La santé intestinale des vollailles

et la lutte contre l'antibiorésistance

Richard Ducatelle

Department of Pathology, Bacteriology and Avian Diseases

Faculty of Veterinary Medicine

Ghent University

Vision 2020

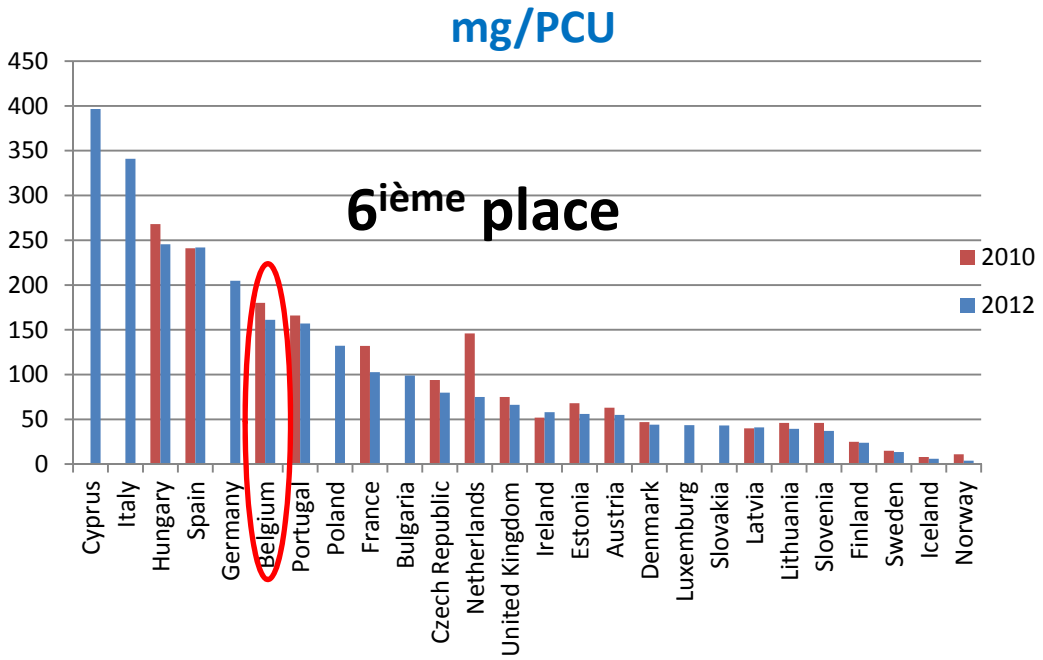
Objectifs stratégiques

-50% d'antibiotiques en moins d'ici 2020

-75% des antibiotiques les plus critiques en moins d'ici 2020

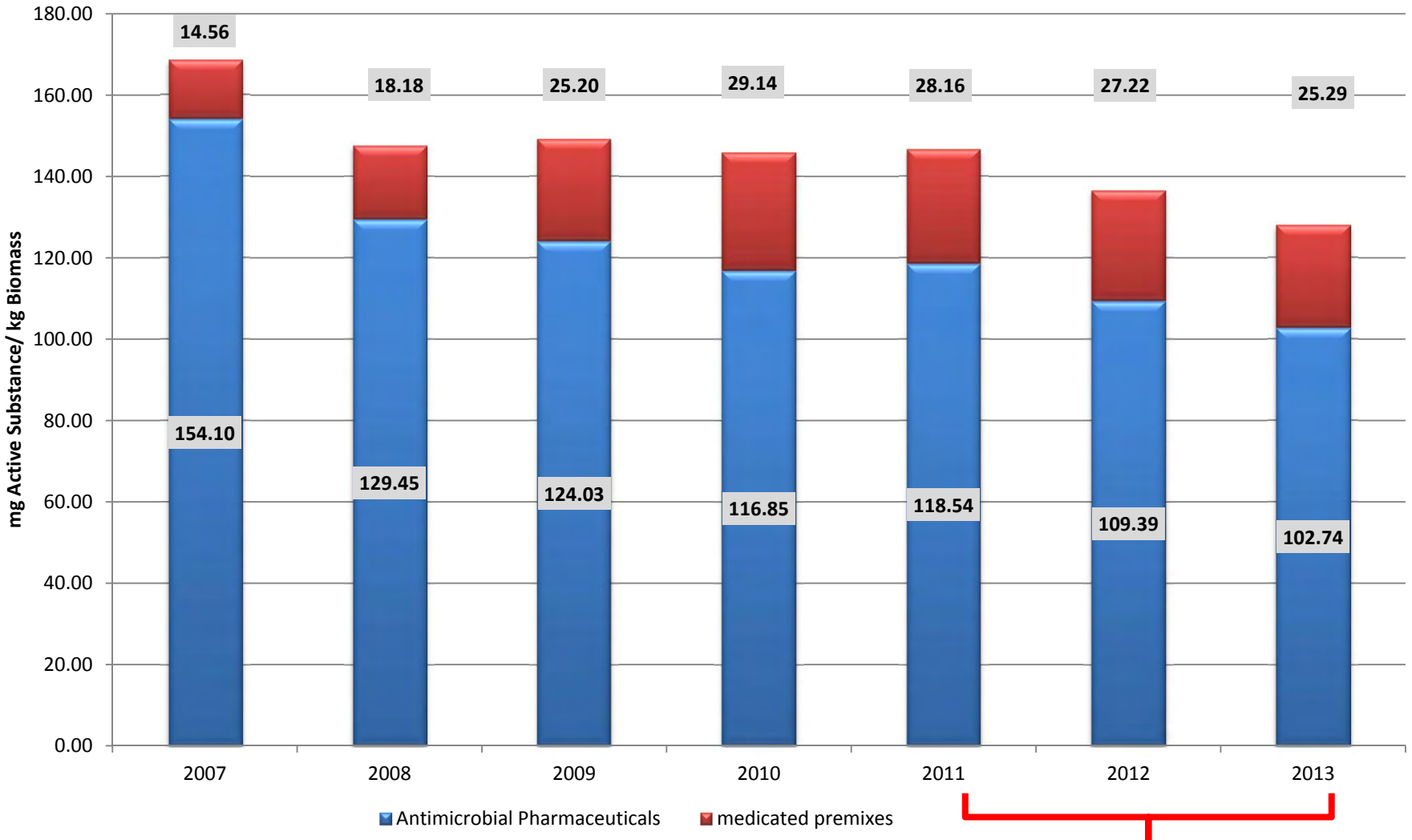
-50% d'aliments médicamenteux en moins d'ici 2017

- **BelVet-SAC:**
  une baisse de 12,7% entre 2011 et 2013
- **ESVAC : Position Belgique**



VISION 2020

Où en est on à l'heure actuelle?



Plus que la moitié des traitements aux antibiotiques
En poulet de chair sont destinés à traiter
Les problèmes de santé intestinale

Dysbiosis

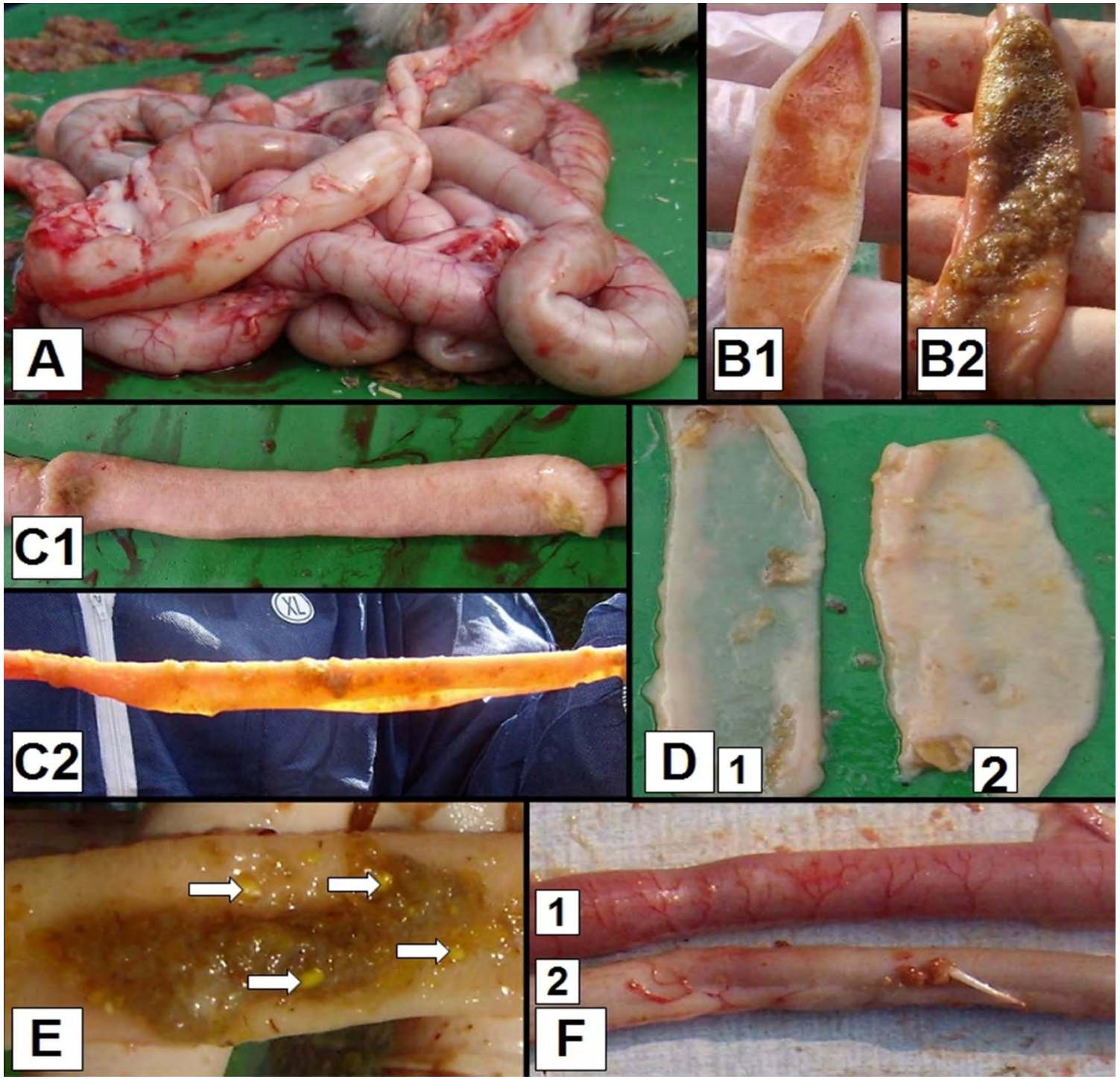
Dysbacteriosis

Feed passage syndrome

Wet litter syndrome

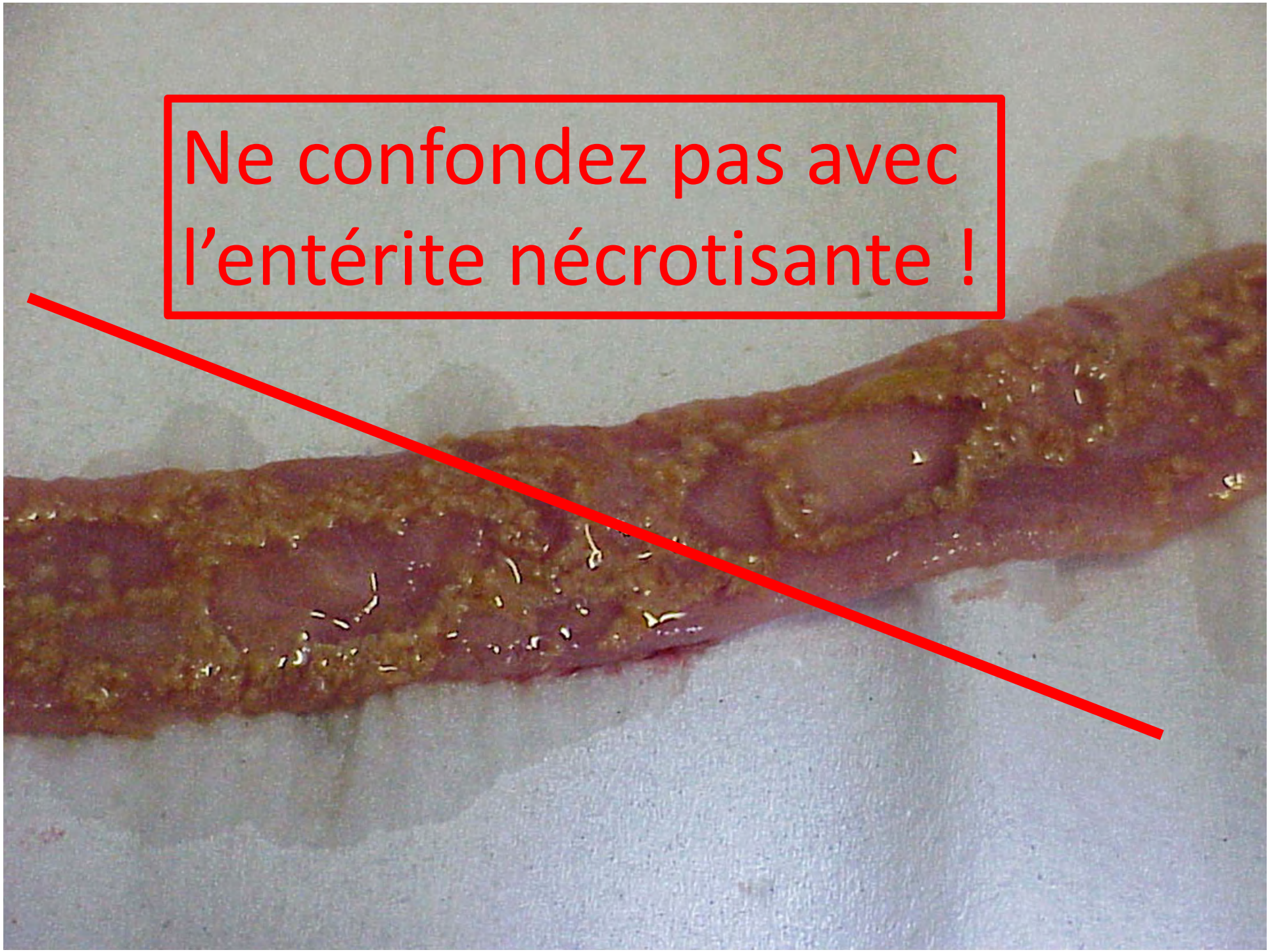
Définition ????

Cause ????



Dysbiosis Score 0-10

Teirlynck et al., Avian Pathol. 2011

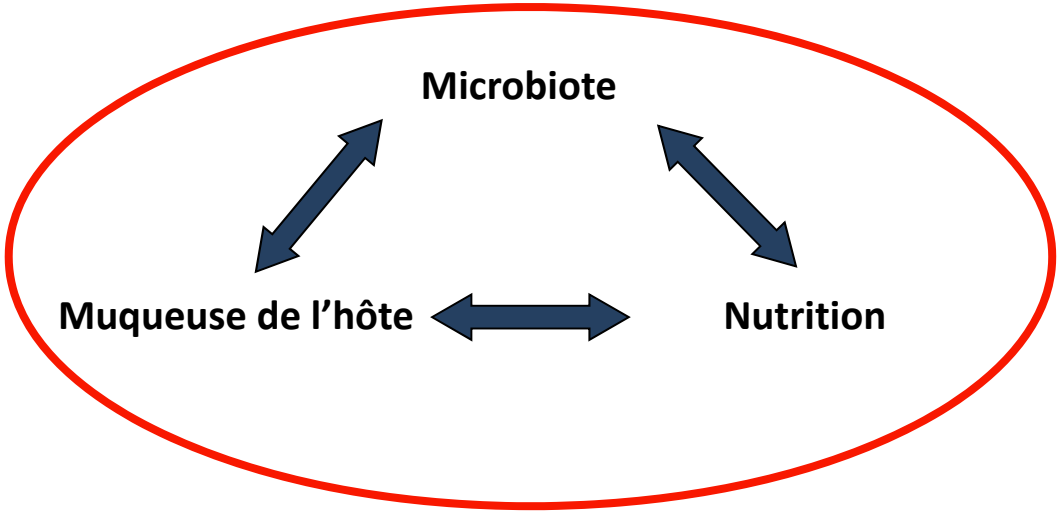

Ne confondez pas avec
l’entérite nécrotisante !

Poulets de chair

Year	Age of reaching of 1.5 kg BW, days
1925	**120**
1960	**51**
1990	**37**
2014*	**28**

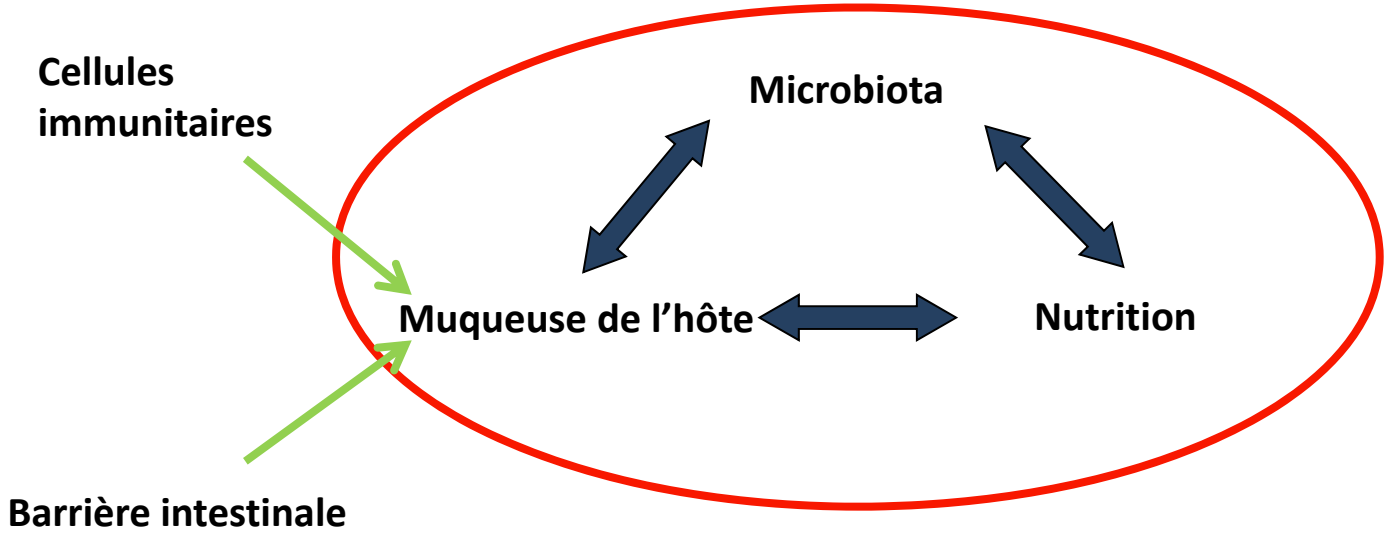
**Ross 308 Performance Objectives, 2014*

L’écosystème de l’intestin

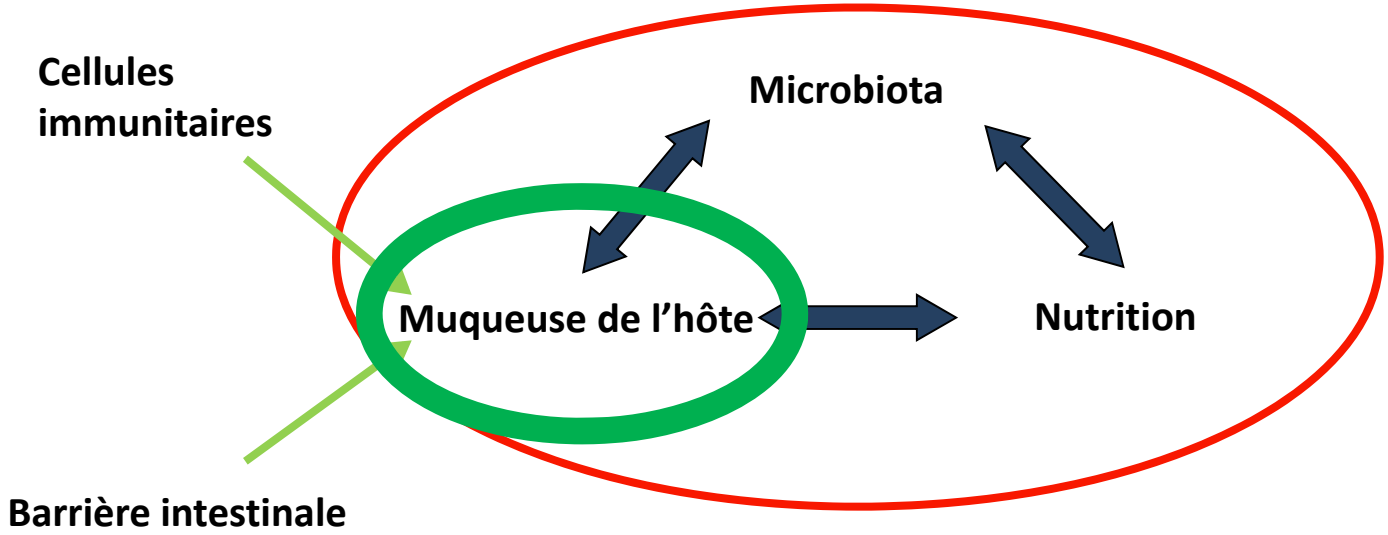


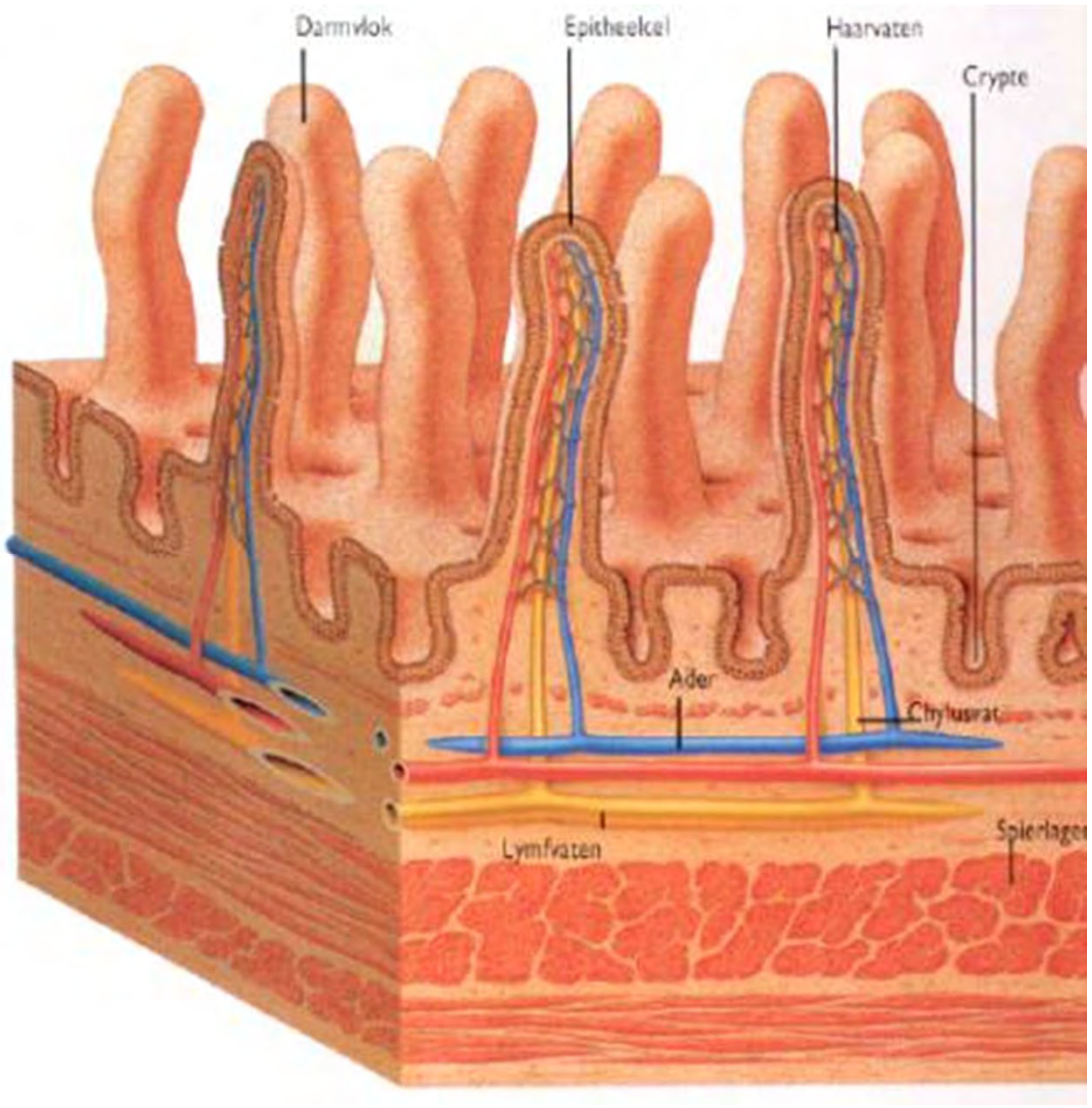
UNIVERSITEIT GENT

L’écosystème de l’intestin

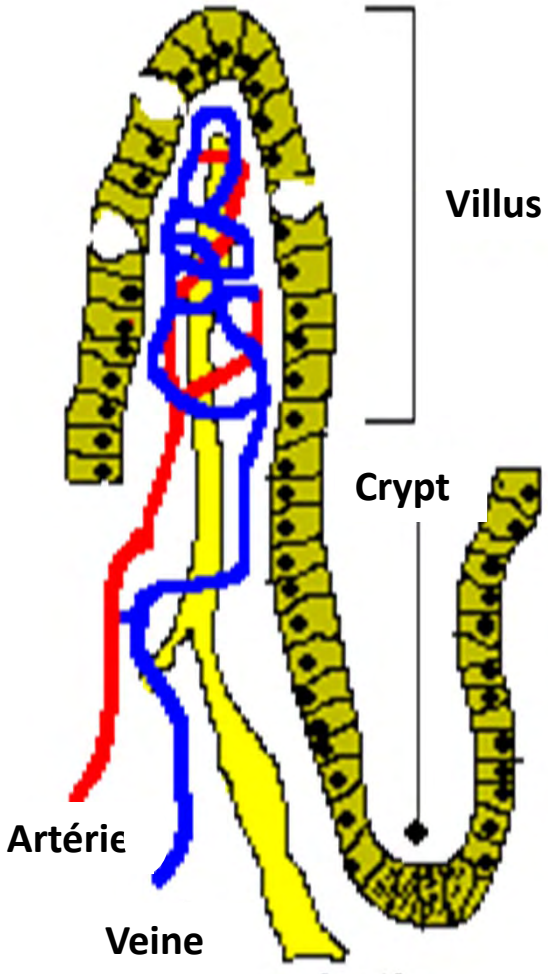


L’écosystème de l’intestin

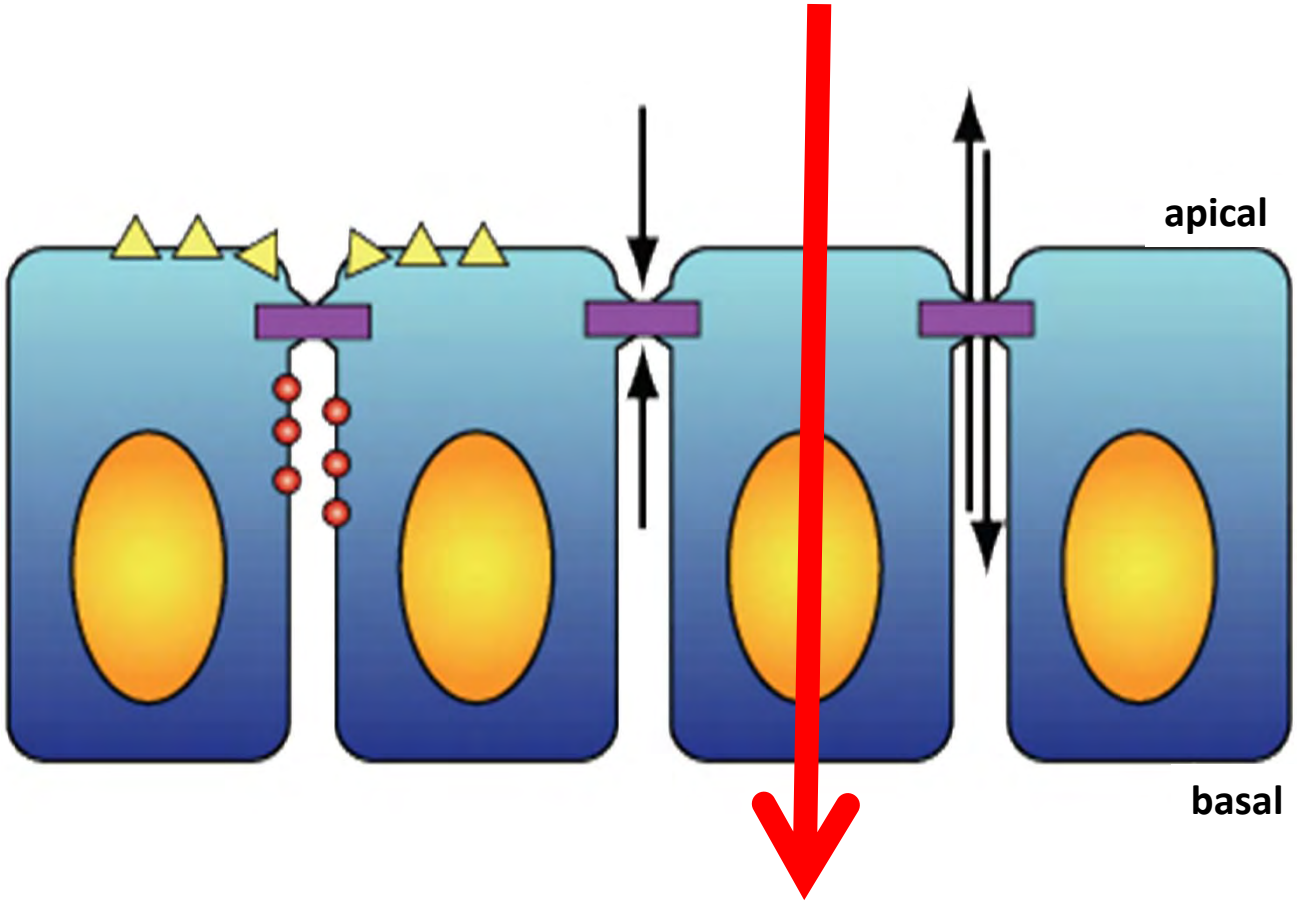




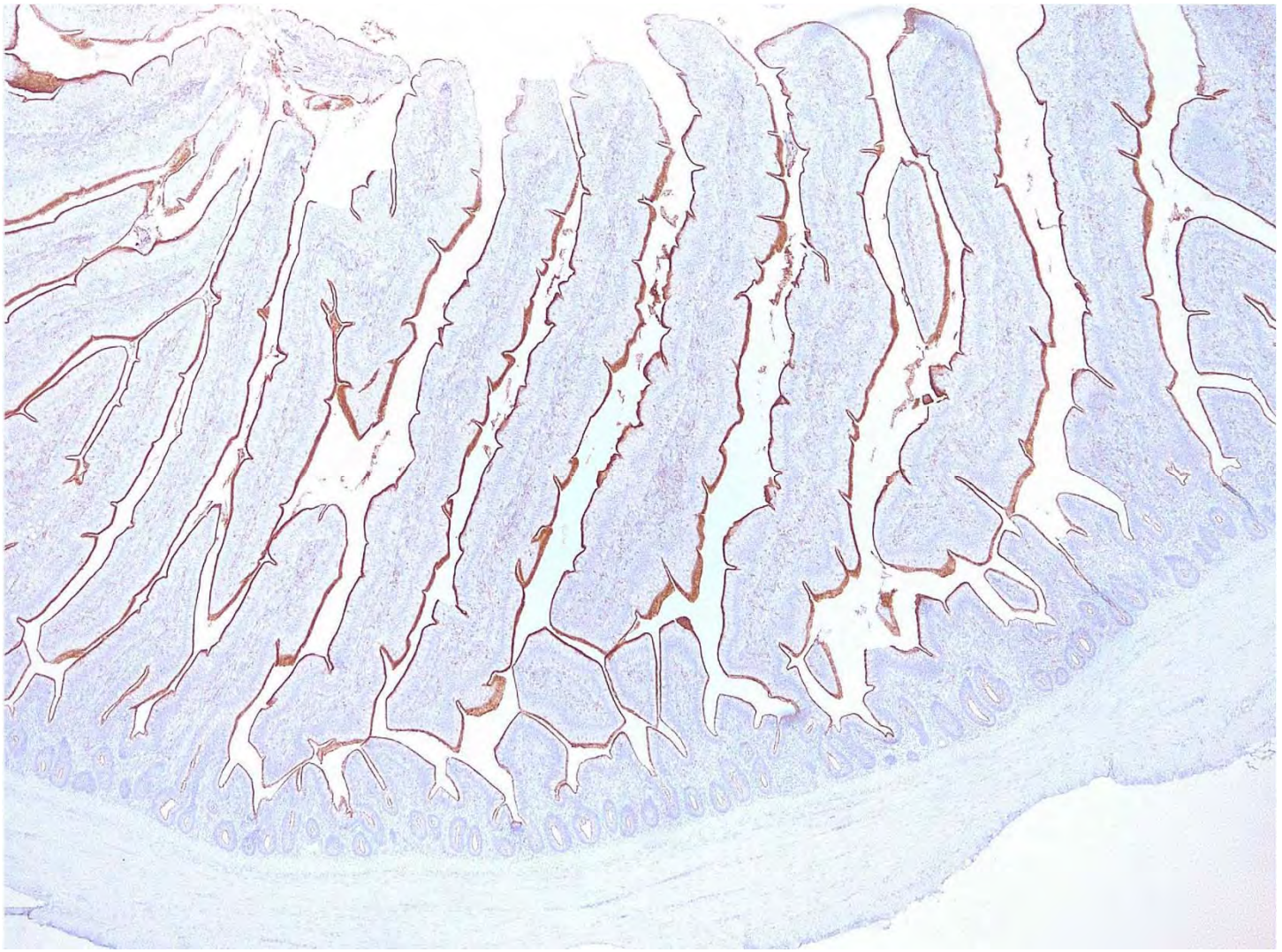
UNIVERSITEIT GENT


Villus
Crypt
Artérie
Veine
Lymphatic

Passage transcellulaire



P-gp, le MDR1 gardien du passage transcellulaire

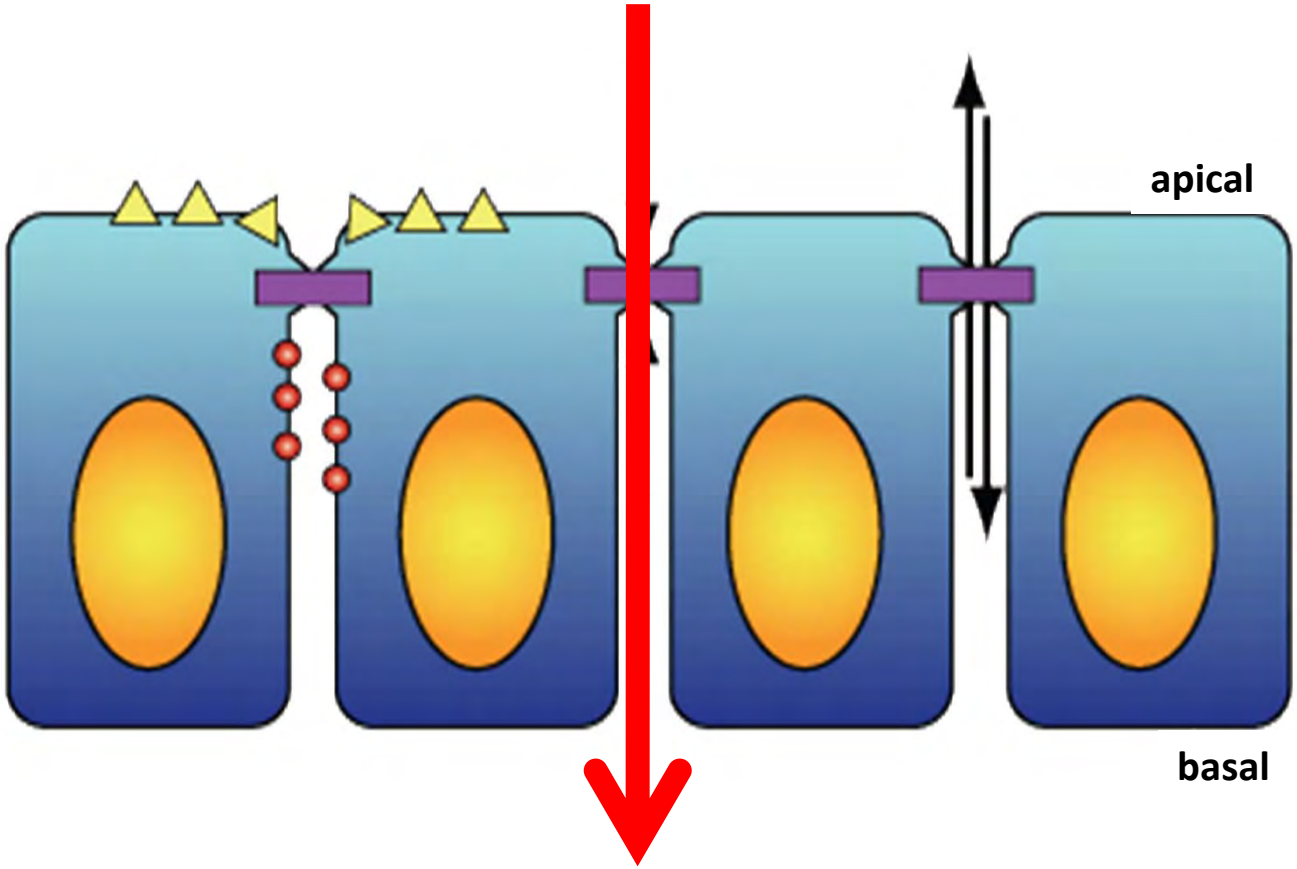


C219 immunohistochimie du P-gp au niveau des microvilosités de la membrane cellulaire apicale

P-gp knock-out mice develop spontaneous intestinal inflammation under SPF conditions.

(Banner et al., 2004)

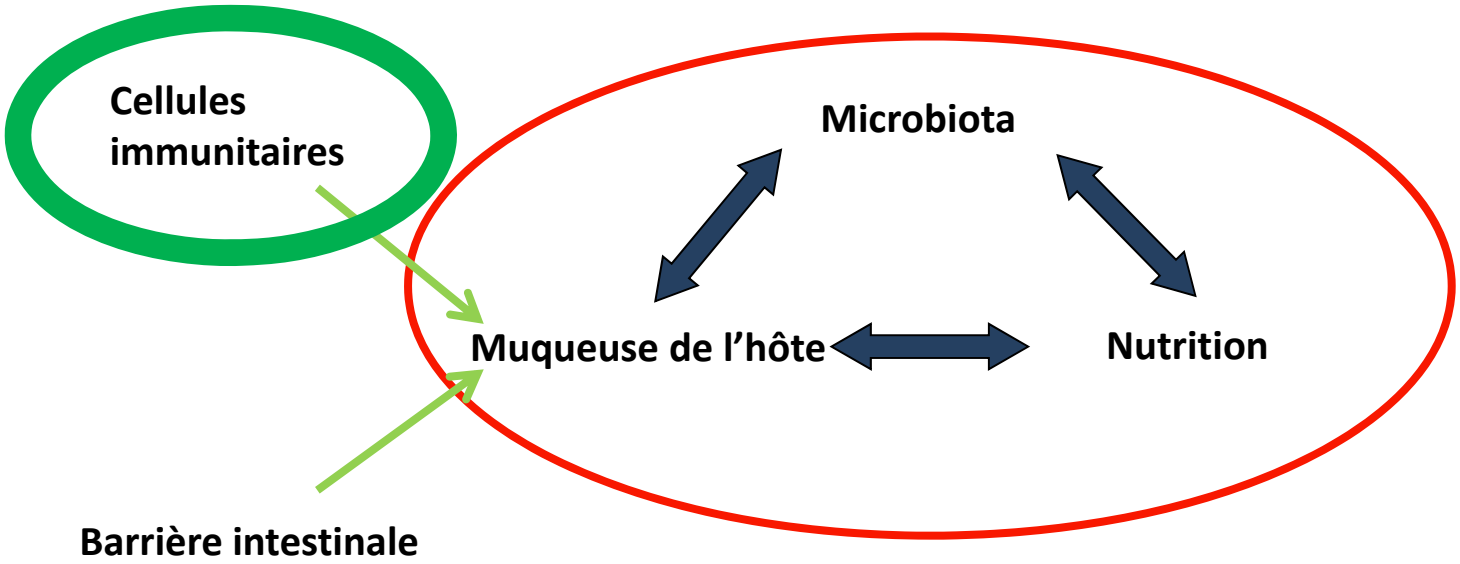
Passage paracellulaire



Facteurs nutritionels stabilisant les jonctions serrés:

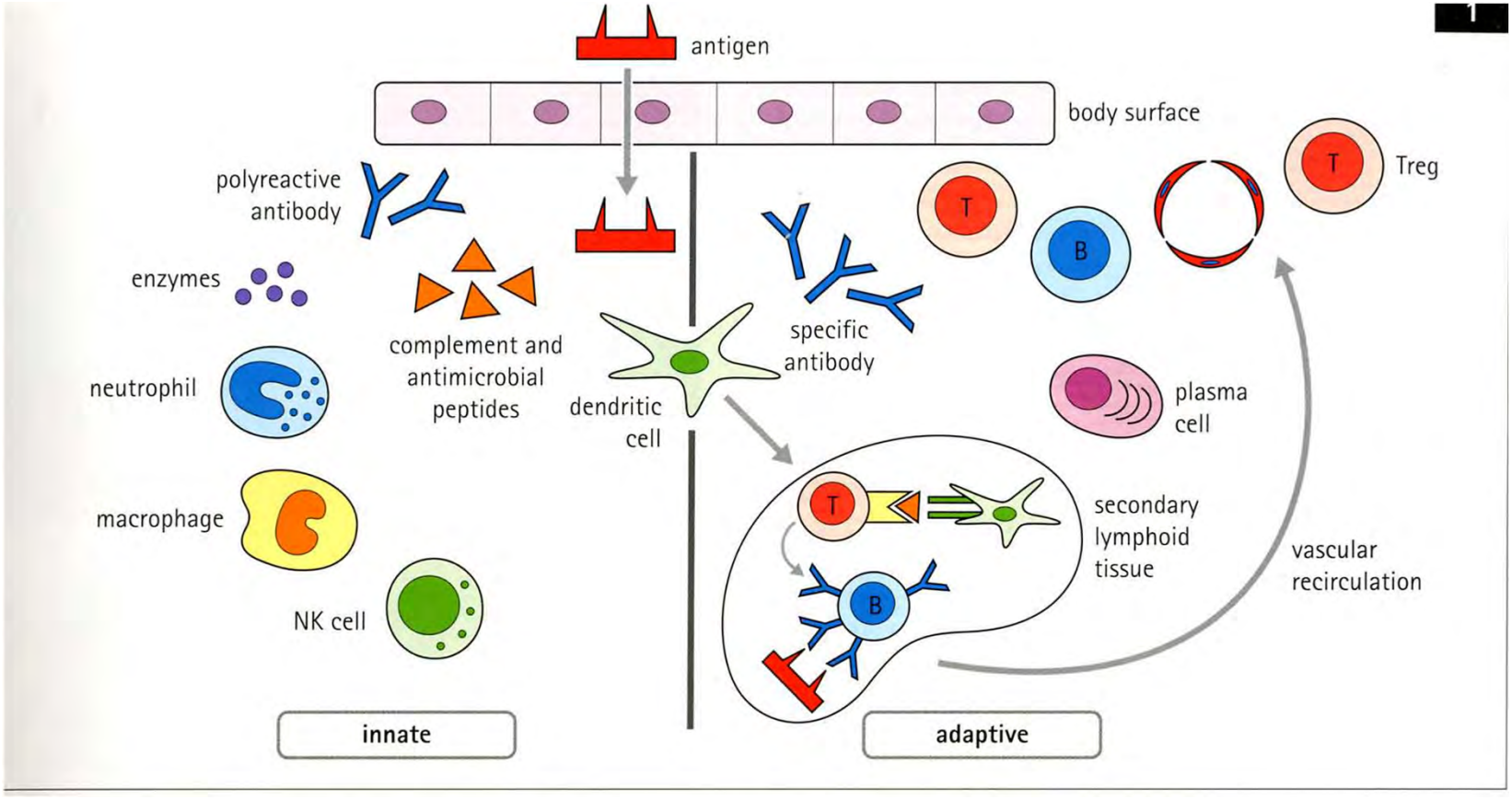
- **Zinc (Ranaldi et al., 2009)**
- **Glutamine (alanyl-glutamine) (Furst et al., 2004)**
- **PUFA (Willemsen et al., 2008)**
- **Polyphenols – flavonoids (quercetin) (Amasheh et al., 2009)**
- **Butyrate**

L’écosystème de l’intestin



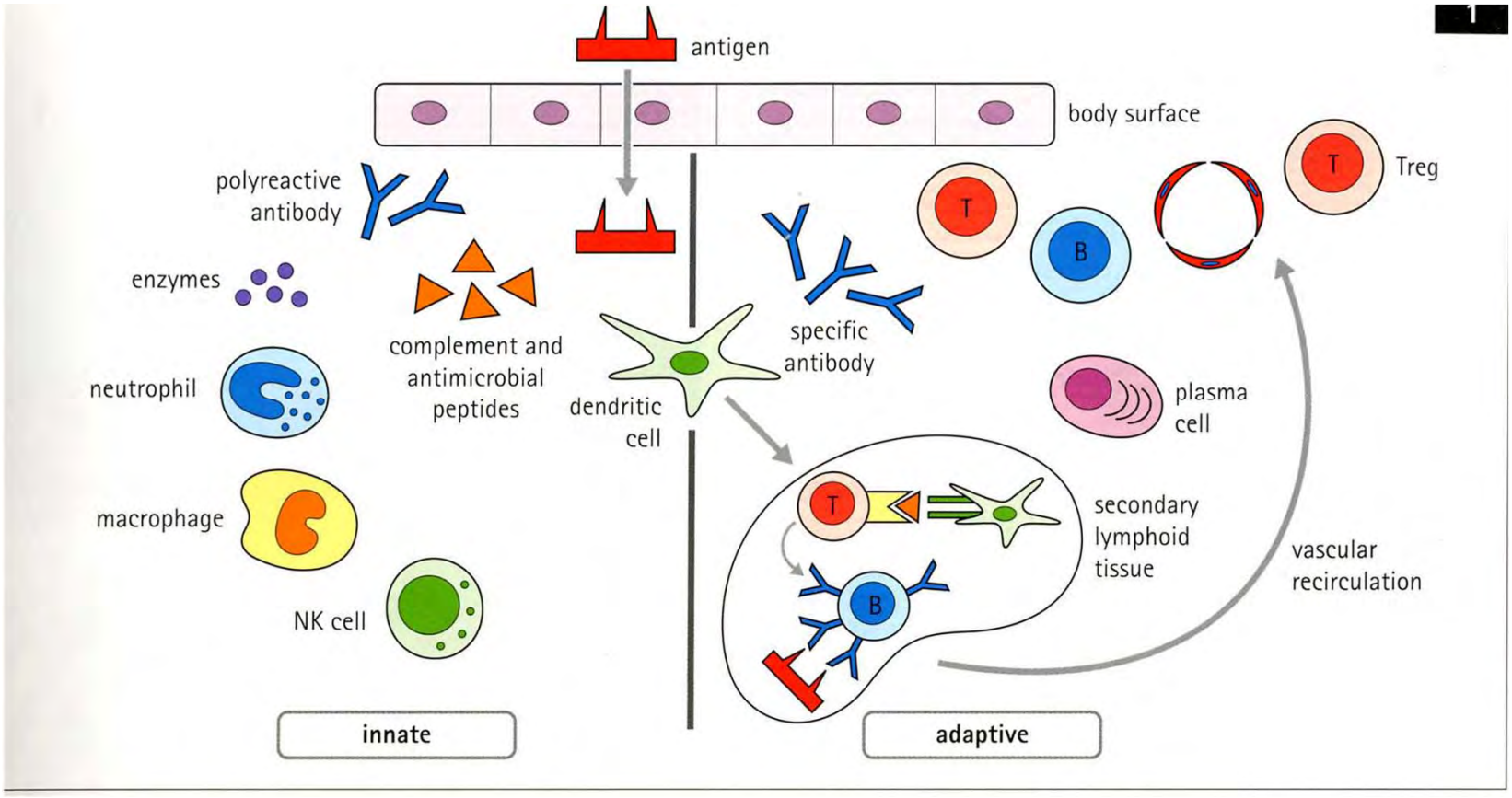
The gastrointestinal tract is the largest immunologic organ in the body.

(Chahine and Bahna, 2010)



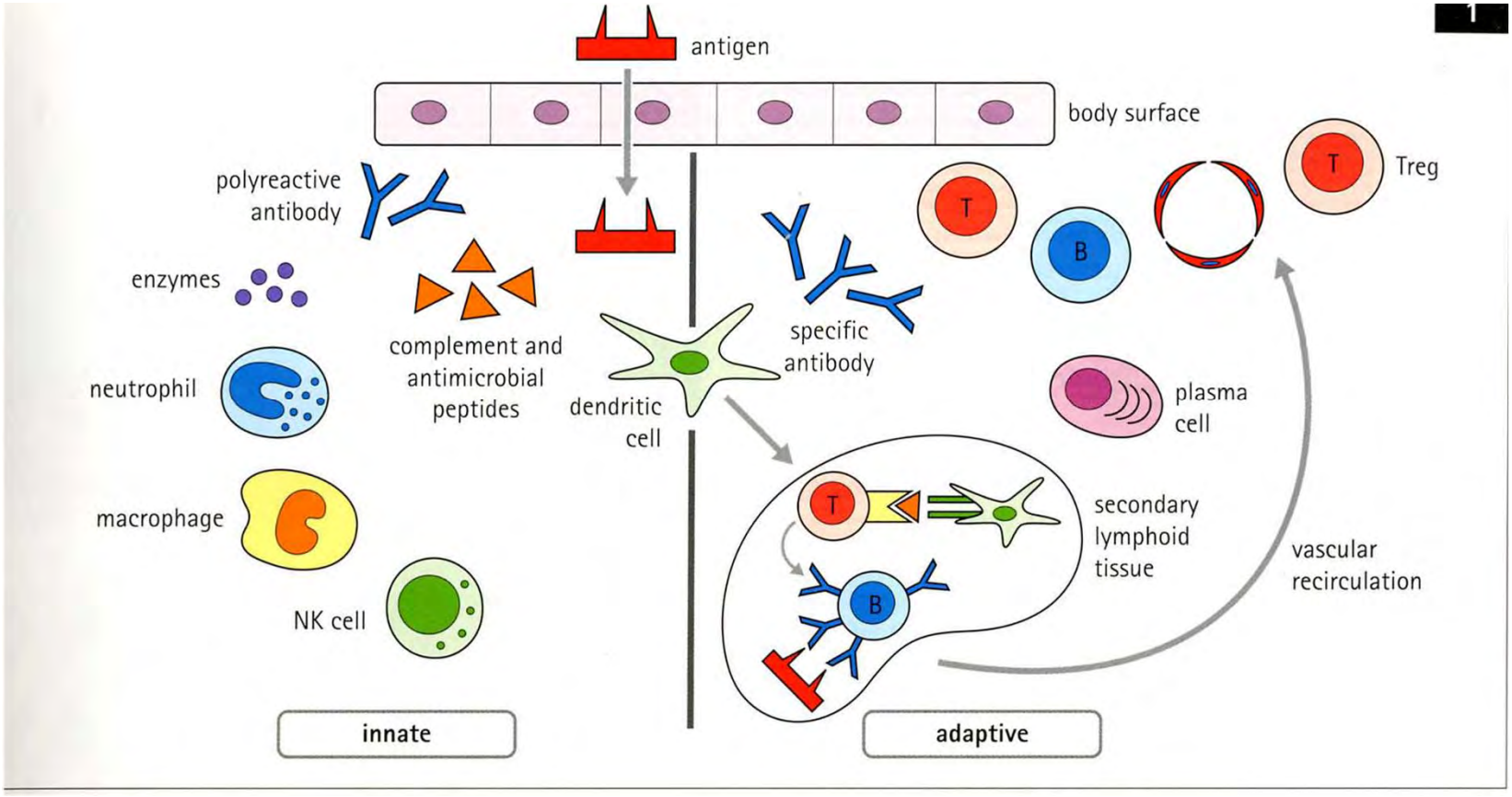
Day and Schulz, 2010

Antigènes = immunogènes = déclanchant une réponse immunitaire= <u>protéines</u>



Day and Schulz, 2010

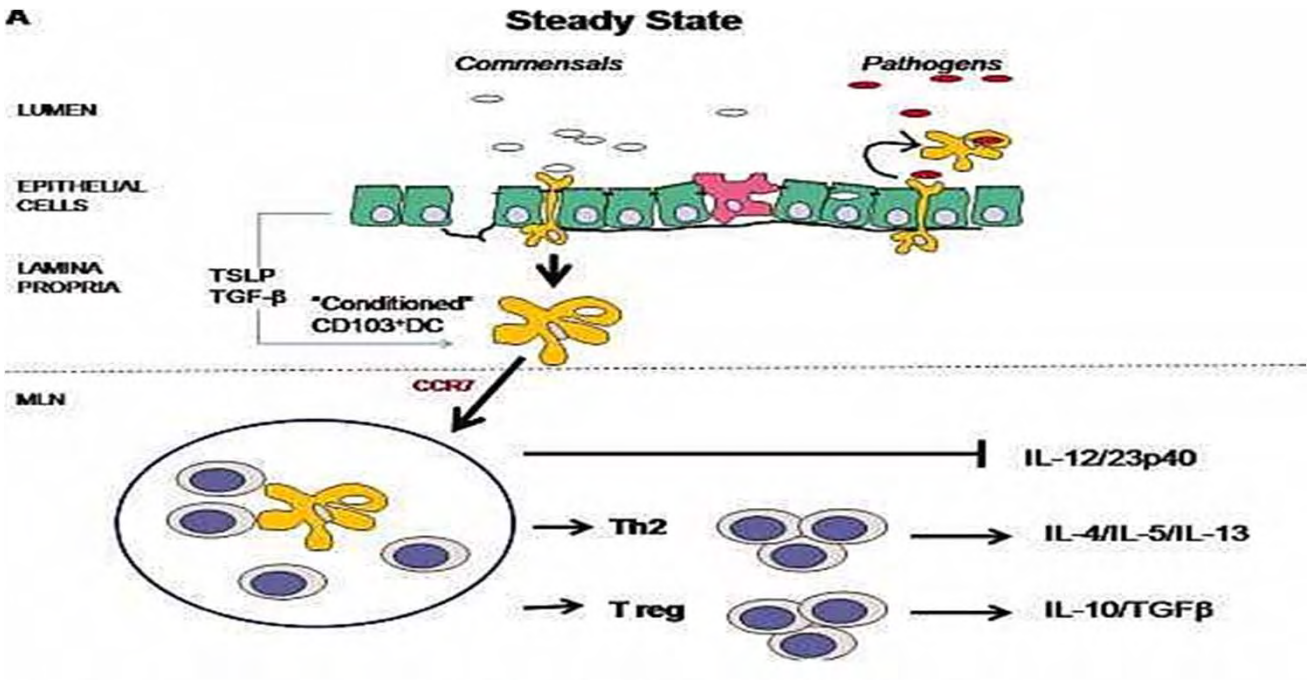
Réponse immunitaire innée= inflammation



Day and Schulz, 2010

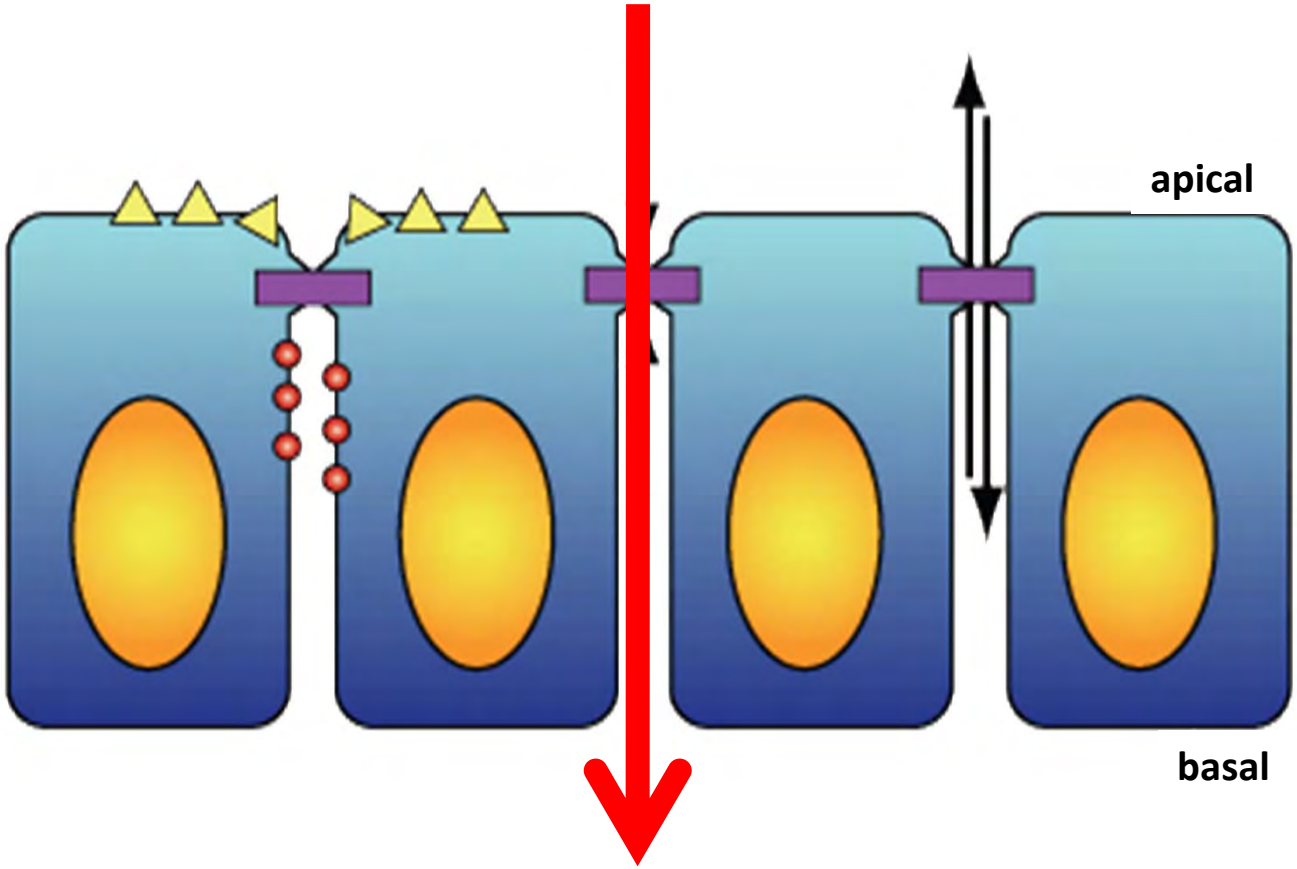
Réponse immunitaire innée= inflammation

Inflammation = fientes humides, litière humide



Tolérance orale

Passage paracellulaire



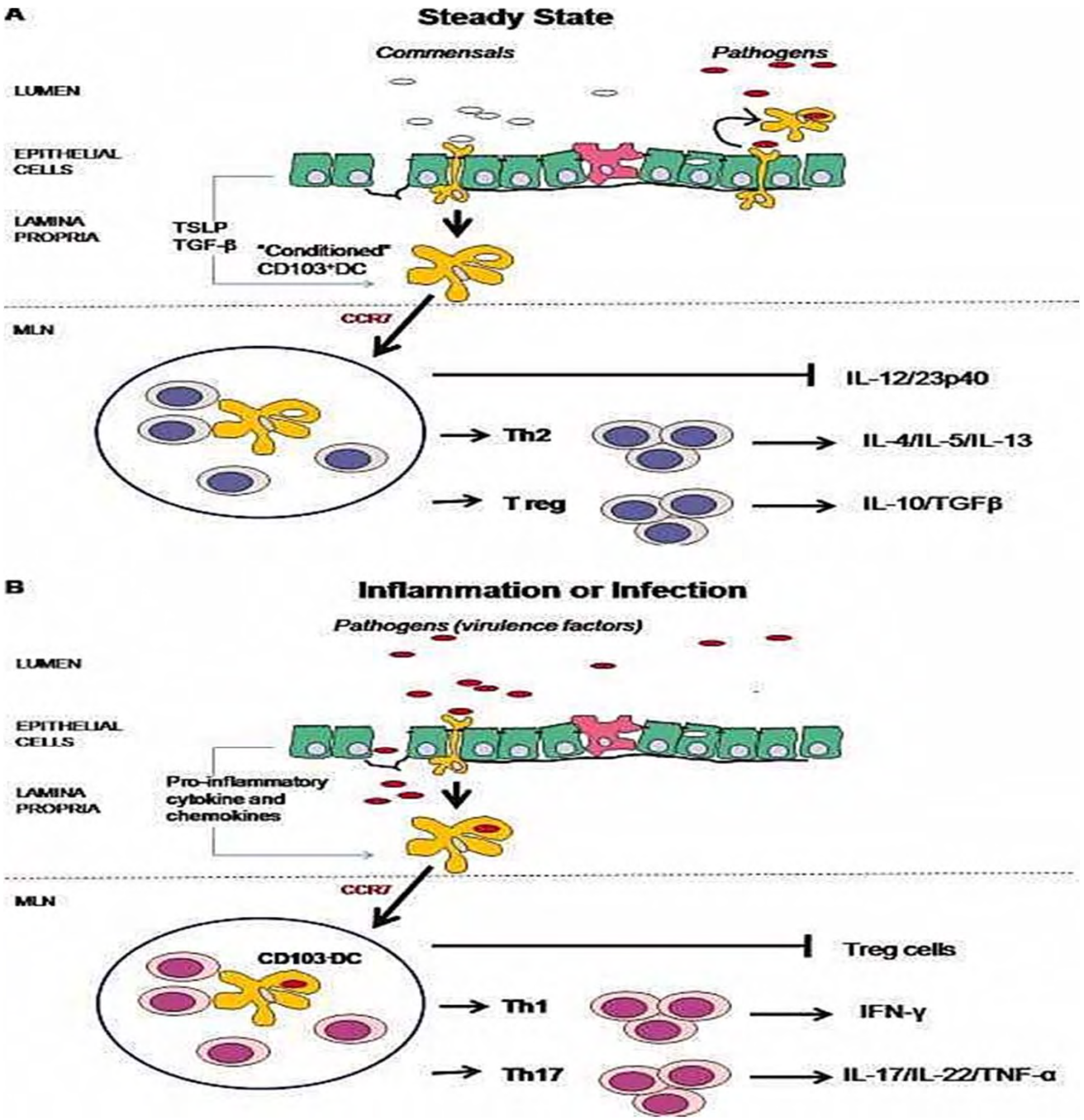
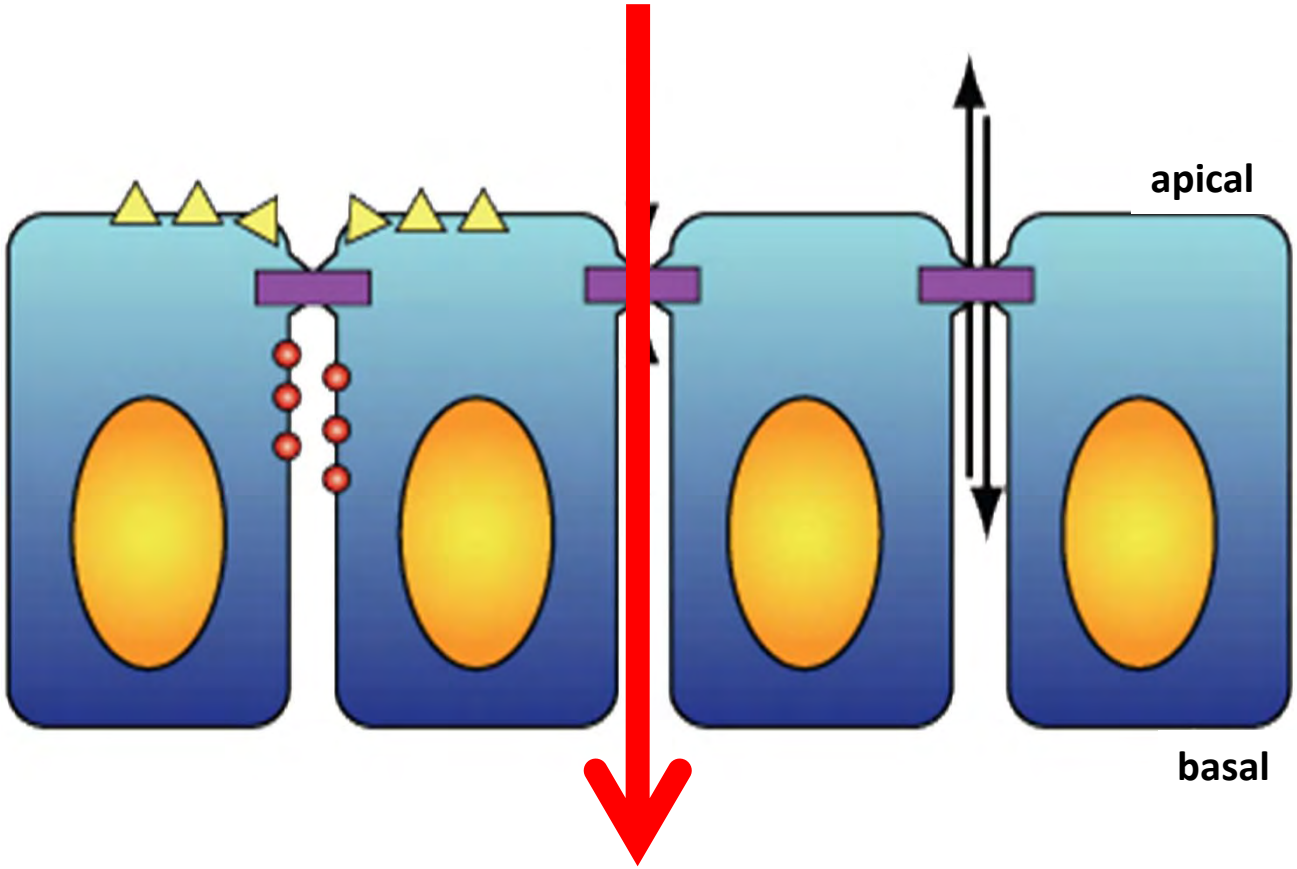

A
Steady State
Commensals
Pathogens
LUMEN
EPITHELIAL CELLS
LAMINA PROPRIA
TSLP
TGF-β
"Conditioned" CD103+DC
CCR7
MLN
IL-12/23p40
Th2
IL-4/IL-5/IL-13
T reg
IL-10/TGFβ
B
Inflammation or Infection
Pathogens (virulence factors)
LUMEN
EPITHELIAL CELLS
LAMINA PROPRIA
Pro-inflammatory cytokine and chemokines
CCR7
MLN
CD103-DC
Treg cells
Th1
IFN-γ
Th17
IL-17/IL-22/TNF-α

Table 1 Main enteric pathogens and /or toxins that modify epithelial TJs and mechanisms used by these pathogens at the TJ level

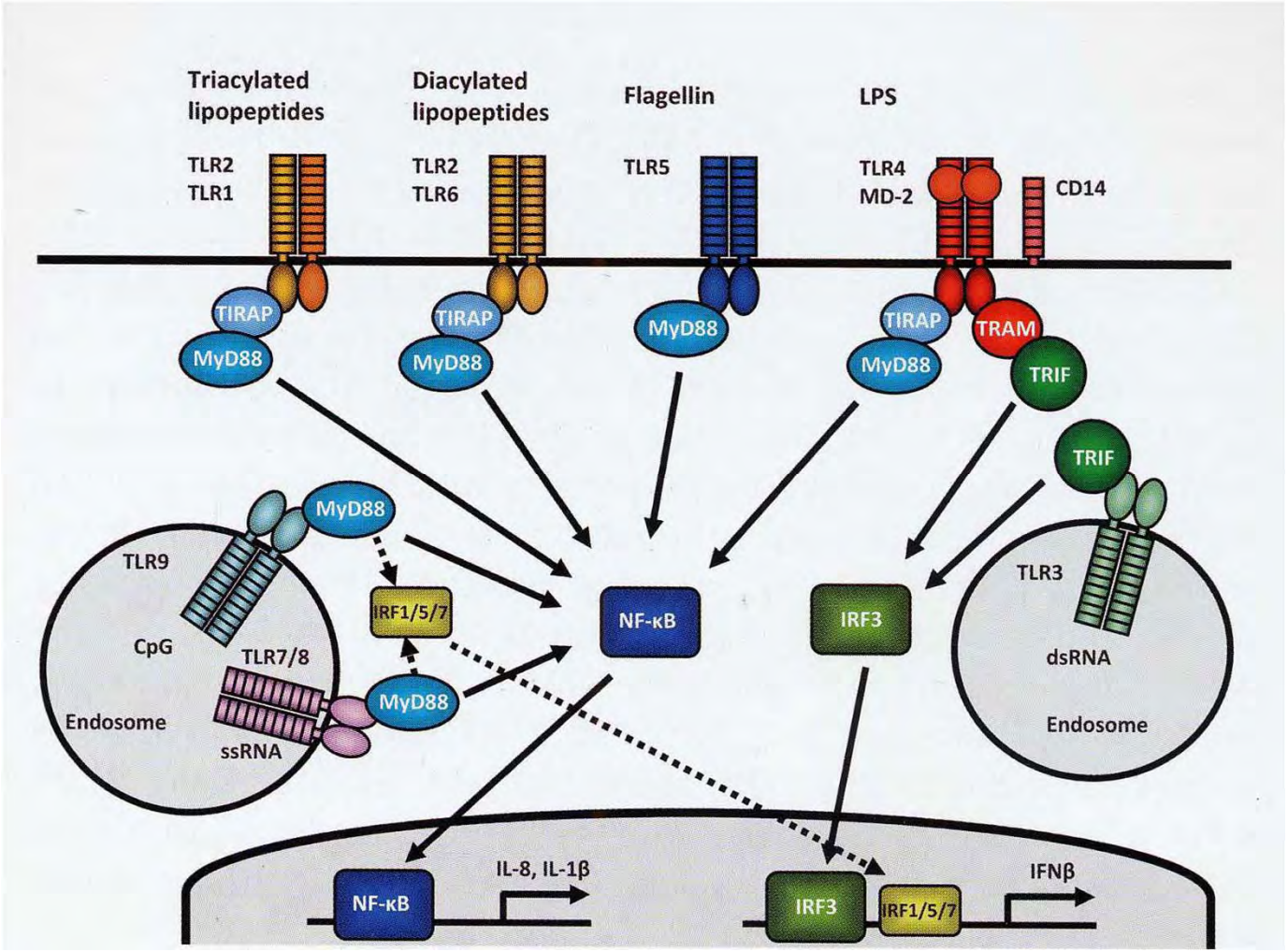
Enteric Pathogens	*Mechanisms*
S. typhimurium *E. coli* (EPEC, EHEC,DAEC) *S. flexneri* *H. pylori* *Y. pseudotuberculosis*	Inducing neutrophil transepithelial migration
C. difficile (toxins A and B) *C. botulinum* (toxins C2 and C3) *C. sordelli* *C. perfringens* (toxin CPE) *L. monocytogenes* *V. cholerae* (toxins RTX and ZOT) *B. fragilis* (toxin bacteroides) *E. coli* (toxin CNF-1)	Remodeling of actin cytoskeleton
E. coli (EPEC, EHEC) *S. flexneri* *H. pylori* (toxin Vac A)	Activation of cellular signal transduction
L. monocytogenes *B. fragilis* *C. difficile* (toxins A) *C. perfringens* (enterotoxin) *S. flexneri* *E. coli* (DAEC)	Modification of TJ proteins

(Hofman, 2003)

Passage paracellulaire

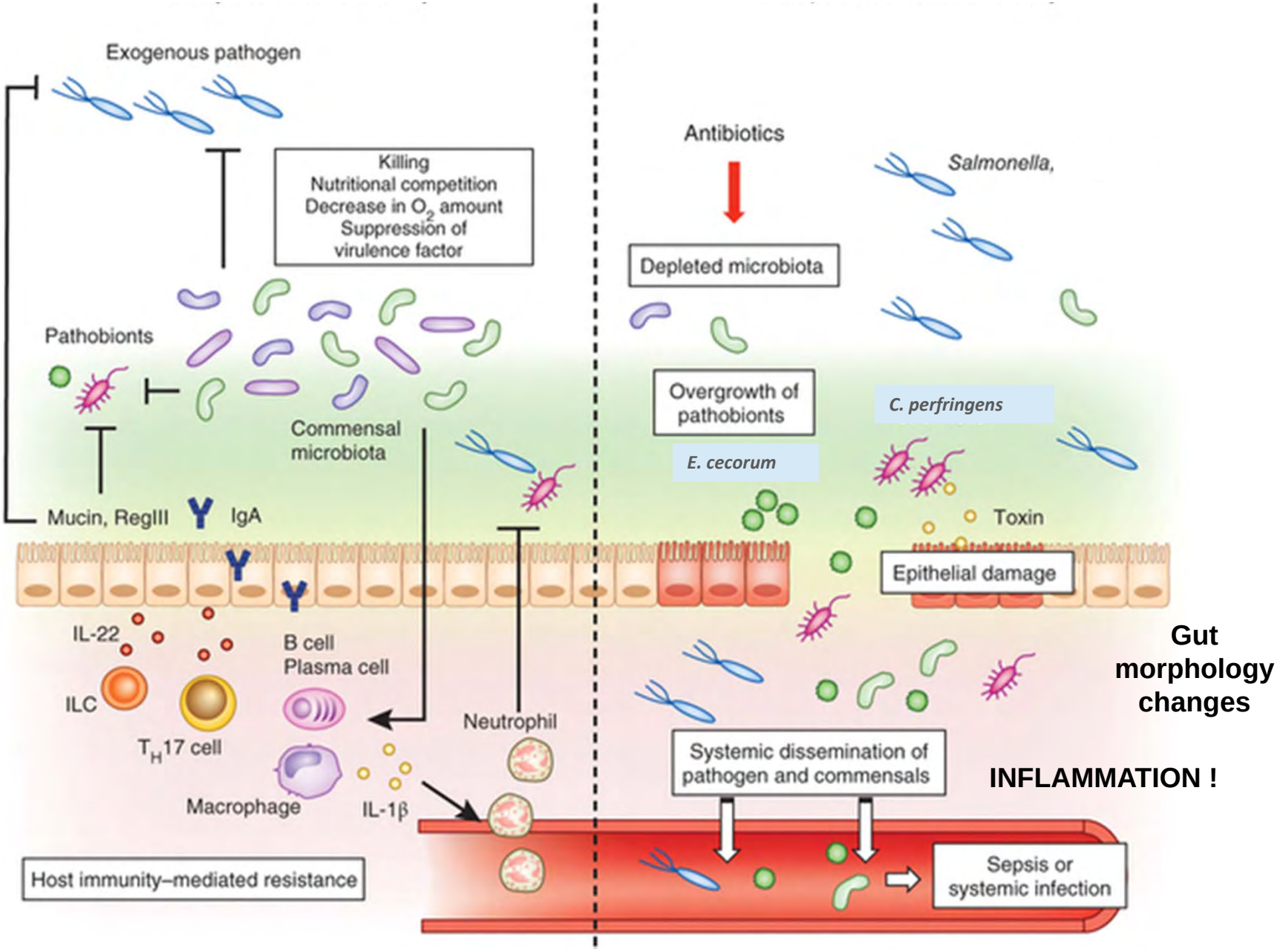


MAMPs and PRRs: Triggers of the innate (inflammatory) immune response



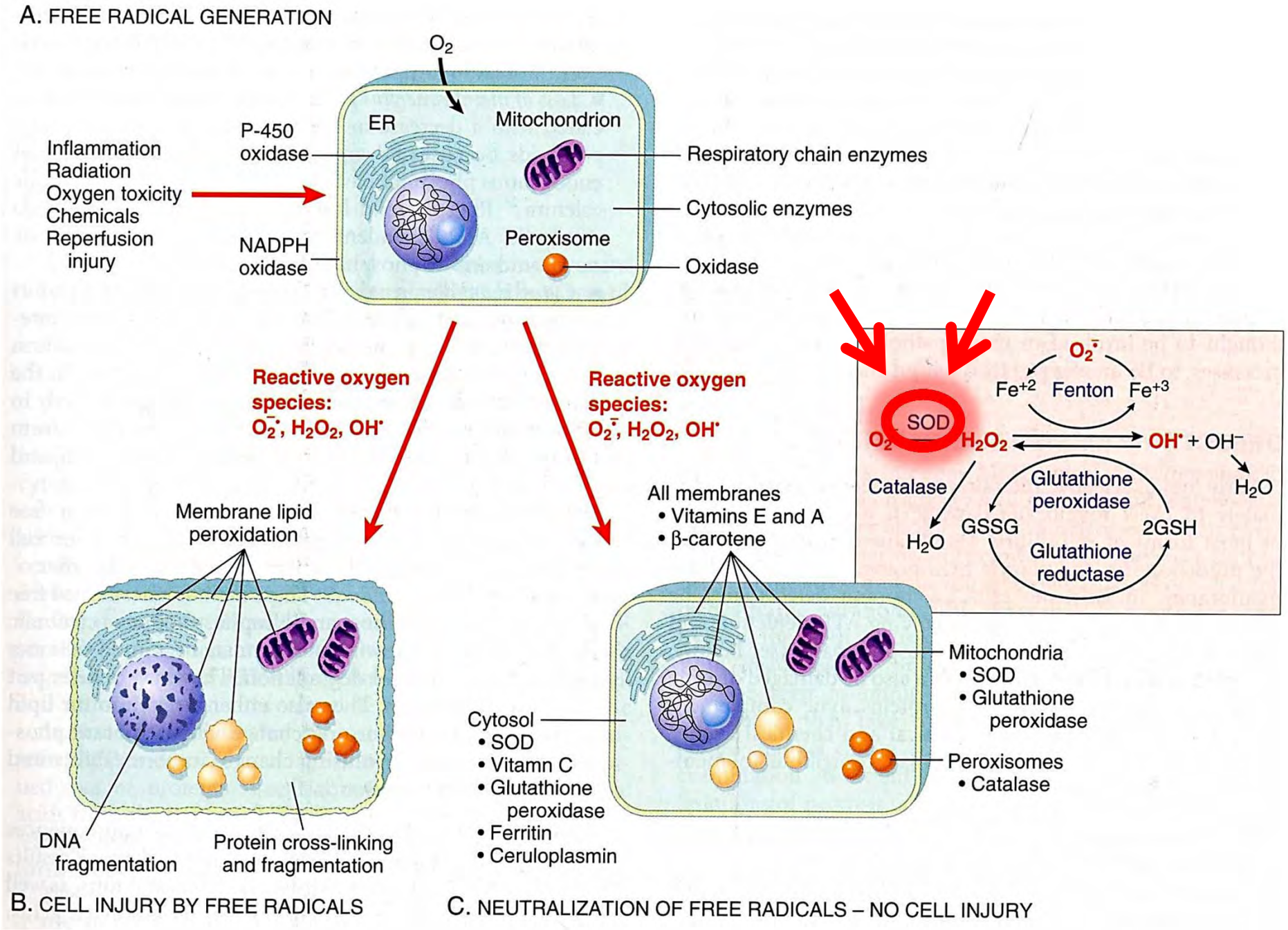
Situation normale

Dysbactériose

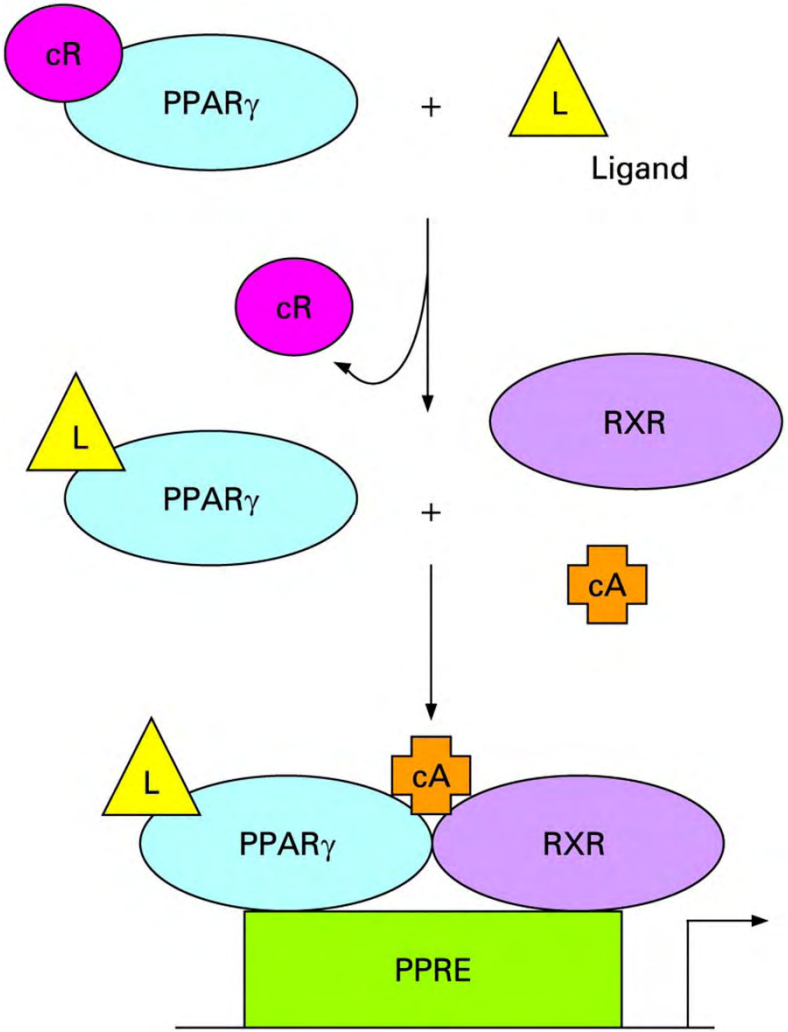


Gut morphology changes

INFLAMMATION !


A. FREE RADICAL GENERATION
O_2
ER
Mitochondrion
P-450 oxidase
Inflammation
Radiation
Oxygen toxicity
Chemicals
Reperfusion injury
NADPH oxidase
Respiratory chain enzymes
Cytosolic enzymes
Peroxisome
Oxidase
Reactive oxygen species:
$O_2^{-\bullet}$, H_2O_2, $OH^\bullet$
Reactive oxygen species:
$O_2^{-\bullet}$, H_2O_2, $OH^\bullet$
$O_2^{-\bullet}$
Fe^{+2}
Fenton
Fe^{+3}
SOD
O_2
H_2O_2
$OH^\bullet$ + OH^-
Catalase
H_2O
Glutathione peroxidase
GSSG
2GSH
Glutathione reductase
H_2O
Membrane lipid peroxidation
DNA fragmentation
Protein cross-linking and fragmentation
B. CELL INJURY BY FREE RADICALS
All membranes
• Vitamins E and A
• β-carotene
Mitochondria
• SOD
• Glutathione peroxidase
Peroxisomes
• Catalase
Cytosol
• SOD
• Vitamn C
• Glutathione peroxidase
• Ferritin
• Ceruloplasmin
C. NEUTRALIZATION OF FREE RADICALS – NO CELL INJURY

Peroxisome proliferator-activated receptor gamma (PPARγ) interagit avec les protéines nucléaires qui agissent comme co-represseurs (cR) et co-activateurs (cA)



Marion-Letellier R et al. Gut 2009;58:586-593

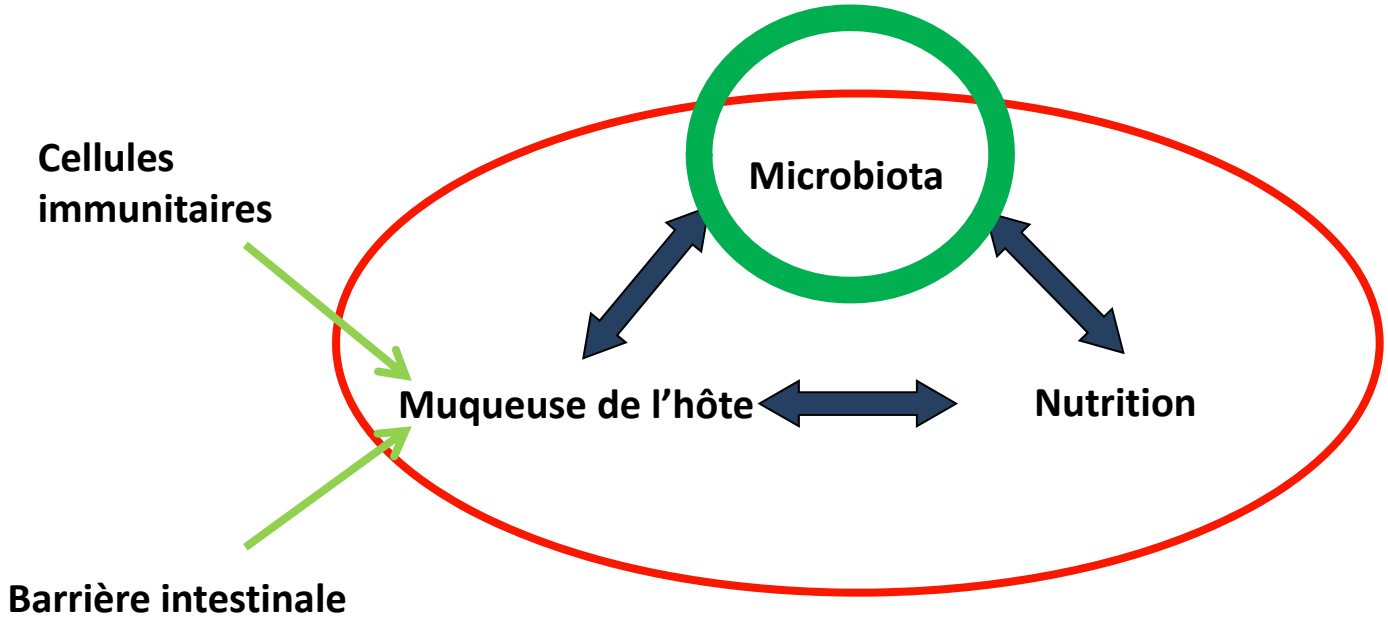
Table 1 Demonstrated anti-inflammatory effects of nutrients through peroxisome proliferator-activated receptor gamma (PPARγ) in intestine

Nutrient	Models
α-Linolenic acid, docosahexaenoic acid	Intestinal epithelial cells[29]
Eicosapentaenoic acid	Intestinal epithelial cells[29]
Conjugated linoleic acid	Intestinal epithelial cells,[30 38 40] dextran sodium sulfate colitis model[5 42]
15-Deoxy-Δ12,14-prostaglandin J2	Intestinal epithelial cells,[6 48] colitis,[6 49] immobilisation-induced stress model[50]
15-Hydroxyeicosatetraenoic acid, 13-Hydroxyoctadecadienoic acid, 13-Oxooctadecadienoic acid,	Intestinal epithelial cells[44 45]
Butyrate	Intestinal epithelial cells[24–26]
Glutamine	Ischaemia–reperfusion rats[54]
Curcumin	TNBS-induced colitis,[59 60 62] sepsis[63]
Capsaicin	Intestinal epithelial cells[65]
Resveratrol	Intestinal epithelial cells[71]
Vitamin E	Intestinal epithelial cells[72]

TNBS, 2,4,6-trinitrobenzene sulfonic acid.

(Marion-Letellier et al., 2009)

L’écosystème de l’intestin



It is estimated that the human microbiota contains as many as 10^{14} bacterial cells, a number that is 10 times greater than the number of human cells present in our bodies.

(Sekirov et al., 2010)

Microbes dans le tube digestif

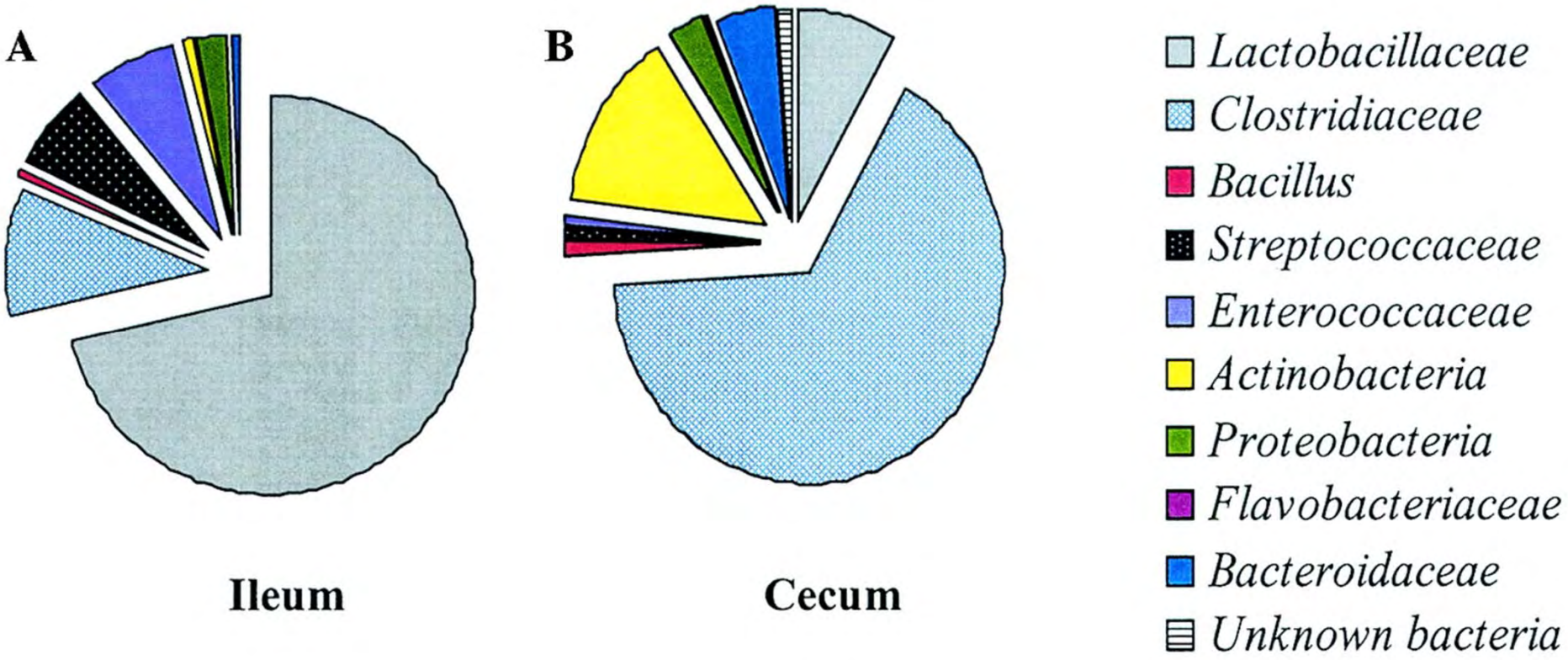
1) Culture sur boites de Pétri

2) Séquençage du gène codant pour 16S r-RNA

3) Q-PCR utlisant class/order/family specific primers

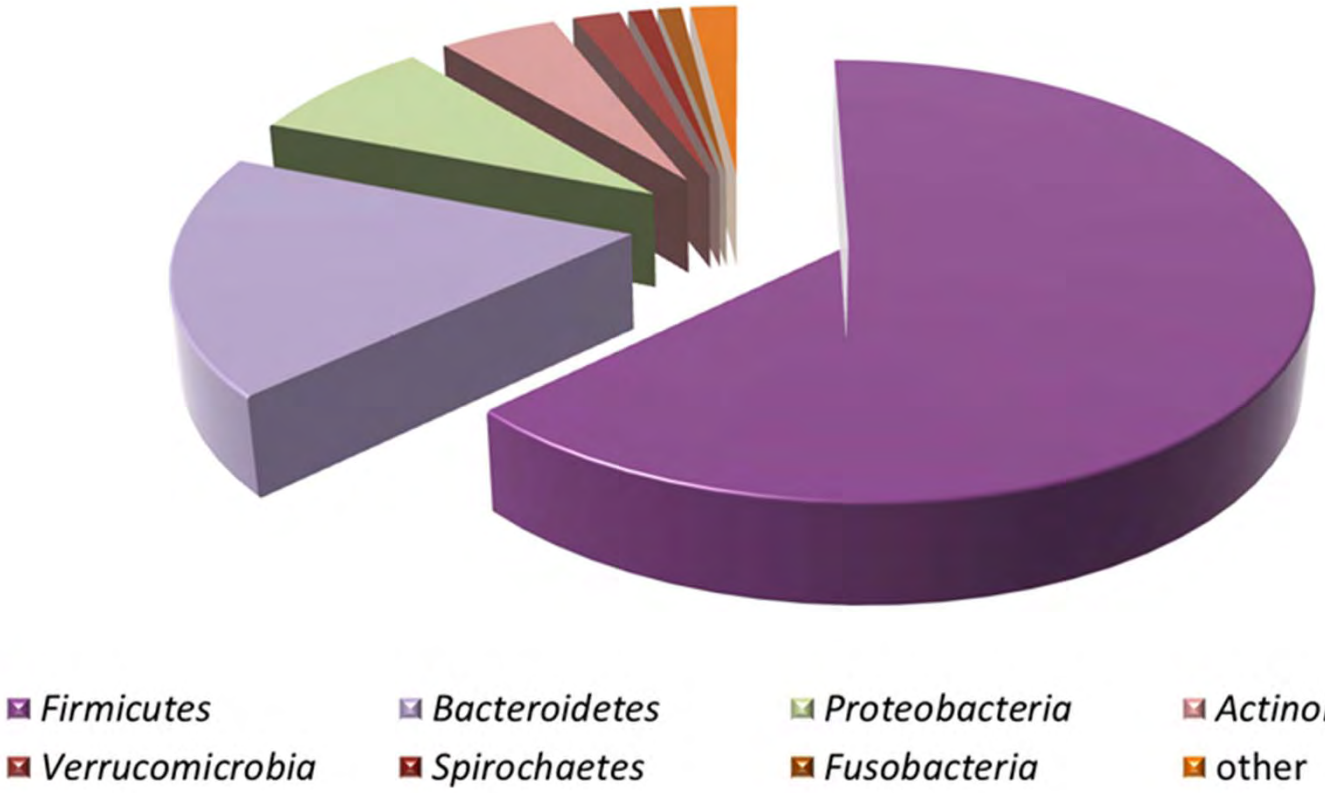
4) Q-PCR utlisant des primers spécifiques pour certaines fonctions

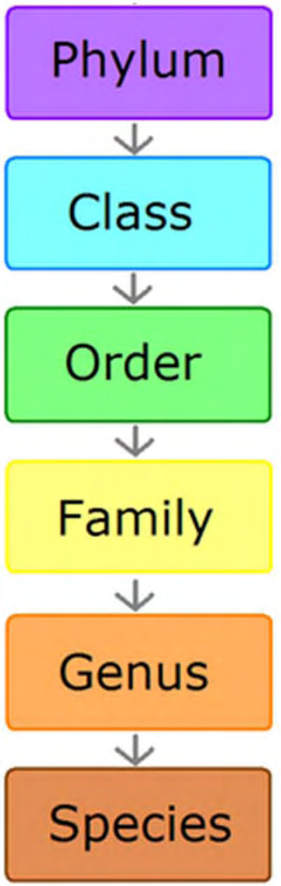
Composition du microbiote dans l' iléon et les Ceca du poulet



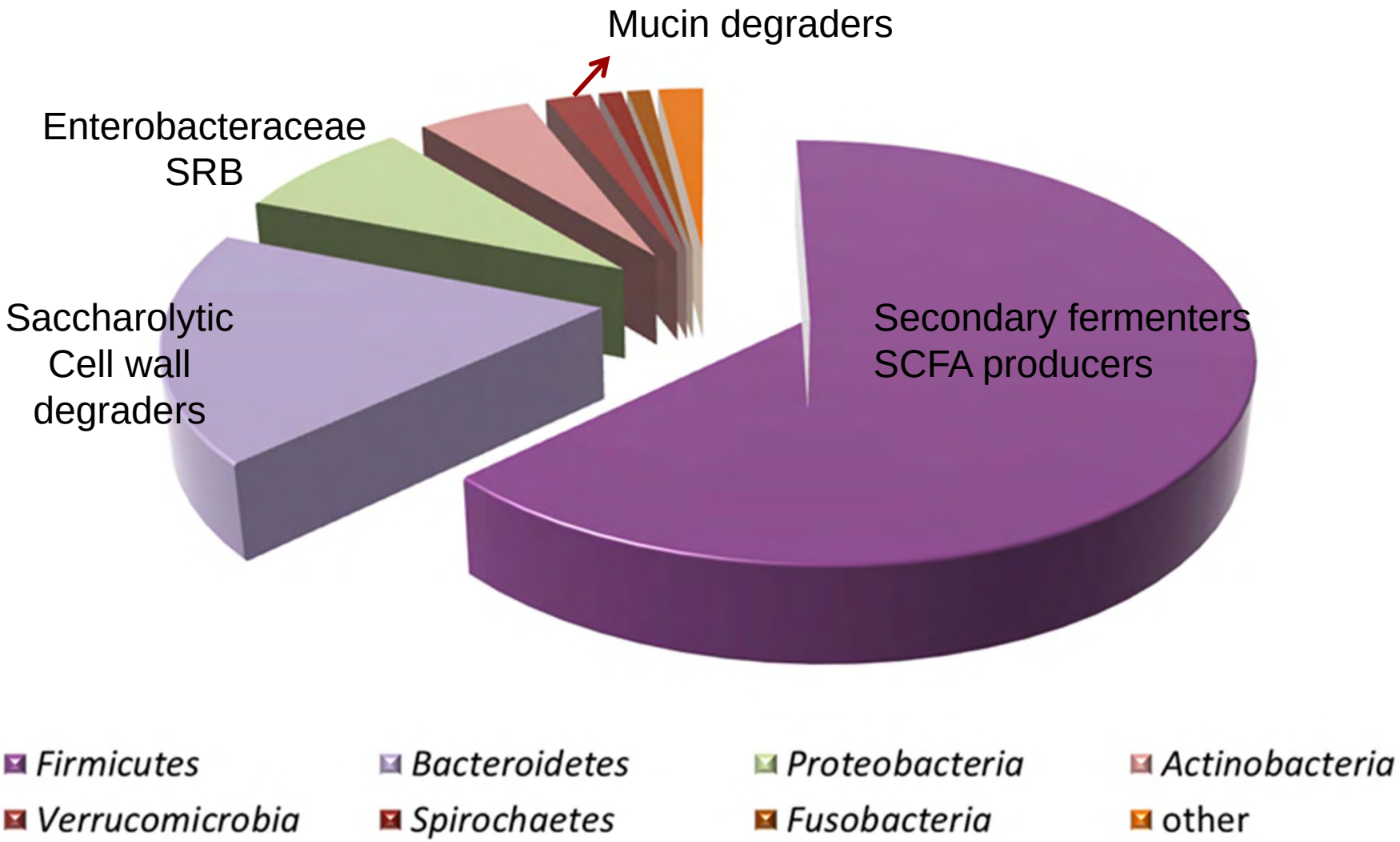
(Lu et al., 2003)

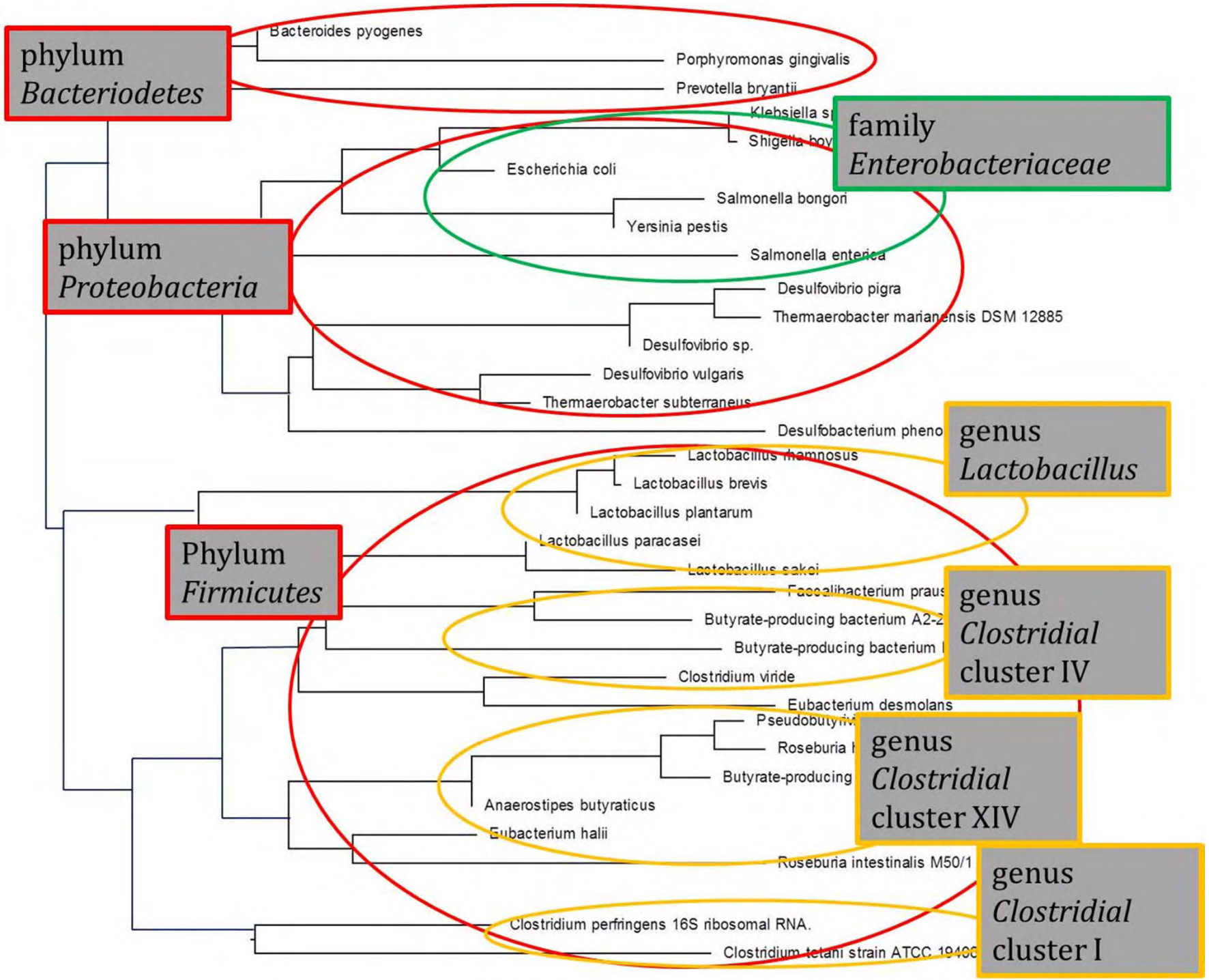
Le microbiote intestinal du poulet

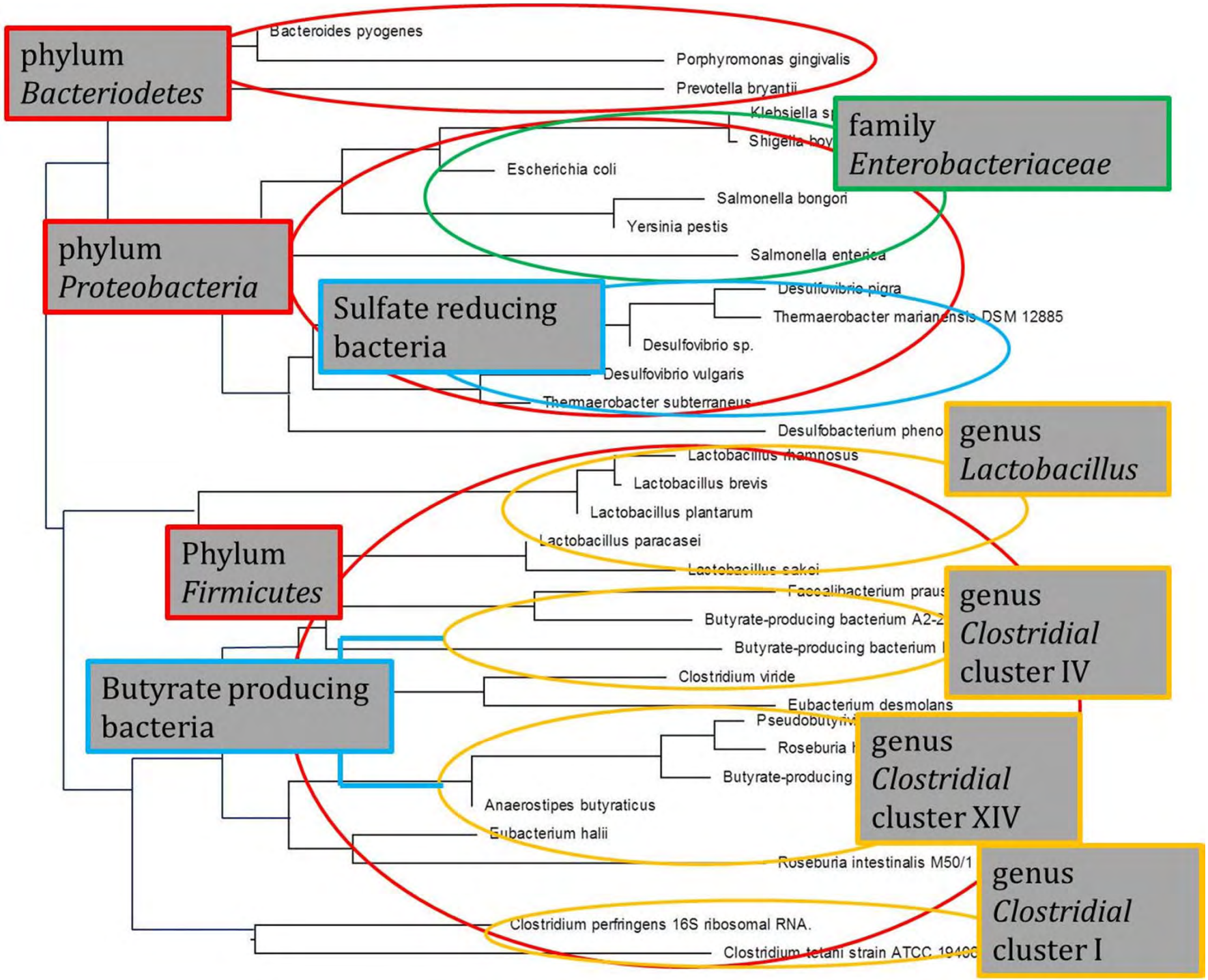


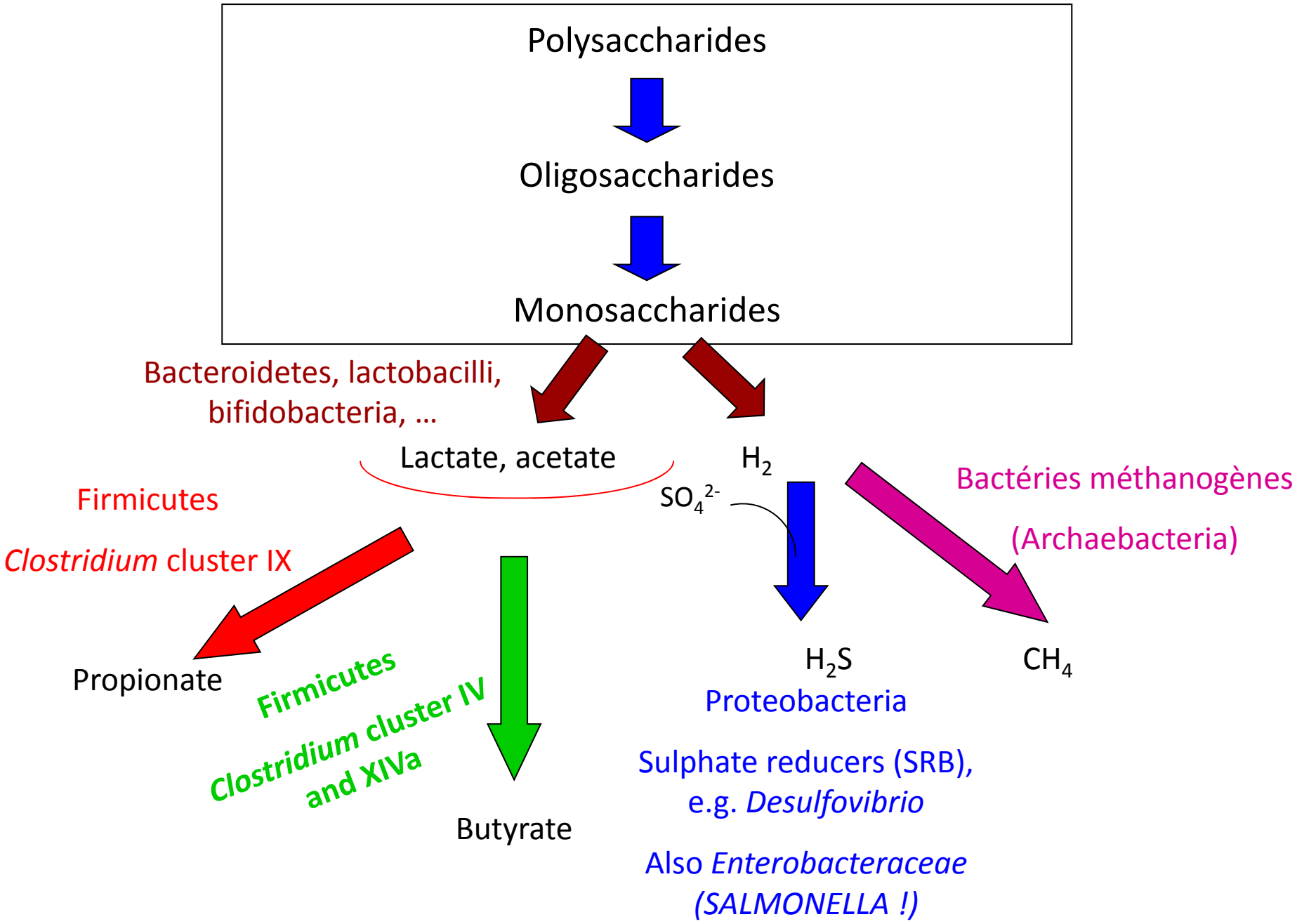


Le microbiote intestinal du poulet




phylum
Bacteriodetes
Bacteroides pyogenes
Porphyromonas gingivalis
Prevotella bryantii
Klebsiella sp
Shigella boy
family
Enterobacteriaceae
Escherichia coli
Salmonella bongori
Yersinia pestis
Salmonella enterica
phylum
Proteobacteria
Desulfovibrio pigra
Thermaerobacter marianensis DSM 12885
Desulfovibrio sp.
Desulfovibrio vulgaris
Thermaerobacter subterraneus
Desulfobacterium pheno
genus
Lactobacillus
Lactobacillus rhamnosus
Lactobacillus brevis
Lactobacillus plantarum
Lactobacillus paracasei
Lactobacillus sakei
Phylum
Firmicutes
Faecalibacterium praus
Butyrate-producing bacterium A2-2
Butyrate-producing bacterium
genus
Clostridial
cluster IV
Clostridium viride
Eubacterium desmolans
Pseudobutyriv
Roseburia
Butyrate-producing
genus
Clostridial
cluster XIV
Anaerostipes butyraticus
Eubacterium halii
Roseburia intestinalis M50/1
genus
Clostridial
cluster I
Clostridium perfringens 16S ribosomal RNA.
Clostridium tetani strain ATCC 1940


phylum
Bacteriodetes
Bacteroides pyogenes
Porphyromonas gingivalis
Prevotella bryantii
family
Enterobacteriaceae
Klebsiella sp
Shigella boy
Escherichia coli
Salmonella bongori
Yersinia pestis
phylum
Proteobacteria
Salmonella enterica
Sulfate reducing
bacteria
Desulfovibrio nigra
Thermaerobacter marianensis DSM 12885
Desulfovibrio sp.
Desulfovibrio vulgaris
Thermaerobacter subterraneus
Desulfobacterium pheno
genus
Lactobacillus
Lactobacillus rhamnosus
Lactobacillus brevis
Lactobacillus plantarum
Phylum
Firmicutes
Lactobacillus paracasei
Lactobacillus sakei
Faecalibacterium praus
genus
Clostridial
cluster IV
Butyrate-producing bacterium A2-2
Butyrate-producing bacterium
Butyrate producing
bacteria
Clostridium viride
Eubacterium desmolans
Pseudobutyriv
Roseburia
genus
Clostridial
cluster XIV
Butyrate-producing
Anaerostipes butyraticus
Eubacterium halii
Roseburia intestinalis M50/1
genus
Clostridial
cluster I
Clostridium perfringens 16S ribosomal RNA.
Clostridium tetani strain ATCC 19406


Polysaccharides
Oligosaccharides
Monosaccharides
Bacteroidetes, lactobacilli, bifidobacteria, …
Lactate, acetate
H2
SO4 2-
Bactéries méthanogènes
(Archaebacteria)
Firmicutes
Clostridium cluster IX
Propionate
Firmicutes
Clostridium cluster IV and XIVa
Butyrate
H2S
CH4
Proteobacteria
Sulphate reducers (SRB), e.g. Desulfovibrio
Also Enterobacteraceae (SALMONELLA !)

Conclusions

1. La dysbiose est un problème très important en poulet de chair
lié à la séléction et à la production intensive

2. La dysbiose est caractérisée par une inflammation de la paroie intestinale
Qui donne lieu à une maldigestion / malabsorption

3. La modification de la flore intestinale joue un rôle important dans la pathogenèse

4. Certains additifs nutritionnels ouvrent des perspectives de prévention

5. Cette approche peut permettre de réduire l'emploi d'antibiotiques