Remote Control of Intestinal Inflammation and Tumorigenesis by the Microbiota

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None to be declared
Pour vivre mieux, plus longtemps
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Redefining what it means to be human

90% 800-1000 species

100 x more genes

100 x more genes
One health initiative

CNS

Multiple sclerosis
EAE

T<sub>H17</sub> cell

T<sub>Reg</sub> cell

T<sub>H17</sub> cell

IL-1β

IL-1R antagonist

Beneficial commensal bacteria

SFB

Gut lumen

Lamina propria

Joint

Arthritis

Peripheral blood

Basophil

Type 1 diabetes
Pancreatitis

Pancreas

Allergic inflammation

Lungs

Towards the Human Colorectal Cancer Microbiome

Original Article
Structural segregation of gut microbiota between colorectal cancer patients and healthy volunteers

Microbial Dysbiosis in Colorectal Cancer (CRC) Patients
Premature aging of microbiota in IBD

Number of spp. vs. Diversity index

Controls- (n=31)  Controls+ (n=15)  CD (n=26)  UC (n=31)

Inflammatory bowel diseases: civilisation illnesses

~ 3.6 millions Europeans and Americans

Young adults

Risk of colorectal cancer x 2

Extraintestinal manifestations

No cure
Host genome shapes the gut microbiota

- Symbiosis = Sensitive balance
- Dysbiosis = Disease risk

- Tolerance
- Inflammation
Lamb1, a novel IBD-predisposing gene

Genome-wide association study of ulcerative colitis identifies three new susceptibility loci, including the HNF4A region

The UK IBD Genetics Consortium & the Wellcome Trust Case Control Consortium 2

7q31.1

ECM1
CDH1
LAMB1
HNF4A
GNA12
A warm tribute to Dr Elisabeth Georges-Labouesse
α6ΔIEC mice developed chronic inflammation

Nat Comm in revision
Compromised hemidesmosomes in α6ΔIEC mice

Control

α6ΔIEC

Plectin Coll. IV

Keratin 8/18 Coll. IV
Enhanced epithelial permeability in $\alpha_6^{\Delta IEC}$ mice
Enhanced epithelial proliferation in $\alpha_6^{\Delta\text{IEC}}$ mice
Defective mucin layer in \( \alpha_{6}^{\Delta_{IEC}} \) mice
Enhanced bacterial attachment to the mutant epithelia
Altered microbiome composition in $\alpha_6^{\Delta IEC}$ mice

Nat Comm in revision
Improved disease severity by antibiotic treatment
Colitis is independent of T/B cells activation
α6ΔIEC mice develop colitis-associated colorectal cancer

![Bar chart and images showing intestinal inflammation and cancer progression in WT and α6ΔIEC mice.](image)
Adaptive immunity is partially involved in dysplasia

- $\alpha_6^{\Delta IEC}$
- Prolapse
- mucus lakes
- rectal mucosa
- Intraepithelial
- Adenocarcinoma
- Infiltrating
- Low Grade Dysplasia

- $\alpha_6^{\Delta IEC}$
- $rag1^{-/-} \alpha_6^{\Delta IEC}$
A bacterial driver-passenger model: beyond the usual suspects
Take-home messages

• A clinically relevant readout integrating gene-environment interactions

• Correcting dysbiosis: novel therapeutic principle

• Towards a better understanding of missing heritability

Post-doc positions available