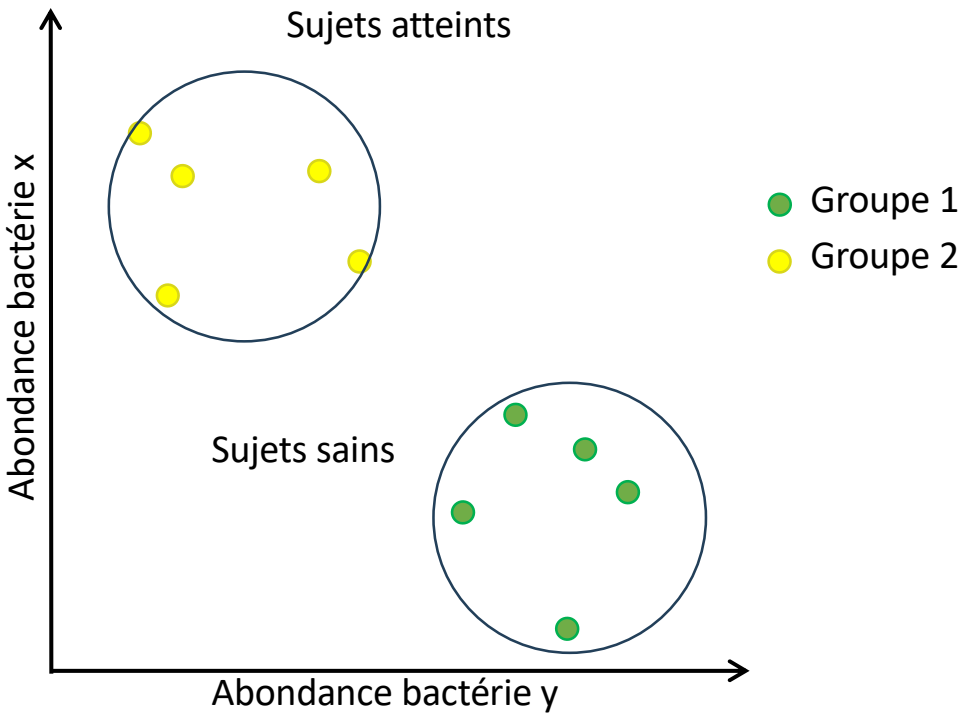


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1 ↓ ↓

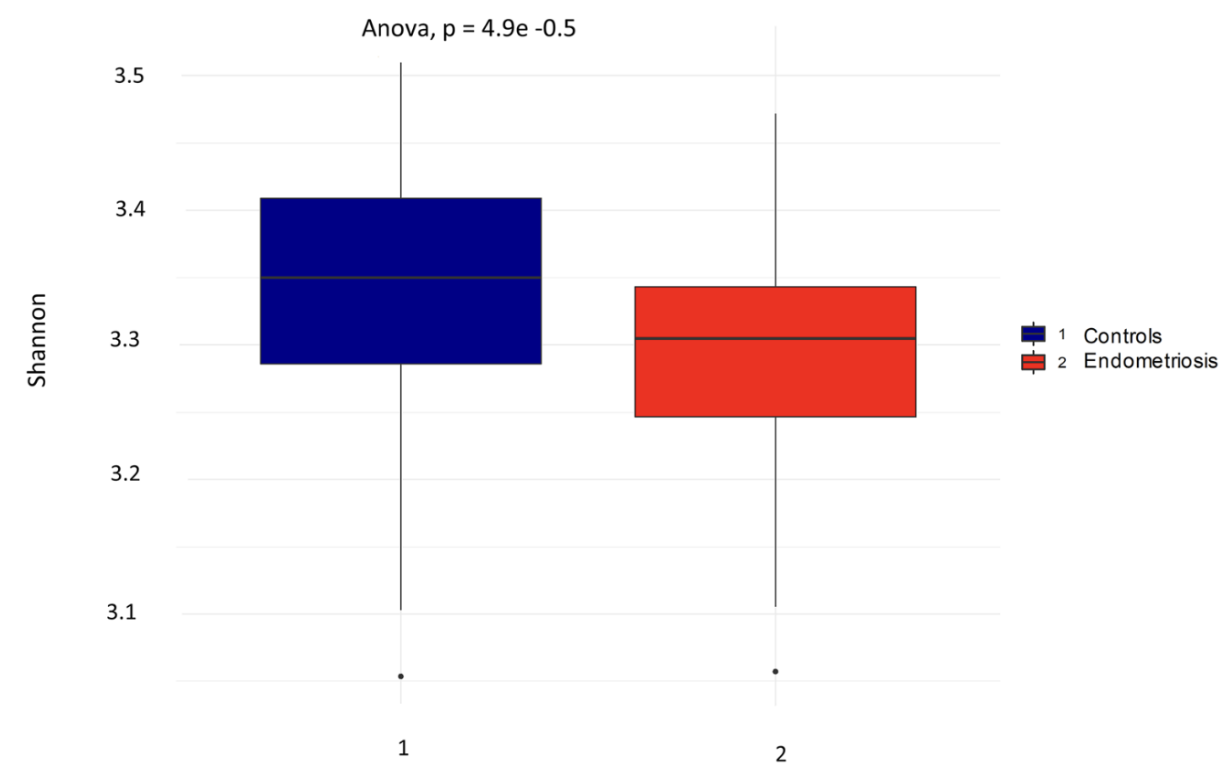
1

0,5 ↓



Diversité β

Microbiote intestinale et endométriose



n = 66 endometriosis vs. 198 controls

Bacteria		Dysregulation
Phyla	<i>Firmicutes to Bacteroidetes ratio</i>	↑
	<i>Bacteroidetes</i>	↑
	<i>Proteobacteria</i>	↑
Species	<i>Escherichia coli</i>	↑
	<i>Streptococcus</i>	↑
	<i>Gardnerella</i>	↑↓
	<i>Clostridium</i>	↓
	<i>Ruminococcus</i>	↓
	<i>Prevotella</i>	↑

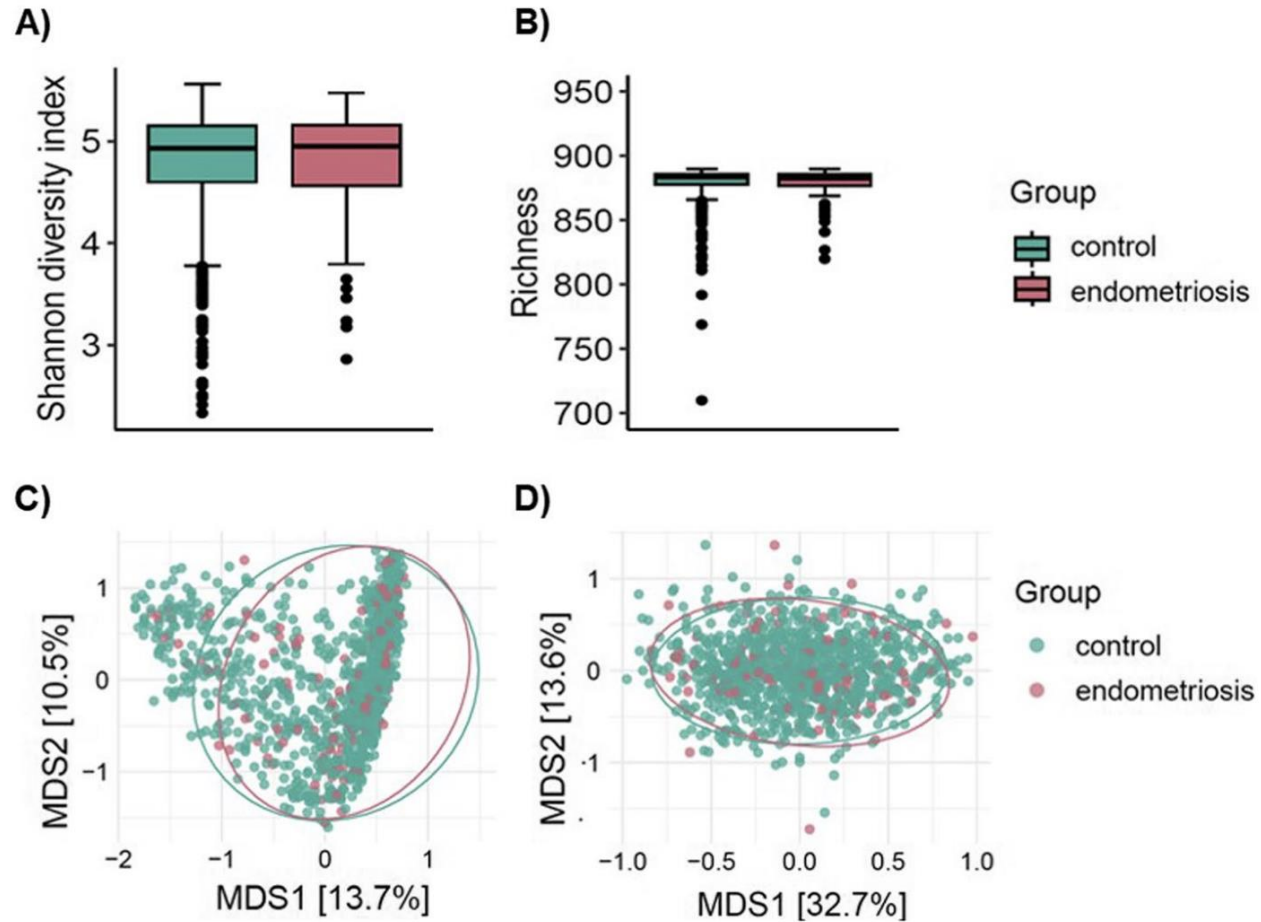
Microbiote intestinal et endométriose



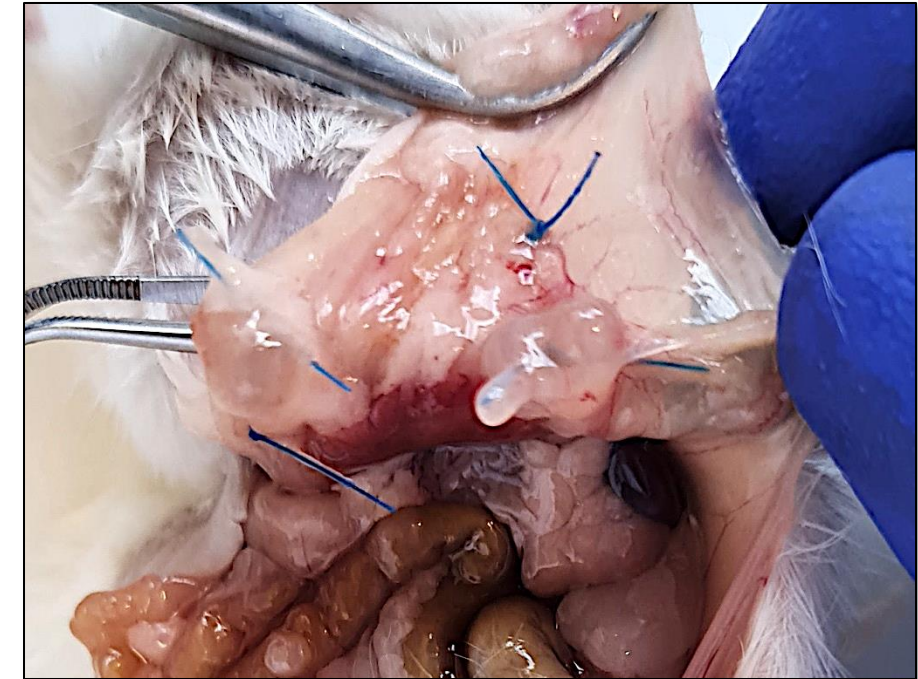
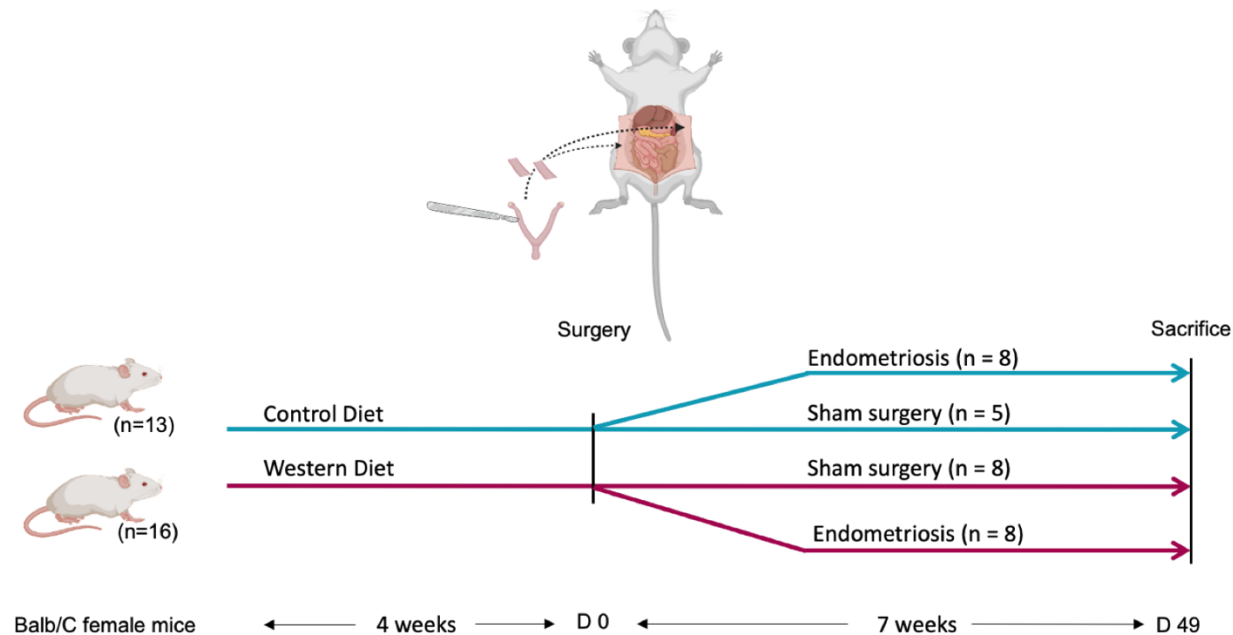
UNIVERSITY OF TARTU

n=1000 femmes (Estonie)
Estonian BioBank

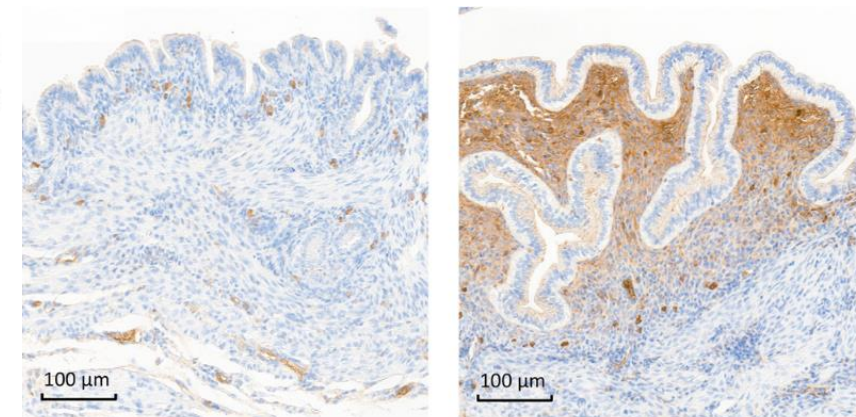
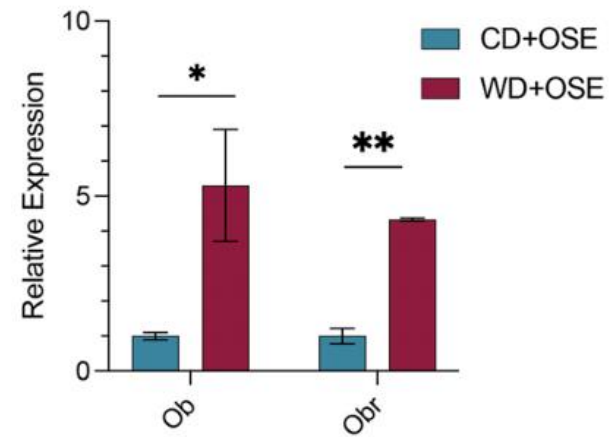
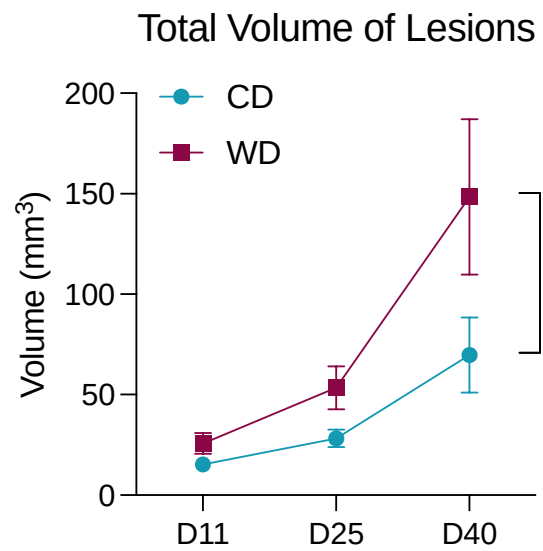
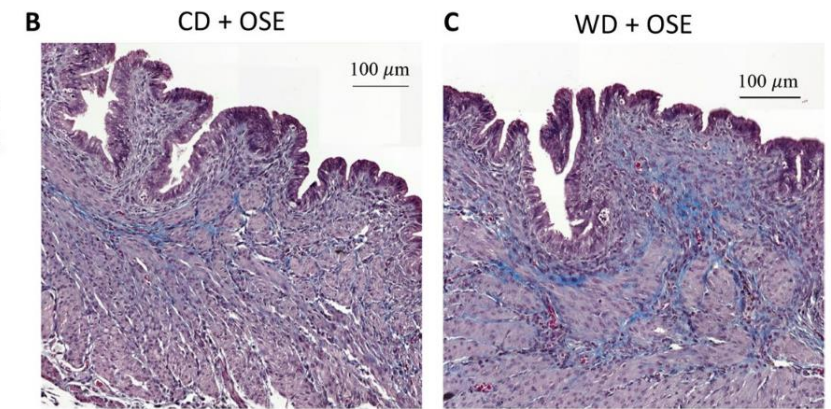
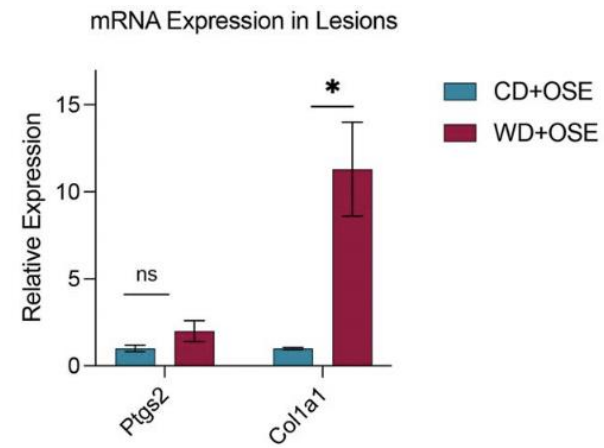
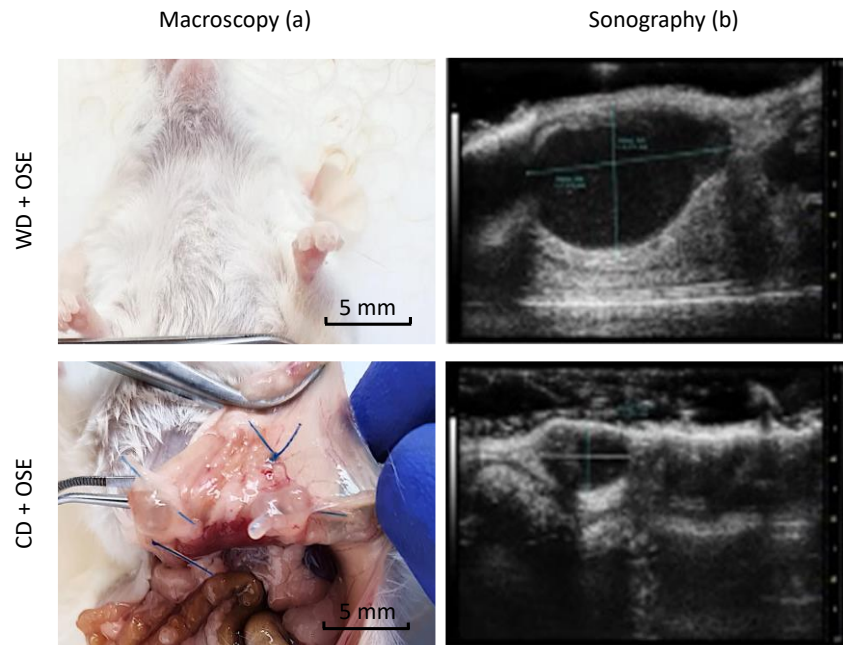
n =136 OSE chir



Western diet promotes endometriotic lesion growth in mice and induces depletion of *Akkermansia muciniphila* in intestinal microbiota

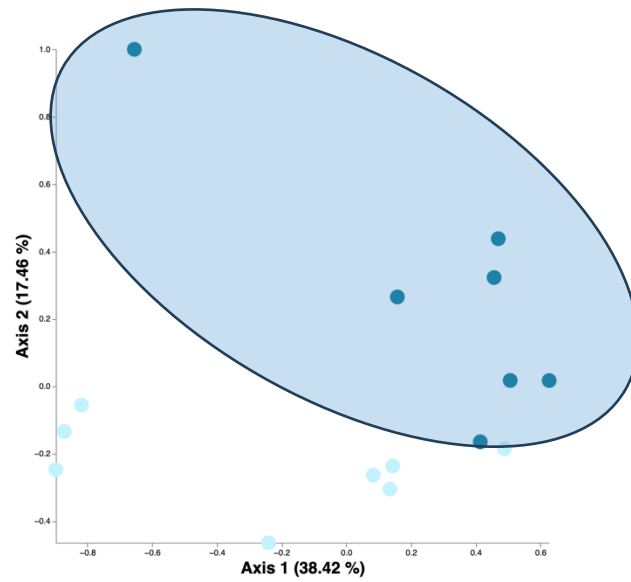


Western diet = High fat + low fiber



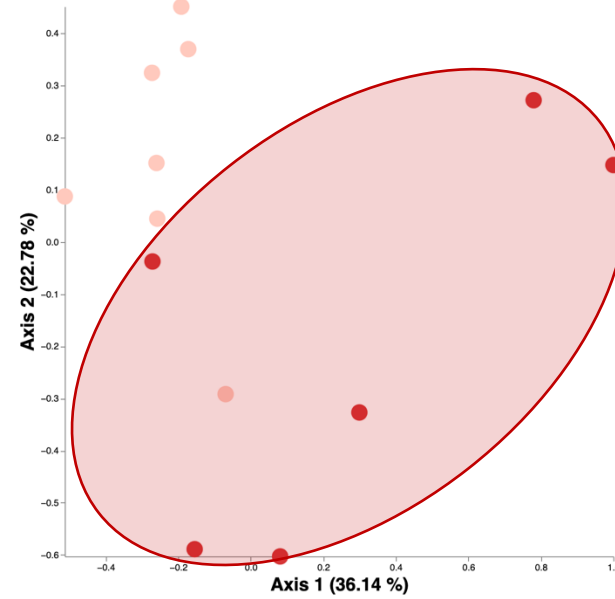


Benoît Chassaing



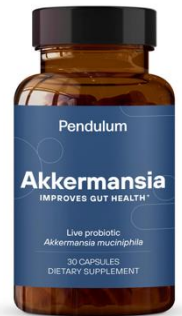
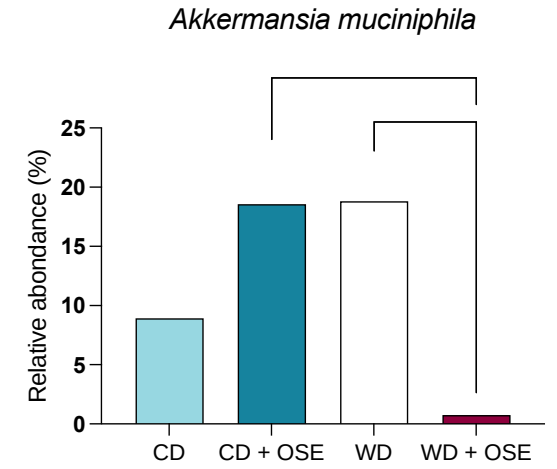
CD Sham
CD + OSE

Permanova P value **0.013**



WD Sham
WD + OSE

Permanova P value **0.004**

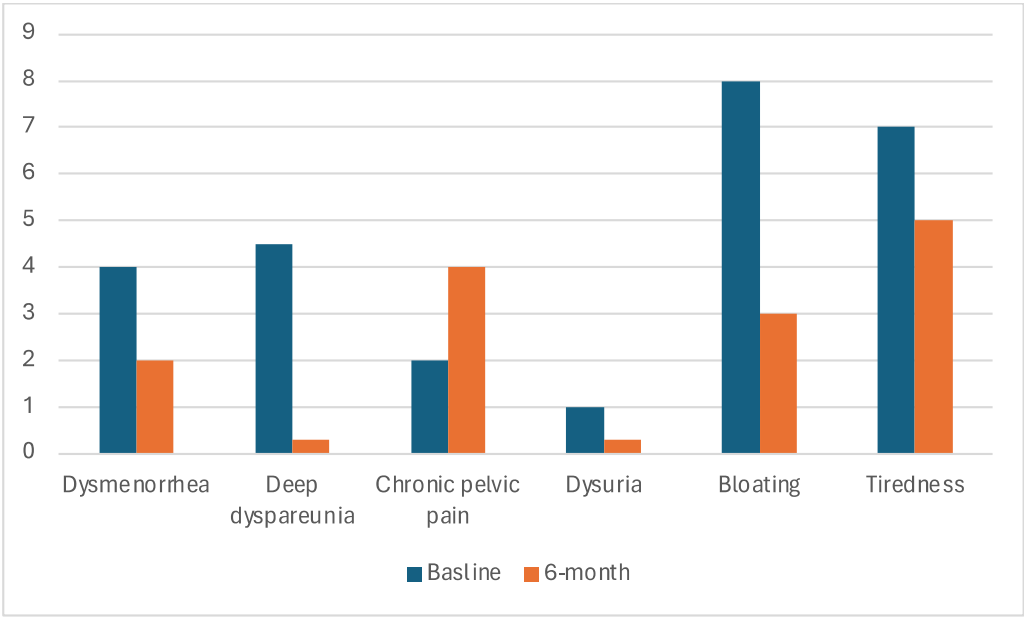


Régimes low FODMAP

	Endometriosis, N = 59	No reported endometriosis, N = 101	P value	Odd's ratio (95% CI)
Adherence to low FODMAP diet	55 (93%)	91 (90%)	0.57	1.5 (0.45–5.05)
Success with low FODMAP diet	43 (72%)	49 (49%)	0.001	3.11 (1.5–6.2)

Moore et al. *Aust N Z J Obstet Gynaecol* 2017

Symptoms associated with endometriosis	Low FODMAP diet		
	N = 22		
	Baseline VAS score (median, IQR)	Six-month VAS score (median, IQR)	P-value ⁴
Dysmenorrhea	4.0 (7.0)	2.0 (4.0)	0.111
Deep dyspareunia	4.5 (6.0)	0.0 (4.0)	0.066
Chronic pelvic pain	2.0 (6.0)	4.0 (6.0)	0.433
Dysuria	1.0 (3.0)	0.0 (0.0)	0.015
Bloating	8.0 (3.8)	3.0 (4.5)	<0.001
Tiredness	7.0 (4.0)	5.0 (5.0)	0.087



van Haaps AP et al. *Human Reprod.* 2023

However, **no recommendations can be made** for any specific non-medical intervention (ie. nutrition) to reduce pain or improve quality of life measures in women with endometriosis, as the potential benefits and harms are unclear.

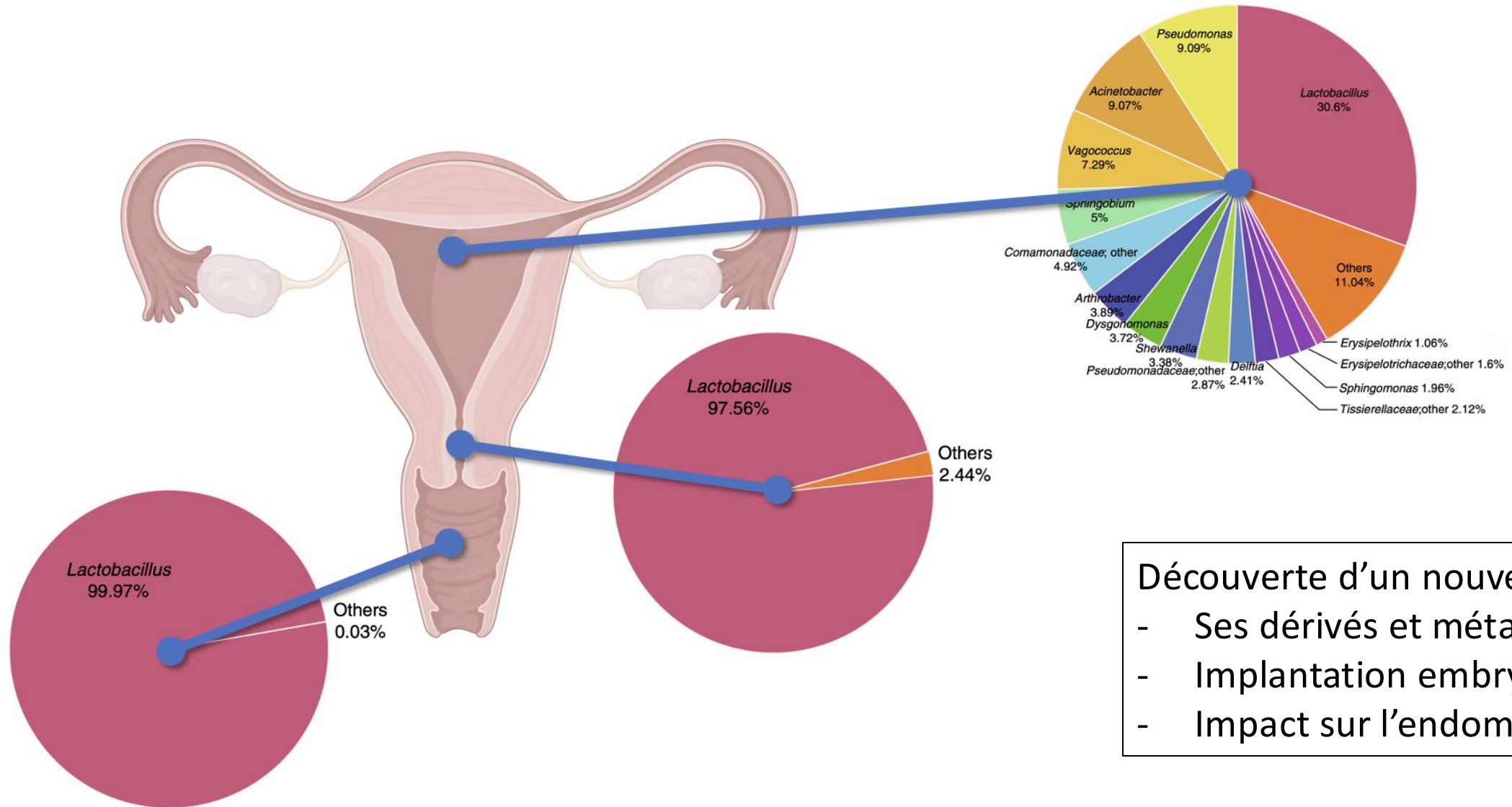
Prise en charge diététique adaptée :

- Bilan nutritionnel
- Adaptation individualisée



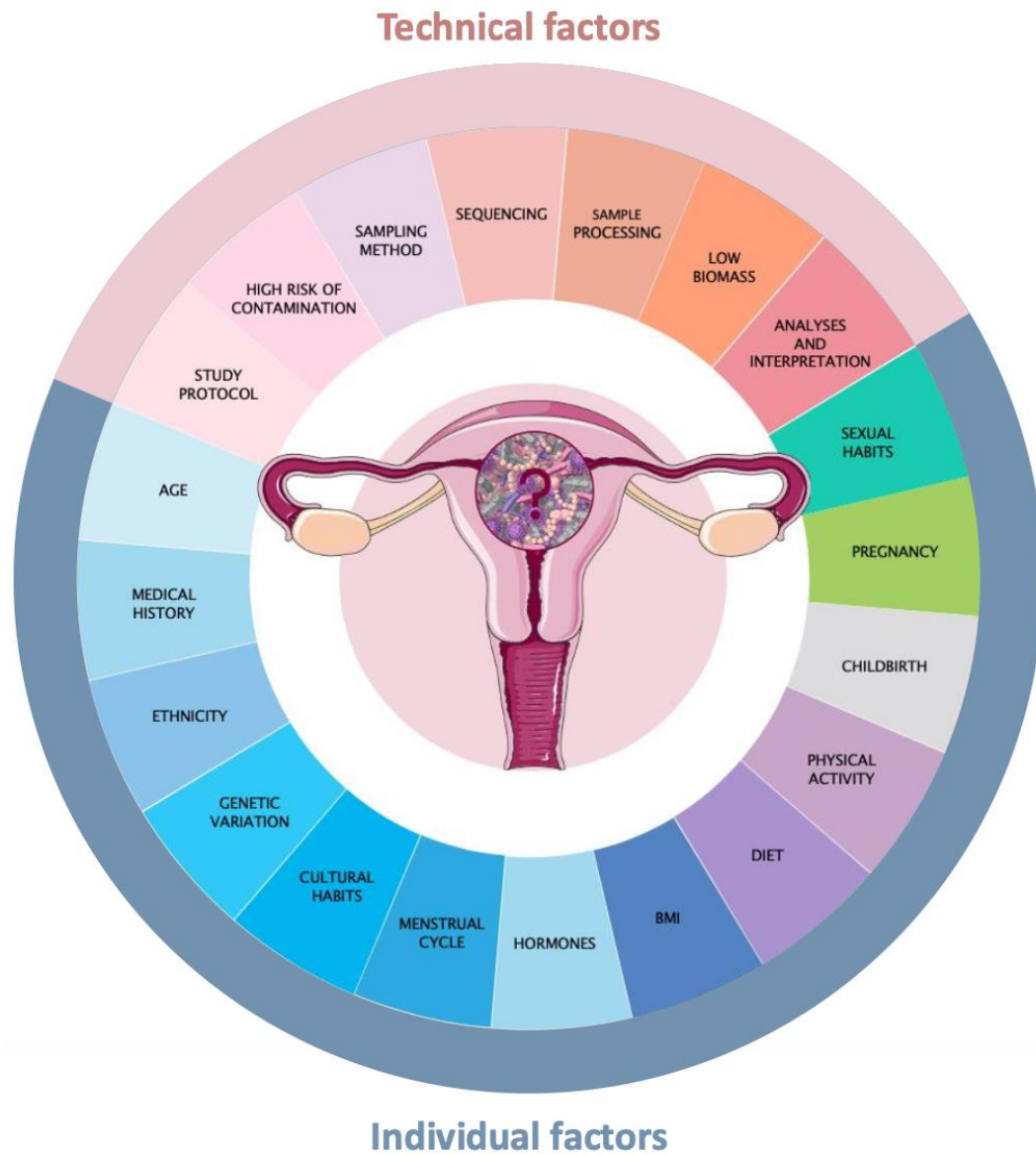
pas de régime sans gluten
pas de régime anti-inflammatoire

Appareil génital



Découverte d'un nouvel acteur :

- Ses dérivés et métabolites ?
- Implantation embryonnaire ?
- Impact sur l'endomètre ?

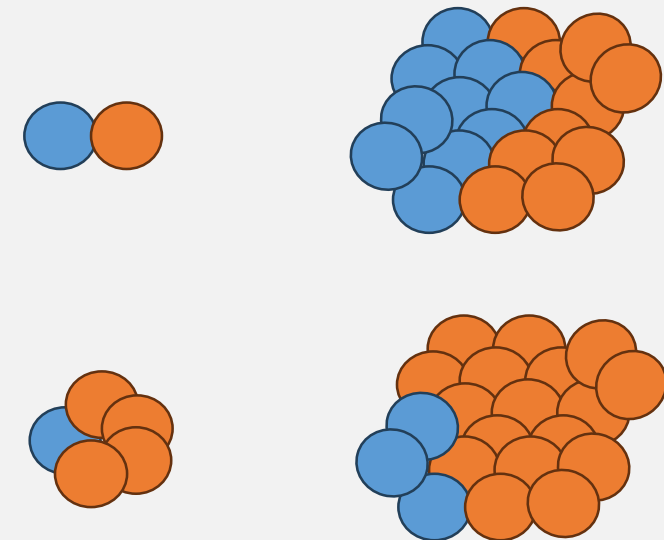


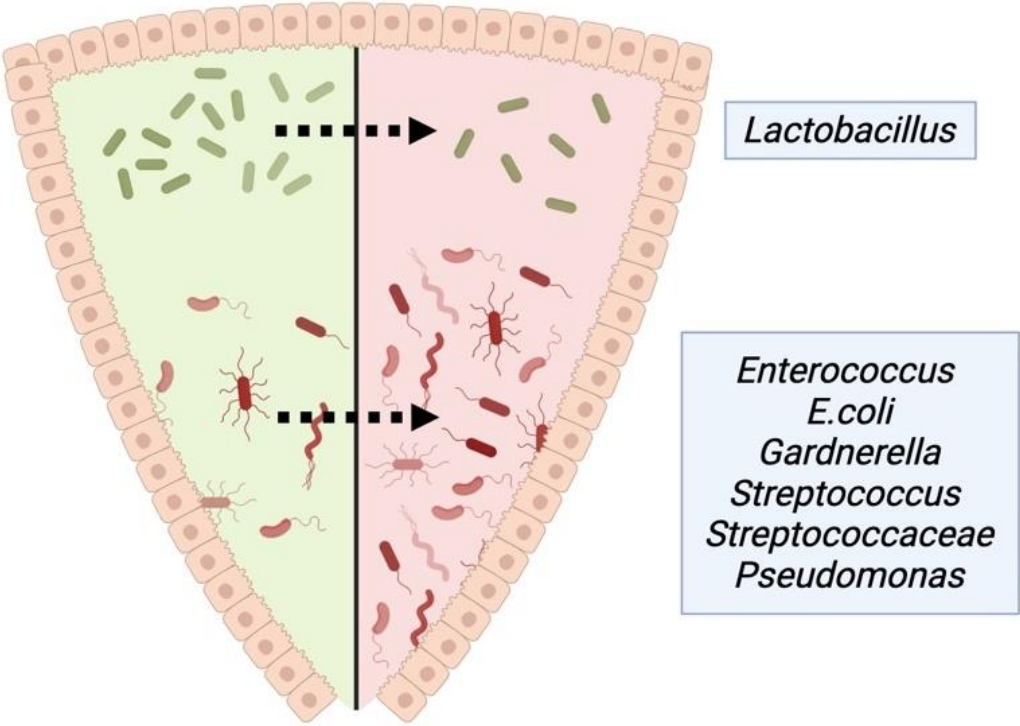
Biomasse faible

VAGIN : 10^8

ENDOMETRE : 10^3

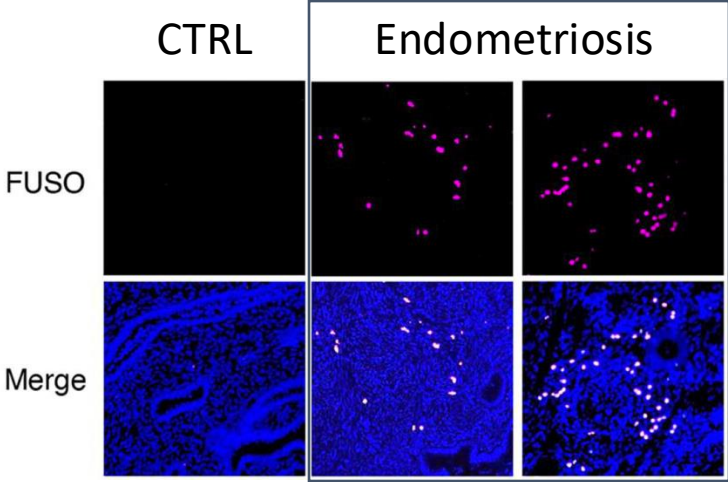
Amplification PCR



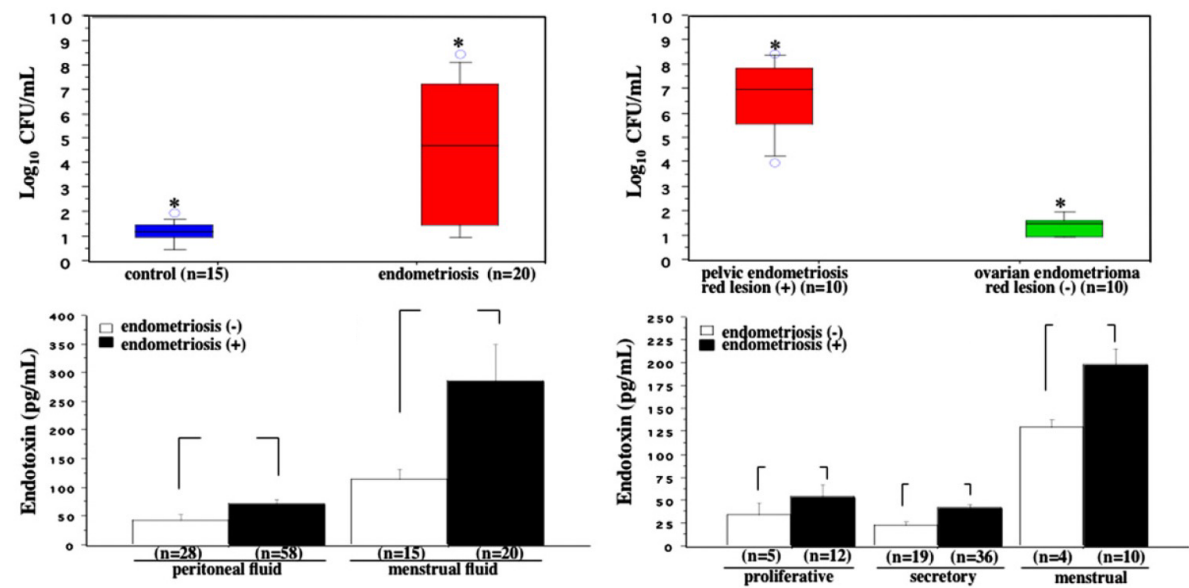
Reference	Design		
Khan et al. 2014	73 EMS vs 55		robota with endometriosis
Khan et al., 2016	32 EMS vs 32		rdnerella, and Streptococcus
Chen et al., 2017	32 EMS vs 16		Moraxellaceae, Staphylococaceae and
Hernandes et al. 2020	10 EMS vs 11		nonas, Acinetobacter, Vagococcus and
Wei et al. 2020	26 EMS vs 11		iversity
Wessels et al. 2021	12 EMS vs 9 c		x) pobium, and Veillonellaceae. x) acteraceae and Streptococcaceae species, ↓ Burkholderiaceae and Ralstonia species

Contribution bactérienne

Fusobacterium infection facilitates the development of endometriosis through the phenotypic transition of endometrial fibroblasts



Muraoka et al. *Sci. Transl. Med* 2023



E.Coli in endometrial sample of 20 endometriosis / 15 control

Les infections d'endométriomes

Abcès tubo-ovariens sur IGH

Terrain femme jeune, RS à risque

Mécanisme ascendant

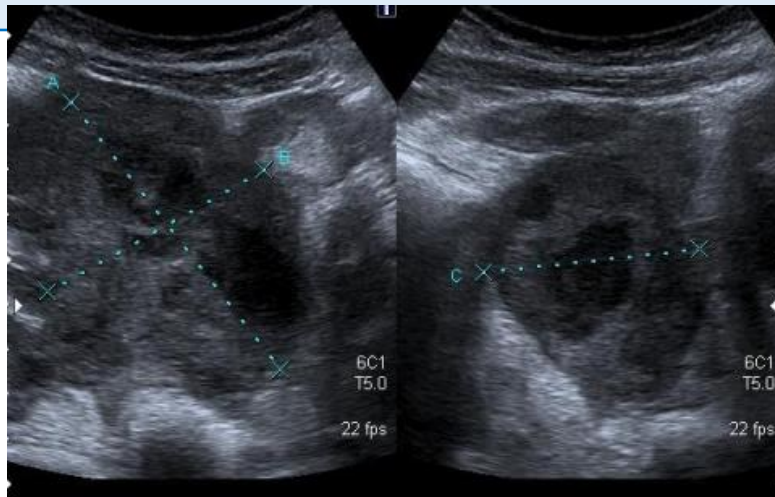
Complexe trompe – ovaire

Associé aux IST (*C. trachomatis* et *N. gonorrhoeae*)

Recommandations :

Drainage chirurgical > 3 cm

ATB par ceftriaxone, métronidazole et doxycycline



Surinfections d'endométriomes

Endométriose

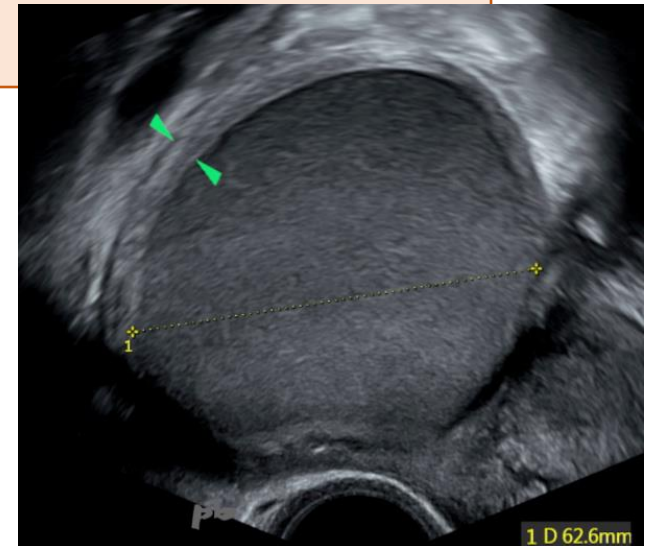
Provenance des pathogènes ?

Limité au kyste ovarien

Jamais associé aux IST

Recommandations :

Aucune



Les infections d'endométrioses

	Patient cohort (n = 69)
Demographic features	
Age (years)*	33.4 ± 5.2
BMI ¹ (kg/m ²)*	24.2 ± 4.7
Gravidity *	0.8 ± 1.1
Parity *	0.3 ± 0.6
Nulliparous, n(%) ^{\$}	51/69 (73.9 %)
Infertility, n(%) ^{\$}	56/69 (81.2 %)
Endometriosis history	
Associated DIE ² , n (%) ^{\$}	63/65 (96.9 %)
Anatomical distribution of DIE ² , n (%) ^{\$}	
Intestine	46/63 (73.0 %)
Ureteral	8/62 (12.9 %)
Bladder	7/63 (11.1 %)



Microbiology and outcomes of tubo-ovarian abscesses: A 5-year cohort of 105 cases

Second surgery during hospitalization for treatment failure, n (%)	20/94 (21.3 %)	vs. <2% pour ATO
Length of hospital stay (days)*	5.2 ± 3.1	
Hospitalization in intensive care, n (%)	1/94 (1.1 %)	
Recurrence, n (%)	29/94 (30.8 %)	vs. 10% pour ATO !
Hospitalization for recurrence, n(%)	26/29 (89.7 %)	
New surgery for recurrence, n(%)	20/29 (69.0 %)	
Ultrasound-guided transvaginal drainage	8/20 (40.0 %)	
Laparoscopy	9/20 (45.0 %)	
Laparotomy	2/20 (10.0 %)	
CT-guided drainage ²	1/20 (5.0 %)	

Parpex et al. *Fertil Steril* 2024
Micheli et al. *J Infection* 2024

	Infections cohort (n = 94)	
Per-operative pus sample documentation	92/94 (98%)	
Positive culture of one or multiple pathogens, n (%)*	60/92 (65%)	
Culture evidencing unique pathogens	48/60 (80%)	
Culture evidencing multiple pathogens, n (%)*	11/60 (18%)	
Type of documentation, n (%)§		
Strict anaerobes	16/70 (23%)	
<i>Bacteroides vulgatus</i>	2/70 (3%)	
<i>Cutibacterium acnes</i>	2/70 (3%)	
<i>Gardnerella vaginalis</i>	2/70 (3%)	
<i>Prevotella denticola</i>	2/70 (3%)	
Enterobacterales	41/70 (59%)	
<i>Escherichia coli</i>	38/70 (54%)	vs. 15% pour ATO
<i>Klebsiella pneumoniae</i>	2/70 (3%)	
<i>Klebsiella oxytoca</i>	1/70 (1%)	
Gram positive cocci	10/70 (14%)	
<i>Enterococcus faecalis</i>	4/70 (6%)	
<i>Streptococcus agalactiae</i>	4/70 (6%)	
DNA amplification by NAAT¹ in vaginal sample, n (%)*	52/94 (55%)	
<i>Chlamydia trachomatis</i>	0/52 (0%)	vs. >20% pour ATO
<i>Neisseria gonorrhoeae</i>	0/52 (0%)	

CONCLUSIONS

Nombreux travaux s'intéressant au microbiote : méthodologie à prendre en compte

Etudes préliminaires prometteuses concernant la symptomatologie de l'endométriose et alimentation.

L'identification d'une signature de microbiote ne préjuge pas de sa fonction (acteurs associés).

Des pistes prometteuses dans la contribution bactérienne/microbiote dans la physiopathologie



Pr Charles Chapron

Professor and Chair, Gynecology Obstetrics II and Reproductive Medicine

Dr Benoît CHASSAING, Institut Pasteur

Pr Caroline CHARLIER, Infectiologie

Institut Cochin



Association agréée par le ministère de la Santé et de la Prévention



ACADEMIE
DU MICROBIOTE
UROGENITAL

Gynaecology

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Medical Unit: G Plu-Bureau, L Maitrot-Mantelet

Reproductive Medicine Unit: P Santulli, M Bourdon, C Maignien, L Melka, A Garcia, D Stroe, L Osmani

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D Vaiman

Laboratory: Immunology

F Batteux, L Doridot, S Chouzenoux

Laboratory: Reproductive Biology

C Patrat, K Pocate, JP Wolf

Statistical Unit. F Goffinet, PY Ancel