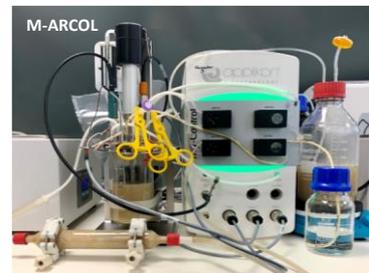


***In vitro* gut simulation platform and its applications in human health: the exemple of obesity**

MEDIS LAB: OUR EXPERTISE

MEDIS is a French research unit specialized in the study of intestinal microbiota and its role in human health and disease. The unit has an internationally recognized expertise in the *in vitro* simulation of human and animal digestive environment, with an original and unique platform in Europe associating digestion, fermentation and absorption gut models (DIGESTiv). Over the last 25 years, MEDIS has adapted its *in vitro* models to reproduce various specific digestive conditions in healthy humans (e.g. different ages or food matrices). Research topics currently evolve towards the *in vitro* simulation of different pathological situations associated to gut microbial dysbiosis (e.g. obesity and inflammatory bowel syndrome -IBS-).



MUCOSAL ARTIFICIAL COLON (M-ARCOL)- OBESE MODEL

In the last decade, the study of gut microbiota and its impact on human health has become a major area of research. This large microbial community, housed throughout the human gastrointestinal tract, performs many biological and metabolic functions and confers benefits to its host. Today, a number of intestinal or extra-digestive pathologies, such as obesity or IBS, are associated with an imbalance in the composition and function of intestinal microbiota so called “dysbiosis”. For technical, reproducibility, regulatory, ethical and cost reasons, *in vitro* gut models are an excellent complement to *in vivo* assays. However, to date, there is rare *in vitro* models of the colonic environment under diseased situation. To overcome this gap, we have recently developed an *in vitro* system reproducing the physicochemical and microbial parameters found in the colonic environment of obese patients.

M-ARCOL (Deschamps et al., 2020 ; Verdier et al. 2021)

Human simulated conditions

- ❖ Body temperature
- ❖ pH
- ❖ Transit time
- ❖ Ileal effluents composition
- ❖ Anaerobiosis
- ❖ Lumen & mucus-associated gut microbiota



↳ set-up with human *in vivo* data

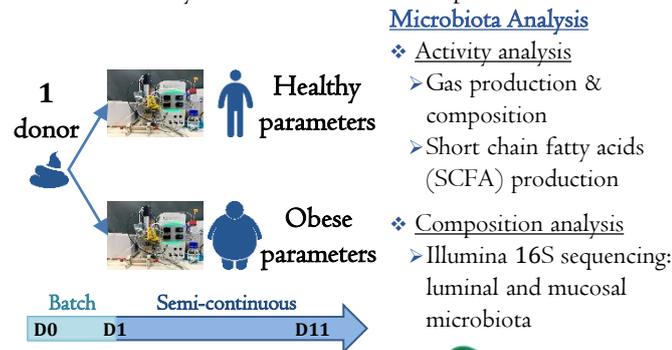
Obese adaptation (vs healthy)

- pH ↘
- Ileal effluents composition
 - Lipids ↗
 - Fibers ↘
 - Starch ↗
 - Salt ↗
 - Primary bile salts ↗

Experimental design

Each stool was used to inoculate two bioreactors ran in parallel, one set-up with healthy parameters, the other with obese ones.

Donors: 4 healthy volunteers and 5 obese patients



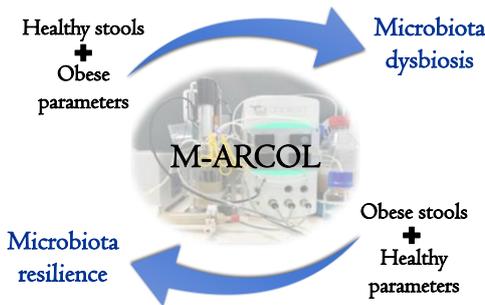
Microbiota Analysis

- ❖ **Activity analysis**
 - Gas production & composition
 - Short chain fatty acids (SCFA) production
- ❖ **Composition analysis**
 - Illumina 16S sequencing: luminal and mucosal microbiota

Main results

Obese parameters vs healthy ones

- ❖ **Activity analysis**
 - Changes in gas profiles
 - More SCFA and associated produced energy
- ❖ **Composition analysis**
 - Lower bacteria diversity
 - Lower abundances of healthy marker populations
 - e.g. *Akkermansiaceae* and *Rikenellaceae*
 - Higher abundances of obese marker populations
 - e.g. *Prevotellaceae* and *Veillonellaceae*



Perspectives and applications

- Obese M-ARCOL model can be used
- as an alternative to *in vivo* animal studies in preclinical phases
 - to perform mechanistic studies on gut microbiota
 - to test strategies aiming to restore gut microbiota eubiosis such as
 - Specific nutrients or diets
 - Pre- or probiotic supplementation
 - Faecal microbiota transplantation

↳ Validated by *in vivo* data in humans